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Mn(III)-BASED OXIDATIVE CYCLIZATION OF 2-((2-ARYLAMINO)ETHYL)MALONATES: SYNTHESIS OF QUINOLINES VIA TETRAHYDROQUINOLINEDICARBOXYLATES†

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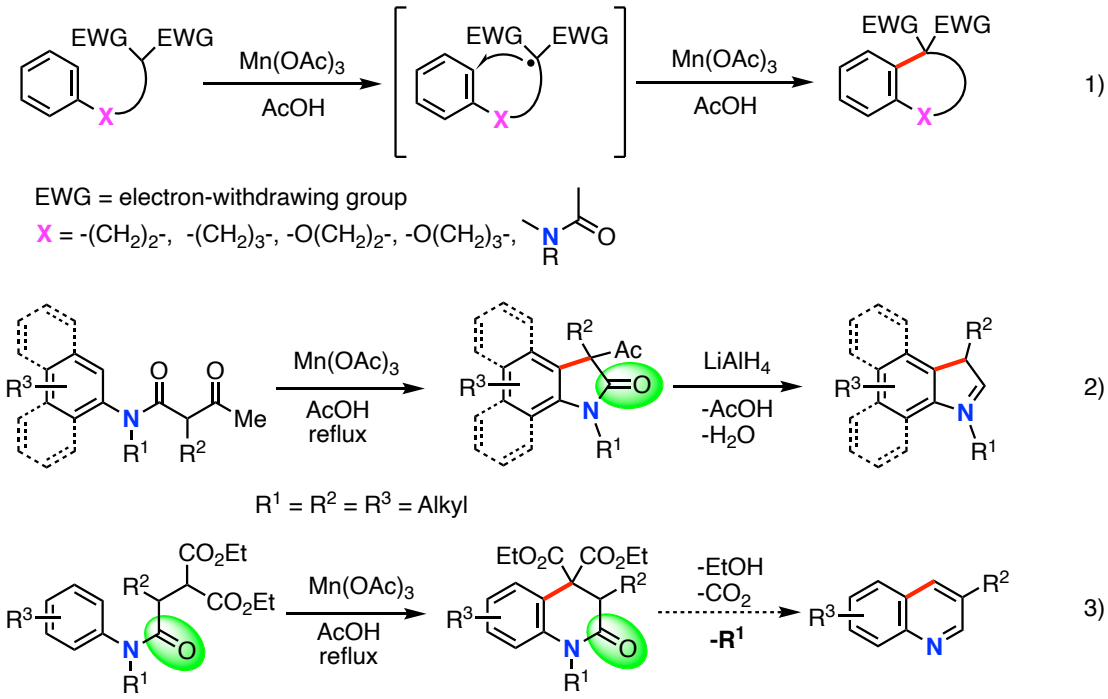
†This paper is dedicated to Professor Yasuyuki Kita on the occasion of his 77th birthday.

Abstract – The synthesis of quinolines from aniline derivatives via the Mn(III)-based oxidative cyclization of 2-(2-(arylamino)ethyl)malonates is described. The 2-(2-(arylamino)ethyl)malonates were prepared in two steps from the substituted anilines. The cyclization of nineteen arylaminoethylmalonates protected by the *N*-acyl and *N*-alkoxycarbonyl groups easily proceeded in the formal 6-*endo* mode regardless of the presence of halo, methyl, and methoxy groups on the aromatic ring, and the corresponding tetrahydroquinolinedicarboxylates were produced in high yields except for the 2,4-dimethoxyphenyl-substituted aminoethylmalonate which occurred by *ipso*-cyclization. The tetrahydroquinolinedicarboxylate could be transformed into quinoline via decarboxylation and deprotective hydrolysis. The characteristic phenomenon in the NMR spectrum of the tetrahydroquinolinedicarboxylates is also discussed.

INTRODUCTION

The cyclization reaction is an important technique for preparing useful organic molecules,[1] in which manganese(III) acetate dihydrate, $Mn(OAc)_3•2H_2O$, is one of the best reagents especially when used in the oxidative cyclization reactions.[2] It is well-known that the Mn(III)-based oxidation of 2'-hydroxychalcones and 2-hydroxybenzophenones affords aurones[3] and 9-xanthenones[4] according to the

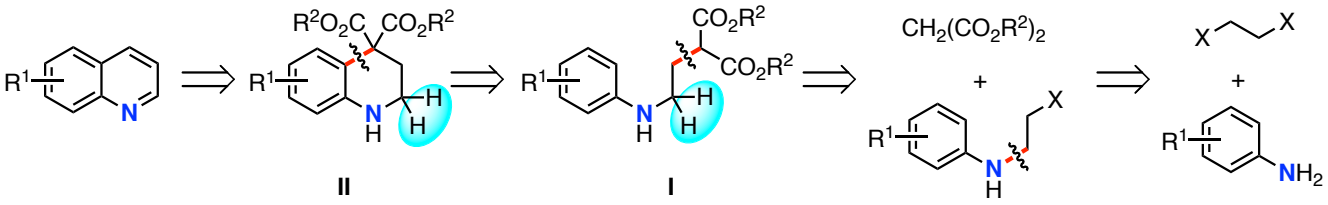
formal 5-*exo* and 6-*endo* C–O bond cyclization. Snider,[5] Citterio,[6] and Chuang[7] reported the efficient carbon-carbon bond cyclization of 3-oxo-9-aryl-6-nonenoates, 1-aryl-7-nonene-1,3-diones, and arylalkylmalonates (Scheme 1, eq. 1), which proceeded in the similar 5-*exo* and 6-*endo* modes to give the corresponding cyclization products, such as octahydrophenanthrenes,[5a] tetrehydroanthracenones,[5b,c] dihydroindenes,[6a] tetrahydronaphthalenes,[2a,6a] dihydrobenzofurans,[5d] chromanes,[8] and dihydrotetraphenediones.[7a] It could also be used for the *N*-alkyl-*N*-aryl-3-oxobutanamides (eq. 2) and (2-(*N*-alkyl-*N*-arylamino)-2-oxoethyl)malonates (eq. 3), producing indolinones[9,10] and dihydroquinolinones based on the reaction.[7c,11] These compounds are important as a starting material for the synthesis of substituted indoles and quinolines, which are indispensable in natural alkaloid synthesis. Although it was easy to prepare the *N*-arylalkanamide starting materials, reduction of lactam carbonyl group and *N*-alkyl deprotection of the cyclization products need at the late stage in order to synthesize the final quinolines (eq. 3) as well as indole derivatives (eq. 2).



Scheme 1. Mn(III)-Based Oxidative Radical Cyclization

We then envisioned the direct preparation of (arylamino)ethylmalonates **I** which would undergo the Mn(III)-based cyclization to provide the dihydroquinolines **II**, then easily converting into the quinolines (Scheme 2). In order to realize this enterprise, we proposed the retrosynthetic scheme from inexpensive commercially-available materials (Scheme 2). The target quinolines would be obtained by the usual decarboxylation of the 2,3-dihydroquinoline-4,4-dicarboxylates **II** probably produced by the key

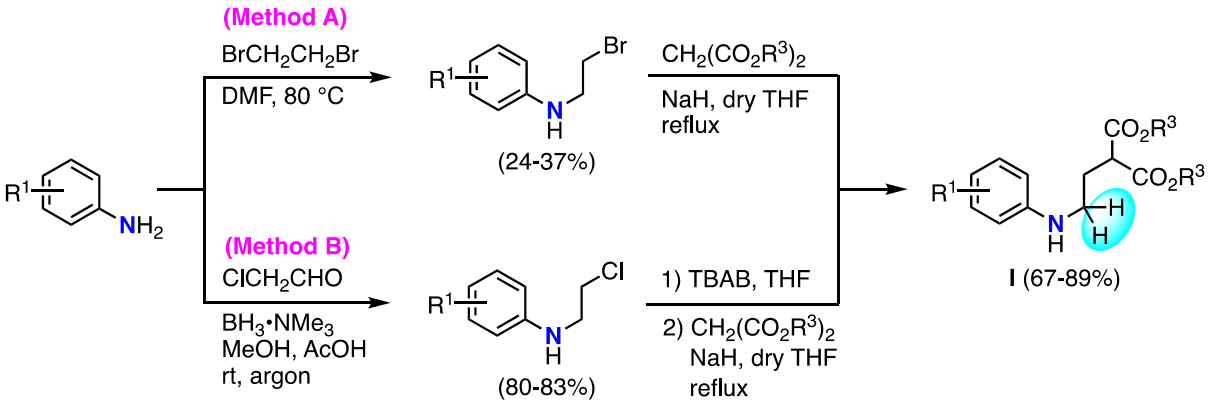
oxidation of the 2-(2-(*N*-arylamino)ethyl)malonates **I**. The arylaminoethylmalonates **I** would be synthesized by the S_N2 reaction of the malonates with arylaminoethyl halides which should be prepared by substitution of anilines with 1,2-dihaloethane. In this paper, a convenient synthesis of quinoline derivatives from familiar anilines via 2,3-dihydroquinoline-4,4-dicarboxylates is described.



Scheme 2. Retrosynthetic Scheme of Quinolines from Anilines

RESULTS AND DISCUSSION

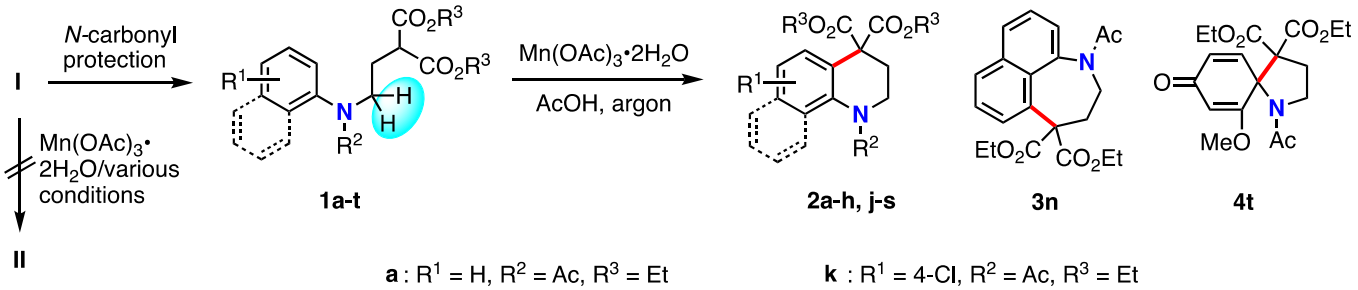
In order to accomplish the proposed synthesis, we commenced the reaction of aniline with 1,2-dibromoethane (Scheme 3, Method A). The substitution efficiently proceeded in *N,N*-dimethylformamide (DMF) as a basic polar aprotic solvent at 80 °C, affording *N*-(2-bromoethyl)aniline up to 33% yield. Although the reaction was carried out under various conditions, no further improvement in the yield could be achieved. The reaction of *N*-(2-bromoethyl)aniline with diethyl malonate smoothly proceeded in dry tetrahydrofuran (THF) using sodium hydride to produce 2-(2-(phenylamino)ethyl)malonate **I** (R^1 = H, R^3 = Et) in 83% yield. On the other hand, aniline underwent reductive amination with α-chloroacetaldehyde in the presence of the borane trimethylamine complex, BH_3•NMe_3, in MeOH containing a catalytic amount of AcOH at room temperature to give *N*-(2-chloroethyl)aniline (R^1 = H) in 80% improved yield compared to *N*-(2-bromoethyl)aniline (R^1 = H) (Scheme 3, Method B). The chloroethylaniline was subjected to a bromine-exchange reaction,[12] which was successively allowed to react with malonate, providing the same phenylaminoethylmalonate. Other various substituted arylaminoethylmalonates **I** were also prepared according to a similar procedure (Scheme 3).



Scheme 3. Preparation of 2-((2-Arylamino)ethyl)malonates

With the key substrate in hand, we initiated a simple, but risky Mn(III)-based oxidative cyclization of the basic secondary amine in the hope of oxidizing the diester enolate prior to the oxidation of the arylamino group, though we are aware that normal aromatic amines are easily oxidized with $Mn(OAc)_3•2H_2O$ to give a mixture of many oxidation products.[13] Contrary to our expectation, the oxidation preferentially occurred at the arylamino group, resulting in a complex mixture. In order to circumvent the oxidation of the arylamino group prior to the diester enolate, we eventually had to protect the amino group with an electron-withdrawing group, such as the acetyl group, which could be easily deprotected at the late stage of the quinoline synthesis. After acetylation of the amino group, the oxidative cyclization of **1a** was then explored (Scheme 4). Gratifyingly, the reaction smoothly proceeded at 70 °C using a stoichiometric amount of the oxidant, and the desired diethyl 1-acetyl-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (**2a**) was obtained in 54% yield together with **1a** unchanged (Table 1, Entry 1). After optimizing the conditions (Entries 2–6), we achieved the best yield of **2a** (84%) (Entry 4). Using other dialkyl malonates **1b** and **1c** also gave a good result (Entries 7 and 8). The cyclization of the *N*-benzoyl-substituted aminoethylmalonate **1d** resulted in the desired tetrahydroquinolinedicarboxylate **2d** in a similar yield of **2a** (compare Entry 9 with 4). The *N*-CO_2Et, *N*-Boc, *N*-Cbz, and *N*-Fmoc protected aminoethylmalonates **1e-h** also gave good results (Entries 10–13), however, the use of the tertiary amine **1i**, *N*-protected by a methyl group, led to a complex mixture and no cyclization products were isolated (Entries 14 and 15).[13] Arylaminoethylmalonates having various substituents on the aromatic group were then protected by the acetyl group except for 2-(2-((4-nitrophenyl)amino)ethyl)malonate,[14] and a similar reaction was carried out under the optimized conditions, resulting in the corresponding tetrahydroquinolinedicarboxylates **2j–s** in synthetically acceptable yields (Entries 16–25). However, the reaction of 2-(2-(*N*-(naphthalen-1-yl)acetamido)ethyl)malonate **1n** produced the tetrahydroquinolinedicarboxylate **2n**

together with 1-acetyl-2,3-dihydronaphtho[1,8-*bc*]azepine-4,4(1*H*)-dicarboxylate **3n** which was formed by the cyclization at the peri position of the naphthyl substituent (Entry 20).[11] In addition, aminoethylmalonate **1r** bearing the *N*-(3-methoxyphenyl) group gave two regioisomers, 7-methoxy **2r** and 5-methoxy **2r'**, as expected (Entry 24).[11] The regioselectivity in the cyclization of **1n** and **1r** was almost equal (Entries 20 and 24). In the case of aminoethylmalonate **1t** bearing the *N*-(2,4-dimethoxyphenyl) group, an *ipso*-cyclization (5-*exo*-*trig* cyclization) preferentially occurred and 8-oxo-1-azaspiro[4.5]deca-6,9-diene-4,4-dicarboxylate **4t** was obtained, although an excess amount of the oxidant was needed to complete the reaction (Entries 26 and 27). A similar *ipso*-cyclization was previously observed in the Mn(III)-mediated oxidation of 2-(2-((2,4-dimethoxyphenyl)(methyl)amino)-2-oxoethyl)malonate, producing 1-methyl-2,8-dioxo-1-azaspiro[4.5]deca-6,9-diene-4,4-dicarboxylate in high yield.[11]



a : R^1 = H, R^2 = Ac, R^3 = Et
b : R^1 = H, R^2 = Ac, R^3 = Me
c : R^1 = H, R^2 = Ac, R^3 = *i*-Pr
d : R^1 = H, R^2 = Bz, R^3 = Et
e : R^1 = H, R^2 = CO_2Et, R^3 = Et
f : R^1 = H, R^2 = Boc, R^3 = Et
g : R^1 = H, R^2 = Cbz, R^3 = Et
h : R^1 = H, R^2 = Fmoc, R^3 = Et
i : R^1 = H, R^2 = Me, R^3 = Et
j : R^1 = 4-F, R^2 = Ac, R^3 = Et
k : R^1 = 4-Cl, R^2 = Ac, R^3 = Et
l : R^1 = 4-Me, R^2 = Ac, R^3 = Et
m : R^1 = 2-Me, R^2 = Ac, R^3 = Et
n : R^1 = 1-Naph, R^2 = Ac, R^3 = Et
o : R^1 = 3,5-$(Me)_2$, R^2 = Ac, R^3 = Et
p : R^1 = 2,4-$(Me)_2$, R^2 = Ac, R^3 = Et
q : R^1 = 4-MeO, R^2 = Ac, R^3 = Et
r : R^1 = 3-MeO, R^2 = Ac, R^3 = Et
s : R^1 = 2-MeO, R^2 = Ac, R^3 = Et
t : R^1 = 2,4-$(MeO)_2$, R^2 = Ac, R^3 = Et

Scheme 4. Oxidation of 2-((2-Arylamino)ethyl)malonates **1a-t**

Table 1. Oxidation of 2-((2-Arylamino)ethyl)malonates **1a-t** with $Mn(OAc)_3$ in AcOH[a]

Entry	Malonate **1**/	R^1	R^2	R^3	**1**:$Mn(OAc)_3$[b]	Temp/°C	min	Product yield/%[c]	Rec. **1**/%[d]
1	**1a**	H	Ac	Et	1:2	70	65	**2a** (54)	24
2	**1a**	H	Ac	Et	1:2	100	38	**2a** (73)	9
3	**1a**	H	Ac	Et	1:2	reflux	20	**2a** (77)	12
4	**1a**	H	Ac	Et	1:3	reflux	30	**2a** (84)	
5	**1a**	H	Ac	Et	1:3	reflux/EtOH[e]	120	**2a** (76)	
6	**1a**	H	Ac	Et	1:4	reflux	20	**2a** (79)	
7	**1b**	H	Ac	Me	1:3	reflux	20	**2b** (84)	
8	**1c**	H	Ac	*i*-Pr	1:3	reflux	20	**2c** (85)	
9	**1d**	H	Bz	Et	1:3	reflux	25	**2d** (83)	

10	**1e**	H	CO_2Et	Et	1:3	reflux	20	**2e** (90)		
11	**1f**	H	Boc	Et	1:3	reflux	25	**2f** (79)		
12	**1g**	H	Cbz	Et	1:3	reflux	20	**2g** (78)		
13	**1h**	H	Fmoc	Et	1:3	reflux	30	**2h** (74)		
14	**1i**	H	Me	Et	1:2	reflux	21	c.m.[f]		
15	**1i**	H	Me	Et	1:2	reflux/EtOH[e]	10	c.m.[f]		
16	**1j**	4-F	Ac	Et	1:3	reflux	38	**2j** (73)		
17	**1k**	4-Cl	Ac	Et	1:3	reflux	40	**2k** (81)		
18	**1l**	4-Me	Ac	Et	1:3	reflux	35	**2l** (90)		
19	**1m**	2-Me	Ac	Et	1:3	reflux	25	**2m** (92)		
20	**1n**	1-Naph	Ac	Et	1:3	reflux	40	**2n** (41)	**3n** (51)	
21	**1o**	3,5-$(Me)_2$	Ac	Et	1:3	reflux	55	**2o** (92)		
22	**1p**	2,4-$(Me)_2$	Ac	Et	1:3	reflux	25	**2p** (64)		
23	**1q**	4-MeO	Ac	Et	1:3	reflux	20	**2q** (91)		
24	**1r**	3-MeO	Ac	Et	1:3	reflux	28	**2r** (45)[g]	**2r'** (48)[h]	
25	**1s**	2-MeO	Ac	Et	1:3	reflux	25	**2s** (94)		
26	**1t**	2,4-$(MeO)_2$	Ac	Et	1:3	reflux	15		**4t** (17)	37
27	**1t**	2,4-$(MeO)_2$	Ac	Et	1:9	reflux	60		**4t** (54)	

[a] The reaction of the malonate **1** (0.5 mmol) was carried out under argon in AcOH (30 mL) except for Entries 5 and 21. [b] Molar ratio. [c] Isolated yield. [d] Recovery of the malonate **1**. [e] EtOH was used as the solvent instead of AcOH. [f] Complex mixture. [g] 7-Methoxydihydroquinoline. [h] 5-Methoxydihydroquinoline.

The NMR spectra of the product tetrahydroquinolinedicarboxylates **2** deserve comment. It could be easy to characterize the cyclization products **2** based on the ^{1}H and ^{13}C NMR spectra in addition to the 2D spectra (see Experimental and Supporting information). For example, the characteristic malonate α-proton (δ 3.42) in the ^{1}H NMR spectrum of **1a** disappeared in that of the product **2a**, which also had one aromatic proton reduced compared to **1a**, and the C-4 quaternary carbon (δ 57.8) substituted two ethoxycarbonyl groups in **2a** was deshielded compared to the malonate α-methine carbon (δ 49.7) in the ^{13}C NMR spectrum of **1a**. These results supported the fact that the oxidative cyclization occurred between the malonate α-methine and the ortho position of the aniline substituent in the reaction of **1a**. These phenomena were also observed in all the other products **2b-h** and **2j-s**. However, the C-2 methylene carbon signal appeared at ca. δ 40 as a very broad peak or did not appear and the C-8a aromatic carbon signal appeared at around 138 ppm as a very weak peak in the ^{13}C NMR spectra of *N*-acetyl-protected **2a-c**, **2j-l**, **2o**, **2q**, **2r**, and **2r'** (see Supporting information). On the other hand, these carbon signals clearly showed in those of the products bearing a substituent at the C-8 position (**2m**, **2n**, **2p**, and **2s**), and *N*-benzoyl **2d** and the *N*-alkoxycarbonyl-protected **2e-h**. The former must be due to the flipping like a pseudo-chair form **A** and twist-boat form **B** of the dihydroquinoline skeleton within the NMR time scale (Figure 1)[15] and the latter should be assigned to the rigid scaffold. The HMQC correlations of **2a** between H-2 methylene proton signals and a broad peak of the C-2 methylene carbon, and the HMBC between

H-2 methylene proton peaks and a weak signal of the C-8a aromatic carbon were definitely observed (Figure 1).

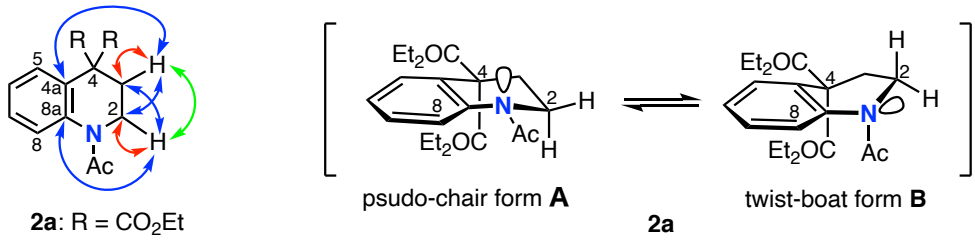
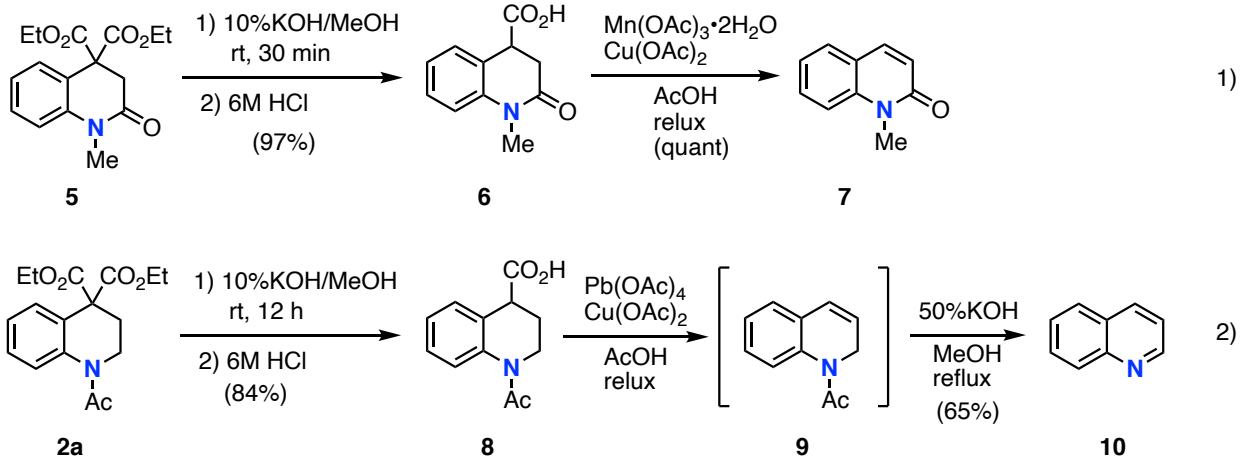


Figure 1. Selected Correlation Based on COSY, HMQC, and HMBC (left) and Flipping of **2a** (right)

With the dihydroquinoline intermediates **2** in hand, we then turned our attention to the final transformation of **2** into quinolines. Since 2-oxo-2,3-dihydroquinoline-4,4-dicarboxylate **5** was previously obtained by the reaction of (2-(*N*-phenylamino)-2-oxoethyl)malonate,[11] the conversion of **5** into the corresponding quinolinone **7** was first investigated (Scheme 5, eq. 1). Fortunately, normal hydrolysis of the dicarboxylate **5** at room temperature gave the monocarboxylic acid **6** followed by oxidative decarboxylation,[16] quantitatively producing **7**. Delighted with this result, we then started the final transformation of tetrahydroquinoline **2a** into the quinoline **10** based on a similar method (Scheme 5, eq. 2). Although the oxidative decarboxylation after hydrolysis was problematic and 1-acetyl-2,3-dihydroquinolin-4(1*H*)-one was also formed, we somehow obtained the desired dihydroquinoline **9**, which was deacetylated under basic conditions to give the quinoline (**10**) of which the spectroscopic data were completely identical with the commercial sample (see Experimental section).[17] The yield of **10** could be improved by further optimization of the reaction conditions. The other dihydroquinolines **2b-h**, **j-s** would also be converted into the corresponding quinolines based on the same procedures.



Scheme 5. Transformation of Dihydroquinoline **2a** into Quinoline (**10**)

CONCLUSION

We demonstrated a useful synthesis of substituted tetrahydroquinolinedicarboxylates **2** using the direct Mn(III)-based oxidative cyclization of 2-(2-(arylamino)ethyl)malonates **1**. The malonates **1** having not only electron-releasing but also electron-withdrawing groups on the aromatic ring efficiently underwent the oxidative cyclization to produce the corresponding tetrahydroquinolines **2**. It was crucial for the cyclization that the electron-withdrawing protective group, such as the acetyl group, was required on the amino nitrogen. We also showed the transformation of **2a** into quinoline (**10**) under familiar conditions, and believe that a variety of substituted quinoline derivatives can be synthesized according to this methodology.

EXPERIMENTAL

Measurements. Melting points were taken using a MP-J3 Yanagimoto micromelting point apparatus and are uncorrected. The IR spectra were measured in $CHCl_3$ or KBr using a Shimadzu 8400 and neat using an IRAffinity-1S FT IR spectrometer with the MIRacle 10 ATR accessary. All the IR data were expressed in cm^{-1}. The NMR spectra were recorded using an AL300 FT-NMR or JNM ECX 500 spectrometer at 300 MHz for the ^1H and at 75 MHz for ^{13}C or at 500 MHz for the ^1H and at 125 MHz for ^{13}C, with tetramethylsilane as the internal standard. The chemical shifts are reported as δ values (ppm) and the coupling constants in Hz. The following abbreviations are used for the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and brs, broad singlet for the ^1H NMR spectra. The EI MS spectra were obtained by a Shimadzu QP-5050A gas chromatograph-mass spectrometer at the ionizing voltage of 70 eV. The high-resolution mass spectra using a JEOL JMS-700 MStation and the elemental analyses using a J-SCIENCE LAB JM10 were performed at the Instrumental Analysis Center, Kumamoto University, Kumamoto, Japan.

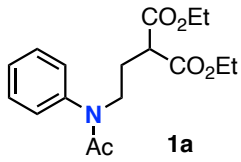
Materials. Diethyl malonate, dimethyl malonate, aniline, 1,2-dibromoethane, acetyl chloride, benzoyl chloride, manganese(II) acetate tetrahydrate, $Mn(OAc)_2•4H_2O$, and tetrabutylammonium bromide (TBAB) were purchased from Wako Pure Chemical Ind., Ltd. Diisopropyl malonate, chloroacetaldehyde, borane trimethylamine complex ($BH_3•NMe_2$), 4-fluoroaniline, 4-chloroaniline, 4-methylaniline, 2-methylaniline, 1-naphthylamine, 3,5-dimethylaniline, 2,4-dimethylaniline, 4-methoxyaniline, 3-methoxyaniline, 2-methoxyaniline, 2,4-dimethoxyaniline, *N*-methylaniline, di-*tert*-butyl dicarbonate, benzyl chloroformate, 9-fluorenylmethyl chloroformate, and sodium hydride (NaH) were purchased from Tokyo Kasei Co., Ltd., and all the commercially-available materials were used as received. Flash column chromatography was performed on silica gel 60N (40-50 mm), which was purchased from Kanto Chemical Co., Inc., and preparative thin layer chromatography (TLC) on Wakogel B-10 and B-5F from Wako Pure Chemical Ind., Ltd. The solvents were commercially-available guaranteed or first-grade and

used as received. Manganese(III) acetate dihydrate, $Mn(OAc)_3•2H_2O$, was synthesized according to our modified method.[10a]

Preparation of Arylaminoethylmalonates 1a-t (Method A). To aniline (10 mmol) in dimethylformamide (DMF) (50 mL), 1,2-dibromoethane (30 mmol) was added, and the mixture was heated at 80 °C for 4 h with stirring. Upon cooling, the reaction mixture was extracted with diethyl ether (Et_2O), and the combined extracts were washed with water, dried over anhydrous $NaSO_4$, then concentrated to dryness. The crude product was separated and purified by column chromatography on silica gel eluting with $CHCl_3$/hexane (6:4 v/v), giving the corresponding *N*-(2-bromoethyl)aniline (24–37%). To a malonate (3.0 mmol) in dry tetrahydrofuran (THF) (3.0 mL), 60% NaH (3.0 mmol) was added and stirred for 20 min. The obtained *N*-(2-bromoethyl)aniline (1.0 mmol) in dry THF (2.0 mL) was then dropwise added to the mixture and heated under reflux for 5 h. Upon cooling, the solvent was removed under reduced pressure and the residue was extracted with $CHCl_3$. The combined extracts were washed with 2M HCl, a saturated aqueous solution of $NaHCO_3$, water, dried over anhydrous $MgSO_4$, then concentrated to dryness. The crude product was separated and purified by column chromatography on silica gel eluting with Et_2O/hexane (3:7 v/v), giving the corresponding 2-(2-(arylamino)ethyl)malonate (67–89%). *N*-Acetyl (Ac), *N*-benzoyl (Bz), and *N*-ethoxycarbonyl (CO_2Et) protections were as follows: acetyl chloride (5.0 mmol), benzoyl chloride (3.0 mmol), or ethyl chloroformate (3.0 mmol) was dropwise added to the obtained 2-(2-(arylamino)ethyl)malonate (1.0 mmol) in dry $CHCl_3$ (5 mL) containing triethylamine (1.0 mmol) at 0 °C, and continued to stir at room temperature for 1 h. The reaction mixture was extracted with $CHCl_3$, and the combined extracts were washed with 2M HCl, a saturated aqueous solution of $NaHCO_3$, water, dried over anhydrous $MgSO_4$, and concentrated to dryness. The obtained crude product was purified by column chromatography on silica gel eluting with Et_2O/hexane (6:4 v/v), giving the corresponding *N*-Ac, *N*-Bz, and *N*-CO_2Et protected arylaminoethylmalonates **1a-e**, **j-t**. The *N*-*tert*-butoxycarbonyl (Boc) protection of diethyl 2-(2-(phenylamino)ethyl)malonate (1.0 mmol) was carried out using di-*tert*-butyl dicarbonate (1.5 mmol) in dry $CHCl_3$ (5 mL) containing triethylamine (1.5 mmol) and *N,N*-dimethyl-4-aminopyridine (1.0 mmol) at room temperature for 5 h, giving *N*-Boc **1f**. The benzyloxycarbonyl (Cbz) protection was conducted using benzyl chloroformate (3.0 mmol) in dry DMF (5.0 mL) containing NaH (1.0 mmol) for 2 h, yielding *N*-Cbz **1g**. The fluorenylmethyloxycarbonyl (Fmoc) protection was carried out using 9-fluorenylmethyl chloroformate (3.0 mmol) in ethyl acetate (AcOEt) (10 mL) containing a 5%$NaHCO_3$ aqueous solution (10 mL) for 1.5 h, yielding *N*-Fmoc **1h** (255 mg, 69%).

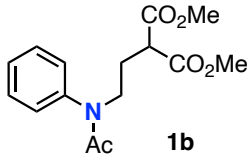
(Method B). To aniline (5 mmol, 0.500 mL) in MeOH (5 mL), chloroacetaldehyde (6 mmol, 1.000 mL), AcOH (0.75 mmol, 0.043 mL) and $BH_3•NMe_3$ (10 mmol, 0.814 g) were added and the mixture was stirred at room temperature for 15 h under argon. The reaction mixture was neutralized by aqueous

ammonia and extracted by $CHCl_3$ and the crude product was purified by column chromatography on silica gel eluting with AcOEt/hexane (2:8 v/v), giving *N*-(2-chloroethyl)aniline (0.680 g, 80% yield). Diethyl malonate (1.5 mmol, 220 mg) was dissolved in dry THF (6 mL) containing 55% NaH (1.5 mmol, 66 mg) with stirring for 20 min, and a dry THF (2 mL) solution of the chloroethylaniline (0.5 mmol, 73 mg) and TBAB (1.5 mmol, 500 mg) was dropwise added to the malonate solution at room temperature. The reaction mixture was then heated under reflux for 15 h. The solvent was removed in vacuo and the residue was extracted with $CHCl_3$. The combined extracts were washed with 2M HCl, a saturated aqueous solution of $NaHCO_3$, water, dried over anhydrous $MgSO_4$, and concentrated to dryness. The obtained crude product was purified by thin-layer chromatography on silica gel developing with Et_2O/hexane (3:7 v/v), giving diethyl 2-(2-(phenylamino)ethyl)malonate (92 mg, 70%). The *N*-protection was performed according to Method A. The physical data of the arylaminoethylmalonates **1a-t** are listed below.



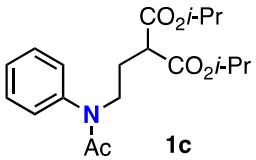
1a

Diethyl 2-(2-(*N*-Phenylacetamido)ethyl)malonate (1a): Yield (301 mg, 94%); yellow liquid; R_f = 0.26 ($CHCl_3$:MeOH = 98:2); IR ($CHCl_3$) ν 1743.5, 1724.2, 1647.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.18 (5H, m, arom H), 4.17 (4H, q, J = 6.9 Hz, OCH_2 ×2), 3.77 (2H, t, J = 6.9 Hz, N-CH_2), 3.42 (1H, t, J = 6.9 Hz, CH), 2.12 (2H, q, J = 6.9 Hz, CH_2), 1.83 (3H, s, Ac), 1.24 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 169.3 (2C) (C=O), 143.0 (arom C), 130.1 (2C), 128.3 (3C) (arom CH), 61.6 (2C) (OCH_2), 49.7 (CH), 47.0, 27.0 (CH_2), 22.8 ($\underline{C}H_3CO$), 14.0 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{24}NO_5$ 322.1654; found 322.1638.



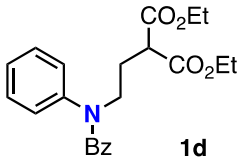
1b

Dimethyl 2-(2-(*N*-Phenylacetamido)ethyl)malonate (1b): Yield (284 mg, 97%); yellow liquid; R_f = 0.23 ($CHCl_3$); IR ($CHCl_3$) ν 1726.2, 1643.2 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.18 (5H, m, arom H), 3.77 (2H, t, J = 6.9 Hz, N-CH_2), 3.72 (6H, s, CH_3 ×2), 3.49 (1H, t, J = 7.2 Hz, CH), 2.12 (2H, q, J = 7.2 Hz, CH_2), 1.83 (3H, s, Ac); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 169.7 (2C) (C=O), 143.0 (arom C), 129.4 (2C), 128.3, 128.2 (2C) (arom CH), 52.1 (2C) (CH_3), 49.3 (CH), 47.0, 27.2 (CH_2), 22.7 ($\underline{C}H_3CO$); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{20}NO_5$ 294.1341; found 294.1328.



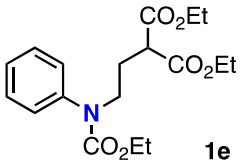
1c

Diisopropyl 2-(2-(*N*-Phenylacetamido)ethyl)malonate (1c): Yield (324 mg, 93%); yellow liquid; R_f = 0.21 ($CHCl_3$); IR ($CHCl_3$) ν 1720.4, 1647.1 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.18 (5H, m, arom H), 5.06-4.98 (2H, m, O-CH ×2), 3.76 (2H, t, J = 7.2 Hz, N-CH_2), 3.34 (1H, t, J = 7.2 Hz, CH), 2.10 (2H, q, J = 7.2 Hz, CH_2), 1.83 (3H, s, Ac), 1.22 (12H, d, J = 6.3 Hz, CH_3 ×4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 168.9 (2C) (C=O), 140.9 (arom C), 130.5 (2C), 128.3 (2C), 128.2 (arom CH), 69.1 (2C) (CH), 50.1 (CH), 47.1, 26.8 (CH_2), 22.8 ($\underline{C}H_3CO$), 21.6 (2C), 21.6 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: [M＋H]$^+$ Calcd for $C_{19}H_{28}NO_5$ 350.1967; found 350.1962.



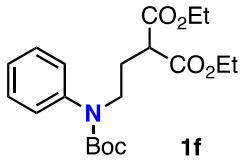
1d

Diethyl 2-(2-(*N*-Phenylbenzamido)ethyl)malonate (1d): Yield (365 mg, 95%); pale yellow liquid; R_f = 0.24 ($CHCl_3$); IR ($CHCl_3$) ν 1728.1, 1635.5 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.03 (10H, m, arom H), 4.25-4.14 (4H, m, OCH_2 ×2), 4.01 (2H, t, J = 7.2 Hz, N-CH_2), 3.48 (1H, t, J = 7.2 Hz), 2.26 (2H, q, J = 7.2 Hz, CH_2), 1.25 (6H, t, J = 7.2 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 169.3 (2C) (C=O), 143.4, 136.1 (arom C), 129.8, 129.4 (2C), 128.9 (2C), 127.90 (2C), 127.87 (2C), 127.0 (arom CH), 61.6 (2C) (OCH_2), 49.8 (CH), 48.3, 26.9 (CH_2), 14.1 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: [M＋H]$^+$ Calcd for $C_{22}H_{26}NO_5$ 384.1811; found 384.1804.



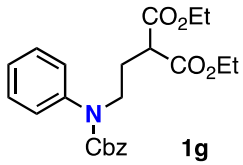
1e

Diethyl 2-(2-((Ethoxycarbonyl)(phenyl)amino)ethyl)malonate (1e): Yield (329 mg, 92%); pale yellow liquid; R_f = 0.23 ($CHCl_3$); IR ($CHCl_3$) ν 1728.1, 1693.4 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.33 (2H, m, arom H), 7.27-7.20 (3H, m, arom H), 4.25-4.09 (6H, m, OCH_2 ×3), 3.76 (2H, t, J = 7.2 Hz, N-CH_2), 3.42 (1H, t, J = 7.2 Hz, CH), 2.15 (2H, q, J = 7.2 Hz, CH_2), 1.23 (9H, t, J = 7.2 Hz, CH_3 ×3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3 (2C), 155.9 (C=O), 141.9 (arom C), 129.3 (2C), 127.3 (2C), 126.9 (arom CH), 61.8 (2C), 61.6 (OCH_2), 49.4 (CH), 48.2, 27.5 (CH_2), 14.6, 14.0 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: [M＋H]$^+$ Calcd for $C_{18}H_{26}NO_6$ 352.1760; found 352.1753.



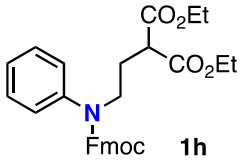
1f

Diethyl 2-(2-((*tert*-Butoxycarbonyl)(phenyl)amino)ethyl)malonate (1f): Yield (288 mg, 76%); yellowish green liquid; R_f = 0.25 (AcOEt:hexane = 2:8); IR ($CHCl_3$) ν 1728.1, 1689.5 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.18 (5H, m, arom H), 4.25-4.11 (4H, m, OCH_2 ×2), 3.71 (2H, t, J = 6.9 Hz, N-CH_2), 3.39 (1H, t, J = 6.9 Hz, CH), 2.14 (2H, q, J = 6.9 Hz, CH_2), 1.43 (9H, s, CH_3 ×3), 1.23 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3 (2C), 154.9 (C=O), 142.4 (arom C), 129.1 (2C), 127.2 (2C), 126.4 (arom CH), 80.4 (O-C), 61.9 (2C) (O-CH_2), 49.5 (CH), 47.9 (CH_2), 28.3 (3C) (CH_3), 27.6 (CH_2), 14.0 (2C) (CH_3); FAB HRMS (acetone/NBA/NaI) *m/z*: $[M+Na]^+$ Calcd for $C_{20}H_{29}NNaO_6$ 402.1893; found 402.1913.



1g

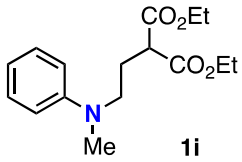
Diethyl 2-(2-(((Benzyloxy)carbonyl)(phenyl)amino)ethyl)malonate (1g): Yield (322 mg, 78%); pale yellow liquid; R_f = 0.17 (Et_2O:hexane = 3:7); IR ($CHCl_3$) ν 1732.0, 1598.9 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.16 (8H, m, arom H), 6.75-6.67 (2H, m, arom H), 4.54 (2H, s, OCH_2), 4.18 (4H, q, J = 6.9 Hz, OCH_2 ×2), 3.47 (2H, t, J = 6.9 Hz, N-CH_2), 3.37 (1H, t, J = 6.9 Hz, CH), 2.25 (2H, q, J = 6.9 Hz, CH_2), 1.25 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4 (3C) (C=O), 148.5, 138.9 (arom C), 129.5 (2C), 128.8 (2C), 127.0, 126.8 (2C), 116.8, 112.6 (2C) (arom CH), 61.6 (2C), 54.4 (OCH_2), 49.7 (CH), 48.9, 26.2 (CH_2), 14.1 (2C) (CH_3); FAB HRMS (acetone/NBA/NaI) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{27}NNaO_6$ 436.1736; found 436.1770.



1h

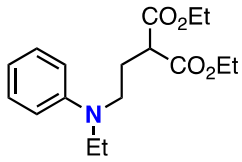
Diethyl 2-(2-((((9*H*-Fluoren-9-yl)methoxy)carbonyl)(phenyl)amino)ethyl)malonate (1h): Yield (345 mg, 69%); pale yellow liquid; R_f = 0.37 (AcOEt:hexane = 3:7); IR ($CHCl_3$) ν 1726.2, 1697.2 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (2H, d, J = 7.6 Hz, arom H), 7.40-7.28 (6H, m, arom H), 7.19-7.15 (5H, m, arom H), 4.36 (2H, brs, OCH_2), 4.22-4.09 (4H, m, OCH_2 ×2), 4.06 (1H, d, J = 6.3 Hz, CH), 3.73 (2H, t, J = 6.9 Hz, N-CH_2), 3.39 (1H, t, J = 6.9 Hz, CH), 2.12 (2H, q, J = 6.9 Hz, CH_2), 1.21 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2 (2C), 155.7 (C=O), 144.0 (2C), 141.4 (3C) (arom C), 129.4

(2C), 127.8 (2C), 127.8 (2C), 127.3, 127.1 (2C), 125.3 (2C), 120.0 (2C) (arom CH), 67.6, 61.6 (2C) (OCH_2), 49.4 (CH), 48.3 (CH_2), 47.1 (CH), 27.4 (CH_2), 14.0 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{30}H_{32}NO_6$ 502.2230; found 502.2231.

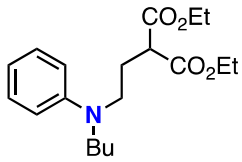


1i

Diethyl 2-(2-(Methyl(phenyl)amino)ethyl)malonate (1i): Yield (164 mg, 56%); pale yellow liquid (lit,[18] bp 190.0 ℃); R_f = 0.47 (AcOEt:hexane = 1:9); IR ($CHCl_3$) *v* 1726.2 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26-7.19 (2H, m, arom H), 6.74-6.68 (3H, m, arom H)), 4.19 (4H, q, *J* = 6.9 Hz, OCH_2 ×2), 3.38 (3H, t, *J* = 6.9 Hz, N-CH_2 and CH), 2.91 (3H, s, N-CH_3), 2.18 (2H, q, *J* = 6.9 Hz, CH_2), 1.25 (6H, t, *J* = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9 (2C) (C=O), 150.1 (arom C), 129.9 (2C), 116.8, 112.6 (2C) (arom CH), 61.6 (2C) (OCH_2), 49.7 (CH), 41.7 (CH_2), 38.3 (N-CH_3), 26.7 (CH_2), 14.1 (2C) (CH_3).

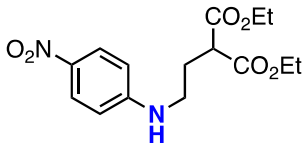


Diethyl 2-(2-(Ethyl(phenyl)amino)ethyl)malonate: Yield (175 mg, 57%); pale yellow liquid; R_f = 0.35 (AcOEt:hexane = 1:9); IR ($CHCl_3$) *v* 1732.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25-7.19 (2H, m, arom H), 6.72-6.64 (3H, m, arom H), 4.19 (4H, q, *J* = 7.2 Hz, OCH_2 ×2), 3.39 (1H, t, *J* = 7.2 Hz, CH), 3.35 (4H, q, *J* = 7.2 Hz, N-CH_2 and CH_2), 2.18 (2H, q, *J* = 7.2 Hz, CH_2), 1.26 (6H, t, *J* = 7.2 Hz, CH_3 ×2), 1.13 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6 (2C) (C=O), 147.9 (arom C), 129.5 (2C), 116.3, 112.5 (2C) (arom CH), 61.6 (2C) (OCH_2), 49.7 (CH), 48.1, 45.1 (NCH_2), 26.7 (CH_2), 14.1 (2C), 12.1 (CH_3); FAB HRMS (acetone/NBA/NaI) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{25}NNaO_4$ 330.1681; found 330.1674.

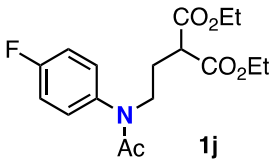


Diethyl 2-(2-(Butyl(phenyl)amino)ethyl)malonate: Yield (191 mg, 57%); pale yellow liquid; R_f = 0.52 (AcOEt:hexane = 1:9); IR ($CHCl_3$) *v* 1726.2 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26-7.18 (2H, m, arom H), 6.71-6.63 (3H, m, arom H), 4.19 (4H, q, *J* = 7.2 Hz, OCH_2 ×2), 3.35 (4H, t, *J* = 7.2 Hz, N-CH_2

×2), 3.25 (1H, t, J = 7.2 Hz, CH), 2.17 (2H, q, J = 7.2 Hz, CH_2), 1.55 (2H, quin, J = 7.2 H, CH_2), 1.37-1.30 (2H, m, CH_2), 1.26 (6H, t = 7.2 Hz, CH_3 ×2), 0.94 (3H, t, J = 7.2 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5 (2C) (C=O), 148.1 (arom C), 129.5 (2C), 116.8, 112.3 (2C) (arom CH), 61.6 (2C) (OCH_2), 50.9 (CH_2), 49.8 (CH), 48.7, 29.3, 26.4, 20.4 (CH_2), 14.1 (2C), 14.0 (CH_3); FAB HRMS (acetone/NBA/NaI) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{29}NNaO_4$ 358.1994; found 358.1996.

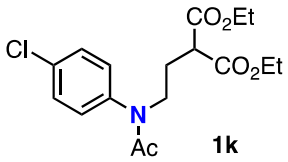


Yield (67 mg, 51%); yellow liquid; R_f = 0.30 (AcOEt:hexane = 3:7); IR ($CHCl_3$) ν 3650 (NH), 1736, 1713 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27-8.22 (2H, m, arom H), 7.88-7.83 (2H, m, arom H), 4.28 (4H, q, J = 6.9 Hz, O-CH_2 ×2), 4.11-4.03 (1H, m, H-CH-N), 3.96-3.89 (1H, m, N-HC-H), 3.71 (1H, dd, J = 8.7, 7.2 Hz, CH), 2.67-2.42 (2H, m, CH_2), 1.33 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 169.5 (C=O), 144.6, 144.3 (arom C), 124.9 (2C), 119.3 (2C) (arom CH), 62.2 (2C) (OCH_2), 50.1 (CH), 47.1 (2C) (NCH_2), 22.0 (2C) (CH_2), 14.2 (2C) (CH_3).



1j

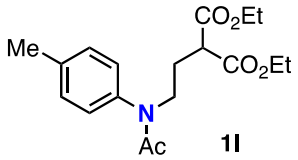
Diethyl 2-(2-(*N*-(4-Fluorophenyl)acetamido)ethyl)malonate (1j): Yield (305 mg, 90%); yellow liquid; R_f = 0.26 ($CHCl_3$); IR ($CHCl_3$) ν 1728.1, 1654.8 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22-7.09 (4H, m, arom H), 4.17 (4H, q, J = 7.2 Hz, OCH_2 ×2), 3.74 (2H, t, J = 7.2 Hz, N-CH_2), 3.42 (1H, t, J = 7.2 Hz, CH), 2.11 (2H, q, J = 7.2 Hz, CH_2), 1.82 (3H, s, Ac), 1.25 (6H, t, J = 7.2 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 169.3 (2C) (C=O), 162.2 (d, $^1J_{(C,F)}$ = 247 Hz), 139.1 (d, $^4J_{(C,F)}$ = 3 Hz), 130.1 (d, $^3J_{(C,F)}$ = 9 Hz), 117.0 (d, $^2J_{(C,F)}$ = 23 Hz), 61.7 (2C) (OCH_2), 49.7 (CH), 47.1, 26.9 (CH_2), 22.7 (CH_3CO), 14.1 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{23}FNO_5$ 340.1560; found 340.1550.



1k

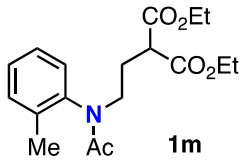
Diethyl 2-(2-(*N*-(4-Chlorophenyl)acetamido)ethyl)malonate (1k): Yield (329 mg, 92%); yellow liquid; R_f = 0.30 ($CHCl_3$); IR ($CHCl_3$) ν 1732.0, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.40 (2H, m,

arom H)), 7.19-7.14 (2H, m, arom H)), 4.17 (4H, q, J = 6.9 Hz, OCH_2 ×2), 3.75 (2H, t, J = 6.9 Hz, N-CH_2), 3.41 (1H, t, J = 6.9 Hz, CH), 2.10 (2H, q, J = 6.9 Hz, CH_2), 1.84 (3H, s, Ac), 1.25 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 169.2 (2C) (C=O), 141.6, 134.1 (arom C), 130.3 (2C), 129.7 (2C) (arom CH), 61.7 (2C) (OCH_2), 49.6 (CH), 47.1, 26.6 (CH_2), 22.7 ($\underline{C}H_3CO$), 14.1 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{23}ClNO_5$ 356.1265; found 356.1278.



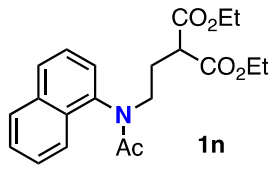
1l

Diethyl 2-(2-(*N*-(4-Methylphenyl)acetamido)ethyl)malonate (1l): Yield (331 mg, 99%); yellow liquid; R_f = 0.27 ($CHCl_3$); IR ($CHCl_3$) ν 1732.0, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23-7.20 (2H, m, arom H)), 7.08-7.05 (2H, m, arom H), 4.17 (4H, q, J = 6.9 Hz, OCH_2 ×2), 3.75 (2H, t, J = 6.9 Hz, N-CH_2), 3.43 (1H, t, J = 6.9 Hz, CH), 2.38 (3H, s, CH_3), 2.10 (2H, q, J = 6.9 Hz, CH_2), 1.82 (3H, s, Ac), 1.24 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 169.4 (2C) (C=O), 140.5, 138.2 (arom C), 130.6 (2C), 128.0 (2C) (arom CH), 61.6(2C) (OCH_2), 49.7 (CH), 46.9, 27.0 (CH_2), 22.7 (CH_3), 21.1 (CH_3), 14.1 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{26}NO_5$ 336.1811; found 336.1803.



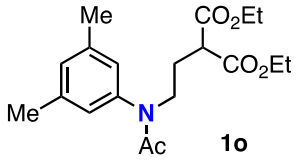
1m

Diethyl 2-(2-(*N*-(2-Methylphenyl)acetamido)ethyl)malonate (1m): Yield (308 mg, 92%); pale yellow liquid; R_f = 0.44 (AcOEt:hexane = 3:7); IR ($CHCl_3$) ν 1728.1, 1643.2 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.26 (3H, m, arom H), 7.25-7.13 (1H, m, arom H), 4.17 (4H, q, J = 7.2 Hz, OCH_2 ×2), 3.44 (2H, t, J = 7.2 Hz, N-CH_2), 3.12 (1H, t, J = 7.2 Hz, CH), 2.24 (3H, s, CH_3), 2.15 (2H, q, J = 7.2 Hz, CH_2), 1.75 (3H, s, Ac), 1.24 (6H, t, J = 7.2 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 169.4, 168.2 (C=O), 141.6, 135.7 (arom C), 131.9, 129.3, 128.7, 127.5 (arom CH), 61.7, 61.5 (OCH_2), 49.8 (CH), 46.0, 27.0 (CH_2), 22.3, 17.5, 14.1, 14.0 (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{26}NO_5$ 336.1811; found 336.1814.



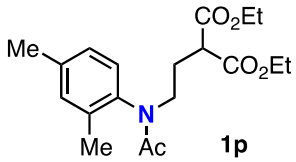
1n

Diethyl 2-(2-(*N*-(Naphthalen-1-yl)acetamido)ethyl)malonate (1n): Yield (297 mg, 80%); yellowish green liquid; R_f = 0.26 ($CHCl_3$); IR ($CHCl_3$) ν 1728.1, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95-7.91 (2H, m, arom H), 7.89 (1H, brs, arom H), 7.61-7.49 (3H, m, arom H), 7.41 (1H, d, J = 9.0 Hz, arom H), 4.42-4.35 (1H, m, N-C$\underline{H_a}$H), 4.23-4.09 (4H, m, OCH_2 ×2), 3.49 (1H, t, J = 6.9 Hz, CH), 3.40-3.31 (1H, m, N-CH$\underline{H_b}$), 2.26-2.17 (2H, m, CH_2), 1.75 (3H, s, Ac), 1.27-1.16 (6H, m, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 169.4, 169.2 (C=O), 139.0, 135.1, 130.4 (arom C), 129.2, 129.0, 127.8, 127.0, 126.7, 125.9, 122.4 (arom CH), 61.62, 61.56 (OCH_2), 49.9 (CH), 46.9, 27.4 (CH_2), 22.3, 14.04, 13.97 (CH_3); FAB HRMS (acetone/NBA) *m/z*: [M＋H]$^+$ Calcd for $C_{21}H_{26}NO_5$ 372.1811; found 372.1806.



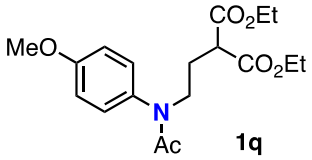
1o

Diethyl 2-(2-(*N*-(3,5-Dimethylphenyl)acetamido)ethyl)malonate (1o): Yield (332 mg, 95%); pale yellow liquid; R_f = 0.28 ($CHCl_3$); IR ($CHCl_3$) ν 1732.0, 1643.2 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.98 (1H, s, arom H), 6.78 (2H, s, arom H), 4.26-4.10 (4H, m, OCH_2 ×2), 3.74 (2H, t, J = 7.2 Hz, N-CH_2), 3.42 (1H, t, J = 7.2 Hz, CH), 2.33 (6H, s, CH_3 ×2), 2.11 (2H, q, J = 7.2 Hz, CH_2), 1.83 (3H, s, Ac), 1.25 (6H, t, J = 7.2 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 169.4 (2C) (C=O), 142.9 (arom C), 139.8 (arom CH), 130.6 (2C) (arom C), 125.8 (2C) (arom CH), 61.6 (2C) (OCH_2), 49.7 (CH), 47.0, 27.0 (CH_2), 22.6, 21.2 (2C), 14.0 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: [M＋H]$^+$ Calcd for $C_{19}H_{28}NO_5$ 350.1967; found 350.1956.



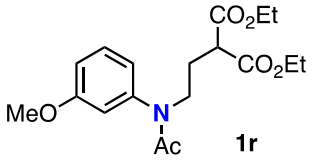
1p

Diethyl 2-(2-(*N*-(2,4-Dimethylphenyl)acetamido)ethyl)malonate (1p): Yield (332 mg, 95%); pale yellow liquid; R_f = 0.38 ($CHCl_3$); IR ($CHCl_3$) ν 1728.1, 1643.2 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (1H, d, J = 1.9 Hz, H-3'), 7.05 (1H, dd, J = 7.9, 1.9 Hz, H-5'), 7.00 (1H, d, J = 7.9 Hz, H-6'), 4.28-4.09 (4H, m, OCH_2 ×2), 3.43 (2H, t, J = 7.2 Hz, N-CH_2), 3.16 (1H, t, J = 7.2 Hz, CH), 2.34 (3H, s, CH_3), 2.18 (3H, s, CH_3), 2.12 (2H, q, J = 7.2 Hz, CH_2), 1.74 (3H, s, Ac), 1.23 (6H, t, J = 7.2 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 169.4, 169.2 (C=O), 139.0, 138.6, 135.3 (arom C), 132.5, 129.0, 128.1 (atom CH), 61.59, 61.55 (OCH_2), 49.8 (CH), 46.1, 27.0 (CH_2), 22.2, 21.0, 17.4, 14.06, 14.03 (CH_3); FAB HRMS (acetone/NBA) *m/z*: [M＋H]$^+$ Calcd for $C_{19}H_{28}NO_5$ 350.1967; found 350.1955.



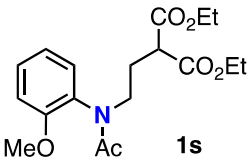
1q

Diethyl 2-(2-(*N*-(4-Methoxyphenyl)acetamido)ethyl)malonate (1q): Yield (333 mg, 95%); yellow liquid; R_f = 0.26 ($CHCl_3$); IR ($CHCl_3$) ν 1732.0, 1645.2 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (2H, d, J = 9.0 Hz, arom CH), 6.93 (2H, d, J = 9.0 Hz, arom CH), 4.25-4.13 (4H, m, OCH_2 ×2), 3.83 (3H, s, OCH_3), 3.73 (2H, t, J = 6.9 Hz, N-CH_2), 3.42 (1H, t, J = 6.9 Hz, CH), 2.11 (2H, q, J = 6.9 Hz, CH_2), 1.82 (3H, s, Ac), 1.25 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 169.3 (2C) (C=O), 159.3, 135.8 (arom C), 129.3 (2C), 115.1 (2C) (arom CH), 61.6 (2C) (OCH_2), 55.6 (OCH_3), 49.7 (CH), 47.0, 27.0 (CH_2), 22.7 ($\underline{C}H_3CO$), 14.1 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{26}NO_6$ 352.1760; found 352.1759.



1r

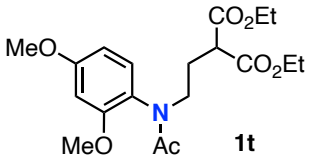
Diethyl 2-(2-(*N*-(3-Methoxyphenyl)acetamido)ethyl)malonate (1r): Yield (333 mg, 95%); yellow liquid; R_f = 0.34 ($CHCl_3$); IR ($CHCl_3$) ν 1728.1, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (1H, t, J = 8.6 Hz, H-5'), 6.90 (1H, dd, J = 8.6, 2,6 Hz, H-6'), 6.78 (1H, m, H-4'), 6.73 (1H, t, J = 2.6 Hz, H-2'), 4.28-4.10 (4H, m, OCH_2 ×2), 3.83 (3H, s, OMe), 3.76 (2H, t, J = 7.2 Hz, N-CH_2), 3.42 (1H, t, J = 7.2 Hz, CH), 2.12 (2H, q, J = 7.2 Hz, CH_2), 1.86 (3H, s, Ac), 1.25 (6H, t, J = 7.2 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 169.3 (2C) (C=O), 160.9, 144.2 (arom C), 130.7, 120.4, 114.1, 113.6 (arom CH), 61.6 (2C) (OCH_2), 55.5 (OCH_3), 49.7 (CH), 47.0, 27.1 (CH_2), 22.6 ($\underline{C}H_3CO$), 14.0 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{26}NO_6$ 352.1760; found 352.1768.



1s

Diethyl 2-(2-(*N*-(2-Methoxyphenyl)acetamido)ethyl)malonate (1s): Yield (326 mg, 93%); yellow liquid; R_f = 0.25 ($CHCl_3$); IR ($CHCl_3$) ν 1726.2, 1643.2 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.31 (1H, m, arom CH), 7.18-7.15 (1H,m, arom CH), 7.02-6.97. (2H, m, arom CH), 4.27-4.10 (4H, m, OCH_2 ×2), 3.85 (3H, s, OCH_3), 3.73 (2H, t, J = 7.5 Hz, N-CH_2), 3.52 (1H, t, J = 7.5 Hz, CH), 2.06 (2H, q, J = 7.5 Hz, CH_2), 1.77 (3H, s, Ac), 1.25 (3H, t, J = 7.5 Hz, CH_3), 1.23 (3H, t, J = 7.5 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 169.6, 169.5 (C=O), 155.6, 131.5 (arom C), 129.78, 129.75, 121.4, 112.1 (arom

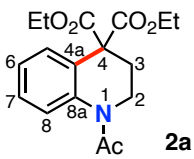
CH), 61.5, 61.4 (OCH_2), 55.5 (OCH_3), 49.6 (CH), 46.7, 27.2 (CH_2), 22.0 ($\underline{C}H_3CO$), 14.08, 14.06 (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{26}NO_6$ 352.1760; found 352.1762.



1t

Diethyl 2-(2-(*N*-(2,4-Dimethoxyphenyl)acetamido)ethyl)malonate (1t): Yield (365 mg, 96%); pale yellow liquid; R_f = 0.26 ($CHCl_3$); IR ($CHCl_3$) *v* 1728.1, 1643.2 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.07 (1H, d, *J* = 8.4 Hz, H-5'), 6.53-6.48 (2H, m), 4.25-4.12 (4H, m, OCH_2 ×2), 3.84 (3H, s, OCH_3), 3.82 (3H, s, OCH_3), 3.68 (2H, t, *J* = 6.9 Hz, N-CH_2), 3.50 (1H, t, *J* = 6.9 Hz, CH), 2.05 (2H, q, *J* = 6.9 Hz, CH_2), 1.77 (3H, s, Ac), 1.27 (3H, t, *J* = 6.9 Hz, CH_3), 1.23 (3H, t, *J* = 6.9 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 169.61, 169.57 (C=O), 160.8, 156.4 (arom C), 130.2 (arom CH), 124.5 (arom C), 104.8, 99.6 (arom CH), 61.5, 61.4 (OCH_2), 55.61, 55.57 (OCH_3), 49.6 (CH), 46.2, 27.1 (CH_2), 21.9 ($\underline{C}H_3CO$), 14.10, 14.07 (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{28}NO_7$ 382.1866; found 382.1859.

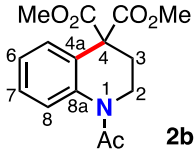
Oxidation of the Arylaminoethylmalonates 1a-t with $Mn(OAc)_3$•$2H_2O$. Arylaminoethylmalonate **1** (0.5 mmol) was dissolved in AcOH (30 mL) and $Mn(OAc)_3$•$2H_2O$ (1.5 mmol) was added. The mixture was heated under reflux in argon until the Mn(III) oxidant was completely consumed and the brown color of Mn(III) turned transparent. The existence of the Mn(III) was monitored by iodine-starch paper and each reaction time is listed in Table 1. After completion of the reaction, the solvent was removed in vacuo and the residue was triturated with 2M HCl (20 mL). The aqueous mixture was extracted with $CHCl_3$ (20 mL × 3) and the combined extracts were washed with a saturated aqueous solution of $NaHCO_3$ (30 mL), water (30 mL), dried over anhydrous $MgSO_4$, then concentrated to dryness. The crude product was separated and purified by thin-layer chromatography on silica gel developing with Et_2O/hexane (8:2 v/v), giving the corresponding tetrahydroquinolinedicarboxylate **2** (Table 1). The solid products were further purified by recrystallization from the appropriate solvent to obtain the analytical samples. The physical properties of the cyclization products are listed in the following section.



2a

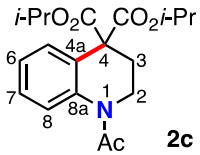
Diethyl 1-Acetyl-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2a): Yield (133.6 mg, 84%); yellow microcrystals; mp 60.0-61.0 °C; R_f = 0.33 (Et_2O:hexane = 8:2); IR ($CHCl_3$) *v* 1728.1, 1743.5, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.19 (4H, m, arom H), 4.26 (4H, q, *J* = 7.2 Hz, OCH_2 ×2),

3.87 (2H, t, J = 6.9 Hz, H-2), 2.53 (2H, t, J = 6.9 Hz, H-3), 2.16 (3H, s, Ac), 1.28 (6H, t, J = 7.2 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 170.0 (2C) (C=O), 138.7 (C-8a), 128.4, 128.0, 125.8, 125.5 (arom CH), 125.5 (C-4a), 62.3 (2C) (OCH_2), 57.8 (C-4), 40.0 (C-2), 32.2 (C-3), 22.9 ($COCH_3$), 14.1 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{22}NO_5$ 320.1498; Found 320.1514. Anal. Calcd for $C_{17}H_{21}NO_5$: C, 63.94; H, 6.63; N, 4.39. Found: C, 64.09; H, 6.62; N, 4.33.



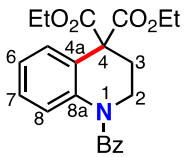
2b

Dimethyl 1-Acetyl-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2b): Yield (125.1 mg, 84%); colorless microcrystals; mp 111.0 °C; R_f = 0.45 (Et_2O:hexane = 8:2); IR ($CHCl_3$) ν 1732.0, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.19 (4H, m, arom H), 3.87 (2H, t, J = 6.9 Hz, H-2), 3.79 (6H, s, OCH_3 ×2), 2.55 (2H, t, J = 6.9 Hz, H-3), 2.16 (3H, s, Ac); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5 (2C), 170.4 (C=O), 138.6 (C-8a), 128.6, 127.9, 125.8, 125.5 (arom CH), 125.5 (C-4a), 57.8 (C-4), 53.3 (2C) (OCH_3), 40.0 (C-2), 32.3 (C-3), 22.8 ($COCH_3$). Anal. Calcd for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.93; H, 5.89; N, 4.84.



2c

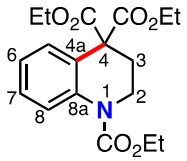
Diisopropyl 1-Acetyl-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2c): Yield (154.1 mg, 85%); colorless needles; mp 73.0 °C; R_f = 0.63 (Et_2O:hexane = 8:2); IR ($CHCl_3$) ν 1724.2, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.29 (2H, m, arom H), 7.23-7.18 (2H, m, arom H), 5.11 (2H, sept, J = 6.0 Hz, O-CH ×2), 3.87 (2H, t, J = 6.9 Hz, H-2), 2.50 (2H, t, J = 6.9 Hz, H-3), 2.16 (3H, s, Ac), 1.27 (12H, d, J = 6.0 Hz, CH_3 ×4); ^{13}C NMR: (75 MHz, $CDCl_3$) δ 170.5, 169.5 (2C) (C=O), 138.7 (C-8a), 128.3, 128.0, 125.6, 125.5 (arom CH), 125.5 (C-4a), 70.0 (2C) (O-CH), 57.7 (C-4), 39.8 (C-2), 32.1 (C-3), 22.9 ($COCH_3$), 21.6 (4C) (CH_3). Anal. Calcd for $C_{19}H_{25}NO_5$: C, 65.69; H, 7.25; N, 4.03. Found: C, 65.61; H, 7.32; N, 4.01.



2d

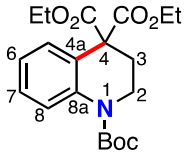
Diethyl 1-Benzoyl-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2d): Yield (163.0 mg, 83%); pale

yellow microcrystals; mp 82.0 °C; R_f = 0.31 ($CHCl_3$); IR ($CHCl_3$) ν 1730.0, 1635.5 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.40 (2H, m, arom H), 7.38-7.23 (4H, m, arom H), 7.06 (1H, td, J = 7.2, 1.6 Hz, arom H), 6.94 (1H, td, J = 7.9, 1.6 Hz, arom H), 6.64 (1H, d, J = 7.9 Hz, arom H), 4.39-4.26 (4H, m, OCH_2 ×2), 3.97 (2H, t, J = 6.9 Hz, H-2), 2.62 (2H, t, J = 6.8 Hz, H-3), 1.31 (6H, t, J = 7.2 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.40, 170.07 (2C) (C=O), 138.7, 135.7, 128.6 (arom C), 130.7, 129.1 (2C), 128.3 (2C), 127.83, 127.80, 126.3, 124.9 (arom CH), 62.4 (2C) (OCH_2), 58.0 (C-4), 41.8 (C-2), 32.3 (C-3), 14.1 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{24}NO_5$ 381.1654; found 382.1664. Anal. Calcd for $C_{22}H_{23}NO_5$: C, 69.28; H, 6,08; N, 3.67. Found: C, 69.14; H, 6,14; N, 3.63.



2e

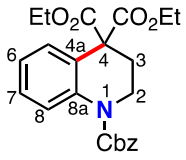
Triethyl 2,3-Dihydroquinoline-1,4,4-tricarboxylate (2e): Yield (161.1 mg, 90%); pale yellow liquid; R_f = 0.69 ($CHCl_3$); IR ($CHCl_3$) ν 1735.8, 1726.2, 1693.4 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (1H, d, J = 8.6 Hz, H-8), 7.40 (1H, dd, J = 8.0, 1.4 Hz, H-5), 7.27 (1H, td, J = 7.5, 1.4 Hz, H-7), 7.08 (1H, td, J = 7.5, 1.4 Hz, H-6), 4.24 (6H, q, J = 6.9 Hz, OCH_2 ×3), 3.86 (2H, t, J = 6.3 Hz, H-2), 2.51 (2H, t, J = 6.3 Hz, H-3), 1.31 (3H, t, J = 6.9 Hz, CH_3), 1.26 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (2C) (O-C=O), 154.6 (N-C=O), 138.2 (C-8a), 129.5, 128.2 (arom CH), 125.3 (C-4a), 124.4, 123.7 (arom CH), 62.19, 62.15 (2C) (OCH_2), 57.3 (C-4), 41.7 (C-2), 31.3 (C-3), 14.53, 13.99 (2C) (CH_3); FAB HRMS (acetone/NBA/NaI) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{23}NNaO_6$ 372.142); found 372.1436.



2f

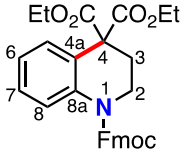
1-(*tert*-Butyl) 4,4-Diethyl 2,3-Dihydroquinoline-1,4,4-tricarboxylate (2f): Yield (159.1 mg, 79%); yellowish green liquid; R_f = 0.71 (AcOEt:hexane = 2:8); IR ($CHCl_3$) ν 1728.1, 1689.5 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (1H, dd, J = 8.4, 1.2 Hz, arom H), 7.38 (1H, dd, J = 8.1, 1.4 Hz, arom H), 7.25 (1H, td, J = 8.0, 1.8 Hz, arom H), 7.06 (1H, td, J = 7.7, 1.3 Hz, arom H), 4.24 (4H, q, J = 7.2 Hz, OCH_2 ×2), 3.80 (2H, t, J = 6.3 Hz, H-2), 2.49 (2H, t, J = 6.3 Hz, H-3), 1.51 (9H, s, CH_3 ×3), 1.26 (6H, t, J = 7.2 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8 (2C), 153.6 (C=O), 138.5 (C-8a), 129.3, 128.0 (arom CH), 125.4 (C-4a), 124.6, 123.4 (arom CH), 81.4 (O-C), 62.1 (2C) (OCH_2), 57.4 (C-4), 41.6 (C-2), 31.4 (C-3), 28.4 (3C), 14.0 (2C) (CH_3); FAB HRMS (acetone/NBA/NaI) *m/z*: $[M+Na]^+$ Calcd for

$C_{20}H_{27}NNaO_6$ 400.1736; found 400.1759.



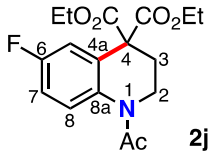
2g

1-Benzyl 4,4-Diethyl 2,3-Dihydroquinoline-1,4,4-tricarboxylate (2g): Yield (151.9 mg, 78%); pale yellow liquid; R_f = 0.48 (AcOEt:hexane = 4:6); IR ($CHCl_3$) ν 1728.1, 1705.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (1H, d, J = 8.1 Hz, arom H), 7.41-7.26 (7H, m, arom H), 7.10 (1H, td, J = 7.1, 1.5 Hz, arom H), 5.23 (2H, s, O-CH_2)), 4.22 (4H, q, J = 7.2 Hz, OCH_2 ×2), 3.89 (2H, t, J = 6.0 Hz, H-2), 2.51 (2H, t, J = 6.0 Hz, H-3), 1.24 (6H, t, J = 7.2 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6 (2C), 154.4 (C=O), 137.9 (C-8a), 136.4 (arom C), 129.4, 128.7 (2C), 128.4, 128.3, 128.2 (2C) (arom CH), 125.3 (C-4a), 124.4, 123.9 (arom CH), 67.8, 62.2 (2C) (OCH_2), 57.3 (C-4), 41.9 (C-2), 31.2 (C-3), 13.9 (2C) (CH_3); FAB HRMS (acetone/NBA/NaI) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{25}NNaO_6$ 434.1580; found 434.1593.



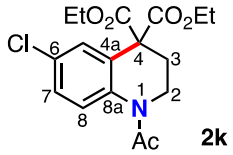
2h

1-((9*H*-Fluoren-9-yl)methyl) 4,4-Diethyl 2,3-Dihydroquinoline-1,4,4-tricarboxylate (2h): In this case, the phenylaminoethylmalonate **1h** (0.3 mmol, 155.9 mg) was used. Yield (114.6 mg, 74%); pale yellow liquid; R_f = 0.48 (AcOEt:hexane = 3:7); IR ($CHCl_3$) ν 1728.1, 1705.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (2H, d, J = 7.6 Hz, arom H), 7.55 (1H, m, arom H), 7.51 (2H, d, J =7.6 Hz, arom H), 7.38 (3H, td, J = 7.6, 2.1 Hz, arom H), 7.28 (2H, td, J = 7.6, 0.9 Hz, arom H), 7.19 (1H, td, J = 7.6, 1.6 Hz, arom H), 7.08 (1H, td, J = 7.6, 1.4 Hz, arom H), 4.57 (2H, d, J = 6.6 Hz, CH_2), 4.25 (1H, t, J = 6.6 Hz, CH), 4.21 (4H, q, J = 6.9 Hz, OCH_2 ×2), 3.81 (2H, t, J = 6.0 Hz, H-2), 2.45 (2H, t, J = 6.0 Hz, H-3), 1.23 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6 (2C), 154.4 (C=O), 144.0 (2C), 141.6 (2C) (arom C), 137.8 (C-8a), 129.4, 128.4, 127.9 (2C), 127.4 (2C) (arom CH), 125.5 (C-4a), 125.2 (2C), 124.6 (arom CH), 124.0 (arom C), 120.2 (2C) (arom CH), 67.7, 62.2 (2C) (OCH_2), 57.2 (C-4), 47.3 (CH), 41.9 (C-2), 31.2 (C-3), 14.0 (2C) (CH_3); FAB HRMS (acetone/NBA/NaI) *m/z*: $[M+Na]^+$ Calcd for $C_{30}H_{29}NNaO_6$ 522.1893; found 522.1926.



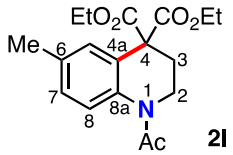
2j

Diethyl 1-Acetyl-6-fluoro-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2j): Yield (129.2 mg, 73%); colorless microcrystals; mp 88.0 °C; R_f = 0.52 ($CHCl_3$); IR ($CHCl_3$) ν 1732.0, 1654.8 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20-7.01 (3H, m, arom H), 4.26 (4H, q, J = 6.9 Hz, OCH_2 ×2), 3.86 (2H, t, J = 6.9 Hz, H-2), 2.52 (2H, t, J = 6.9 Hz, H-3), 2.14 (3H, s, Ac), 1.28 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 169.6 (2C) (C=O), 159.7 (d, $^1J_{(C,F)}$ = 287 Hz, C-6), 134.6 (C-8a), 126.9 (d, $^3J_{(C,F)}$ = 8 Hz, C-8), 119.7 (d, $^3J_{(C,F)}$ = 9 Hz, C-4a), 115.4 (2C) (d, $^2J_{(C,F)}$ = 22 Hz, C-5 and C-7), 62.3 (2C) (OCH_2), 57.5 (C-4), 39.7 (C-2), 31.8 (C-3), 22.6 ($CO\underline{C}H_3$), 13.9 (2C) (CH_3). Anal. Calcd for $C_{17}H_{20}NFO_5$: C, 60.53; H, 5.98; N, 4.15. Found: C, 60.69; H, 6.08; N, 4.15.



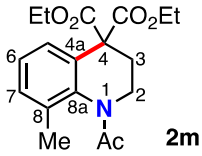
2k

Diethyl 1-Acetyl-6-chloro-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2k): Yield (142.5 mg, 81%); yellow liquid; R_f = 0.52 ($CHCl_3$); IR ($CHCl_3$) ν 1745.5, 1726.2, 1652.9 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.24 (3H, m, arom H), 4.27 (4H, q, J = 6.9 Hz, OCH_2 ×2), 3.85 (2H, t, J = 6.6 Hz, H-2), 2.52 (2H, t, J = 6.6 Hz, H-3), 2.16 (3H, s, Ac), 1.29 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR: (75 MHz, $CDCl_3$) δ 170.1, 169.5 (2C) (C=O), 137.0 (C-8a), 131.0 (C-6), 128.5, 126.5 (2C) (arom CH), 126.5 (C-4a), 62.3 (2C) (OCH_2), 57.3 (C-4), 40.2 (C-2), 31.7 (C-3), 22.8 ($CO\underline{C}H_3$), 13.9 (2C) (CH_3). FAB HRMS (acetone/NBA/NaI) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{20}NClNaO_5$ 376.0928; found 376.0930.



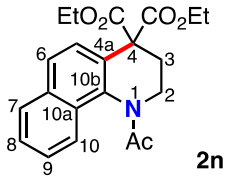
2l

Diethyl 1-Acetyl-6-methyl-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2l): Yield (146.0 mg, 90%); red liquid; R_f = 0.40 ($CHCl_3$); IR ($CHCl_3$) ν 1728.1, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23-7.05 (3H, m, arom H), 4.26 (4H, q, J = 6.9 Hz, OCH_2 ×2), 3.84 (2H, t, J = 6.9 Hz, H-2), 2.51 (2H, t, J = 6.9 Hz, H-3), 2.35 (3H, s, CH_3), 2.14 (3H, s, Ac), 1.28 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 170.0 (2C) (C=O), 136.0, 135.7 (arom C), 129.1, 128.3, 125.3 (arom CH), 125.3 (C-4a), 62.3 (2C) (OCH_2), 57.3 (C-4), 39.4 (C-2), 32.2 (C-3), 22.8 ($CO\underline{C}H_3$), 21.2 CH_3), 14.1 (2C) (CH_3); FAB HRMS (acetone/NBA/NaI) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{23}NNaO_5$ 356.1474; found 356.1494.



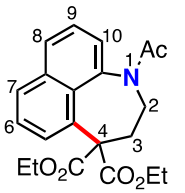
2m

Diethyl 1-Acetyl-8-methyl-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2m): Yield (154.5 mg, 92%); yellow liquid; R_f = 0.41 (AcOEt:hexane = 3:7); IR ($CHCl_3$) ν 1728.1, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28-7.03 (3H, m, arom H), 4.77-4.67 (1H, m, H-CH), 4.32 (4H, q, J = 7.2 Hz, OCH_2 ×2), 3.07-3.01 (1H, m, HC-H), 2.92-2.84 (1H, m, H-CH), 2.26 (3H, s, CH_3), 2.24-2.19 (1H, m, HC-H), 1.84 (3H, s, CH_3), 1.34 (3H, t, J = 7.2 Hz, CH_3), 1.24 (3H, t, J = 7.2 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 170.0, 169.6 (C=O), 137.8, 135.3, 134.3 (arom C), 131.0, 126.9, 124.0 (arom CH), 62.2 (2C) (OCH_2), 58.6 (C-4), 38.7 (C-2), 32.5 (C-3), 21.0, 17.3, 14.12, 14.01 (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{24}NO_5$ 334.1654; found 334.1650.



2n

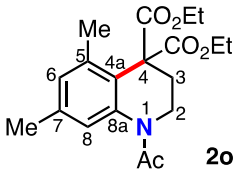
Diethyl 1-Acetyl-2,3-dihydrobenzo[*h*]quinoline-4,4(1*H*)-dicarboxylate (2n): Yield (78.5 mg, 41%); pale yellow liquid; R_f = 0.57 (AcOEt:hexane = 3:7); IR ($CHCl_3$) ν 1726.2, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (1H, d, J = 8.2 Hz, arom H), 7.84 (1H, d, J = 8.2 Hz, arom H), 7.44 (2H, td, J = 7.8, 3.1 Hz, arom H), 7.21 (1H, d, J = 8.2 Hz, arom H), 7.18 (1H, d, J = 8.2 Hz, arom H), 5.16-5.06 (1H, m, H-2), 4.45-4.31 (2H, m, OCH_2), 4.28-4.15 (2H, m, OCH_2), 3.23-3.14 (1H, m, H-3), 2.99-2.90 (1H, m, H'-3), 2.64-2.53 (1H, m, H'-2), 1.70 (3H, s, Ac), 1.33 (3H, t, J = 7.2 Hz, CH_3), 1.29 (3H, t, J = 7.2 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0, 171.2, 170.0 (C=O), 138.6, 136.0, 135.4, 129.6 (arom C), 129.5, 129.1, 127.9, 126.5, 125.9, 125.7 (arom CH), 63.5, 62.3 (OCH_2), 61.9 (C-4), 42.7 (C-2), 34.6 (C-3), 22.5 ($COCH_3$), 14.0, 13.9 (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{24}NO_5$ 370.1654; found 370.1627.



3n

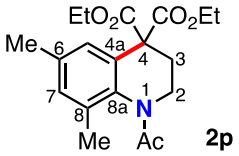
Diethyl 1-Acetyl-2,3-dihydronaphtho[1,8-*bc*]azepine-4,4(1*H*)-dicarboxylate (3n): Yield (96.8 mg, 51%); colorless microcrystals; mp 128-129 °C; R_f = 0.67 (AcOEt:hexane = 3:7); IR ($CHCl_3$) ν 1730.0,

1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91-7.85 (2H, m, arom H), 7.79 (1H, d, J = 8.8 Hz, arom H), 7.76 (1H, td, J = 6.8, 1.8 Hz, arom H), 7.52 (1H, td, J = 6.8, 1.8 Hz, arom H), 7.42 (1H, d, J = 8.6 Hz, arom H), 4.89 (1H, dt, J = 14.1, 7.9 Hz, H_a-2), 4.37 (2H, q, J = 7.2 Hz, OCH_2), 4.31-4.09 (2H, m, OCH_2), 3.21 (1H, ddd, J = 11.3, 7.9, 5.0 Hz, H_b-2), 2.95 (1H, ddd, J = 11.3, 7.9, 5.0 Hz, H_a-3), 2.39 (1H, dt, J = 14.1, 7.9 Hz, H_b-3), 1.73 (3H, s, Ac), 1.35 (3H, t, J = 7.2 Hz, CH_3), 1.25 (3H, t, J = 7.2 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0, 170.2, 169.6 (C=O), 135.6, 134.0, 130.6, 129.4 (arom C), 128.7, 127.3, 127.0, 126.8, 124.3, 123.2 (arom CH), 62.45, 62.37 (OCH_2), 58.5 (C-4), 39.5 (C-2), 33.6 (C-3), 23.0 ($CO\underline{C}H_3$), 14.11, 14.02 (CH_3). Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.00; H, 6.33; N, 3.80.



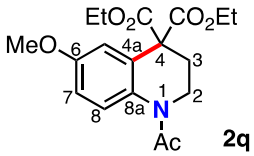
2o

Diethyl 1-Acetyl-5,7-dimethyl-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2o): Yield (134.6 mg, 92%); yellow liquid; R_f = 0.48 (AcOEt:hexane = 4:6); IR ($CHCl_3$) ν 1728.1, 1647.1 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (1H, brs, arom H), 6.82 (1H, brs, arom H), 4.30-4.14 (4H, m, OCH_2 ×2), 3.84 (2H, t, J = 6.9 Hz, H-2), 2.53 (2H, t, J = 6.9 Hz, H-3), 2.31 (3H, s, CH_3), 2.25 (3H, s, CH_3), 2.03 (3H, s, Ac), 1.26 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.61 (2C), 170.55 (C=O), 138.6, 137.2 (2C), 136.7 (arom C), 130.2, 124.1 (arom CH), 62.2 (2C) (OCH_2), 57.0 (C-4), 39.5 (C-2), 34.1 (C-3), 22.7, 20.9, 20.3, 13.9 (2C) (CH_3); FAB HRMS (acetone/NBA/NaI) *m/z*: $[M + Na]^+$ Calcd for $C_{19}H_{25}NNaO_5$ 370.1630; found 370.1625.



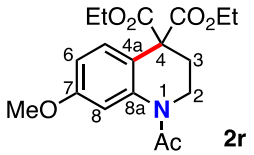
2p

Diethyl 1-Acetyl-6,8-dimethyl-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2p): Yield (111.8 mg, 64%); pale yellow liquid; R_f = 0.43 (AcOEt:hexane = 4:6); IR ($CHCl_3$) ν 1728.1, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.07 (1H, brs, arom H), 6.82 (1H, brs, arom H), 4.74-4.68 (1H, m, $\underline{H}$-CH), 4.40-4.34 (4H, m, OCH_2 ×2), 4.25-4.07 (1H, m, HC-$\underline{H}$), 3.05-2.83 (2H, m, CH_2), 2.33 (3H, s, CH_3), 2.21 (3H, s, CH_3), 1.84 (3H, s, CH_3), 1.35 (3H, t, J = 7.5 Hz, CH_3), 1.24 (3H, t, J = 7.5 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 170.1 (2C) (C=O), 136.5, 135.2, 134.8, 133.9 (arom C), 131.6, 124.7 (arom CH), 62.2 (2C) (OCH_2), 58.6 (C-4), 38.7 (C-2), 32.6 (C-3), 21.3, 21.0, 17.3, 14.1, 14.0 (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M + H]^+$ Calcd for $C_{19}H_{26}NO_5$ 348.1811; found 348.1799.



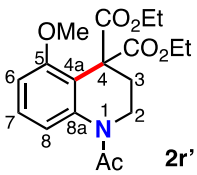
2q

Diethyl 1-Acetyl-6-methoxy-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2q): Yield (162.6 mg, 91%); colorless needles; mp 88.0 °C; R_f = 0.51 ($CHCl_3$); IR ($CHCl_3$) ν 1730.0, 1637.5 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (1H, brs, arom H), 6.88-6.85 (2H, brs, arom H), 4.26 (4H, q, J = 6.9 Hz, OCH_2 ×2), 3.84 (2H, t, J = 6.9 Hz, H-2), 3.81 (3H, s, OCH_3), 2.51 (2H, t, J = 6.9 Hz, H-3), 2.12 (3H, brs, Ac), 1.28 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 170.0 (2C) (C=O), 157.4 (C-6), 138.2 (C-8a), 126.2 (arom CH), 113.6 (C-4a), 113.4 (2C) (arom CH), 62.3 (2C) (OCH_2), 58.4 (C-4), 55.6 (OCH_3), 39.9 (C-2), 32.2 (C-3), 22.5 ($CO\underline{C}H_3$), 14.1 (2C) (CH_3). Anal. Calcd for $C_{18}H_{23}NO_6$: C, 61.88; H, 6.64; N, 4.01. Found: C, 61.92; H, 6.61; N, 4.03.



2r

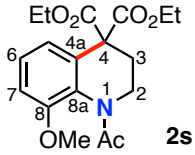
Diethyl 1-Acetyl-7-methoxy-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate(2r): Yield (78.1 mg, 45%); pale red microcrystals; mp 84.0 °C; R_f = 0.67 ($CHCl_3$); IR ($CHCl_3$) ν 1728.1, 1652.9 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (1H, d, J = 8.9 Hz, H-5), 6.81 (1H, brs, H-8), 6.76 (1H, dd, J = 8.6 Hz, H-6), 4.24 (4H, q, J = 6.9 Hz, OCH_2 ×2), 3.87 (2H, t, J = 6.6 Hz, H-2), 3.81 (3H, s, OCH_3), 2.50 (2H, t, J = 6.6 Hz, H-3), 2.22 (3H, s), Ac, 1.27 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5 (2C), 170.3 (C=O), 159.4 (C-7), 139.7 (C-8a), 129.4 (C-5), 111.0 (C-4a), 110.5 (C-6), 102.5 (C-8), 62.2 (2C) (OCH_2), 56.9 (C-4), 55.5 (OCH_3), 40.6 (C-2), 32.1 (C-3), 23.2 ($CO\underline{C}H_3$), 14.1 (2C) (CH_3). Anal. Calcd for $C_{18}H_{23}NO_6$: C, 61.88; H, 6.64; N, 4.01. Found: C, 61.90; H, 6.89; N, 4.04.



2r'

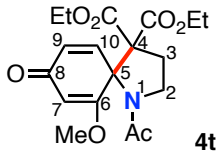
Diethyl 1-Acetyl-5-methoxy-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2r'): Yield (83.9 mg, 48%); pale red liquid; R_f = 0.57 ($CHCl_3$); IR ($CHCl_3$) ν 1728.1, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (1H, t, J = 9.0 Hz, H-7), 6.91 (1H, brs, H-8), 6.80 (1H, d, J = 8.2 Hz, H-6), 4.18 (4H, q, J = 6.9 Hz, OCH_2 ×2), 3.83 (2H, t, J = 6.6 Hz, H-2), 3.79 (3H, s, OCH_3), 2.52 (2H, t, J = 6.6 Hz, H-3), 2.16 (3H, s, Ac), 1.24 (6H, t, J = 6.9 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 170.4 (2C) (C=O),

157.4 (C-5), 139.6 (C-8a), 128.3 (C-7), 117.9 (C-8), 113.6 (C-4a), 109.0 (C-6), 61.8 (2C) (OCH_2), 56.3 (OCH_3), 54.9 (C-4), 40.4 (C-2), 33.3 (C-3), 23.1 ($CO\underline{C}H_3$), 14.1 (2C) (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{24}NO_6$ 350.1604; found 350.1621.



2s

Diethyl 1-Acetyl-8-methoxy-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (2s): Yield (171.1 mg, 94%); pale yellow liquid; R_f = 0.53 ($CHCl_3$); IR ($CHCl_3$) *v* 1728.1, 1651.0 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (1H, t, *J* = 8.0 Hz, H-6), 6.96 (1H, d, *J* = 8.6 Hz, H-7), 6.83 (1H, d, *J* = 8.0 Hz, H-5), 4.53 (1H, dd, *J* = 19.0, 8.0 Hz, H_a-2), 4.35 (2H, q, *J* = 7.2 Hz, OCH_2), 4.28-4.06 (2H, m, OCH_2), 3.85 (3H, s, OCH_3), 3.13 (1H, t, *J* = 8.7 Hz, H_b-2), 2.83 (1H, td, *J* = 11.7, 3.3 Hz, H_a-3), 2.23 (1H, dt, *J* = 13.5, 8.7 Hz, H_b-3), 1.93 (3H, s, Ac), 1.34 (3H, t, *J* = 7.2 Hz, CH_3), 1.23 (3H, t, *J* = 7.2 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0, 169.9, 169.4 (C=O), 153.6 (C-8), 135.2 (C-8a), 127.8 (C-4a), 127.3 (C-6), 118.3 (C-5), 111.6 (C-7), 62.34, 62.28 (OCH_3), 58.4 (C-4), 55.7 (OCH_3), 39.0 (C-2), 32.8 (C-3), 21.2 ($CO\underline{C}H_3$), 14.1, 14.0 (CH_3); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{24}NO_6$ 350.1604; found 350.1625.

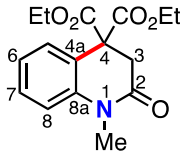


4t

Diethyl 1-Acetyl-6-methoxy-8-oxo-1-azaspiro[4.5]deca-6,9-diene-4,4-dicarboxylate (4t): In this case, the (2,4-dimethoxyphenyl)aminoethylmalonate **1t** (0.3 mmol, 117.3 mg) was used. Yield (61.1 mg, 54%); brown liquid; R_f = 0.05 (Et_2O); IR ($CHCl_3$) *v* 1728, 1662, 1628, 1599 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (1H, d, *J* = 9.5 Hz, H-9), 6.23 (1H, d, *J* = 10.5 Hz, H-10), 5.56 (1H, s, H-7), 4.30-4.14 (4H, m, OCH_2 ×2), 3.92-3.83 (2H, m, CH_2), 3.66 (3H, s, OCH_3), 3.16 (1H, m, H_a-3), 2.19 (1H, m, H_b-3), 2.10 (3H, s, Ac), 1.25 (3H, t, *J* = 7.2 Hz, CH_3), 1.16 (3H, t, *J* = 7.2 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.4 (C-6), 171.8 (C-8), 169.5, 168.3 (C=O), 166.6 (N-Ac), 144.4 (C-9), 128.7 (C-9), 103.6 (C-7), 67.4 (C-5), 67.0 (C-4), 62.5, 62.3 (OCH_2), 56.0 (OCH_3), 47.1 (C-2), 31.3 (C-3), 23.6 ($CO\underline{C}H_3$), 13.9, 13.5 (CH_3); MS *m/z* (rel intensity) 366.2 (M+H, 100), 292.2 (20), 250.2 (18), 152.1 (645), 136.1 (11), 77.0 (7); FAB HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{24}NO_7$ 366.1553; found 366.1570.

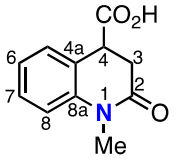
Preparation of 2-Oxo-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate 5 and Conversion into Quinolinone 7. The dihydroquinolinone **5** was prepared by the Mn(III)-based oxidation of diethyl 2-(2-(methyl(phenyl)amino)-2-oxoethyl)malonate (5 mmol, 1.543 g) according to the literature.[11] The dihydroquinolinone **5** (1.5 mmol, 0.5155 g) was dissolved in MeOH (10 mL) and a 10% KOH aqueous

solution (5 mL) was added. The aqueous solution was stirred at room temperature for 30 min, washed with AcOEt, acidified with 6M HCl until no bubbles, then extracted with AcOEt. The combined extracts were dried over anhydrous $MgSO_4$ and concentrated to dryness. The solid obtained was recrystallized using $CHCl_3$ to give the oxotetrahydroquinoline-4-carboxylic acid **6** (339.8 mg, 98%). The acid **6** (1.0 mmol, 211.4 mg) was oxidized by $Mn(OAc)_3$•$2H_2O$ (2.0 mmol, 575.7 mg) in the presence of $Cu(OAc)_2$ (1.0 mmol, 181.9 mg) in boiling AcOH (15 mL) for 40 min,[15] giving the desired quinolinone **7** (162.2 mg, 99.5%) after the usual work-up. The physical data are shown below.



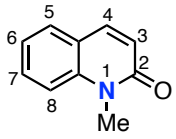
5

Diethyl 1-Methyl-2-oxo-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (5): Yield (1.365 g, 90%); colorless cubics; mp 86-87 °C (lit,[11] mp 86-87 °C); R_f = 0.47 (Et_2O:hexane = 8:2); IR ($CHCl_3$) ν 1757, 1734, 1688 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (1H, td, J = 7.5, 1.5 Hz, H-7), 7.31 (1H, dd, J = 8.0, 1.0 Hz, H-8), 7.11 (1H, td, J = 7.5, 1.5 Hz, H-6), 7.04 (1H, dd, J = 8.0, 1.0 Hz, H-5), 4.32-4.22 (4H, m, OCH_2 ×2), 3.34 (3H, s, N-CH_3), 3.24 (2H, s, H-3), 1.27 (6H, t, J = 7.3 Hz, CH_3 ×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1 (2C) (C=O), 166.8 (C-2), 139.9 (C-8a), 129.5, 127.9, 123.3 (arom CH), 122.8 (C-4a), 115.5 (arom CH), 62.6 (2C) (OCH_2), 57.0 (C-4), 38.1 (N-CH_3), 29.7 (C-3), 14.1 (2C) (CH_3). Anal. Calcd for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.90; H, 6.35; N, 4.62.



6

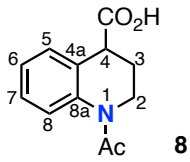
1-Methyl-2-oxo-1,2,3,4-tetrahydroquinoline-4-carboxylic acid (6): Yield (339.8 mg, 98%); colorless microcrystals; mp 171-173 °C (lit,[19] mp 175-176 °C); R_f = 0.50 ($CHCl_3$); IR ($CHCl_3$) ν 3600-2300 (OH), 1736, 1641 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (1H, brs, CO_2H), 7.34-7.31 (2H, m, arom H), 7.07 (1H, t, J = 7.5 Hz, arom H), 7.01 (1H, d, J = 7.5 Hz, arom H), 3.86 (1H, dd, J = 6.0, 3.5 Hz, H-4), 3.34 (3H, s, N-CH_3), 3.05 (1H, dd, J = 16.0, 3.5 Hz, H_a-3), 2.79 (1H. dd, J = 16.0, 6.0 Hz, H_b-3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4 (C=O), 168.7 (C-2), 140.1 (C-8a), 129.2, 129.1, 123.4 (arom CH), 122.2 (C-4a), 115.4 (arom CH), 41.9 (C-4), 33.4 (C-3), 29.8 (N-CH_3); MS *m/z* (rel intensity) 205 (M^+, 36), 160 (100), 132 (38), 117 (24), 77 (22).



7

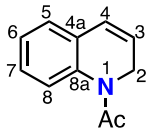
1-Methylquinolin-2(1*H*)-one (7): Yield (79.0 mg, 98%); colorless needles; mp 74-75 °C (lit,[20] mp 175-176 °C); R_f = 0.33 ($CHCl_3$); IR ($CHCl_3$) ν 1651 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (1H, d, J = 9.0 Hz, H-8), 7.55-7.53 (2H, m, arom H), 7.34 (1H, d, J = 9.0 Hz, H-4), 7.22 (1H, t, J = 8.0 Hz, arom H), 6.70 (1H, d, J = 9.0 Hz, H-3), 3.70 (3H, s, N-CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.4 (C-2), 140.1 (C-8a), 139.1, 130.7, 128.8, 122.2, 121.8, 114.2 (arom CH), 120.7 (C-4a), 29.5 (N-CH_3); MS *m/z* (rel intensity) 159 (M^+, 100), 130 (64), 116 (9), 101 (16), 89 (18), 77 (27).

Conversion of 2a into Quinoline 10. The treatment of **2a** (0.22 mmol, 70.4 mg) in MeOH (3 mL) with a 10% KOH aqueous solution (6 mL) was carried out at room temperature for 12 h. After the work-up described above, tetrahydroquinolinecarboxylic acid **8** (40.6 mg, 84%) was obtained. The acid **8** (0.3 mmol, 64.9 mg) underwent oxidative decarboxylation with $Pb(OAc)_4$ (0.6 mmol, 278 mg) and $Cu(OAc)_2$ (0.6 mmol, 110.4 mg) in boiling AcOH (5 mL) for 24 h, affording the dihydroquinoline **9** (51.3 mg) including 1-acetyl-2,3-dihydroquinolin-4(1*H*)-one. Using $Mn(OAc)_3$ instead of $Pb(OAc)_4$ also gave a similar result. Finally, dihydroquinoline **9** (0.3 mmol, 51.3 mg) in MeOH (3 mL) was treated with a 50% KOH aqueous solution (1.4 mL) at reflux temperature for 24 h. Water was added and the aqueous mixture was extracted with CH_2Cl_2, which was washed with brine and concentrated to dryness. The crude product was separated by thin-layer chromatography developing with Et_2O/hexane (8:2 v/v), giving the desired quinoline **10** (30.4 mg, 65%). The final transformation of **9** (0.5 mmol, 88.4 mg) into quinoline was also conducted with a 50% H_2SO_4 aqueous solution in MeOH (5 mL) at reflux temperature for 24 h, giving quinoline **10** (38.3 mg, 58%). The physical properties of the products are listed below.



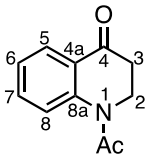
8

1-Acetyl-1,2,3,4-tetrahydroquinoline-4-carboxylic acid (8): Yield (40.6 mg, 84%); colorless microcrystals; mp 168-170 °C; R_f = 0.12 (AcOEt); IR ($CHCl_3$) ν 3500-2100 (OH), 1751, 1676 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.6 (1H, brs, CO_2H), 7.44-7.13 (4H, m, arom H), 3.96 (1H, m, H-CH), 3.81 (1H, t, J = 6.0 Hz, H-4), 3.45 (1H, m, HC-H), 2.25-2.19 (1H, m, H-CH), 2.11 (3H, s, Ac), 2.04-1.98 (1H, m, HC-H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 174.9 (O-C=O), 169.7 ($COCH_3$), 139.1 (C-8a), 129.2 (2C), 127.4, 125.5 (arom CH), 125.3 (C-4a), 55.1 (C-2), 42.9 (C-4), 27.4 (C-3), 23.4 ($COCH_3$); MS *m/z* (rel intensity): 220.2 (M+H, 18), 154.1 (100), 136.1 (90), 89.0 (25), 77.0 (21); HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{14}NO_3$ 220.0974; found 220.0974.

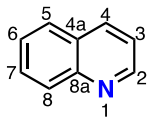


9

1-Acetyl-1,2-dihydroquinoline (9): Colorless microcrystals; mp 39-40 °C (lit,[21] mp 39-40 °C); R_f = 0.89 (EtOAc); IR ($CHCl_3$) ν 1653 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22-7.10 (4H, m, arom H), 6.53 (1H, d, J = 9.5 Hz, H-4), 6.08 (1H, m, H-3), 4.46 (2H, brs, H-2), 2.20 (3H, s, Ac); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8 ($\underline{C}OCH_3$), 150.2 (C-8a), 129.2, 128.1, 127.1, 126.2, 125.6, 123.8 (arom CH), 124.4 (C-4a), 41.1 (C-2), 22.2 (N-CH_3); MS *m/z* (rel intensity): 173 (M^+, 18), 130 (100), 102 (8), 77 (17).



1-Acetyl-2,3-dihydroquinolin-4(1*H*)-one : Yield (26.0 mg, 35%); pale yellow microcrystals; mp 89-91 °C (lit,[22] mp 91.5-92.5 °C); R_f = 0.64 (AcOEt); IR ($CHCl_3$) ν 1689, 1654 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (1H, d, J = 7.4 H, arom H), 7.49 (1H, t , J = 8.0 Hz, arom H), 7.37 (1H, br, arom H), 7.22 (1H, t, J = 8.0 Hz, arom H), 4.18 (2H, t, J = 6.0 Hz, H-2), 2.74 (2H, t, J = 6.0 Hz, H-3), 2.28 (3H, s, Ac); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.1 (C-4), 169.5 ($\underline{C}OCH_3$), 144.6 (C-8a), 134.2, 127.9, 125.7, 124.2 (arom CH), 126.2 (C-4a), 43.9 (C-2), 39.6 (C-3), 23.2 (CO$\underline{C}H_3$); MS *m/z* (rel intensity) 220.2 (M+H, 18), 154.1 (100), 136.1 (90), 89.0 (25), 77.0 (21); HRMS (acetone/NBA) *m/z*: $[M+H]^+$ Calcd for $C_{11}H_{12}NO_2$ 190.0868; found 190.0856.



10

Quinoline (10): Yield (30.4 mg, 65%); pale yellow liquid; R_f = 0.63 (Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.92 (1H, d, J = 6.5 Hz, H-2), 8.16-8.10 (2H, m, arom H), 7.81 (1H, d, J = 8.0 Hz, arom H), 7.74-7.70 (1H, m, arom H), 7.57-7.52 (1H, m, arom H), 7.40-7.37 (1H, m, arom H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.4 (C-2), 148.3 (C-8a), 136.1, 129.5, 129.4 (arom CH), 128.3 (C-4a), 127.8, 126.5, 121.1 (arom CH); MS *m/z* (rel intensity): 129 (M^+, 100), 102 (24), 76 (10), 64 (11).

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