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TRANSFORMATIONS OF METHYL 2-BENZOYLAMINO-2-OXO-BUTANOATE. THE SYNTHESIS OF OXAZOLO[4,5–*c*]QUINOLINE AND 1-SUBSTITUTED 1*H*-IMIDAZOLE-4-CARBOXYLATE DERIVATIVES

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Abstract – Methyl 2-benzoylamino-2-oxobutanoate (**1**) was transformed with aromatic amines (**2a–d**) into methyl 2-arylamino-2-(benzoylamino)but-2-enoates (**3a–d**) Cyclization of compounds (**3a–c**) in polyphosphoric acid affords a mixture of oxazolo[4,5–*c*]quinoline derivatives (**4a–c**) and 1-aryl-2-phenyl-5-methyl-1*H*-imidazole-4-carboxylates (**5a–c**), while compound **3d** gives a mixture of 9-bromo- (**4d**) and 7-bromooxazolo[4,5–*c*]quinoline derivative (**4d´**)

INTRODUCTION

In the literature only limited number of syntheses of oxazolo[4,5–*c*]quinolines are described. They are obtained from 3-amino-4-hydroxyquinolines,[1] from isatoic anhydrides with α-isocyanoacetates,[2] by Beckmann rearrangement of 3-acyl-4-hydroxy-2-quinolone oximes,[3] and from 4-azido-2(1*H*)-quinolones by thermolysis in the presence of carboxylic acids and polyphosphoric acid.[4] Many oxazoloquinoline derivatives have been found in the last decades to show antihypertensive and dopaminergic properties[5] and antiulcer,[6] anticancer,[7] antiallergic,[8] antidepressive,[9] or herbicidal acrivity.[10] Recently, immunomodulating effects of quinolines containing a carbamoyl group have been described[11] and for inducing cytokine biosynthesis.[12]

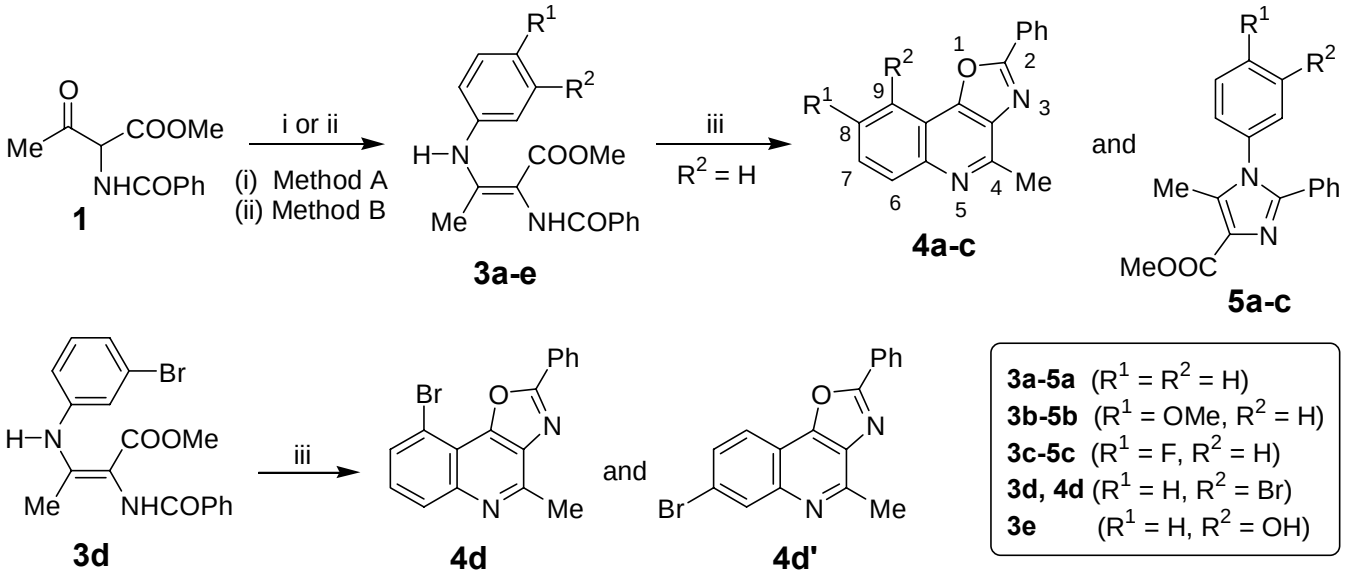
There has been only a limited number of syntheses of imidazoles described in the literature in which the acyclic precursors containing C–N–C–C–N structural element have been used.[13] They are cyclizations of α-acylaminoamidines,[14] α-acylaminothiocarboxylic acid amides,[15] α-acylaminocarboxylic acids amides,[16] hydrazones,[17] *N*-substituted derivatives of α-aminocarbonitriles,[18] *N*-substituted 1,2-diaminoalkanes,[19] and bisamides of oxalic acid.[20]

Substituted alkyl 2-acylamino-3-dimethylaminopropenoates and related compounds as masked

α-formyl-α-amino acids have turned out to be versatile reagents in the synthesis of many heterocyclic systems.[21] 3-Arylainopropenoates without 2-acylamino substitutent have been found as suitable intermediates for the preparaton of 1,4-dihydro-4-oxoquinoline derivatives.[22] The latter compounds have been further used also for the preparation of oxazoloquinoline derivatives.[23] In connection with this research, methyl 2-benzoylamino-3-oxobutanoate (**1**), prepared from hippuric acid by treatment with *N*,*N*-dimethylacetamide in the presence of phosphoryl chloride, followed by hydrolysis with hydrochloric acid in methanol, has been employed for the synthesis of 1-substituted 4-benzoylamino-3-methyl-5(2*H*)-pyrazolones.[24]

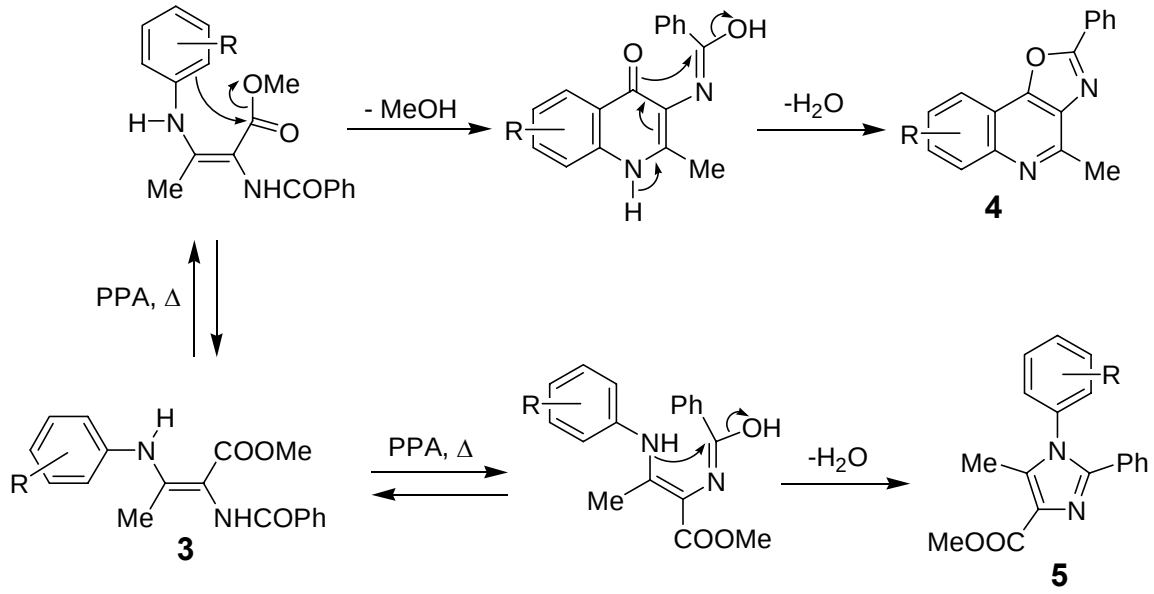
RESULTS AND DISCUSSION

In this paper we report on the transformation of **1** with aromatic amines (**2a–e**) into methyl 3-arylamino-2-benzoylaminobut-2-enoates (**3a–e**) by heating for several hours in the presence of catalytic amounts of *p*-toluenesulfonic acid (PTSA), either in benzene (method A) or in ethanol (Method B), with yields 52–79% in ethanol and 9–74% in benzene. Heteroaromatic amines, such as 2-aminopyridine, 2-amino-4-methylpyridine, and 2-amino-5-chloropyridine did not react under these conditions. When compounds (**3a–c**) were heated in polyphosphoric acid (PPA) at 130–140°C for 1–2.5 h, followed by neutralization of the reaction mixture with saturated solution of sodium hydrogen carbonate two products were isolated in each case. Both componenets were separated by column chromatography to give 2-phenyl-4-metyloxazolo[4,5–*c*]quinoline derivatives (**4a–c**) and 1-aryl-5-methyl-1*H*-imidazole-4-carboxylates (**5a–c**) in moderate yields. In the case of **3d**, the isomeric 7-bromo- (**4d**) and 9-bromo-4-methyl-2-phenyloxazolo[4,5-*c*]quinoline (**6d**) were isolated in 14 and 24% yields, respectively (Scheme 1).



Scheme 1. (i) Ar–NH_2 (**2a–e**), benzene, PTSA (cat.), reflux, Dean-Stark (Method A); (ii) Ar–NH_2 (**2a–e**), EtOH, PTSA (cat.), reflux (Method B); (iii) PPA, 130–140°C, then chromatographic separation.

The formation of the products can be explained in the following way. The cyclization of compounds (**3**) can take place between the methoxycarbonyl group and aromatic ring at *ortho* positon in regard to the amino group to form 3-benzoylamino substituted 4-oxo-1,4-dihydroquinoline intermediate followed by cyclodehydration taking place between benzoylamino and potential hydroxy group at the 4 position in quinoline ring to give oxazolo[4,5–*c*]quinoline derivatives (**4**). This latter reaction is analogous to the cyclization of 3-amino-4-oxo-1,2-dihydroquinoline in the presence of acetic anhydride reported recently.[1x] The concurrent reaction is cyclization taking place between the amino group attached to the aromatic ring and carbonyl group of the benzoylamino group to give imidazole derivatives (**4**) (Scheme 2).



Scheme 2

The structures of new compounds are based on elemental analyses, ^{1}H NMR spectra, MS spectral data and X-Ray determination. The ^{1}H NMR spectra of compounds (**3**) exhibit only one set of signals. The NOESY spectrum of **3b** in DMSO-d_6 at 302 K shows the NOE between the protons of the methyl group attached to the double bond and proton attached to the nitrogen atom of the benzoylamino group on one side, and between the proton attached to the nitrogen atom of the arylamino group and the protons of the methoxycarbonyl group, thus indicating that compounds (**3**) exist in the (*E*)-configuration (Figure 1).

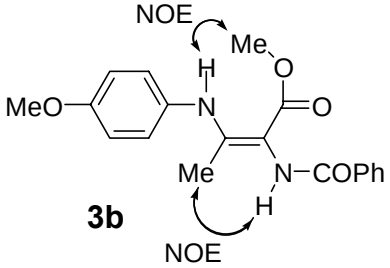


Figure 1

The structures of compounds (**4**) were determined by ^{1}H NMR spectra. Compound (**4a**) shows besides five protons of the 2-phneyl group four aromatic protons belonging to thequinoline ring. Compounds (**4a-c**) show three protons for quinoline part of the molecule with the corresponding coupling constants indicating that the substituents are attached at 8-position. Compound (**4d**) exhibits three protons for quinoline nucleus at δ = 7.55 ppm (H_7), 7.87 ppm (H_8) and 8.15 ppm (H_6) with the coupling contants $J_{6,7}$ = 8.5 Hz, $J_{6,8}$ = 1.0 Hz, and $J_{7,8}$ = 7.6 Hz, confirming that the bromine is attached at 9-position. Compound (**6d**) exhibits three protons at δ = 7.73 ppm (H_8), 8.11 ppm (H_9), and 8.37 (H_6) with the coupling constants $J_{6,8}$ = 1.9 Hz, $J_{6,9}$ = 0.4 Hz, and $J_{8,9}$ = 8.6 Hz indeicating that the bromine is attached at 7-position. The structure of compound (**4c**) was confirmed also by X-Ray analysis (Figure 2).

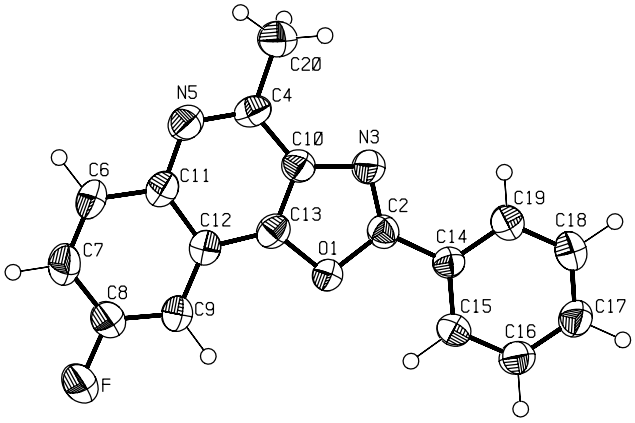


Figure 2. The asymmetric unit showing atom labels of the non-hydrogen atoms. Ellipsoids are plotted at 50% probability level.

Compouds (**5**) show besides the aromatic protons for groups attached at 1- and 2-postion a singlet in the range at δ =2.40–2.41 ppm for the methyl group at 5-position and at δ = 3.86–3.95 ppm for ester methyl group at 4-position.

X-Ray Structure Determination

$C_{17}H_{11}N_2OF$, M_r=278.3, monoclinic $P2_1$, No.: 4, a=3.84190(10), b=10.8035(3), c=15.7459(6) Å, V=653.12(4) Å^3, Z=2, D_x=1.415 Mg/m^3, MoKα radiation, λ=0.71069 Å, μ=0.10 mm^{-1}.

Diffraction data were collected on the Nonius-Kappa CCD Diffractometer at room temperature using graphite monochromatized MoKα radiation. The crystal dimensions were 0.20 × 0.15 × 0.50 mm. The entire reciprocal sphere was covered by ϕ and ω scans of 2^o per frame. The data collection was performed using the Nonius Collect Software[25] while the indexing and scaling of the data were performed using

DENZO and SCALEPACK.[26] The merging of the reflections up to the minimum d value of 0.77 Å gave R_{int}=0.040 for 1549 unique reflections of which 1035 were observed (I > 1.5σ(I)). Absorption correction was not performed due to small absorption coefficient.

The structure was solved using SIR92 program[27] while the refinement and plotting were done using Xtal3.4[28] program package. The solution program provided all non-hydrogen atoms, which were refined with anisotropic displacement factors. The hydrogen atoms could be found among the peaks in the difference Fourier map but were not stable in the refinement. They were stabilized using restraints on bond lengths and angles. Regina weighting scheme[29] was applied. The refinement of 214 variables on F_o magnitudes of 1035 reflections and 33 restraints ended with R=0.054, R_w=0.057. Maximal shift/error was 0.051 and maximal and minimal residual electron densities in the difference Fourier map were 0.37 and –0.32 e/Å^3.

Final atomic coordinates and equivalent atomic displacement parameters are given in Table 1, bond distances and angles are presented in Table 2. The asymmetric unit with atom labels is shown in Figure 2. It consists of one planar molecule. No unusual short contacts were found in the packing diagram.

Table 1. Fractional Coordinates and Equivalent Temperature Factors (Å^2). U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U_{eq}
F	0.8946(15)	-0.1979(7)	0.1288(2)	0.101(3)
O(1)	0.4578(9)	0.1482(8)	0.3405(2)	0.046(2)
N(3)	0.3776(11)	0.3555(8)	0.3298(3)	0.048(2)
N(5)	0.7081(13)	0.3075(8)	0.1134(3)	0.053(3)
C(2)	0.3597(12)	0.2577(9)	0.3787(3)	0.043(3)
C(4)	0.5814(12)	0.3709(9)	0.1781(3)	0.048(3)
C(6)	0.8852(15)	0.1171(9)	0.0514(3)	0.057(3)
C(7)	0.9320(18)	-0.0094(9)	0.0546(3)	0.066(4)
C(8)	0.8448(18)	-0.0727(8)	0.1275(4)	0.065(4)
C(9)	0.7210(16)	-0.0170(8)	0.1980(3)	0.057(3)
C(10)	0.5003(14)	0.3103(8)	0.2542(3)	0.045(3)
C(11)	0.7509(14)	0.1812(8)	0.1210(3)	0.049(3)
C(12)	0.6703(14)	0.1117(9)	0.1952(3)	0.047(3)
C(13)	0.5478(13)	0.1849(8)	0.2598(3)	0.045(3)
C(14)	0.2591(13)	0.2510(9)	0.4663(3)	0.042(2)
C(15)	0.3168(14)	0.1453(9)	0.5142(3)	0.048(3)
C(16)	0.2279(16)	0.1424(9)	0.5987(3)	0.056(3)
C(17)	0.0777(16)	0.2443(9)	0.6355(3)	0.057(3)
C(18)	0.0201(14)	0.3505(9)	0.5882(3)	0.054(3)
C(19)	0.1123(13)	0.3546(8)	0.5038(3)	0.048(3)
C(20)	0.5304(9)	0.5073(4)	0.1679(2)	0.069(4)

Table 2: Bond Distances (Å) and Bond Angles(°) with e.s.d.'s in parentheses.

F-C(8)	1.366(12)	C(7)-C(8)	1.389(10)
O(1)-C(2)	1.385(11)	C(8)-C(9)	1.363(9)
O(1)-C(13)	1.387(7)	C(9)-C(12)	1.404(13)
N(3)-C(2)	1.310(11)	C(10)-C(13)	1.370(13)
N(3)-C(10)	1.386(8)	C(11)-C(12)	1.433(9)
N(5)-C(4)	1.334(9)	C(12)-C(13)	1.384(9)
N(5)-C(11)	1.378(13)	C(14)-C(15)	1.382(12)
C(2)-C(14)	1.449(6)	C(14)-C(19)	1.394(11)
C(4)-C(10)	1.410(9)	C(15)-C(16)	1.386(7)
C(4)-C(20)	1.495(10)	C(16)-C(17)	1.380(12)
C(6)-C(7)	1.379(14)	C(17)-C(18)	1.382(12)
C(6)-C(11)	1.411(9)	C(18)-C(19)	1.389(7)

C(2)-O(1)-C(13)	103.6(7)	N(5)-C(11)-C(6)	117.7(6)
C(2)-N(3)-C(10)	104.3(7)	N(5)-C(11)-C(12)	124.1(6)
C(4)-N(5)-C(11)	119.2(6)	C(6)-C(11)-C(12)	118.2(8)
O(1)-C(2)-N(3))	114.4(5)	C(9)-C(12)-C(11)	120.7(6)
O(1)-C(2)-C(14)	117.2(7)	C(9)-C(12)-C(13)	126.4(6)
N(3)-C(2)-C(14)	128.4(8)	C(11)-C(12)-C(13)	112.9(8)
N(5)-C(4)-C(10)	120.5(8)	O(1)-C(13)-C(10)	107.7(6)
N(5)-C(4)-C(20)	118.3(6)	O(1)-C(13)-C(12)	127.8(8)
C(10)-C(4)-C(20)	121.2(6)	C(10)-C(13)-C(12)	124.5(6)
C(7)-C(6)-C(11)	120.6(6)	C(2)-C(14)-C(15)	121.2(7)
C(6)-C(7)-C(8)	118.9(6)	C(2)-C(14)-C(19)	119.3(7)
F-C(8)-C(7)	117.5(6)	C(15)-C(14)-C(19)	119.5(5)
F-C(8)-C(9)	118.6(6)	C(14)-C(15)-C(16)	120.2(7)
C(7)-C(8)-C(9)	123.9(8)	C(15)-C(16)-C(17)	120.4(7)
C(8)-C(9)-C(12)	117.7(6)	C(16)-C(17)-C(18)	119.9(5)
N(3)-C(10)-C(4)	131.2(8)	C(17)-C(18)-C(19)	120.1(7)
N(3)-C(10)-C(13)	110.0(6)	C(14)-C(19)-C(18)	120.0(7)
C(4)-C(10)-C(13)	118.8(6)		

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^{1}H NMR spectra were obtained on a Bruker Avance DPX 300 (300 MHz) spectrometer with $CDCl_3$ as solvent and TMS as the internal standard. Mass spectra were obtained on an Autospeck Q spectrometer. The microanalyses for C, H, and N were obtained on a Perkin-Elmer CHN *Analyser* 2400. Column chromatography was performed on silica gel (Silica gel 60, 0.035–0.070 mm, Fluka).

Methyl 2-benzoylamino-3-oxobutanoate (**1**) was prepared according to the procedure reported in the literature.[24]

General Procedure for the Preparation of Methyl 2-Benzoylamino-3-arylaminobut-2-enoates (3).

Procedure A. A mixture of aromatic amine (**2**) (0.001 mol), methyl 2-benzoylamino-3-oxobutanoate (**1**) (0.235 g, 0.001 mol), benzene (5 mL), and a catalytic amount of PTSA was heated under reflux for 1–11.5

h. A Dean-Stark water trap was used to remove the water formed during the reaction. The volatile components were evaporated *in vacuo*, the residue was triturated with diethyl ether (3 mL) or ethanol (4 mL), cooled, and the precipitate was collected by filtration to give **3**.

Procedure B. A mixture of aromatic amine (**2**) (0.001 mol), methyl 2-benzoylamino-3-oxobutanoate (**1**) (0.235 g, 0.001 mol), ethanol (4 mL), and a catalytic amount of PTSA was heated under reflux for 4–11.5 h. The volatile components were evaporated *in vacuo*, the residue was triturated with ether (3 mL) or ethanol (3 mL), cooled, and the precipitate was collected by filtration to give **3**.

The following compounds were prepared in this manner:

Methyl 3-Anilino-2-benzoylaminobut-2-enoate (3a). This compound was prepared from **1** and aniline (**2a**) (0.093 g, 0.001 mol), reflux for 11 h (Procedure A) or 14 h (Procedure B); trituration with ether. Yield: 0.245 g (79%, Procedure A) or 0.158 g (51%, Procedure B); mp 129–133°C (from ethanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.08 (3H, s, CH_3), 3.72 (3H, s, OCH_3), 7.04 (1H, br s, NH), 7.11–7.23 (3H, m, Ph), 7.31–7.39 (2H, m, Ph), 7.44–7.57 (3H, m, Ph), 7.85–7.91 (2H, m, Ph), 10.83 (1H, br s, NH). *Anal*. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.83; H, 5.97; N, 9.11.

Methyl 2-Benzoylamino-3-[(4-methoxyphenyl)amino]but-2-enoate (3b). This compound was prepared from **1** and 4-methoxyaniline (**2b**) (0.123 g, 0.001 mol), reflux for 4 h (Procedure A) or 11.5 h (Procedure B); trituration with ether. Yield: 0.252 g (74%, Procedure A) or 0.225 g (66%, Procedure B); mp 122–126°C (from mixture of diethyl ether and ethanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.99 (3H, s, CH_3), 3.71 (3H, s, OCH_3), 3.81 (3H, s, 4-OCH_3), 6.88 (2H, d, J = 8.7 Hz, 2H of Ar), 7.02 (1H, br s, NH), 7.08 (2H, d, J = 8.7 Hz, 2H of Ar), 7.43–7.57 (3H, m, Ph), 7.84–7.90 (2H, m, Ph), 10.63 (1H, br s, NH). *Anal*. Calcd for $C_{19}H_{20}N_2O_4$: C, 67.05; H, 5.92; N, 8.23. Found: C, 67.19; H, 6.04; N, 8.41.

Methyl 2-Benzoylamino-3-[(4-fluorophenyl)amino]but-2-enoate (3c). This compound was prepared from **1** and 4-fluoroaniline (**2c**) (0.111 g, 0.001 mol), reflux for 3.5 h (Procedure A) or 4 h (Procedure B); trituration with ethanol. Yield: 0.184 g (56%, Procedure A) or 0. 246 g (75%, Procedure B); mp 170–173°C (from ethanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.01 (3H, s, CH_3), 3.72 (3H, s, OCH_3), 7.01–7.15 (5H, m, C_6H_4 and NH), 7.44–7.58 (3H, m, Ph), 7.84–7.90 (2H, m, Ph), 10.69 (1H, br s, NH). *Anal*. Calcd for $C_{18}H_{17}N_2O_3F$: C, 65.84; H, 5.22; N, 8.53. Found: C, 65.78; H, 5.34; N, 8.45.

Methyl 2-Benzoylamino-3-[(3-bromophenyl)amino]but-2-enoate (3d). This compound was prepared from **1** and 3-bromoaniline (**2d**) (0.172 g, 0.001 mol), reflux for 5 h (Procedure A) or 6.5 h (Procedure B); trituration with ethanol. Yield: 0.035 g (9%, Procedure A) or 0.202 g (52%, Procedure B); mp 143–148°C

(from ethanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.09 (3H, s, CH_3), 3.72 (3H, s, OCH_3), 7.04 (1H, br s, NH), 7.07 (1H, m, *J* = 1.1, 1.5, 7.9 Hz, 1H of Ar), 7.21 (1H, dd, *J* = 7.9, 8.7 Hz, 1H of Ar), 7.29–7.34 (2H, m, *J* = 1.1, 1.5, 8.7 Hz, 2H of Ar), 7.45–7.58 (3H, m, Ph), 7.85–7.90 (2H, m, Ph), 10.83 (1H, br s, NH). *Anal*. Calcd for $C_{18}H_{17}N_2O_3Br$: C, 55.54; H, 4.40; N, 7.20. Found: C, 55.65; H, 4.52; N, 7.00.

Methyl 2-Benzoylamino-3-[(3-hydroxyphenyl)amino]but-2-enoate (3e). This compound was prepared from **1** and 3-hydroxyaniline (**2e**) (0.109 g, 0.001 mol), reflux for 1 h (Procedure A) or 8 h (Procedure B); trituration with ethanol. Yield: 0.101 g (31%, Procedure A) or 0.150 g (46%, Procedure B); mp 175–179°C (from ethanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.07 (3H, s, CH_3), 3.64 (3H, s, OCH_3), 6.28 (1H, br s, OH), 6.36–6.70 (3H, m, 3H of Ar), 7.12 (1H, br s, NH), 7.16 (1H, m, 1H of Ar), 7.45–7.58 (3H, m, Ph), 7.85–7.92 (2H, m, Ph), 10.76 (1H, br s, NH). *Anal*. Calcd for $C_{18}H_{18}N_2O_4$: C, 66.25; H, 5.56; N, 8.58. Found: C, 66.02; H, 5.63; N, 8.69.

General Procedure for the Preparation of Substituted 4-Methyl-2-phenyl[1,3]oxazolo-[4,5–*c*]quinolines (4) and Methyl 1-Aryl-5-methyl-2-phenyl-1*H*-imidazole-4-carboxylates (5). A mixture of methyl 3-arylamino-2-benzoylaminobut-2-enoate (**3**) (0.001 mol) and PPA (1.5 g) was heated at 130–140°C for 50 min–2.5 h. The solution was cooled and the saturated aqueous solution of $NaHCO_3$ (20–30 mL) was added. The precipitate was collected by filtration and the crude mixture of **4** and **5** was separated and purified by column chromatography. Fractions containing the products **4** and **5** were combined, respectively, and evaporated *in vacuo* to give analytically pure compounds (**4**) and (**5**). The following compounds were prepared in this manner:

4-Methyl-2-phenyl[1,3]oxazolo[4,5–*c*]quinoline (4a) and Methyl 5-Methyl-1,2-diphenyl-1*H*-imidazole-4-carboxylate (5a). A mixture of **4a** and **5a** was prepared from methyl 3-anilino-2-benzoylaminobut-2-enoate (**2a**) (0.310 g, 0.001 mol) and PPA, heating for 50 min. Column chromatography: first **4a** (petroleum ether–ethyl acetate, 5:1), then **5a** (ethyl acetate).

Compound (**4a**). Yield: 0.052 g (20%); mp 158–161°C; MS: *m/z* = 260 (M^+). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.05 (3H, s, CH_3), 7.55–7.60 (3H, m, Ph), 7.63 (1H, ddd, *J* = 1.2, 7.0, 8.1 Hz, H_7), 7.73 (1H, ddd, *J* = 1.5, 7.0, 8.5 Hz, H_8), 8.18 (1H, ddd, *J* = 0.7, 1.2, 8.5 Hz, H_9), 8.25 (1H, ddd, *J* = 0.7, 1.5, 8.1 Hz, H_6), 8.33–8.38 (2H, m, Ph). *Anal*. Calcd for $C_{17}H_{12}N_2O$: C, 78.44; H, 4.65; N, 10.76. Found: C, 78.48; H, 4.65; N, 11.00.

Compound (**5a**): Yield: 0.041 g (14%); mp 132–135°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.41 (3H, s, CH_3), 3.95 (3H, s, OCH_3), 7.15–7.25 (5H, m, Ph), 7.34–7.38 (2H, m, Ph), 7.45–7.50 (3H, m, Ph). *Anal*. Calcd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58. Found: C, 73.74; H, 5.71; N, 9.31.

8-Methoxy-4-methyl-2-phenyl[1,3]oxazolo[4,5–*c*]quinoline (4b) and Methyl 1-(4-Methoxyphenyl)-5-methyl-2-phenyl-1*H*-imidazole-4-carboxylate (5b). A mixture of **4b** and **5b** was prepared from methyl 2-benzoylamino-3-[(4-methoxyphenyl)amino]but-2-enoate (**3b**) (0.340 g, 0.001 mol) and PPA, heating for 1 h. Column chromatography: first **4b** (petroleum ether–ethyl acetate, 5:1), then **5b** (ethyl acetate). Microanalyses for C, H, and N for compounds (**4b**) and (**5b**) were not completely satisfactory. The best values are given below. The identity of compounds was confirmed by HRMS.

Compound (**4b**). Yield: 0.038 g (13%); mp 140–142°C. MS: *m/z* = 290 (M^+), HRMS: Calcd: 290.106350, Found: 290.105528. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.00 (3H, s, CH_3), 4.02 (3H, s, OCH_3), 7.36 (1H, dd, *J* = 3.0, 9.4 Hz, H_7), 7.48 (1H, d, *J* = 3.0 Hz, H_9), 7.56–7.60 (3H, m, Ph), 8.06 (1H, d, *J* = 9.4 Hz, H_6), 8.34–8.39 (2H, m, Ph). *Anal*. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 73.94; H, 5.02; N, 9.13.

Compound (**5b**). Yield: 0.029 g (9%); mp 137–141°C. MS: *m/z* = 322 (M^+), HRMS: Calcd: 322.132540, Found: 322.131743. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.40 (3H, s, CH_3), 3.86 (3H, s, OCH_3), 3.95 (3H, s, OCH_3), 6.96 (2H, d, *J* = 9.0 Hz, 2H of Ar), 7.09 (2H, d, *J* = 9.0 Hz, 2H of Ar), 7.17–7.27 (3H, m, Ph), 7.37–7.41 (2H, m, Ph). *Anal*. Calcd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.24; H, 5.92; N, 8.11.

8-Fluoro-4-methyl-2-phenyl[1,3]oxazolo[4,5–*c*]quinoline (4c) and Methyl 1-(4-Fluorophenyl)-5-methyl-2-phenyl-1*H*-imidazole-4-carboxylate (5c). A mixture of **4c** and **5c** was prepared from methyl 2-benzoylamino-3-[(4-fluorophenyl)amino]but-2-enoate (**3c**) (0.328 g, 0.001 mol) and PPA, heating for 2.5 h. Column chromatography (ether): first **4c** then **5c**.

Compound (**4c**). Yield: 0.181 g (65%); mp 168–170°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.05 (3H, s, CH_3), 7.43–7.50 (1H, ddd, J_{H6H7} = 9.0, J_{H7H9} = 3.0, $^3J_{FH7}$ = 8.7 Hz, H_7), 7.55–7.61 (3H, m, Ph), 7.83 (1H, dd, J_{H7H9} = 3.0, $^3J_{FH9}$ = 8.7 Hz, H_9), 8.16 (1H, dd, J_{H6H7} = 9.0, $^4J_{FH6}$ = 5.1 Hz, H_6), 8.32–8.37 (2H, m, Ph). *Anal*. Calcd for $C_{17}H_{11}N_2OF$: C, 73.37; H, 3.98; N, 10.07. Found: C, 73.32; H, 3.82; N, 9.98.

Compound (**5c**). Yield: 0.099 g (32%); mp 188–190°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.41 (3H, s, CH_3), 3.95 (3H, s, OCH_3), 7.17 (4H, m, C_6H_4), 7.20–7.27 (3H, m, Ph), 7.32–7.37 (2H, m, Ph). *Anal*. Calcd for $C_{18}H_{15}N_2OF$: C, 69.67; H, 4.87; N, 9.03. Found: C, 69.74; H, 4.63; N, 8.93.

9-Bromo-4-methyl-2-phenyl[1,3]oxazolo-[4,5–*c*]quinoline (6d) and 7-Bromo-4-methyl-2-phenyl-[1,3]oxazolo[4,5–*c*]quinoline (4d') A mixture of **4d** and **4d'** was prepared from methyl 2-benzoylamino-3-[(3-bromophenyl)amino]but-2-enoate (**3d**) (0.389 g g, 0.001 mol) and PPA, heating for 1.5 h. Column chromatography: first **4d** (petroleum ether–ethyl acetate, 5:1) then **4d'** (ethyl acetate).

Compound (**4d**). Yield: 0.047 g (14%); mp 195–196°C. MS: *m/z* = 338 (M^+), 340 (M^++2). ^{1}H NMR (300

MHz, $CDCl_3$): δ 3.03 (3H, s, CH_3), 7.55–7.61 (3H, m, Ph), 7.73 (1H, dd, J = 1.9, 8.6 Hz, H_8), 8.11 (1H, dd, J = 0.4, 8.6 Hz, H_9), 8.31–8.37 (2H, m, Ph), 8.37 (1H, dd, J = 0.4, 1.9 Hz, H_6). *Anal*. Calcd for $C_{17}H_{11}N_2O_2Br$: C, 60.20; H, 3.27; N, 8.26. Found: C, 60.48; H, 3.07; N, 8.20.

Compound (**4d'**). Yield: 0.081 g (24%); mp 185–186°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.05 (3H, s, CH_3), 7.55 (1H, dd, J = 7.6, 8.5 Hz, H_7), 7.57–7.62 (3H, m, Ph), 7.87 (1H, dd, J = 1.0, 7.6 Hz, H_8), 8.15 (1H, dd, J = 1.0, 8.5 Hz, H_6), 8.35–8.41 (2H, m, Ph). *Anal*. Calcd for $C_{17}H_{11}N_2O_2Br$: C, 60.20; H, 3.27; N, 8.26. Found: C, 60.36; H, 3.04; N, 8.19.

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