HETEROCYCLES, Vol. 92, No.10 , 2016, pp. 1761 - 1783. © 2016 The Japan Institute of Heterocyclic Chemistry
Received, 17th June, 2016, Accepted, 9th August, 2016, Published online, 18th August, 2016
DOI: 10.3987/REV-16-845

DIAZONAPHTHOQUINONES: SYNTHESIS, REACTIONS AND APPLICATIONS

Dina I. A. Othman[1,2] and Mitsuru Kitamura[2]*

[1]Department of Pharmaceutical Organic Chemistry, Faculty of Pharmacy, Mansoura University, Mansoura 35516, Egypt. [2]Department of Applied Chemistry, Kyushu Institute of Technology, 1-1 Sensuicho, Tobata, Kitakyushu, 804-8550 Japan, kita@che.kyutech.ac.jp

Abstract – This review deals with synthesis and reactions of diazonaphthoquinones during the past 6 years. Various substituted diazonaphthoquinones have been prepared by the reaction of the appropriate naphthol and 2-azido-1,3-dimethylimidazolinium chloride (ADMC) in short direct pathway. This method is likely to find wide spread uses in organic synthesis and material chemistry such as for preparing photoresists. In this review, different metal catalyzed reactions are investigated and applied successfully to the synthesis of important aromatic compounds. In addition, total synthesis of some natural compounds has been attempted using this recently developed diazo-transfer methodology. It is hoped that this compilation, in combination with the previously published literatures on diazo-transfer reaction, will provide useful, up-to-date and comprehensive foundation and reference sources for individuals interested in the same field.

CONTENTS

1. INTRODUCTION

Recently, orthodiazonaphthoquinones [1-diazo-2(1*H*)-naphthalenones (**1**) and 2-diazo-1(2*H*)-naphthalenones (**2**)], have been the subject of much interest because of their unique structures, reactivity and few known preparative method (Figure1).[1] They are unique cyclic α-diazocarbonyl compounds, which are used as building blocks candidates for many aromatic functional materials, such as solar cells, metal ligands and antioxidants.[2,3] The Wolff rearrangement of 1,2-diazonaphthoquinones is the key reaction of photoresists, therefore they are exclusively used as photoresist materials, such as Novolak–diazonaphthoquinone resists.[4-6] However, the development of diverse reactions has been partially limited due to their difficult synthesis.[1]

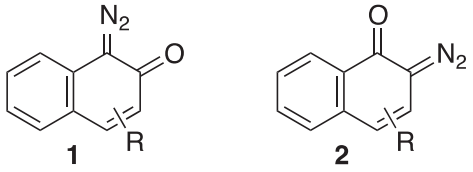
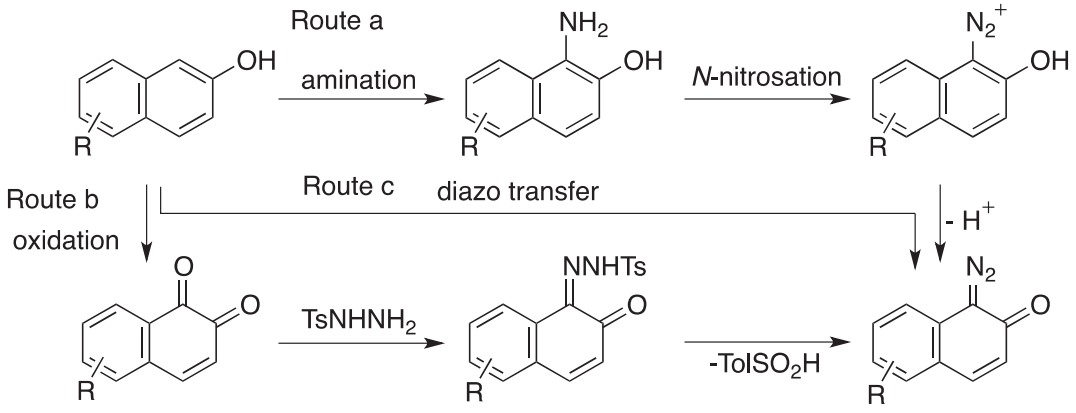


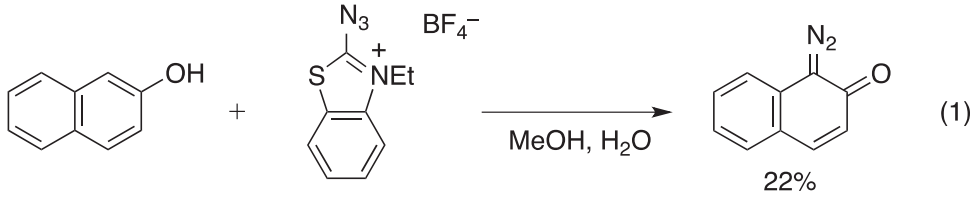
Figure 1. Orthodiazonaphthoquinones (DNQ)

Generally, diazonaphthoquinones are synthesized from naphthols using different pathways, either by diazotization of aminophenol derivatives followed by deprotonation (Route a)[7] or by monosulfonylhydrazonation of quinones followed by elimination of sulfinic acid (Route b),[8] as illustrated in Scheme 1. Multi-step reaction and the requirement of regioselective transformation were the main drawbacks of both routes, thus diazo-transfer reaction (Route c) was found to be the shortest direct synthetic method of diazonaphthoquinones although it is not so popular one.[9]



Scheme 1. Synthesis of diazonaphthoquinones from 2-naphthol

In 1978, Balli *et al*. have synthesized 2-azido-3-ethylbenzothiazolium tetrafluoroborate, as an efficient reagent for diazo-transfer reaction to naphthol, but this method suffered from low yield (eq. 1).[10] Thus, the development of short efficient direct method for the synthesis of diazonaphthoquinones has become an urgent need.

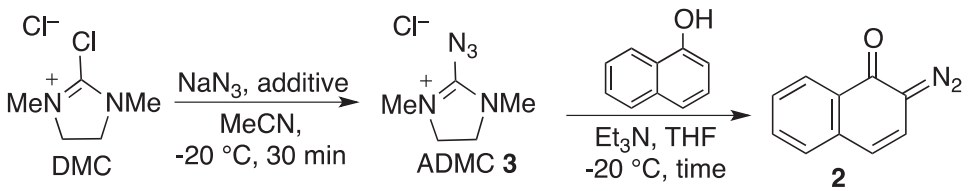


Recently, we found that 2-azido-1,3-dimethylimidazolinium salts act as efficient and safe diazo-transfer reagents giving easily isolated and high yielded diazo products.[11-15] 2-Azido-1,3-dimethylimidazolinium chloride (ADMC) (**3**) could be used for the diazo-transfer reaction to naphthols to give corresponding various diazonaphthoquinones in good yield. Furthermore, we developed a new synthetic method of substituted naphthols by the metal-catalyzed reaction of diazonaphthoquinones, which could be applied for the synthetic study of natural products. In this review, we describe our efforts on the synthesis and application toward development of synthetic method of diazonaphthoquinones.

2. SYNTHETIC METHOD

Synthesis of diazonaphthoquinones by diazo-transfer reaction of reaction 2-azido-1, 3-dimethylimidazolinium chloride (ADMC) (3) with naphthols

Initially, the reaction of 1-naphthol with ADMC **3** was examined. To a solution of ADMC **3**, prepared by reaction of chloroimidazolinium chloride (DMC) with sodium azide, 1-naphthol and triethylamine were added using acetonitrile at -20 °C, as shown in Scheme 2. It is worth noting that; using 15-crown ether for such reaction was proved to be very effective in decreasing the reaction time and giving more clean reaction mixture. Protic solvent was not to be preferred, because diazonaphthoquinone products decomposed to naphthol in an aqueous solution. The choice of base was also important in this diazo-transfer reaction. Using Et_3N, *i*-Pr_2NEt and K_2CO_3 led to good yield. In contrast, using less basic bases, such as aromatic bases (imidazole, pyridine, 4-dimethylaminopyridine), were not suitable for the production of diazonaphthoquinone and using DBU (1,8-diazobicyclo[5.4.0]undec-7-ene) resulted in unknown products.

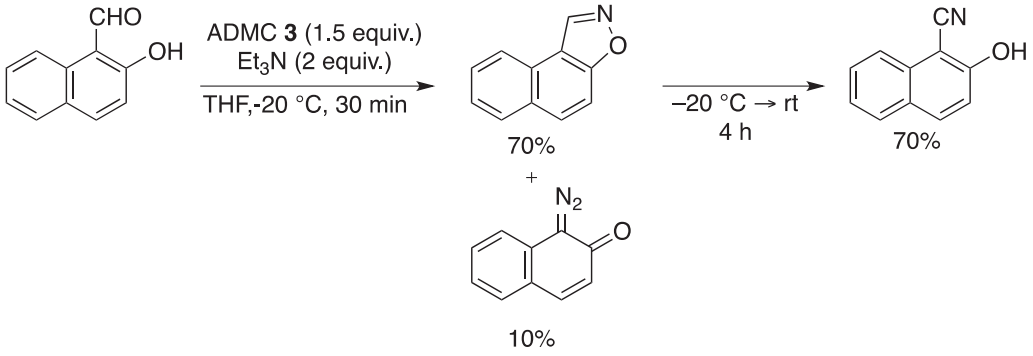


Additive	Time	Yield (%)
–	40 min	76
15-crown -5	30 min	83

Scheme 2. Representative diazo-transfer reaction pathway using 1-naphthol

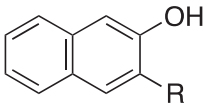
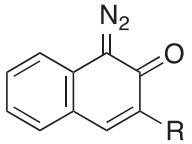
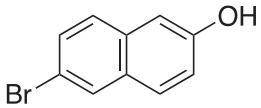
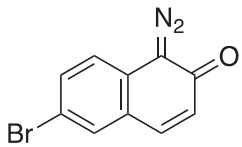
In Table 1, the results of the diazo-transfer reaction for various naphthols and related compounds are shown. 1-Nonsubstituted 2-naphthols were converted to 1-diazotized compounds in good yields (entries 1-5); while 1-substituted 2-naphthols did not yield corresponding diazo compounds (entries 6, 7). 2-Nonsubstituted 1-naphthol gave 2-diazo derivatives in good yields without influence of the substituent on C(3) or C(4) on naphthol (entries 8-15). The reaction of 2-alkyl-1-naphthol became complex and 4-diazotized compound was formed in low yield (entry 16). Anthrone (equivalent to anthracen-9-ol) gave the corresponding diazo compound (**4)** in good yield (entry 17), but phenol could not be used in the diazotization reaction (entry 18).

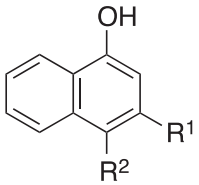
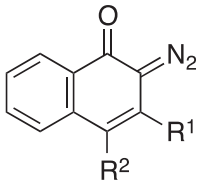
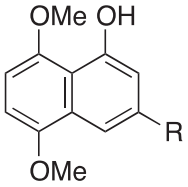
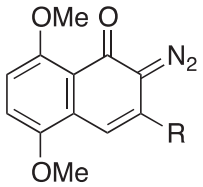
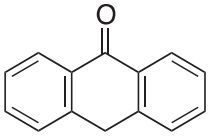
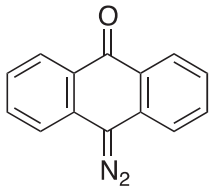
Interestingly, 1-formyl-2-naphthol gave isoxazole derivative as a major product, which is further transformed to nitrile under stirring for 4 h at rt, as shown in Scheme 3.



Scheme 3. Behavior of 1-formyl-2-naphthol toward diazo transfer reaction with ADMC **3**

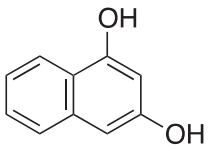
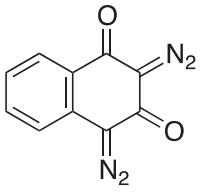
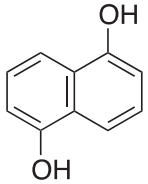
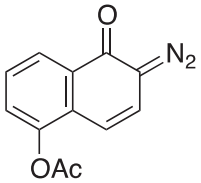
Table 1. Representative reactions of some naphthols with ADMC **3**[a]

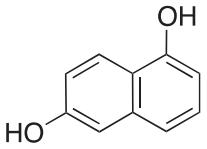
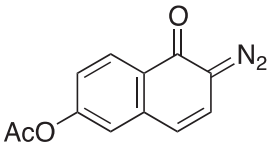
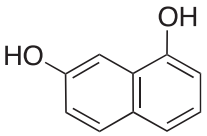
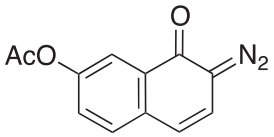
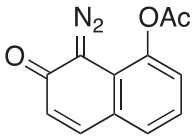
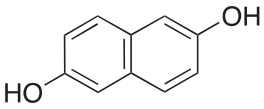
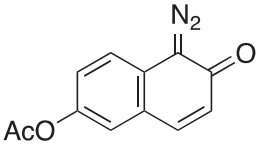
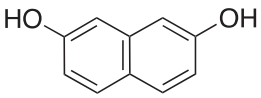
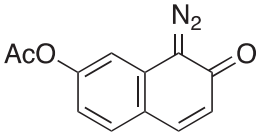
Entry	ArOH	Time	Product	Yield (%)
				
1	R = CH_2OTBS	0.5 h	R = CH_2OTBS	81
2	R = CO_2Me	1 h	R = CO_2Me	75
3	R = CO_2Ph	1 h	R = CO_2Ph	62
4	R = CONHPh	1 h	R = CONHPh	60 [93][b]
5		1 h		79
6	1-bromo-2-naphthol	3 h	-[c]	
7	BINOL	2 h	-[d]	

				
8	R^1 = H, R^2 = OMe	1 h	R^1 = H, R^2 = OMe	73
9	R^1 = H, R^2 = Cl	1 h	R^1 = H, R^2 = Cl	81
10	R^1 = CH_2OTBS, R^2 = H	1 h	R^1 = CH_2OTBS, R^2 = H	72
11	R^1 = CO_2Me, R^2 = H	2 h	R^1 = CO_2Me, R^2 = H	98
12	R^1 = CO_2Ph, R^2 = H	2 h	R^1 = CO_2Ph, R^2 = H	97
13	R^1 = CO_2Ph, R^2 = OMe	2 h	R^1 = CO_2Ph, R^2 = OMe	94
				
14[e]	R = (*E*)-CH=CH-Ph	3 h	R = (*E*)-CH=CH-Ph	89
15	R = CO_2Et	4 h	R = CO_2Et	60
16	2-butyl-1-naphthol	1 h	-[c]	
17		0.1 h	 **4**	[86][b,f]
18	PhOH	2 h[g]	-[d]	

[a]Unless otherwise noted, the reactions were carried out at -20 °C by stirring a mixture of ArOH (1 equiv.) and Et_3N (2 equiv.) in THF with a solution of ADMC **3** (1.5 equiv.), which was prepared using DMC (1.5 equiv.), sodium azide (NaN_3) (1.7 equiv.), and 15-crown-5 (30 mol%) in MeCN. [b]The yield was determined by ^{1}H NMR spectroscopy. [c]Complex mixture. No compounds were identified. [d]Ar-OH was recovered. [e]Molar ratio: DMC/NaN_3/naphthol/Et_3N = 5/5/1/5. [f]Anthraquinone was obtained in 7% yield. [g]At room temperature.

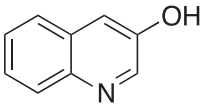
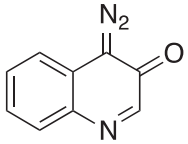
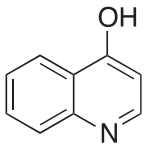
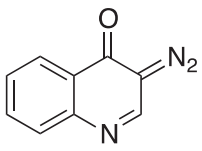
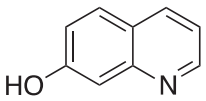
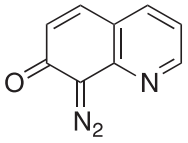
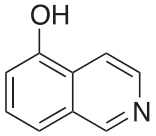
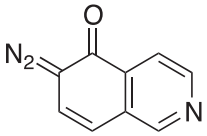
Table 2. Reactions of naphthalenediols with ADMC **3**[a]

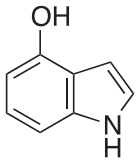
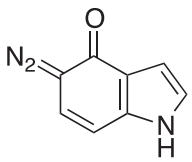
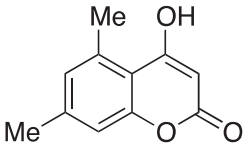
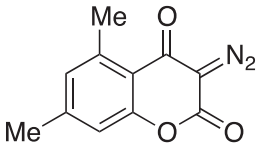
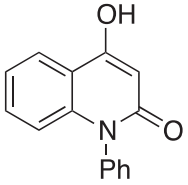
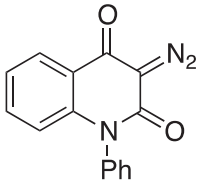
Entry	Naphthalenediol	Time	Products	Yield (%)
1		0.1 h		80[b]
2[c]		1 h		56

3[c]		1 h		41
4[c]		0.5 h	 	40 20
5[c]		1 h		31
6[c]		0.5 h		40

[a]Unless otherwise noted, the reactions were carried out at -20 °C by stirring a mixture of ArOH and Et_3N (2 equiv.) in THF with a solution of ADMC **3** (1.5 equiv.), which was prepared from DMC (1.5 equiv.), sodium azide (1.7 equiv.) and 15-crown-5 (30 mol%) in MeCN. [b]3.0 equiv. of **3** was used. [c]After the diazotization reaction was performed, the crude products were treated with acetic anhydride and pyridine.

Table 3. The diazo-transfer reaction of some heterocyclic scaffolds and the novel resulted diazotized products.[a,b]

Entry	Ar-OH	Products	Yield (%)
1			80%
2			42%
3			70%
4			35%

5			40%
6			74%
7			82%

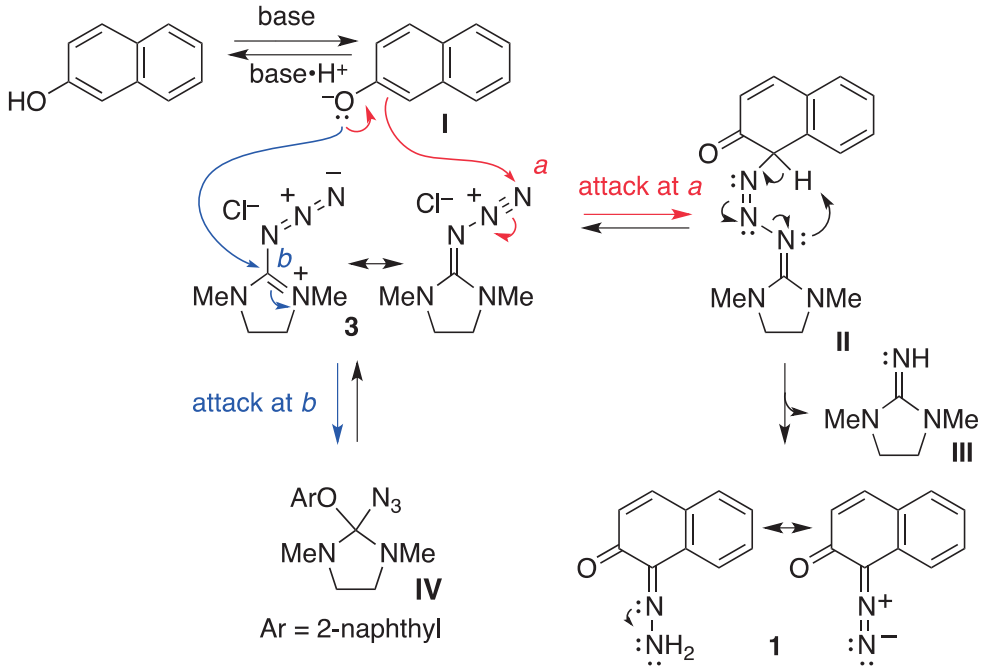
[a]Reaction conditions: the reactions were carried out at -20 °C by stirring a mixture of Ar-OH (1 equiv.) and Et_3N (2 equiv.) in THF with a solution of ADMC **3** (1.5 equiv.), which was prepared using DMC (1.5 equiv.) and sodium azide (NaN_3) (1.7 equiv.) in MeCN. [b]Unpublished results.

The results of the reaction for naphthalenediols are shown in Table 2. The formation of mono diazotized compounds was observed in most cases except for 1,3-naphthalenediol which gave the bis diazotized compound in 80% yield when 3 equiv. of **3** was used (entry 1). Subsequent acetylation of the monodiazotized products was performed so as to facilitate its isolation.

For the importance of diazo compounds in both semiconductor manufacturing and medicinal chemistry and in order to expand the applicability of this newly developed diazo-transfer methodology, the behavior of another OH group-containing heterocyclic scaffolds was explored as shown in Table 3.[16] Some derivatives of quinoline, isoquinoline, indole and 4-hydroxycoumarin were transformed to corresponding diazotized compounds in moderate to good yield.

A plausible mechanism for the reaction between ADMC **3** and 2-naphthol in the presence of a base is shown in Scheme 4. The reaction pathway depends on the base used. Naphtholate **I** will be formed from 2-naphthol and the base at equilibrium when the used base has a conjugate acid with an acidity constant similar to that of naphthol ($pK_a \approx 10$). Naphtholate **I** will then attack the terminal nitrogen in **3** (the position *a* in **3**) to form intermediate **II**. Intermediate **II** will then undergo intramolecular proton abstraction to afford the corresponding diazo compound **1** and guanidine **III**. The reverse reaction will occur when naphtholate **I** attacks the central carbon in the guanidinium (the position *b* in **3**), and naphtholate **I** and 2-naphthol will be reformed at equilibrium. In contrast, naphtholate **I** will be kinetically formed when a strong base ($pK_{aH} > 10$) is used, and a hard oxygen nucleophile will attack the most positive position *b* in **3** to form **IV**. In this case, the reverse reaction will be slow because naphtholate **I** is

predominantly formed from 2-naphthol. Naphtholate **I** will hardly be formed when a weak base is used; therefore diazonaphthoquinone **1** will not be formed efficiently.



Scheme 4. Plausible diazo-transfer reaction mechanism and the vital role of the base

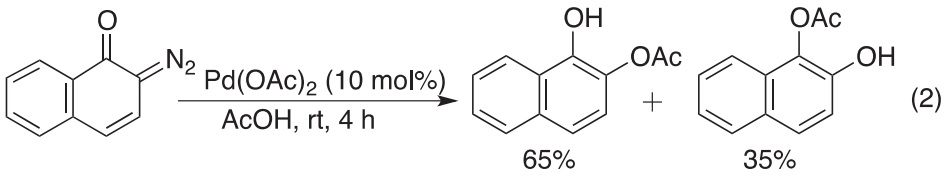
3. APPLICATIONS OF DIAZO-TRANSFER REACTION

The recently developed reaction was involved in many attractive chemical applications, either in different metal-catalyzed reaction with the aim to get efficient aromatic compounds or in total synthesis of natural compounds.

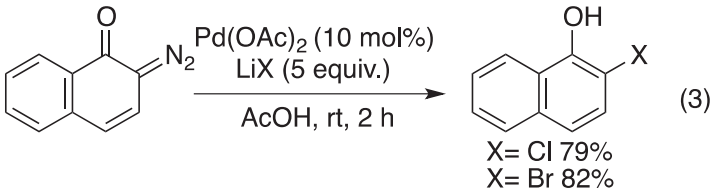
3-1. METAL-CATAYZED REACTION

Pd-Catalyzed formal OH insertion reaction of acetic acid

Similar to catechol derivatives, 1,2-naphthalenediols are very attractive candidates for aromatic functional materials, such as solar cells, metal ligands, and antioxidants.[3,17] However, to date, few useful processes have been reported for their synthesis.[18] In 2011, the synthesis of 1,2-naphthalenediol derivatives was first achieved *via* Pd(II)-catalyzed formal O-H insertion reaction of 1,2-diazonaphthoquinones to acetic acid (eq. 2).[19]

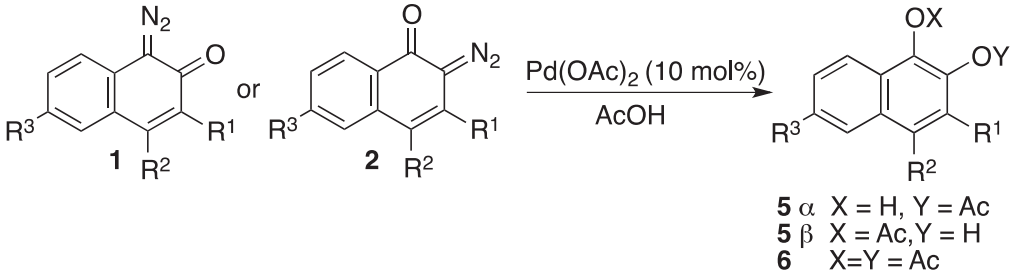


Several reaction conditions were examined to obtain naphthalenediol monoacetate, which was then subjected to hydrolysis to yield the desired naphthalene diol. It was found that, rhodium(II) acetate, cupper salts (CuI, CuCl, $CuCl_2$, $Cu(OAc)_2$), or $PdCl_2$ were ineffective while palladium(II) acetate was found to be the most efficient catalyst for the O-H insertion reaction of diazonaphthoquinone. Then, synthesis of different 1,2-naphthalenediol derivatives from various diazonaphthoquinones was attempted (Table 4). It was observed that, the reactions of 1-diazonaphthoquinones required slightly higher temperature than those of 2-diazonaphthoquinones. Furthermore, it was found that the Pd(II)-catalyzed reaction performed in the presence of lithium halides produced halonaphthols comparable to the Sandmeyer reaction, as shown in eq. 3. In similar manner, $Pd(OAc)_2$-catalyzed O-H insertion reaction of typical acyclic α-diazocarbonyl compounds was proved to yield acetoxy dicarbonyl compounds smoothly.



(3)

Table 4. Synthesis of 1,2-naphthalenediol derivatives by the reaction diazonaphthoquinones and acetic acid



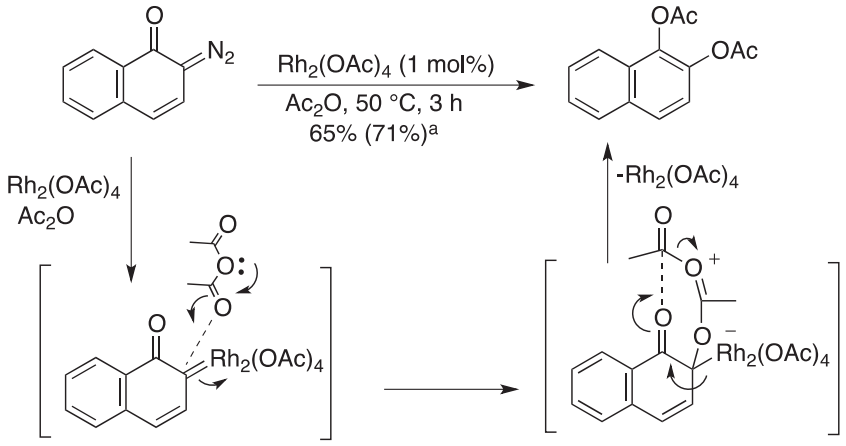
Entry	**1**/**2**	R^1	R^2	R^3	Conditions	Yield (%)
1	**1**	H	H	H	50 °C, 1 h	**5** 79 (65:35)[a]
2	**1**	H	H	Br	50 °C, 4 h	**5** 67 (63:37)[a]
3	**1**	CO_2Me	H	H	50 °C, 6 h	**5** 85 (>99: <1)[a]
4	**1**	CONHPh	H	H	50 °C, 5 h	**5** 68 (>99: <1)[a]
5[b]	**2**	H	OMe	H	rt, 5 min	complex mixture
6[b]	**2**	H	OMe	H	rt, 20 min	**6** 66[c]
7	**2**	H	Cl	H	rt, 24 h	**5** 51 (53: 47)[a]

[a]The ratio of **5**α/**5**β after the purification with column chromatography (SiO_2). The position of acetyl group is undetermined. [b]5 mol% $Pd(OAc)_2$ was used. [c]After the Pd-catalyzed reaction, crude compounds were treated with acetic anhydride and pyridine.

Rh-Catalyzed reaction with acetic anhydride

Exclusively, Scheme 5 illustrates the practical and efficient $Rh_2(OAc)_4$-catalyzed reaction of 1,2-diazonaphthoquinones with acetic anhydride to form 1,2-naphthalenediol diacetates. Thus, protected 1,2-naphthalenediol derivatives could be synthesized and isolated efficiently. In this reaction, cupper salts and Pd catalyst were found to be inefficient while in the presence of Rh(II) acetate, diacetate products were obtained smoothly in good yield.[20] The possible reaction mechanism for the formation of naphthalenediol diacetates is illustrated in Scheme 5.

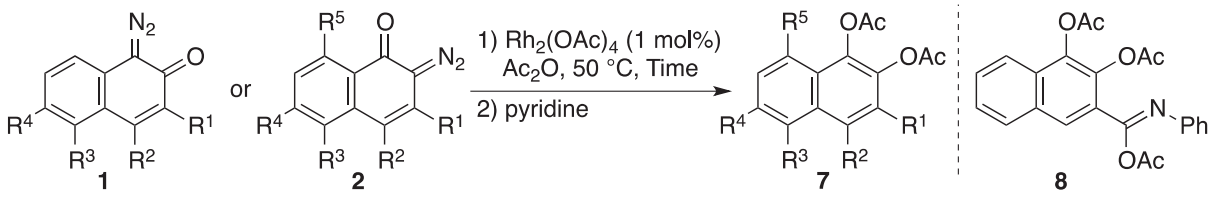
The scope and limitations of the $Rh_2(OAc)_4$-catalyzed formation of 1,2-naphthalenediol diacetates from 1,2-diazonaphthoquinones are shown in Table 5. In all experiments, pyridine should be added to the reaction mixture following the reaction with catalytic $Rh_2(OAc)_4$ in acetic anhydride.



[a]After the Rh-catalyzed reaction, pyridine was added and the reaction mixture was stirred at 50 °C for 1 h.

Scheme 5. Synthesis of 1,2 naphthalenediol diacetate and the possible reaction mechanism

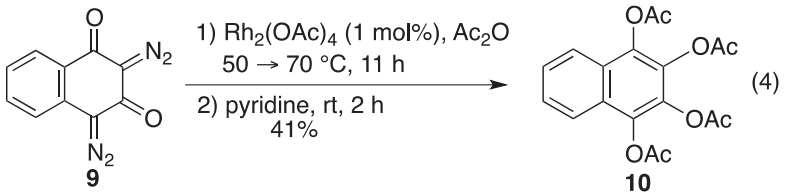
Table 5. Synthesis of various naphthalenediol diacetates **7** from 1,2-diazonaphthoquinones



Entry	**1**/**2**	R^1	R^2	R^3	R^4	R^5	Time (h)	Yield (%)
1	**1**	H	H	H	H	H	6	66
2	**1**	H	H	H	Br	H	9	76
3	**1**	CO_2Me	H	H	H	H	2	81
4	**1**	CONHPh	H	H	H	H	8[a]	13[b]
5	**2**	H	OMe	H	H	H	3	44
6	**2**	H	Cl	H	H	H	4	45
7	**2**	CO_2Et	H	OMe	H	OMe	11[a]	88

[a]Rh-catalyzed reaction was carried out at 70 °C [b] Compound **8** was obtained in 78% yield.

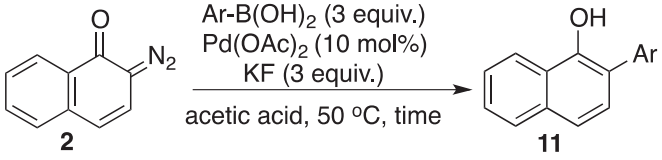
In addition, the Rh-catalyzed reaction of 2,4-bis(diazo)-1,2,3,4-tetrahydronaphthalene-1,3-dione (**9**) was examined to yield 1,2,3,4-tetra(acetoxy)naphthalene **(10)** in moderate yield (eq. 4).



Pd-Catalyzed cross coupling reaction with arylboronic acid

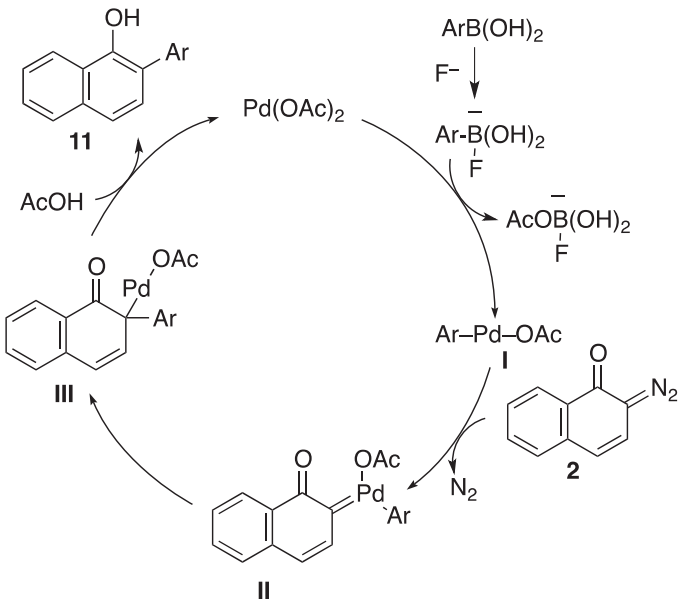
Introduction of substituents to aromatic compounds is a very important process in organic synthesis. Regioselective arylation of 1-naphthol remains one of the most difficult issues in the synthesis of the substituted phenol derivatives, so that the first palladium-catalyzed cross-coupling reaction of diazonaphthoquinone and arylboronic acid has been attempted, providing a novel access to biaryl compounds (Table 6).[21] It was proved that, using $Pd(OAc)_2$ as catalyst, instead of Pd(0), had a greater effect on the yield. In addition, using acetic acid as solvent made the reaction media more clean than using other solvent. Moreover, addition of fluoride anion was effective in such reaction as previously mentioned in Suzuki-Miyaura coupling reaction.[22]

Table 6. Pd-Catalyzed coupling of diazonaphthoquinone and various arylboronic acids



Entry	Ar	Time (h)	Yield (%)
1	Ph	3	76
2	*o*-MeC_6H_4	3	56
3	*o*-$MeOC_6H_4$	3	40
4	*m*-$MeOC_6H_4$	2	53
5	*p*-Me	3	67
6	*p*-$MeOC_6H_4$	4	25
7	*p*-$CF_3C_6H_4$	5	34
8	1-naphthyl	4	47

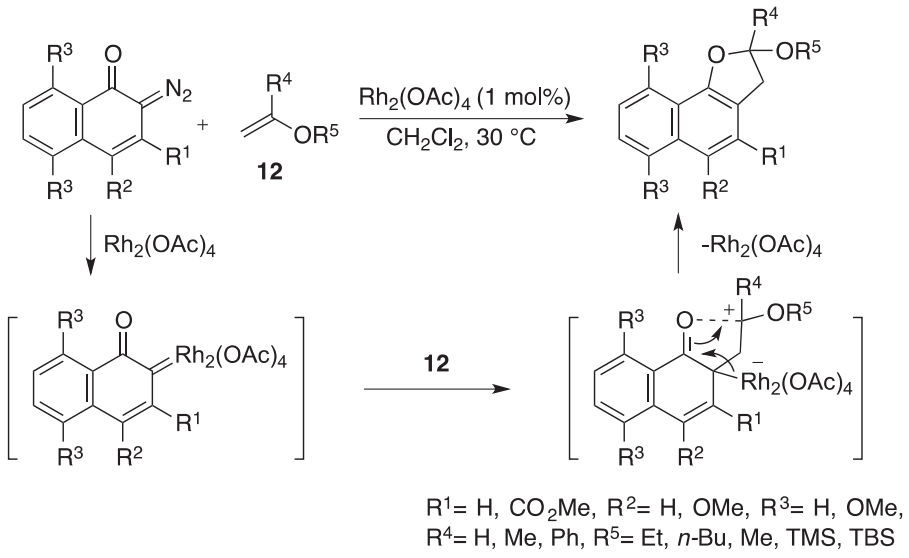
The most believable reaction mechanism is shown in Scheme 6, which is the Pd(II)-catalytic cycle *via* the migratory insertion of a palladium carbene complex.[23,24] The reaction is initiated by the transmetallation of arylboronic acid by the aid of F^- and $Pd(OAc)_2$ to generate intermediate **I**, which reacts with diazonaphthoquinone (**2**) to form palladium carbene complex **II**. Migratory insertion of the aryl group to the carbene carbon occurs, generating palladium complex **III**. Finally, protonation of acetic acid to **III** affords the coupling product (**11**) and regenerates $Pd(OAc)_2$.



Scheme 6. Proposed cross coupling reaction mechanism

Diazonaphthoquinones act as aryl donor

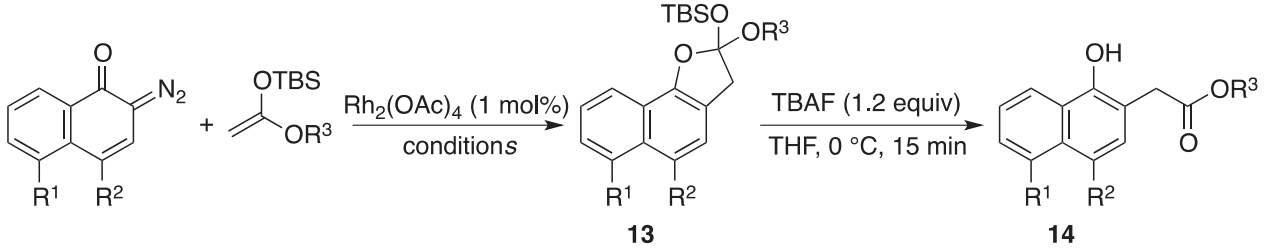
Another application is that, the synthesis of the naphthofuran derivatives with its reported interesting biological activities.[25] It was proved that dihydronaphthofuran derivatives could be synthesized by Rh-catalyzed intermolecular cycloaddition reaction of diazonaphthoquinones with enol ethers (**12)** (Scheme 7).[26] No improvement of the yield was observed either by using $Rh_2(OCOCF_3)$ or under Kraus reaction condition.[27] Moreover, no cycloadduct product was formed in absence of Rh catalyst. In addition, it was observed that, 2-diazonaphthoquinone having an electron-donating group at C-4 position efficiently afforded dihydronaphthofuran in high yield.



Scheme 7. $Rh_2(OAc)_4$-Catalyzed cycloaddition reaction of 2-diazonaphthoquinones with enol ethers

Furthermore, this methodology was extended to the synthesis of α-arylcarbonyl compounds. The $Rh_2(OAc)_4$-catalyzed cycloaddition reaction of 2-diazonaphthoquiones with ketene acetals was examined and the obtained naphthofuran derivatives were then transformed to the corresponding α-naphthyl esters in high yield by treatment with tetrabutylammonium fluoride (TBAF) (Table 7). In entry 6, the formation of the corresponding lactone was observed with 6% yield.

Table 7. Synthesis of dihydronaphthofurans (**13)** and α-(1-hydroxy-2-naphthyl) esters (**14)** by the reaction of diazonaphthoquinones and ketene acetals



13 **14**

Entry	R^1	R^2	R^3	Condition[a]	Time (h)	Yield (%)	
						13	**14**
1	H	H	Et	A	1	76	88
2	H	H	Me	A	1	51	66
3	H	H	*t*Bu	B	1.5	80	99
4	H	OMe	Et	A	0.75	82	80
5	H	Cl	Et	A	0.75	70	80
6	OAc	H	Et	A	0.5	53	66

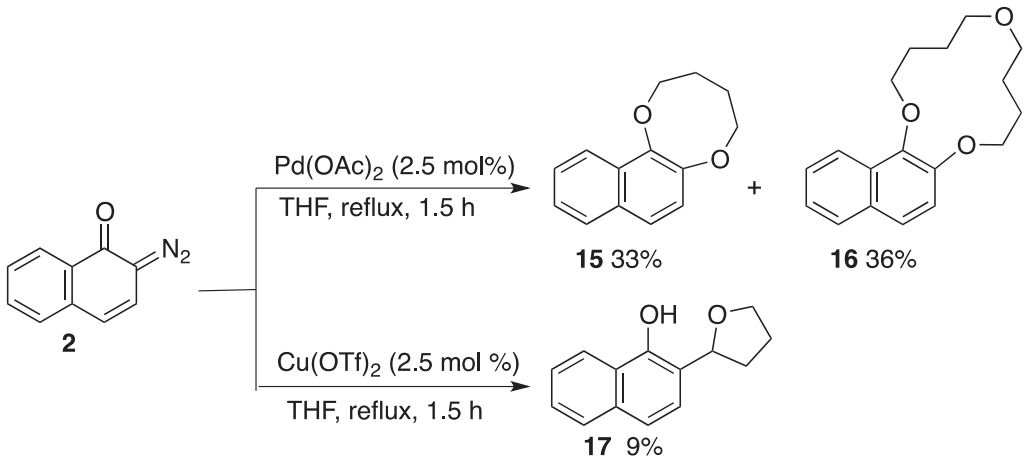
[a]Condition A: $Rh_2(OAc)_4$ (1 mol%), ketene silyl acetal (1.2 equiv.), CH_2Cl_2, 40 °C. Condition B: $Rh_2(OAc)_4$ (1 mol%), ketene silyl acetal (1.2 equiv.), $ClCH_2CH_2Cl$, 80 °C.

It is worth noting to mention that a similar α-(1-hydroxy-2-naphthyl) ester was previously prepared from 1-naphthol in eight steps.[28] Interestingly, this method provides more rapid synthesis *via* diazotization of 1-naphthol followed by $Rh_2(OAc)_4$-catalyzed reaction with ketene silyl acetal and finally ring opening with TBAF. To the best of our knowledge, this novel method was the first to describe that diazonaphthoquinones could be used as aryl donors for the metal-catalyzed α-arylation of ester enolate equivalents.

Pd-Catalyzed macrocyclization reaction with cyclic ether

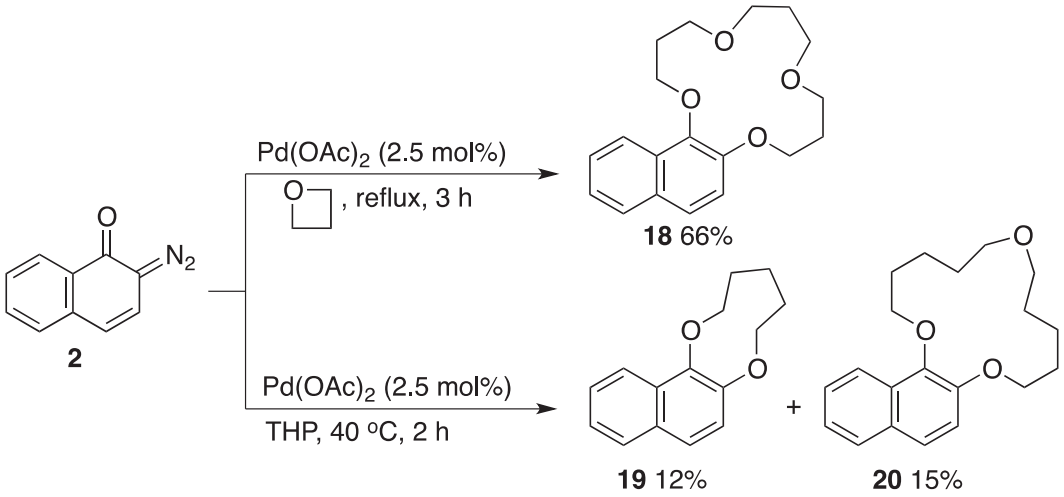
$Pd(OAc)_2$ was found to be an efficient catalyst for several coupling reactions of 1,2-diazonaphthoquinones. Unexpectedly, new method for the synthesis of medium-sized/macrocyclic ethers was developed, during the evaluation of the stability of 2-diazonaphthoquinone (**2**) when refluxed with catalytic amount of $Pd(OAc)_2$ using various solvents (CH_2Cl_2, toluene, benzene, MeCN and THF).[29] As a result, new method for the efficient synthesis of protected 1,2-naphthalenediols has been explored. As

shown in Scheme 8, cyclic ethers (**15**) and (**16**) were obtained in reasonable yield using the determined optimum cyclization conditions. It was found that lower temperature (45 °C) and using Rh, $PdCl_2$ and $Pd(OCOCF_3)_2$ catalysts were not efficient for such cyclization. Moreover, no cyclic ethers were obtained upon the addition of a halide anion (LiCl) or during the use of Cu reagents, except for $Cu(OTf)_2$ and $Cu(OTf)\cdot C_6H_5$, a minor amount of C-H insertion product **(17)** was formed.



Scheme 8. $Pd(OAc)_2$-Catalyzed macrocyclization of 2-diazonaphthoquinone with THF

Next, during investigation of the $Pd(OAc)_2$-catalyzed cyclization reaction using different diazonaphthoquinones substrates, it was found that introduction of a C-3 substituent was efficient for the selective formation of 8-membered ring cyclic ethers (**15**). On the other hand, the expected cyclization products were not generated using 4-methoxy-2-diazonaphthoquinone but only a dimerization product was obtained in 10% yield.



Scheme 9. Pd-Catalyzed cyclization of 2-diazonaphthoquinone with oxetane and THP

In addition, examination of $Pd(OAc)_2$-catalyzed reaction of 2-diazonaphthoquinone with oxetane and tetrahydropyrane (THP) was proved to yield 15-membered cyclic ether (**18)** and a mixture of 9-membered cyclic ether (**19**) and 15-membered ether (**20**), respectively (Scheme 9). It was observed that the reactions of 1-diazonaphthoquinone proceeded smoothly in a similar manner.

Rh-Catalyzed intramolecular C-H insertion reaction

β-Phenylnaphthalene lactones derivatives are widely used as intermediates for the synthesis of many bioactive natural products, such as polyketides and biaryl compounds (Figure 2).[30]

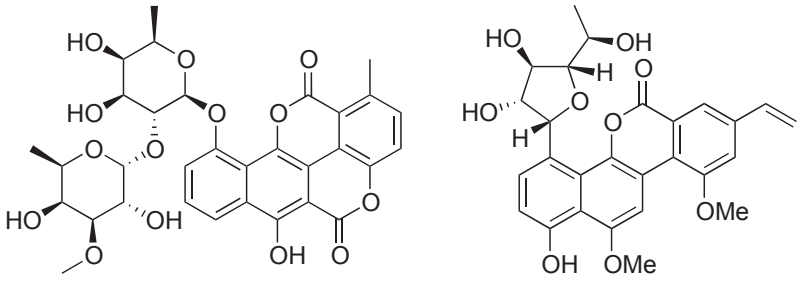
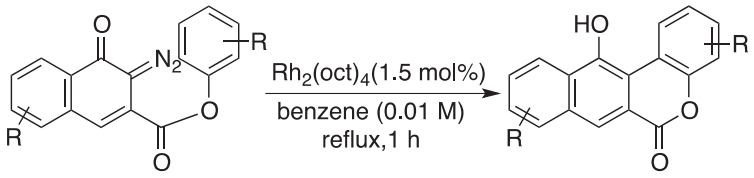


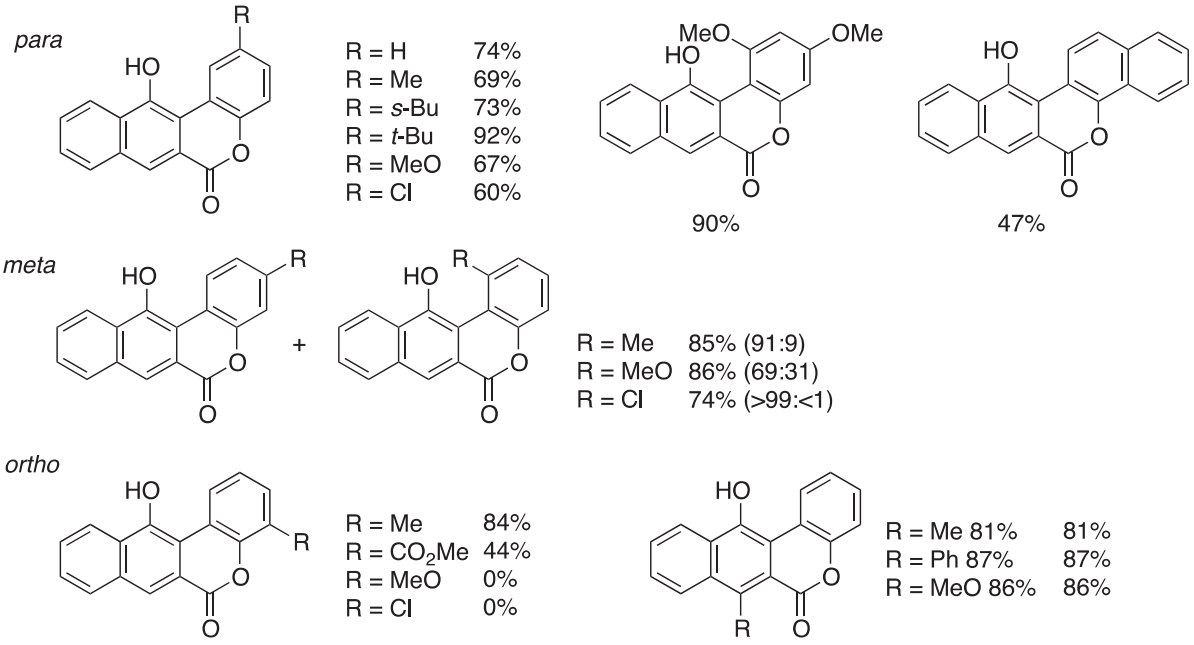
Figure 2. Natural products containing β-phenylnaphthalene lactone moiety

Although Pd-catalyzed intramolecular biaryl coupling of halogenated aryl carboxylic acid aryl esters was reported to be the most efficient method, it suffered from several problems such as a limited accessibility of starting haloaryl compounds, the reproducibility of the reaction and the harsh reaction conditions.[31] We developed novel method for the synthesis of β-phenylnaphthalene lactones using Rh-catalyzed intramolecular formal C-H insertion cyclization reaction of 3-aryloxycarbonyldiazonaphthoquinones (Table 8).[32]

Judging from these results, it is apparent that there are two potential reaction sites for the formation of 6-membered ring in case of meta-monosubstituted phenyl esters. The C-C bond cyclization is favored at the para position of the substituent R due to less steric hindrance. In case of ortho-monosubstituted phenyl esters, regioselectivity of the present intramolecular Rh-catalyzed cyclization is largely dependent on the type of substituent on aromatic ring. Finally, the introduction of a methyl, phenyl or methoxy substituent at the 4-position to 3-aryloxycarbonyl-2-diazonaphthoquinone efficiently afforded the cyclized products in high yield.

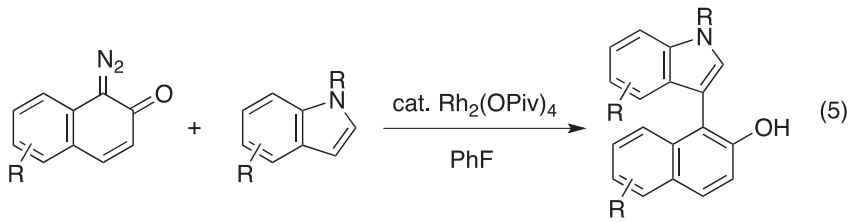
Table 8. Rh-Catalyzed cyclization of various 3-aryloxycarbonyldiazonaphthoquinones





Rh-Catalyzed reaction with indole

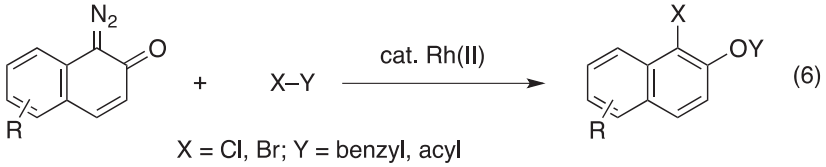
Baral *et al*. have developed a regioselective direct 3-arylation of indoles with 1-diazonaphthalen-2-(1*H*)-ones (**1**) by rhodium(II) pivalate-catalyzed cross-coupling reaction, yielding a variety of novel 3-naphthylindoles in high yield (eq. 5).[33]



(5)

Rh-Catalyzed reaction with benzyl/acyl halides

An efficient synthesis of different halonaphthalenyl ethers and esters was achieved via Rh(II)-catalyzed reaction of diazo compounds with benzyl halides or acid halides, respectively (eq.6)[34]

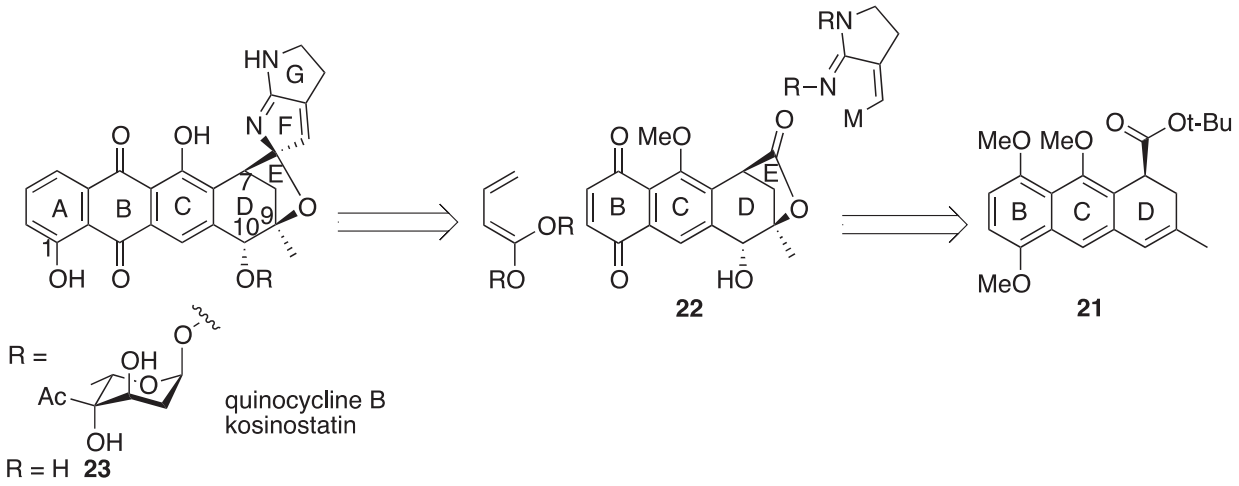


(6)

3-2. SYNTHETIC STUDY OF NATURAL COMPOUNDS

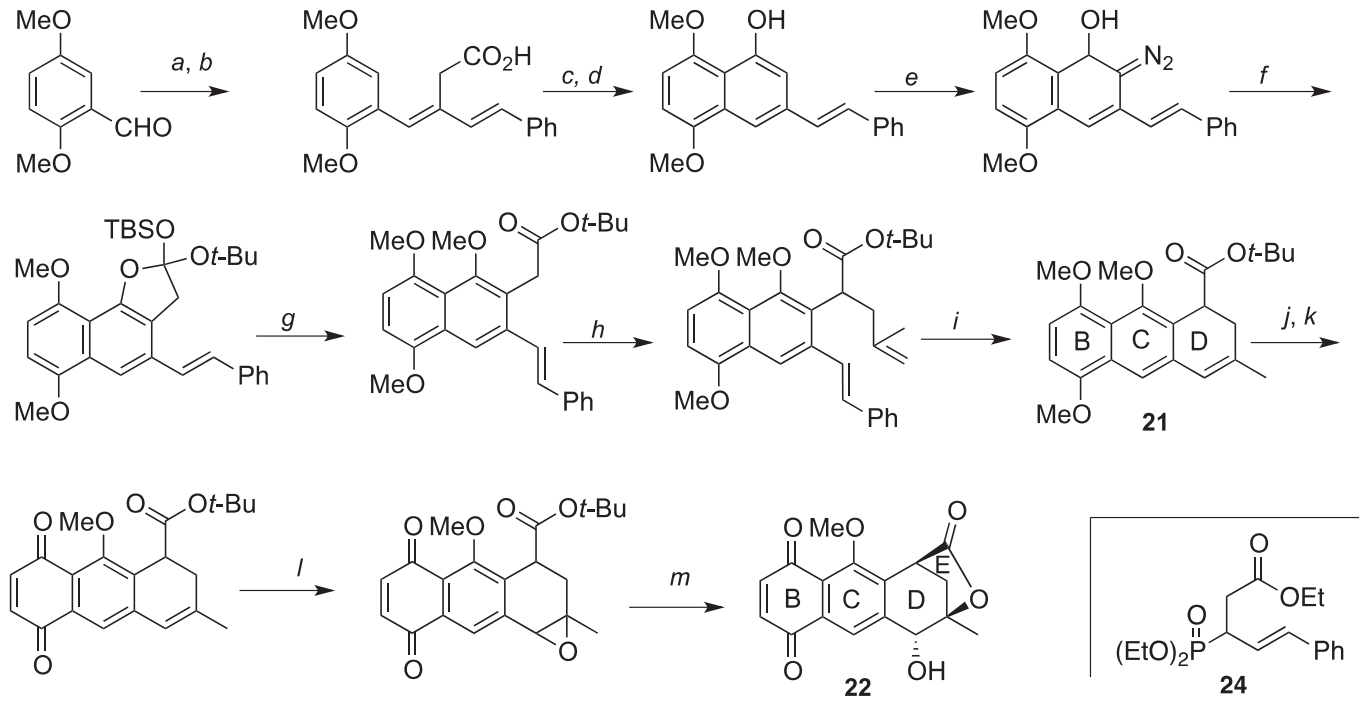
Synthetic study of kosinostatin

One of the most efficient applications of the recently developed diazo-transfer reaction is the synthesis of lactone (**22**), which corresponds to the BCDE ring fragment of kosinostatin aglycon (**23**).[35,36] This aglycon (**23**) constitutes the core structure of the quinocycline/isoquinocyline antibiotics with their unique structure and several biological activities (Scheme 10).[37]



Scheme 10. Retrosynthesis of kosinostatin/quinocycline B

The D ring of lactone (**22**) was characterized with three carbon chiral centers, which assumed to be constructed by the oxidative cyclization of alkenyl carboxylic acid. Therefore, ester BCD ring (**21**) was set as its precursor and it was synthesized *via* two routes. First, compound (**21**) was synthesized from 2,5-dimethoxybenzaldehyde by the combination of typical known transformations including efficient application of non-aqueous OsO_4 oxidation in the presence of $PhB(OH)_2$.[32] Unfortunately this pathway required 15 long steps and suffered from some difficulties. One of its main drawbacks was ortho-alkoxycarbonylmethylation of 1-naphthol. As a result, this process was improved by alkoxycarbonylmethylation using the recently developed diazonaphthoquinone. Scheme 11 illustrates that ester (**21**) was successfully synthesized in 9 steps from the same starting aldehyde applying Horner-Wittig reaction. By this new developed synthetic route, the number of reaction steps was reduced to 9 steps and the total yield was increased to 8.6% instead of 3.4%. Finally, **21** was stereoselectively converted to lactone (**22**) *via* trifluoroacetic acid-mediated cyclization of the 3,4-epoxy- cyclohexanecarboxylic acid derivative.

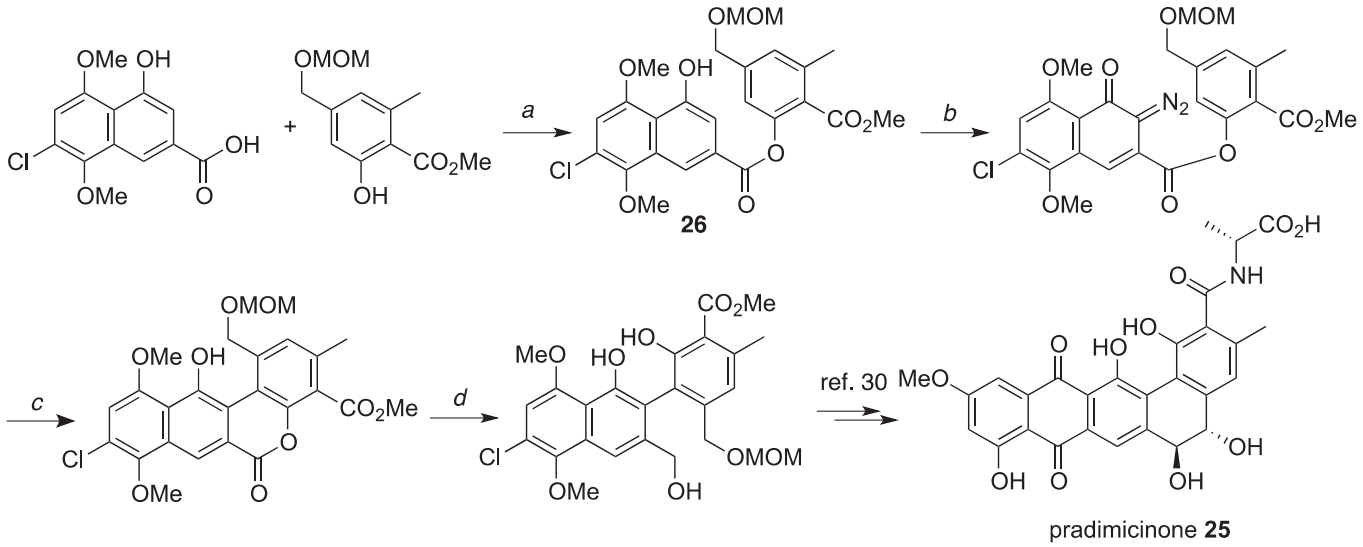


Reagents and conditions: a) phosphonate **24** (1.2 equiv.), NaH (3 equiv.), THF, -78 °C to rt, 3.5 h (75%); b) 10 M KOH aq *n*-Bu_4NBr (0.1 equiv.), 1,4-dioxane, 90 °C, 24 h; c) NaOAc (2 equiv.), Ac_2O, 140 °C, 7 h; d) K_2CO_3, MeOH, 1,4-dioxane, rt, 4.5 h (3 steps 42%); e) DMC (5 equiv.), NaN_3 (5 equiv.), MeCN, -25 °C, 1.5 h, Et_3N (2.5 equiv.), THF, -25 °C to rt, 3 h (89%); f) CH_2=C(OTBS)(O*t*-Bu) (2 equiv.), 1 mol% $Rh_2(OAc)_4$, 40 °C, 1 h (45%); g) *n*-Bu_4NF (2 equiv.), MeI (10 equiv.), $Na_2S_2O_4$ (0.1 equiv.), THF, rt, 1.5 h (91%); h) CH_2=C(CH_3)CH_2Br, NaH, 45 °C, 3 h (91%); i) 5 mol% Grubbs 2nd cat., toluene, 80 °C, 12 h (82%); j) CF_3CO_2H, CH_2Cl_2, rt, 1.5 h (quant.); k) $Ce(NH_4)_2(NO_3)_6$, MeCN, H_2O, 0 °C, 10 min; l) *m*-CPBA, $NaHCO_3$, CH_2Cl_2, rt, 2.5 h; m) CF_3CO_2H, CH_2Cl_2, 0 °C, 40 min (3 steps 31%).

Scheme 11. Synthesis of BCD ring fragment **21** and BCDE ring lactone **22**

Synthetic study of pradimicinone

Another interesting application was the synthesis of pradimicinone (**25**).[32] As shown in Scheme 12, the diazo-transfer reaction of ADMC (**3**) to polysubstituted 1-naphthol afforded diazonaphthoquinone in the presence of 15-crown-5. Then Rh-catalyzed cyclization reaction followed by reduction of the formed lactone afforded triol, successfully. According to previously reported literature, this triol underwent several transformations to yield pradimicinone (**25**).



Reagents and conditions: a) 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDCl), *N,N*-dimethyl-4-aminopyridine, CH_2Cl_2, rt, 2 h (51%). b) DMC (4.5 equiv.), NaN_3 (4.4 equiv.), 15-crown-5 (30 mol%), MeCN, -20 °C, 1 h: then **26**, Et_3N (2 equiv.), THF, -30 °C, 6 h. c) $Rh_2(oct)_4$, (1.5 mol%), benzene, reflux, 2.5 h. d) $NaBH_4$ (4.0 equiv.), THF, MeOH, -45 °C, 4 h (3 steps 55%).

Scheme 12. Formal synthesis of pradimicinone (**25**)

4. CONCLUSION

Here, we briefly reviewed the current progress of the synthetic chemistry on diazonapthoquiones, which are efficiently prepared through short direct pathway and have high chemical reactivity toward several types of metal-catalyzed reactions, such as O-H or C-H insertion reaction. Further studies on more wide applications of diazo-transfer reactions are in progress. This survey attempts to summarize the synthetic methods, reactions and applications for future studies to be done in the same field.

ACKNOWLEDGEMENTS

We thank Prof. Tatsuo Okauchi (Kyushu Institute of Technology) for his helpful discussion.

REFERENCES

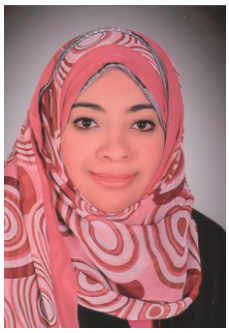
1. For a review, see: V. V. Ershov, G. A. Nikiforov, and C. R. H. I. de Jonge, *Quinone Diazides*, Elsevier, Amsterdam, 1981.
2. a) M. E. Bodini and V. Arancibia, *Trans. Met. Chem*., 1997, **22**, 150; b) M. C. Foti, E. R. Johnson, M. R. Vinqvist, J. S. Wright, L. R. C. Barclay, and K. U. Ingold, *J. Org. Chem*., 2002, **67**, 5190; c) E. Pino, A. Aspée, C. López-Alarcón, and E. Lissi, *J. Phys. Org. Chem.*, 2006, **19**, 867.
3. a) C. R. Rice, M. D. Ward, M. K. Nazeeruddin, and M. Grätzel, *New J. Chem.*, 2000, **24**, 651; b) R. Mosurkal, J.-A. He, K. Yang, L. A. Samuelson, and J. Kumar, *J. Photochem. Photobiol*. *A*: *Chem*.,

2004, **168**, 191; c) T. Lu, P. Shao, I. Mathew, A. Sand, and W. Sun, *J. Am. Chem. Soc.*, 2008, **130**, 15782; d) I. Hod, M. Shalom, Z. Tachan, S. Rühle, and A. Zaban, *J. Phys. Chem. C,* 2010, **114**, 10015; e) B.-K. An, W. Hu, P. L.Burn, and P. Meredith, *J. Phys. Chem. C*, 2010, **114**, 17964; f) R. Sánchez-de-Armas, J. Oviedo, M. Á. S. Miguel, and J. F. Sanz, *J. Phys. Chem. C,* 2011, **115**, 11293.

4. For reviews, see: a) A. Reiser, H. Y. Shih, T. F. Yeh, and J. P. Huang, *Angew. Chem.*, 1996, **108**, 2610; *Angew. Chem., Int. Ed. Engl.* 1996, **35**, 2428; b) A. Reiser, J. P. Huang, X. He, T. F. Yeh, S. Jha, H. Y. Shih, M. S. Kim, Y. K. Han, and K. Yan, *Eur. Polym. J*., 2002, **38**, 619; c) K. i. Fukukawa and M. Ueda, *Polym. J*., 2008, **40**, 281.
5. a) M. Yagihara, Y. Kitahara, and T. Asao, *Chem. Lett.*, 1974, **3**, 1015; b) N. P. Hacker and N. J. Turro, *Tetrahedron Lett*., 1982, **23**, 1771; c) G. Bucher and W. Sander, *J. Org. Chem.*, 1992, **57**, 1346; d) J. I. K. Almstead, B. Urwyler, and J. Wirz, *J. Am. Chem. Soc.,* 1994, **116**, 954; e) G. G. Qiao, J. Andraos, and C. Wentrup, *J. Am. Chem. Soc.*, 1996, **118**, 5634; f) N. C. de Lucas, J. C. Netto-Ferreira, J. Andraos, J. Lusztyk, B. D. Wagner, and J. C. Scaiano, *Tetrahedron Lett.*, 1997, **38**, 5147; g) S. Murata, J. Kobayashi, C. Kongou, M. Miyata, T. Matsushita, and H. Tomioka, *J. Org. Chem.*, 2000, **65**, 6082; h) W. Kirmse, *Eur. J. Org. Chem.*, 2002, **14**, 2193; i) N. K. Urdabayev and V. V. Popik, *J. Am. Chem. Soc.*, 2004, **126**, 4058.
6. K. Bahadur, Somia Magar, and Y. R. Lee, *Org. Lett*., 2013, **15**, 4288.
7. a) L. C. Anderson and M. J. Roedel, *J. Am. Chem. Soc*., 1945, **67**, 955; b) J. D. C. Anderson, R. J. W. Le Fevre, and I. R. Wilson, *J. Chem. Soc*., 1949, 2082; c) W. Sander, G. Bucher, H. Wandel, E. Kraka, D. Cremer, and W. S. Sheldrick, *J. Am. Chem. Soc*., 1997, **119**, 10660.
8. a) M. P. Cava, R. L. Litle, and D. R. Napier, *J. Am. Chem. Soc*., 1958, **80**, 2257; b) N. P. Hacker and N. J. Turro, *Tetrahedrone Lett*., 1982, **23**, 1771; c) P. J. N. Brown, J. I. G. Cadogan, I. Gosney, A. Johnstone, R. M. Paton, and N. H. Wilson, *J. Chem. Soc., Perkin Trans. 2*, 1996, 2303; d) V. F. Ferreira, A. Jorqueira, K. Z. Leal, H. R. X. Pimentel, P. R. Seidl, M. N. da Silva, M. C. B. V. da Silva, M. C. B. V. da Souza, A. V. Pinto, J. L.Wardell, and S. M. S. V. Wardell, *Magn. Reson. Chem*., 2006, **44**, 481.
9. a) T. Ye and M. A. Mckervey, *Chem. Rev*., 1994, **94**, 1091; b) Z. Zhang and J. Wang, *Tetrahedron*, 2008, **64**, 6577; c) M. Regitz, *Angew. Chem., Int. Ed. Engl*., 1967, **6**, 733; d) A. Padwa and D. J. Austin, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 1797.
10. H. Balli, V. Muller, and A. Sezen-Gezgin, *Helv. Chim. Acta*, 1978, **61**, 104.
11. Review: M. Kitamura, *J. Synth. Org. Chem. Jpn.,* 2014, **72**, 14.
12. Diazo-transfer to 1,3-carbonyl compounds, see: a) M. Kitamura, N. Tashiro, and T. Okauchi, *Synlett*, 2009, 2943; b) M. Kitamura, N. Tashiro, S. Miyagawa, and T. Okauchi, *Synthesis*, 2011, 1037.

13. Diazo-transfer to primary amines, see: a) M. Kitamura, M. Yano, N. Tashiro, S. Miyagawa, M. Sando and T. Okauchi, *Eur. J. Org. Chem.*, 2011, **3**, 458; b) M. Kitamura, S. Kato, M. Yano, N. Tashiro, Y. Shiratake, M. Sando, and T. Okauchi, *Org. Biomol. Chem.*, 2014, **12**, 4397.
14. a) M. Kitamura, N. Tashiro, R. Sakata, and T. Okauchi, *Synlett*, 2010, 2503; b) M. Kitamura, R. Sakata, N. Tashiro, A. Ikegami, and T. Okauchi, *Bull. Chem. Soc. Jpn.,* 2015, **88**, 824.
15. Other reaction: a) M. Kitamura, N. Tashiro, Y. Takamoto, and T. Okauchi, *Chem. Lett*., 2010, **39**, 732; b) M. Kitamura, T. Koga, M. Yano, and T. Okauchi, *Synlett*, 2012, 133; c) M. Kitamura, K. Murakami, Y. Shiratake, and T. Okauchi, *Chem. Lett*., 2013, **42**, 691.
16. Unpublished results.
17. a) P. Stahl, L. Kissau, R. Mazitschek, A. Huwe, P. Furet, A. Giannis, and H. Waldmann, *J. Am. Chem. Soc*., 2001, **123**, 11586; b) T. Lu, P. Shao, I. Mathew, A. Sand, and W. Sun, *J. Am. Chem. Soc*., 2008, **130**, 15782; c) S. Madan and C. H. Cheng, *J. Org. Chem*., 2006, **71**, 8312.
18. a) K. L. Platt and F. Oesch, *J. Org. Chem*., 1983, **48**, 265; b) J. L. Zambrano and R. Dorta, *Synlett*, 2003, 1545; c) J. K. Crandall, M. Zucco, R. S. Kirsch, and D. M. Coppert, *Tetrahedron Lett*., 1991, **32**, 5441.
19. M. Kitamura, M. Kisanuki, R. Sakata, and T. Okauchi, *Chem. Lett*., 2011, **40**, 1129.
20. M. Kitamura, M. Kisanuki, and T. Okauchi, *Eur. J. Org. Chem*., 2012, **5**, 905.
21. M. Kitamura, R. Sakata, and T. Okauchi, *Tetrahedron Lett.*, 2011, **52**, 1931.
22. a) S. W. Wright, D. L. Hageman, and L. D. McClure, *J. Org. Chem.*, 1994, **59**, 6095; b) T. Kirschbaum, C. A. Briehn, and P. Bäuerle, *J. Chem. Soc., Perkin Trans. 1*, 2000, 1211.
23. C. Peng, Y. Wang, and J. Wang, *J. Am. Chem. Soc*., 2008, **130**, 1566.
24. a) K. L. Greenman, D. S. Carter, and D. L. Van Vranken, *Tetrahedron*, 2001, **57**, 5219; b) K. L. Greenman and D. L. Van Vranken, *Tetrahedron*, 2005, **61**, 6438; c) S. K. J. Devine and D. L.Van Vranken, *Org. Lett*., 2007, **9**, 2407; d) J. Barluenga, P. Moriel, C. Valdés, and F. Aznar, *Angew. Chem. Int. Ed.*, 2007, **46**, 5587; e) S. Chen and J. Wang, *Chem. Commun*., 2008, 4198; f) Q. Xiao, J. Ma, Y. Yang, Y. Zhang, and J. Wang, *Org. Lett.*, 2009, **11**, 4732; g) Z. Zhang, Y. Liu, M. Gong, X. Zhao, Y. Zhang, and J. Wang, *Angew. Chem. Int. Ed*., 2010, **49**, 1139; h) A. Khanna, I. D. U. A. Premachandra, P. D. Sung, and D. L. Van Vranken, *Org. Lett*., 2013, **15**, 3158; i) A. Khanna, I. D. U. A. Premachandra, P. D. Sung, and D. L. Van Vranken, *Org. Lett*., 2013, **15**, 3694; j) E. S. Gutman, V. Arredondo, and D. L. Van Vranken, *Org. Lett*., 2014, **16**, 5498; k) M. Kitamura, R. Yuasa, and D. L. Van Vranken, *Tetrahedron Lett.*, 2015, **56**, 3027. 66; l) I. D. U. A. Premachandra, T. Nguyen, C. Shen, E. Gutman, and D. L. Van Vranken, *Org. Lett*., 2015, **17**, 5464.
25. V. S. P. R. Lingam, D. H. Dahale, K. Mukkanti, B. Gopalan, and A. Thomas, *Tetrahedron Lett*., 2012, **53**, 5695.

26. M. Kitamura, K. Araki, H. Matsuzaki, and T. Okauchi, *Eur. J. Org. Chem.*, 2013, **23**, 5045.
27. G. A. Kraus, J. O. Nagy, and J. DeLano, *Tetrahedron*, 1985, **41**, 2337.
28. M. Yoshida, M. Higuchi, and K. Shishido, *Org. Lett.,* 2009, **11**, 4752.
29. M. Kitamura, M. Kisanuki, K. Kanemura, and T. Okauchi, *Org. Lett*., 2014, **16**, 1554.
30. a) N. Ueberschaar, Z. Xu, K. Scherlach, M. Metsa-Ketela, T. Bretschneider, H.-M. Dahse, H. Görls, and C. Hertweck, *J. Am. Chem. Soc*., 2013, **135**, 17408; b) S. Horii, H. Fukase, E. Mizuta, K. Hatano, and K. Mizuno, *Chem. Pharm. Bull*., 1980, **28**, 3601; c) G. Bringmann and D. Menche, *Angew. Chem. Int. Ed.*, 2001, **40**, 1687; d) T. Matsumoto, T. Hosoya, and K. Suzuki, *J. Am. Chem. Soc*., 1992, **114**, 3568; e) A. Hager, D. Mazunin, P. Mayer, and D. Trauner, *Org. Lett*., 2011, **13**, 1386; f) M. Tamiya, K. Ohmori, M. Kitamura, H. Kato, T. Arai, M. Oorui, and K. Suzuki, *Chem. Eur. J.*, 2007, **13**, 9791; g) M. Kitamura, K. Ohmori, T. Kawase, and K. Suzuki, *Angew. Chem. Int. Ed*., 1999, **38**, 1229; h) K. Ohmori, M. Tamiya, M. Kitamura, H. Kato, M. Oorui, and K. Suzuki, *Angew. Chem. Int. Ed*., 2005, **44**, 3871.
31. a) T. Harayama and H. Yasuda, *Heterocycles*, 1997, **46**, 61; b) Q. J. Zhou, K. Worm, and R. E. Dolle, *J. Org. Chem.,* 2004, **69**, 5147; c) H. Abe, K. Nishioka, S. Takeda, M. Arai, Y. Takeuchi, and T. Harayama, *Tetrahedron Lett.*, 2005, **46**, 3197; d) S. R. Taylor, A. T. Ung, and S. G. Pyne, *Tetrahedron*, 2007, **63**, 10889; e) O. C. Arellano and A. C. Vargas, *Tetrahedron Lett*., 2010, **51**, 602; f) J. Luo, Y. Lu, S. Liu, J. Liu, and G. Denga, *Adv. Synth. Catal*., 2011, **353**, 2604; g) S. Luo, F. X. Luo, X. S. Zhang, and Z. J. Shi, *Angew. Chem. Int. Ed.*, 2013, **52**, 10598.
32. M. Kitamura, S. Takahashi, and T. Okauchi, *J. Org. Chem*., 2015, **80**, 8406.
33. E. R. Baral, Y. R. Lee, and S. H. Kim, *Adv. Synth. Catal.*, 2015, **357**, 2883.
34. E. R. Baral, Y. R. Lee, S. H. Kim, and Y. J. Wee, *Synthesis*, 2016, **48**, 579.
35. M. Kitamura, K. Kubo, S. Yoshinaga, H. Matsuzaki, K. Ezaki, T. Matsuura, D. Matsuura, N. Fukuzumi, K. Araki, and M. Narasaki, *Tetrahedron Lett.*, 2014, **55**, 1653.
36. Synthetic study of quinocycline/isoquinocyline derivatives, see: a) J. Cordes, K. Harms, and U. Koert, *Org. Lett*., 2010, **12**, 3808; b) M. A. Breuning, K. Harms, and U. Koert, *Org. Lett.,* 2011, **13**, 1402; c) M. Dischmann, T. Frassetto, M. A. Breuning, and U. Koert, *Chem. Eur. J*., 2014, **20**, 11300.
37. a) D. B. Cosulich, J. H. Mowat, R. W. Broschard, J. B. Patrick, and W. E. Meyer, *Tetrahedron Lett*., 1964, **3**, 453; b) J. H. Mowat, R. W. Broschard, J. B. Patrick, and W. E. Meyer, *Tetrahedron Lett*., 1964, **5**, 750; c) A. Tulinsky, *J. Am. Chem. Soc.*, 1964, **86**, 5368; d) T. Furumai, Y. Igarashi, H. Higuchi, N. Saito, and T. Oki, *J. Antibiot*., 2002, **55**, 128; e) Y. Igarashi, H. Higuchi, T. Oki, and T. Furumai, *J. Antibiot*., 2002, **55**, 134; f) M. Y. El-Naggar, *J. Microbiol*., 2007, **45**, 262.



Dina Othman was born in Kuwait in 1985. She had her Bachelor Degree in Pharmaceutical Science from faculty of pharmacy, Mansoura University, Egypt (2007), where she worked as administrator in pharmaceutical organic chemistry department. She received her M. Sc. degree in Pharmaceutical Organic Chemistry, about the synthesis of novel benzofuran derivatives as antitumor agents (2013). She has become assistant lecturer in the same department, faculty of pharmacy, Mansoura University, Egypt (2013). She took many courses about the principle of highly qualified learning process (FLDP) and attended many international workshops on computational molecular modelling and drug discovery. (2014). Then, she is appointed as PhD research student to Professor Mitsuru Kitamura's group at Kyushu Institute of Technology, Japan (2015), executing joint supervision system between Egypt and Japan. Her research interest is design and synthesis of different heterocycles with interesting biological activities such as, antitumor and antiviral activities.

Mitsuru Kitamura was born in Takamatsu, Japan, in 1971 and received his B.Sc. in 1994 and M. Sc. in 1996 from Keio University. He received his Ph.D. in 1999 from Tokyo Institute of Technology under the direction of Professor Keisuke Suzuki. Then, he was appointed as research associate in Professor Koichi Narasaka's group at the University of Tokyo. In 2005, he moved to Kyushu Institute of Technology as associate professor, and promoted to full professor in 2015. He was a recipient of the Chemical Society of Japan Award for Young Chemists (2005) and Award for a Creative Young Chemist, Kyushu-Yamaguchi Branch, the Society of Synthetic Organic Chemistry, Japan (2011). His research interest is development of new synthetic method of amino compounds/nitrogen heterocycles and natural product synthesis.