Sixth International Electronic Conference on Synthetic Organic Chemistry (ECSOC-6), 1-30 September
[A013]

Synthesis of benzodifuran derivatives by using 2-aryl-1,4-benzoquinones

Vasyl S. Matiychuk, Roman L. Martyak, Mykola D. Obushak*

Department of Organic Chemistry, Ivan Franko National University of Lviv,
Kyryla & Mefodiya 6, Lviv 79005, Ukraine.
E-mail: obushak@in.lviv.ua

Received: July 2002 / Uploaded August 2002

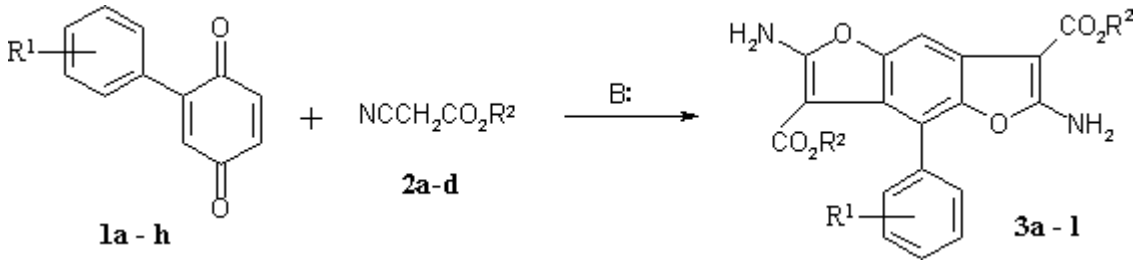
Abstract: 2-Aryl-1,4-benzoquinones (aryl = RC_6H_4, R = H, 4-Me, 3-CF_3, 4-COOH, 3-Cl, 4-Cl, 4-F, 4-NO_2) react with methyl ethyl, propyl and allyl cyanoacetates in the presence of some bases to form dialkyl 2,6-diamino-4-arylfuro[2',3':4,5]benzo[b]furan-3,7-dicarboxylates**.** Regardless of the reagents ratio benzodifuran derivatives are formed selectively. Only in reaction 2-(4-nitrophenyl)-1,4-benzoquinone with ethyl cyanoacetate 2-amino-5-hydroxy-4-(4-nitrophenyl)benzo[b]furan-3-carboxylate is formed as minor component.

Key words: benzoquinone, 2-aryl-1,4-benzoquinones, cyclizations, heterocycles, benzodifuran derivatives, cyanoacetic esters, arylation, Meerwein reaction.

It is known that interaction of quinones with various C-nucleophiles is often not finished by 1,4-addition. In the presence of other functional groups intramolecular cyclization takes place to form condensed heterocyclic compounds [1]. However, mainly 1,4-benzoquinone and also disubstituted quinones were investigated in these reactions. Due to asymmetry of monosubstituted 1,4-benzoquinones a formation of different isomers is possible in the reactions with C-nucleophiles. Therefore, such quinones are studied considerably less in these reactions, but in published works [1–7] some contradictions which concerned their regioselectivity took place. It was reported that toluquinone and 2-chloro-1,4-benzoquinone react with ethyl acetoacetate or ethyl benzoylacetate to form linear furo[2',3':4,5]benzo[b]furan isomers [2, 3]. Under changed the reaction conditions benzofuran derivatives (1:1 adduct) was received, moreover CH-acid added in position 5 of 2-aryl-1,4-benzoquinones [2]. Subsequently evidences were found that 1:1 adduct formed as a result of nucleophilic attack in position 6 [4]. The condensation of ethyl benzoylacetate with toluquinone has been reported to lead to two benzofuran isomers [4, 5]. However, for one of them in these works a different structure was assigned. The ratio 1:1 and 1:2 adducts largely depends on reaction conditions [6, 7]. From result obtained at analysis of interaction of 2-acetyl-1,4-benzoquinone with CH-acid is possible to make the conclusion that the electron-withdrawing groups in quinone ring direct nucleophilic attack to position 3 [8–10]. Unsubstituted quinone react mainly with cyanoacetic esters to form dialkyl 2,6-diaminofuro[2',3':4,5]benzo[b]furan-3,7-dicarboxylate [11, 12]. In this report

interaction of 2-aryl-1,4-benzoquinones **1a–h** with cyanoacetic esters **2a-d** is investigated. Compounds **1a–h** are prepared by arylation of the 1,4-benzoquinone with arenediazonium chlorides [13–15].

In similar reactions quinone derivatives may react with one or two molecules of CH-acid by the type of Michael reaction [16–19] with followed cyclization to derivatives of benzofuran and benzodifuran respectively. We have established that quinones **1a–h** react with cyanoacetic esters **2a-d** to form benzodifuran derivatives **3a–l** (Scheme 1).



1: R^1=H (**a**), 4-Me (**b**), 3-CF_3 (**c**), 4-COOH (**d**), 3-Cl (**e**), 4-Cl (**f**), 4-F (**g**), 4-NO_2 (**h**);

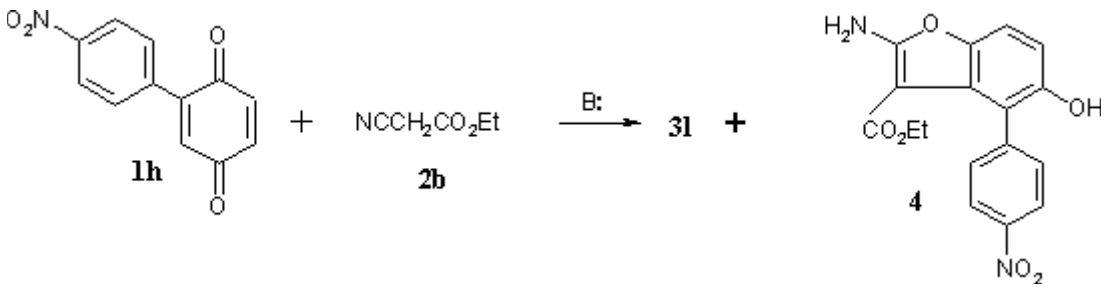
2: R^2=Me (**a**), Et (**b**), Pr (**c**), Allyl (**d**).

Scheme 1

Table 1. Benzodifuran derivatives 3a–l

3	***R^1***	***R^2***	***Yield, %***
a	H	Me	50
b	3-CF_3	Me	42
c	4-F	Me	54
d	H	Me	49
e	4-Me	Et	56
f	4-COOH	Et	46
g	3-Cl	Et	44
h	4-NO_2	Et	31
i	H	Pr	34
j	4-F	Pr	38
k	H	Allyl	58
l	4-Cl	Allyl	62

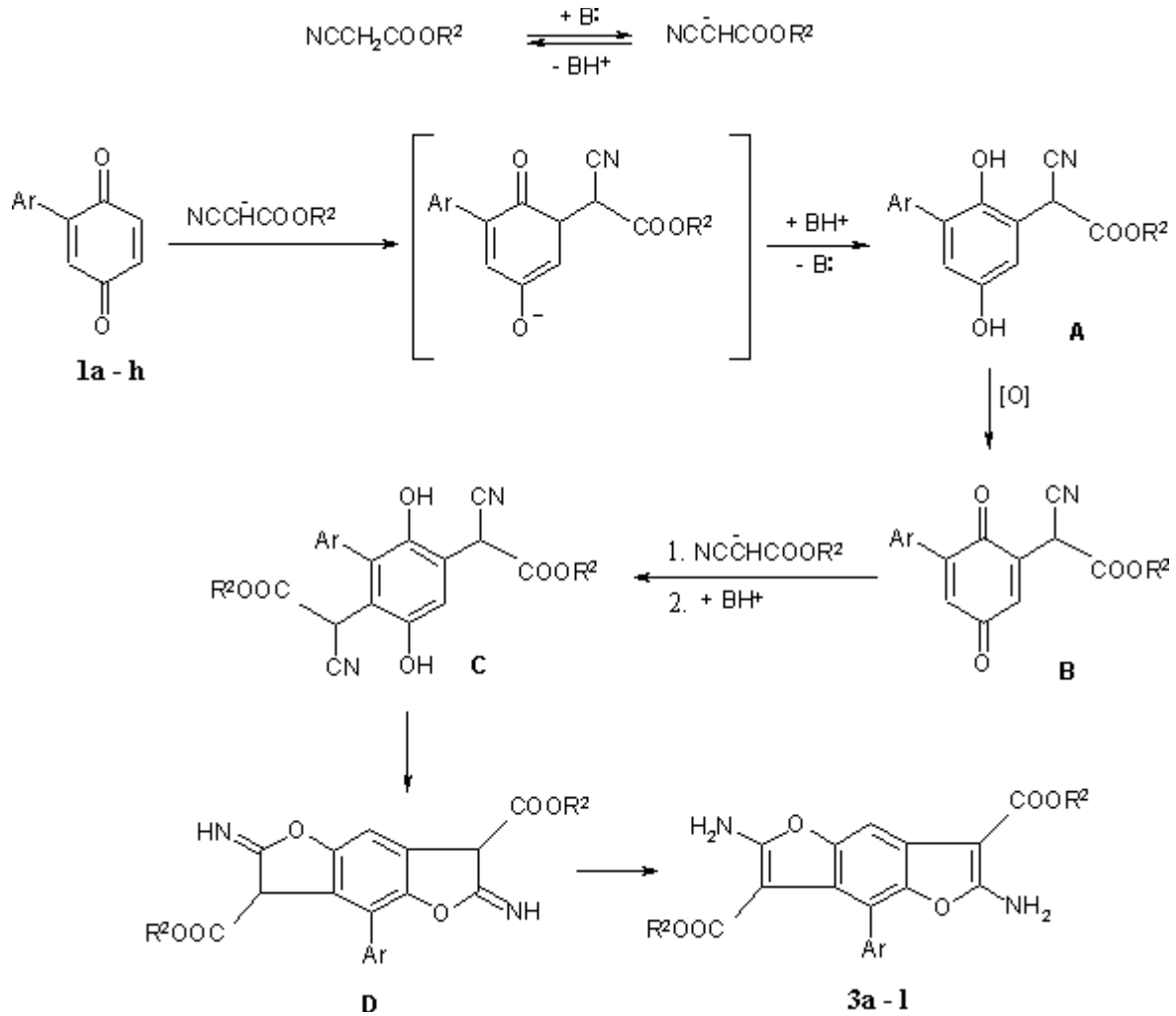
Reaction was carried out in alcohol in the presence of bases (ammonium hydroxide, piperidine, alcoholates). Arylquinones with *ortho*-substituents in aromatic ring were practically unreactive in this reaction. In those cases benzodifuran or benzofuran derivatives are not isolated in pure form.
The interesting particularity of the reaction is that regardless of the reagents ratio benzodifuran derivatives are formed selectively. Only in the reaction of ethyl cyanoacetate **2b** with 2-(4-nitrophenyl)-1,4-benzoquinone **1h** minor component – ethyl 2-amino-5-hydroxy-4-(4-nitrophenyl)benzo[b]furan-3-carboxylate **4** (Scheme 2) – is formed besides of benzodifuran **3h** (**3h**:**4** = 77:23).



Scheme 2

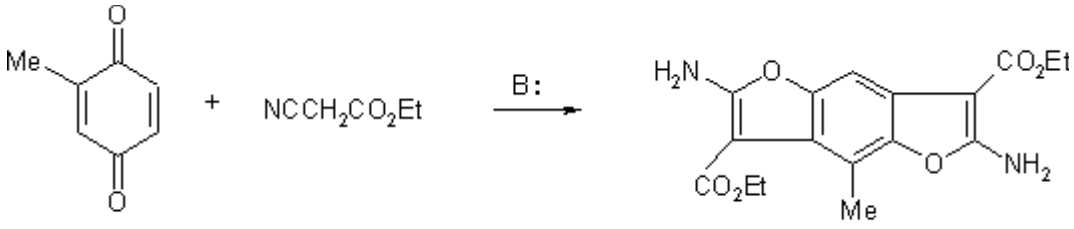
Probable mechanism of this reaction includes several stages (Scheme 3). Carbanion of cyanoacetic ester reacts with quinones **1a–h** by the type of Michael reaction with the formation of hydroquinone **A**. The latter is oxidized by starting quinone to substituted quinone **B**. In the next stage another molecule of cyanoacetic ester is added to quinone **B**. Finally intramolecular cyclization takes place due to interaction of hydroxy and nitrile groups of hydroquinone **C**.

The principal stage of this process evidently is fast oxidation of adduct **A** to substituted quinone **B**. In that case when primary addition product **A** had not time to oxidize, its intramolecular cyclization takes place to form benzofuran derivative **4**. Electron-withdrawing substituents in aromatic ring of compounds **1a–h** (R^1=NO_2) naturally favour to such reaction route.



Scheme 3

In ^{1}H NMR spectra of compounds **3a–l** two sets of signals of ester groups protons are observed. It is explained by shielding of one of ester groups by aryl substituent. Indeed in ^{1}H NMR spectrum of diethyl 2,6-diamino-4-methylfuro[2',3':4,5]benzo[b]furan-3,7-dicarboxylate **5**, was obtained by interaction of ethyl cyanoacetate with toluquinone (Scheme 4), signals of CO_2Et-groups protons practically coincide.



5

Scheme 4

Conclusions

So, during the interaction of arylquinones with cyanoacetic esters the reaction is not stoped on the stage of the addition of one molecule of nucleophilic reagent. Adduct 1:2 is formed and its intramolecular cyclization leads to benzodifuran derivatives.

References

1. Kutyrev A.A. and Moskva V.V. *Usp. Khim. (Chem. Rev. USSR)* **1991**, *60*, 134.
2. Grinev A.N. and Terent'ev A.P. *Zh. Obshch. Khim. (J. Gen. Chem. USSR)* **1958**, *28*, 78.
3. Grinev A.N., Pan Bon-Khvar, Frosin V.N. and Terent'ev A.P. *Zh. Obshch. Khim. (J. Gen. Chem. USSR)* **1956**, *26*, 561.
4. McPherson H.L. and Ponder B.W. *J. Heterocycl. Chem.* **1978**, *15*, 43.
5. Grinev A.N., Venevtseva N.K. and Terent'ev A.P. *Zh. Obshch. Khim. (J. Gen. Chem. USSR)* **1958**, *28*, 1850.
6. Kornilov M.Yu., Makovetskii V.P., Turov A.V. and Dzvinchuk I.B. *Khim. Geterotsikl. Soedin. (Chem. Heterocycl. Compds)* **1980**, 22.
7. Jeffreys J.A.D. *J. Chem. Soc.* **1959**, 2153.
8. Fumagalli S.E. and Eugster C.H. *Helv. Chim. Acta* **1971**, *54*, 959.
9. Kuckländer U., Herweg-Wahl U., Massa W. and Baum G. *Chem. Ber.* **1987**, *120*, 1791.
10. Kuckländer U., Herweg-Wahl U., Poll W. and Rickerich L. *Chem. Ber.* **1988**, *121*, 1841.
11. Derkosch J. and Specht I. *Monatsh. Chem.* **1961**, *92*, 542.
12. Napier R.J., Shand C.A., Thomson R.H., Cheng L., Griffiths J. and Greenhalgh C.W. *J. Chem. Res. Miniprint* **1983**, 480.
13. Obushak M.D., Matiychuk V.S. and Martyak R.L. *Khim. Geterotsikl. Soedin. (Chem. Heterocycl. Compds)* **2001**, 986.
14. Brassard P. and L'Écuyer P. *Can. J. Chem.* **1958**, *36*, 700.
15. Kvalnes D.E. *J. Am. Chem. Soc.* **1934**, *56*, 2478.
16. Christoffers J. *Synlett* **2001**, *6*, 723.
17. King T.J. and Newall C.E. *J. Chem. Soc.* **1965**, 974.
18. Makovetskii V.P., Dzvinchuk I.B., Yaremenko V.V. and Svishchuk A.A. *Ukr. Khim. Zh. (Ukrainian J. Chem.)* **1979**, *45*, 652.
19. Makovetskii V.P., Dzvinchuk I.B., Volovenko Yu.M. and Svishchuk A.A. *Khim. Geterotsikl. Soedin. (Chem. Heterocycl. Compds)* **1979**, 129.