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A NEW METHOD OF ß-KETO ALKYL CHAIN INTRODUCTION INTO 1,4-NAPHTHOQUINONE

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Photochemical reaction of 2,3-disubstituted 1,4-naphthoquinone with 2-methoxy-1-alkene and subsequent hydrolysis afforded 2-(2-alkanonyl)-1,4-naphthoquinone derivatives.

Recently, a lot of synthetic methods for naturally occurring and/or antitumor antibiotic quinonoid compounds have been investigated.[1)] One of the most important steps in the synthetic pathway to these quinones is a functionalized alkyl chain introduction into the quinone skeleton. However, in spite of many studies on allylation[1a-g)] and acylation[1a,c,h)] of quinones, direct ß-keto alkyl chain introduction into quinones has never been investigated so far because of its difficulty.

Here, we wish to report a new method for a direct ß-keto alkyl chain introduction into 1,4-naphthoquinone by using the photochemical reaction of 2,3-disubstituted 1,4-naphthoquinone (**1**) with alkoxylated ethylene (**2**). When 2-methoxy-1-alkenes (**2**a-d) were used as starting ethylene, for example, 2-(2-alkanonyl)-3-chloro-1,4-naphthoquinones (**3**a-d) were obtained in the photochemical reaction with 2,3-dichloro-1,4-naphthoquinone (**1**a). A benzene solution (25 ml) of 2,3-dichloro-1,4-naphthoquinone (**1**a; 1 mmol) and isopropenyl methyl ether (**2**a; 2 mmol)[2)] was irradiated with a high pressure Hg arc lamp (300 W) in the presence of pyridine (2 mmol) at room temperature for 3 h. The reaction mixture was concentrated in vacuo and subjected to column chromatography on silica gel. An addition product (**3**a) was isolated. The structure of this product (**3**a) was

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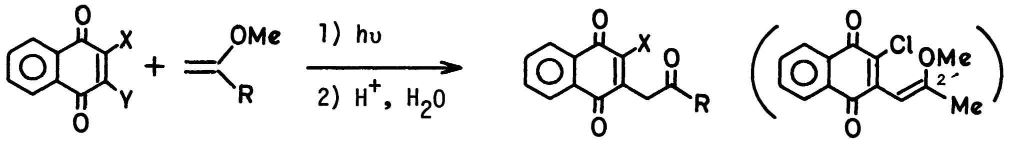
Table 1. Photochemical Reaction of 2,3-Disubstituted 1,4-Naphthoquinone (1a-c) with 2-Methoxy-1-alkene (2a-d)



1a-c 2a-d 3a-f 4

Quinone	Ethylene	Product 3	(Yield/%)a)
1a; X=Y=Cl	2a; R=CH_3	3a; X=Cl,R=CH_3	(67)
1a	2b; R=n-C_4H_9	3b; X=Cl,R=n-C_4H_9	(45)
1a	2c; R=n-C_5H_{11}	3c; X=Cl,R=n-C_5H_{11}	(43)
1a	2d; R=n-C_6H_{13}	3d; X=Cl,R=n-C_6H_{13}	(35)
1b; X=Y=Br	2a	3e; X=Br,R=CH_3	(65)
1c; X=OMe,Y=Br	2a	3f; X=OMe,R=CH_3	(20)

a) Isolated yield based on starting quinone 1 consumed.

assigned to 2-chloro-3-(2-propanonyl)-1,4-naphthoquinone by its ^{1}H-NMR,3) IR, and mass spectra. Thin layer chromatography (TLC) analysis of the reacting mixture revealed that ethylene adduct (4) was formed. However, column chromatography on silica gel of the reaction mixture resulted in the isolation of a product 3a. The ethylene adduct (4) was not obtained. Namely, the isolated product (3a) was produced by hydrolysis of the ethylene adduct (4) in silica gel column. Formation of the ethylene adduct (4) would be understood in terms of the similarity to the photochemical reaction of 2,3-disubstituted 1,4-naphthoquinone with 1,1-diarylethylene reported previously.4)

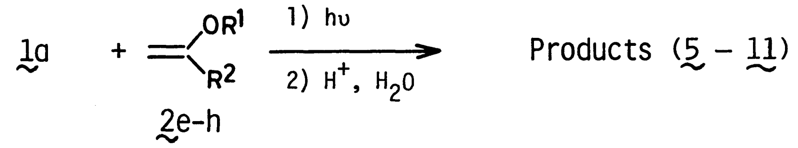
Other 2-methoxy-1-alkenes (2b-d)2) gave successfully the corresponding 2-(2-alkanonyl)-3-chloro-1,4-naphthoquinones (3b-d)3) in the reaction with 2,3-dichloro-1,4-naphthoquinone (1a) followed by hydrolysis.5) The results are summarized in Table 1.

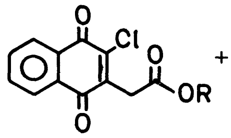
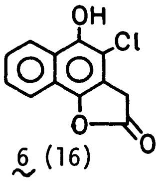
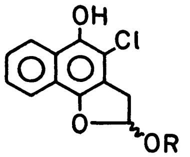
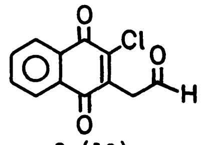
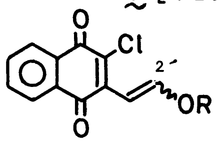
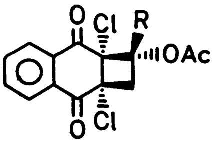
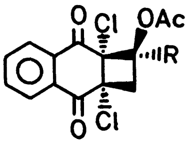
Hence, 2-methoxy-1-alkenes (2a-d) were all reactive for the photochemical reaction with 2,3-dichloro-1,4-naphthoquinone (1a) to yield ß-keto alkylated 1,4-naphthoquinones (3a-d) after hydrolysis without any difficulties.

This direct ß-keto alkylating method of 1,4-naphthoquinone was further extended to syntheses of 2-bromo-3-(2-propanonyl)-1,4-naphthoquinone (3e) and 2-methoxy-3-(2-propanonyl)-1,4-naphthoquinone (3f). When isopropenyl methyl ether (2a) was submitted to the photochemical reaction with 2,3-dibromo-1,4-naphthoquinone (1b) and 2-bromo-3-methoxy-1,4-naphthoquinone (1c), β-keto alkylated 1,4-naphthoquinones such as 3e and 3f[3] were obtained, respectively, after hydrolysis[5] as shown in Table 1.

Contrary to these behaviors of 2-methoxy-1-alkenes (2a-d), when alkyl vinyl ethers (2e,f) were subjected to the reaction with 1a, several products (5-9) were isolated as depicted in Table 2. The products (5-8) would be produced by hydrolysis and/or subsequent other reaction of the ethylene adduct (9) formed by the photo-reaction. Vinyl acetates (2g,h) as starting ethylene, however,

Table 2. Photochemical Reaction of 2,3-Dichloro-1,4-naphthoquinone (1a) with Vinyl Ether (2e,f) and Vinyl Acetate (2g,h)



Ethylene	Products (Yield/ %)[a]
2e; R^1=Et,R^2=H	 5 [R=Et] (19) +  6 (16) +  7 [R=Et] (12) +  8 (10) +  9 [R=Et] (1)
2f; R^1=^{n}Bu,R^2=H	5 [R=^{n}Bu] (20) + 6 (10) + 7 [R=^{n}Bu] (12) + 8 (14) + 9 [R=^{n}Bu] (1)
2g; R^1=Ac,R^2=H	 10 [R=H] +  11 [R=H] (1.3/1) mixture (97)
2h; R^1=Ac,R^2=Me	10 [R=Me] (46) + 11 [R=Me] (18) + 3a (11)

[a] Isolated yield based on starting quinone 1a consumed.

gave cyclobutane adducts (**10** and **11**) via photochemical $[\pi 2s+\pi 2s]$ cycloaddition.[6]

Thus, the facile photochemical reaction of 2,3-disubstituted 1,4-naphthoquinones (**1**a-c) with 2-methoxy-1-alkenes (**2**a-d) provides us a new useful method for direct ß-keto alkyl chain introduction into 1,4-naphthoquinone.

References

1) a) K.Maruyama, H.Uno, and Y.Naruta, Chem. Lett., 1983, 1767; b) Y.Naruta, H.Uno, and K.Maruyama, Tetrahedron Lett., 22, 5221 (1981); c) Y.Naruta, H.Uno, and K.Maruyama, J. Chem. Soc., Chem. Commun., 1981, 1277; d) T.Kometani, Y.Takeuchi, and E.Yoshii, J. Org. Chem., 48, 2311 (1983); e) Y.Naruta, J. Am. Chem. Soc., 102, 3774 (1980); f) Y.Naruta, J. Org. Chem., 45, 4097 (1980); g) L.F.Fieser, J. Am. Chem. Soc., 48, 3201 (1926); h) J.M.Bruce and E.Cutts, J. Chem. Soc., C, 1966, 449.

2) Starting ethylenes (**2**a,e-h) are commercially available. Other ethylenes (**2**b-d) were prepared by the method described in the literature.[7]

3) The ^{1}H-NMR data of typical compounds (δ; in $CDCl_3$); **3**a: 8.08 (2H,m), 7.72 (2H,m), 4.00 (2H,s), 2.36 (3H,s). **3**b: 8.16 (2H,m), 7.80 (2H,m), 4.01 (2H,s), 2.66 (2H,t,J=7 Hz), 1.2-1.9 (4H,m), 0.96 (3H,t,J=7 Hz). **3**c: 8.16 (2H,m), 7.77 (2H,m), 4.00 (2H,s), 2.66 (2H,t,J=7 Hz), 1.2-2.0 (6H,m), 0.96 (3H,br-t, J=7 Hz). **3**d: 8.18 (2H,m), 7.81 (2H,m), 4.01 (2H,s), 2.66 (2H,t,J=7 Hz), 1.1-1.9 (8H,m), 0.92 (3H,br-t,J=7 Hz). **3**e: 8.16 (2H,m), 7.78 (2H,m), 4.08 (2H,s), 2.37 (3H,s). **3**f: 8.11 (2H,m), 7.76 (2H,m), 4.18 (3H,s), 3.78 (2H,s), 2.33 (3H,s).

4) K.Maruyama, S.Tai, and T.Otsuki, Chem. Lett., 1983, 843; K.Maruyama, T.Otsuki, and K.Mitsui, J. Org. Chem., 45, 1424 (1980).

5) Hydrolysis was completely performed by treatment of the reaction mixture with diluted aq. HCl solution after irradiation.

6) Whether the ethylene adducts such as **4** and **9** or the cyclobutane adducts such as **10** and **11** are formed in the photo-reaction depends upon the electronegativity of the starting ethylene. This will be discussed elsewhere in detail.

7) P.F.Hudrlik and A.M.Hudrlik, J. Org. Chem., 38, 4254 (1973).

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