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A NOVEL SYNTHESIS OF β-KETO ALKYLATED 1,4-QUINONE

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Many β-keto alkylated 1,4-quinones were synthesized facilely by photochemical reaction of 2-methyl- or 2-methoxy-1,4-quinones with 2-methoxy- or 2-trimethylsilyloxy-1-alkenes and subsequent oxidation of the photo-products under acidic conditions.

Recently, quinonoid compounds have attracted much attention because of their expected bioactivities. Most important step in the synthetic pathways to these quinones is an introduction of a functionalized alkyl chain into the quinone skeleton.$^{1)}$ Although many studies on allylation$^{1a-g)}$ and acylation$^{1f-h)}$ of quinones have been done, β-keto alkylation of quinones has never been investigated so far. Previously, we reported a facile synthetic method of 2-(2-alkanonyl)-3-halogeno-1,4-naphthoquinones.$^{2)}$ Here we wish to report a novel method for introducing a β-keto alkyl chain into 2-methyl- and 2-methoxy-1,4-quinones.

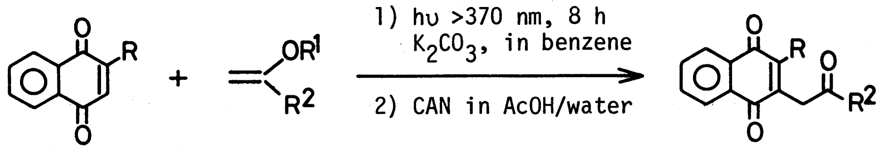
Typically, a benzene solution (25 ml) of 2-methyl-1,4-naphthoquinone (1a; 1 mmol) and isopropenyl methyl ether (2a; 2 mmol)$^{4a)}$ was irradiated (>370 nm) with a high pressure Hg lamp (300 W) through a Toshiba UV-39 glass filter in the presence of potassium carbonate (0.5 mmol) at room temperature for 8 h.$^{3a)}$ The reaction mixture was filtered and the filtrate was concentrated in vacuo. The residue was treated with cerium(IV) ammonium nitrate (CAN; 2 mmol) in aqueous acetic acid (acetic acid / water = 20 ml / 10 ml) overnight. After usual work-up of the reaction mixture followed by column chromatography on silica gel, a product (3a) was isolated. The structure of this product (3a) was assigned to 2-methyl-3-(2-propanonyl)-1,4-naphthoquinone by its physical data as follows: yellow needles (from hexane-chloroform), mp 132.5-133.5 °C. ^{1}H-NMR ($CDCl_3$): δ 8.03 (2H, m), 7.67 (2H, m), 3.82 (2H, s), 2.33 (3H, s), 2.13 (3H, s). IR(KBr): 1710, 1660, 1300, 1170, 710 cm^{-1}. MS: m/e=228 (M^+). Found 228.0769. Calcd for $C_{14}H_{12}O_3$: M, 228.0786.[3b)]

Similarly, other 2-methoxy-1-alkenes (2b-d)[4b)] gave the corresponding 2-(2-alkanonyl)-3-methyl-1,4-naphthoquinones (3b-d)[5)] in the reaction with 2-methyl-1,4-naphthoquinone (1a). Furthermore, 2-trimethylsilyloxy-1-alkenes (2e-k)[4c)] were also reactive for the reaction with 1a to afford successfully the corresponding 2-(2-alkanonyl)-3-methyl-1,4-naphthoquinones (3b-h).[5)] The results are summarized in Table 1.

Other 1,4-quinones such as 2-methoxy-1,4-naphthoquinone (1b) and 2-methyl-1,4-benzoquinones (4a-d) were applicable to the present reaction with isopropenyl methyl ether (2a) (Table 1 and Table 2). Many β-keto alkylated 1,4-quinones such as 2-methoxy-3-(2-propanonyl)-1,4-naphthoquinone (3i) and 2-methyl-3-(2-propanonyl)-1,4-benzoquinones (5a-d) were obtained.

Thus, the present reaction provides us a novel method of wide applicability for introducing a β-keto alkyl chain into 1,4-quinones.

Table 1. Syntheses of 2-methyl- and 2-methoxy-3-(2-alkanoyl)-1,4-naphthoquinones

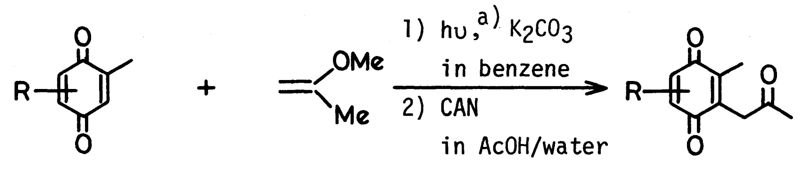


1 2 3

Quinone	Ethylene	Quinone conversion	Product (Yield/%)[a)]
1a; R=Me	2a; R^1=R^2=Me	84%	3a; R=R^2=Me (75)
1a	2b; R^1=Me,R^2=n-C_4H_9	65%	3b; R=Me,R^2=n-C_4H_9 (66)
1a	2c; R^1=Me,R^2=n-C_5H_{11}	68%	3c; R=Me,R^2=n-C_5H_{11} (65)
1a	2d; R^1=Me,R^2=n-C_6H_{13}	70%	3d; R=Me,R^2=n-C_6H_{13} (76)
1a	2e; R^1=$SiMe_3$,R^2=C_2H_5	60%	3e; R=Me,R^2=C_2H_5 (48)
1a	2f; R^1=$SiMe_3$,R^2=n-C_3H_7	59%	3f; R=Me,R^2=n-C_3H_7 (44)
1a	2g; R^1=$SiMe_3$,R^2=n-C_4H_9	57%	3b (47)
1a	2h; R^1=$SiMe_3$,R^2=n-C_5H_{11}	66%	3c (45)
1a	2i; R^1=$SiMe_3$,R^2=n-C_6H_{13}	56%	3d (54)
1a	2j; R^1=$SiMe_3$,R^2=iso-C_3H_7	57%	3g; R=Me,R^2=iso-C_3H_7 (46)
1a	2k; R^1=$SiMe_3$,R^2=iso-C_4H_9	51%	3h; R=Me,R^2=iso-C_4H_9 (43)
1b; R=OMe	2a	82%	3i; R=OMe,R^2=Me (70)

a) Isolated yield based on starting quinone consumed.

Table 2. Syntheses of 2-methyl-3-(2-propanonyl)-1,4-benzoquinones



4 2a 5

Quinone	quinone conversion (Irradiation time)		Product (Yield/%)b)
4a; R=H	98%	(5 h)	5a; R=H (27)
4b; R=5-Me	96%	(3.5 h)	5b; R=5-Me (55)
4c; R=6-Me	93%	(6 h)	5c; R=6-Me (59)
4d; R=5,6-Me_2	93%	(2 h)	5d; R=5,6-Me_2 (40)

a) Irradiated by high pressure Hg lamp without using the UV-39 glass filter.

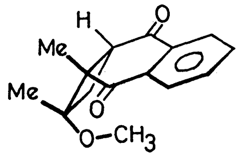
b) Isolated yield based on starting quinone consumed.

References

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

2) K. Maruyama, T. Otsuki, and S. Tai, Chem. Lett., 1984, 371.

3) a) The photochemical reaction of 1a with 2a produced primarily a cyclobutane adduct (6) as a major product6) via photochemical [π2s+π2s] cycloaddition. When irradiation was carried out directly with a high pressure Hg lamp without using the glass filter, another product (7) was formed accompanying with 6. The product (7) would be understood to result from an intramolecular hydrogen abstraction reaction of 6 in the excited state. When the photoreaction was performed in the absence of K_2CO_3, other products (3a, 8, and 9) were formed instead of 6. b) The cyclobutane adduct (6) was treated with acetic acid under atmospheric conditions to yield 9 and 3a. Thus, a possible reaction pathway was depicted in Scheme 1.



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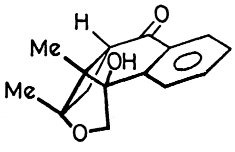

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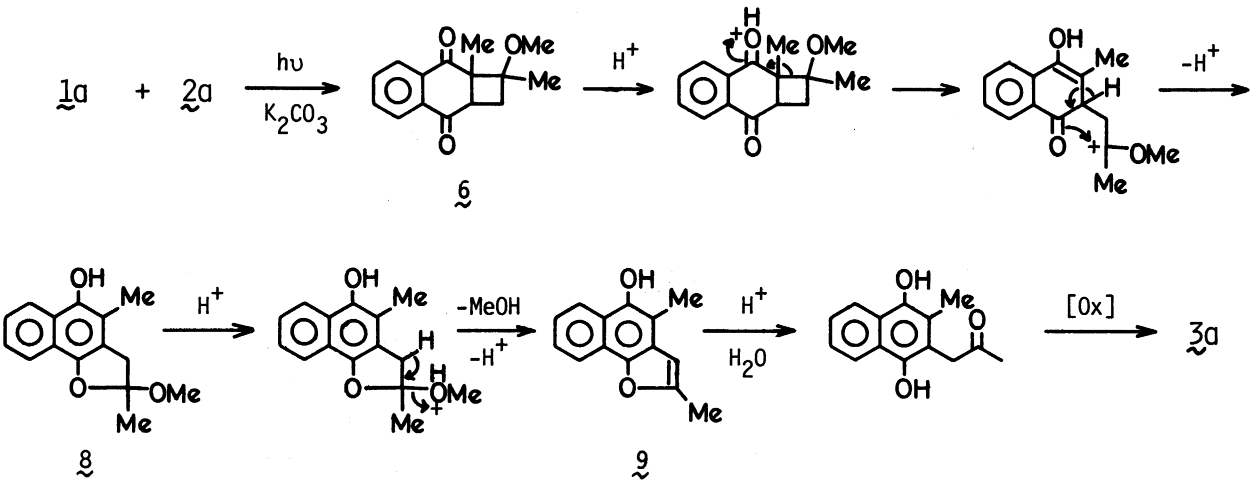

Scheme 1. Possible reaction pathway.

4) a) Ethylene (2a) is commercially available. b) Ethylenes (2b-d) were prepared by the method described in the literature: P. F. Hudrlik and A. M. Hudrlik, J. Org. Chem., 38, 4254 (1973). c) Ethylenes (2e-k) were synthesized by the method described in the literature: H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, J. Org. Chem., 34, 2324 (1969).

5) ^{1}H-NMR data of typical compounds ; δ (in $CDCl_3$): 3b: 8.08 (2H, m), 7.72 (2H, m), 3.82 (2H, s), 2.64 (2H, t, J=7 Hz), 2.15 (3H, s), 1.1-1.9 (4H, m), 0.94 (3H, t, J=7 Hz). 3c: 8.06 (2H, m), 7.70 (2H, m), 3.80 (2H, s), 2.62 (2H, t, J=7 Hz), 2.14 (3H, s), 1.1-1.9 (6H, m), 0.91 (3H, br-t, J=7 Hz). 3d: 8.08 (2H, m), 7.71 (2H, m), 3.82 (2H, s), 2.63 (2H, t, J=7 Hz), 2.14 (3H, s), 1.1-1.9 (8H, m), 0.91 (3H, br-t, J=7 Hz). 3e: 8.12 (2H, m), 7.76 (2H, m), 3.85 (2H, s), 2.68 (2H, q, J=7 Hz), 2.16 (3H, s), 1.13 (3H, t, J=7 Hz). 3f: 8.06 (2H, m), 7.70 (2H, m), 3.81 (2H, s), 2.62 (2H, t, J=7 Hz), 2.15 (3H, s), 1.68 (2H, sextet, J=7 Hz), 0.97 (3H, t, J=7 Hz). 3g: 8.12 (2H, m), 7.76 (2H, m), 3.92 (2H, s), 2.89 (1H, septet, J=7 Hz), 2.15 (3H, s), 1.24 (6H, d, J=7 Hz). 3h: 8.06 (2H, m), 7.69 (2H, m), 3.79 (2H, s), 2.49 (2H, d, J=7 Hz), 2.21 (1H, nonet, J=7 Hz), 2.13 (3H, s), 0.98 (6H, d, J=7 Hz).

6) The regio- and stereoselectivities of the cycloaddition reaction were explained by taking into consideration the frontier orbital interaction between 1a and 2a.[7)]

7) M. D. Rozeboom, I. -M. Tegmo-Larsson, and K. N. Houk, J. Org. Chem., 46, 2338 (1981); G. Desimoni and G. Tacconi, Chem. Rev., 75, 651 (1975).

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