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A NEW ROUTE TO 3-ALKYL-2,5-DI-t-BUTYL-2,4-CYCLOPENTADIENONES FROM 4-ALKYL-2,6-DI-t-BUTYLPHENOLS[1]

A. Nishinaga,* K. Nakamura, and T. Matsuura

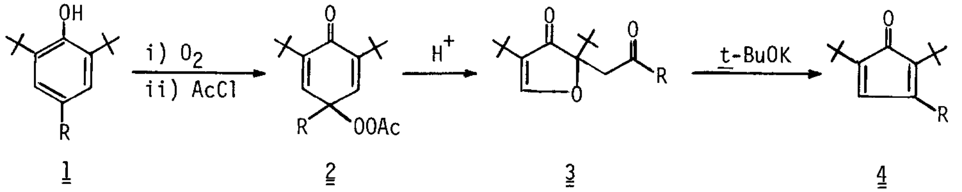
Department of Synthetic Chemistry, Faculty of Engineering,
Kyoto University, Kyoto, Japan

Base-catalyzed reaction of 5-acylmethyl-2,5-di-t-butyl-4-oxa-2-cyclopentenones selectively derived from 4-alkyl-2,6-di-t-butylphenols via three steps involving oxygenation, acetylation, and acid-treatment gave 3-alkyl-2,5-di-t-butyl-2,4-cyclopentadienones in excellent yield.

Previously, we have reported a one-step method for the synthesis of 3-substituted 2,5-di-t-butyl-2,4-cyclopentadienones involving t-BuOK-catalyzed oxygenation of 4-aryl-2,6-di-t-butyl- and 2,4,6-tri-t-butyl- phenols in t-BuOH at 70 °C.[2,3] This method is based on characteristic reactivity of these phenols that under the reaction conditions they are oxygenated selectively at the ortho position affording epoxy-o-quinols, which undergo base-catalyzed intramolecular decomposition to give the cyclopentadienones.[4] The method is, therefore, invalid for other 4-alkyl-2,6-di-t-butylphenols, because they are always oxygenated only at the para position to give peroxy-p-quinols or epoxy-p-quinols[5] which give different products from cyclopentadienones by base-catalyzed reaction.[6]

We now find that base-catalyzed reaction of 5-acylmethyl-2,5-di-t-butyl-4-oxa-2-cyclopentenones 3 gives 3-alkyl-2,5-di-t-butyl-2,4-cyclopentadienones 4 in excellent yield. Since cyclopentenones 3 are readily obtained by acid-treatment of peroxy-p-quinol acetates 2,[7] the present method provides a new effective route to 3-alkyl-2,5-di-t-butyl-2,4-cyclopentadienones from 4-alkyl-2,6-di-t-butylphenols.

A solution of equimolar amounts of 3 and t-BuOK in t-BuOH was heated at 70 °C under nitrogen atmosphere until the reaction was completed. The reaction time required was dependent on the nature of the substituent R in 3 (Table 1). Chromatographic separation (silica gel) of the reac-



a; R = Me b; R = Et c; R = n-Pr d; R = i-Pr e; R = cyclo-C_5H_9

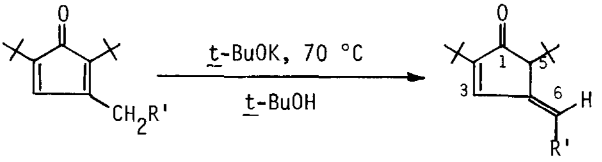
Table 1. Formation of Cyclopentadienones 4 from Base-catalyzed Reaction of 3.[a]

4	Reaction Time[b] (min)	Yield (%)	M.p.(B.p.)[c] (°C)/mmHg	IR(Nujol) ν_{CO} (cm^{-1})	UV(EtOH) $\lambda_{max}(\varepsilon)$ (nm)	^{1}HNMR($CDCl_3$), δ (ppm) t-Bu	R	C=CH
4a	40	69[d]	(85-86)/2	1700	416(410)	1.13, 1.22	2.03[f]	6.13[m]
4b	30	96	(78-80)/2	1710	416(414)	1.14, 1.23	1.09[g] 2.44[h]	6.26[n]
4c	30	91[d]	(142-143)/2	1700	416(446)	1.14, 1.22	0.99[i] 1.42, 2.41[l]	6.22[n]
4d	150	81	65-66	1710[e]	416(475)	1.14, 1.23	0.97[j] 1.88[k]	6.24[n]
4e	150	91	47-49	1710[e]	416(483)	1.13, 1.24	1.4-1.9[l] 3.3-3.7[l]	6.37[n]

[a] A solution of 3 (0.4 mmol) in t-BuOH (8 ml) containing t-BuOK (0.4 mmol) was heated at 70 °C under N_2. The mixture was poured into an ice-cooled aqueous NH_4Cl solution and extracted with pentane. The product 4 was isolated by silica gel chromatography and purified by distillation. [b] Required for completion of the reaction. [c] Distilled at a reduced pressure (2mm Hg) and satisfactory analytical data were obtained: C, ±0.3%; H, ±0.27%. [d] Isomeric products 5a and 5c were also obtained in 24% and 7% yield, respectively. [e] Nujol paste. [f] d, J = 0.5 Hz. [g] t, J = 7.7 Hz [h] q, J = 7.7 Hz. [i] t, J = 7.5 Hz. [j] d, J = 6.5 Hz. [k] sep, J = 6.5 Hz. [l] m. [m] q, J = 0.5 Hz. [n] broad s.

tion mixture gave cyclopentadienones 4 as orange-red liquids, among which 4d and 4e were crystallized. Analytical and spectral data of 4 (Table 1) are in good agreement with the structure.

In the reaction of 3a and 3c, isomeric products 5a and 5c were also obtained in 24% and 7% yield, respectively. The products 5 should result from further reaction of 4 with the base. Actually, when 4a-c were treated with t-BuOK in t-BuOH at 70 °C under nitrogen atmosphere, 5a-c[8] were obtained quantitatively. Thus, with an excess of the base the reaction of 3 resulted in the predominant formation of 5, except for the cases with 3d and 3e where no isomerization of 4 took



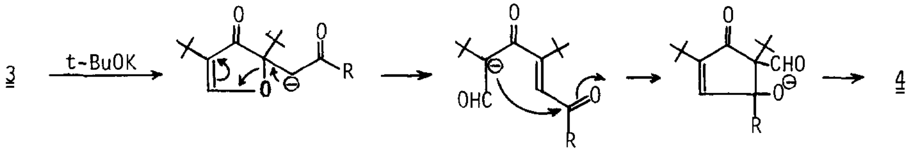
4

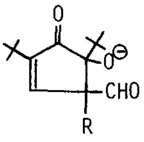
5

a; R' = H b; R' = Me c; R' = Et

place. These observations indicate that cyclopentadienones 4 having a methyl or methylene group adjacent to the ring at the 3-position are unstable in the presence of a strong base such as *t*-BuOK, whereas those with a methine group such as 3d and 3e are stable because the isomerization of the latter compounds is sterically hindered. This is implicated in the fact that the base-catalyzed isomerization of 4b and 4c gives only 5b and 5c but not the other stereo isomer around the *exo*-double bond.

A reasonble mechanism for the formation of 4 involves deprotonation from the methylene group in 3 followed by rearrangement initiated by the resulting carbanion leading to an intermediate 6 as depicted in the following scheme. Interestingly, the intermediate 6 is analogous to the in-





6

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termediate 7 (R = substituted phenyl) confirmed for the formation of 4 (R = substituted phenyl) in the base-catalyzed oxygenation of phenols 1 (R = substituted phenyl).[4] Attempts to isolate 6 were, however, unsuccessful.

The base-catalyzed reaction of 3 depended on the nature of solvent and reaction temperature. In N,N-dimethylformamide, even with an equimolar amount of *t*-BuOK, only 5a was obtained (70 °C, 10 min; yield, 99%). In ethanol or tetrahydrofuran, a complicated mixture including small amounts of 4a and 5a was obtained. At a low temperature, the *t*-BuOK catalyzed reaction of 3 resulted in the quantitative formation of bicyclo[3.2.1]-8-oxa-octane-3,6-dione derivatives formed by the Michael addition of a carbanion generated at the acyl group -COR to the enone system in 3, which will be published elsewhere. The different product formation dependent on the reaction temperature indicates that deprotonation occurs on both sides of the carbonyl group of the acylmethyl group in **3** and that the base-catalyzed ring opening of **3** is the rate determining step in the formation of **4**.

References and Notes

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8) **5a**: colorless liquid, b.p. 81-83 °C/5 mm Hg; IR(Film), 1710 cm^{-1}; UV(EtOH), λ_{max} 272 nm (log ε, 4.01); ^{1}HNMR(CDCl$_3$), δ 0.99 (s, 9H), 1.21 (s, 9H), 7.32 (d,d, 1H, J = 0.8, 0.6 Hz), 2.48 (d,d, 1H, J = 0.8, 0.5 Hz), 5.11 (d,d,d, 1H, J = 1.0, 0.8, 0.8 Hz), 5.30 (d,d,d, 1H, J = 1.0, 0.6, 0.5 Hz).

5b: colorless liquid, b.p. 82-84 °C/2 mm Hg; IR(Film), 1700 cm^{-1}; UV(EtOH), λ_{max} 289 nm (log ε, 4.00); ^{1}HNMR(CDCl$_3$), δ 0.96 (s, 9H), 1.22 (s, 9H), 7.64 (d, 1H, J = 1.0 Hz), 2.42 (d, 1H, J = 0.8 Hz), 5.57 (d,d,q, 1H, J = 1.0, 0.8, 7.3 Hz), 1.90 (d, 3H, J = 7.3 Hz).

5c: colorless liquid, b.p. 105-106 °C/2 mm Hg; IR(Film), 1695 cm^{-1}; UV(EtOH), λ_{max} 289 nm log ε, 4.04); ^{1}HNMR(CDCl$_3$), δ 0.96 (s, 9H), 1.22 (s, 9H), 7.61 (d, 1H, J = 1.0 Hz), 2.42 (d, 1H, J = 0.8 Hz), 5.53 (d,d,t, 1H, J = 1.0, 0.8, 7.7 Hz), 0.97 (t, 3H, J = 7.0 Hz), 2.33 (d,q, 2H, J = 7.7, 7.0 Hz). All the compounds **5** gave satisfactory analytical results: C, ±0.27%; H, ±0.25%. The decoupling technique with ^{1}HNMR of **5a** confirmed assignment of the chemical shifts of the olefinic protons and their coupling constants. Thus, the signals at δ = 5.11, 5.30, and 7.32 were reasonably assigned for R'(H), H_6, and H_3, respectively. The coupling constants $J_{H_3-H_6}$, $J_{H_3-R'}$, $J_{H_5-H_6}$, $J_{H_5-R'}$, and $J_{H_6-R'}$ were determined as 0.8, 0.6, 0.8, 0.5, and 1.0 Hz, respectively. Coupling constants $J_{H_3-H_6}$ and $J_{H_5-H_6}$ observed for all the other compounds **5** were 1.0 and 0.8 Hz, respectively. These data are compatible with the structure of **5**.

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