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ACYLATION OF 4-SUBSTITUTED 6-HYDROPEROXY-2,6-DI-t-BUTYL-2,4-CYCLOHEXADIENONES

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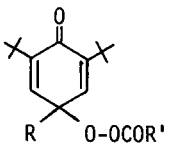
Acylation of 4-aryl-2,6-di-t-butyl- and 2,4,6-tri-t-butyl- 6-hydroperoxy-2,4-cyclohexadienones gave unexpected products, 4-acyloxy-5,6-epoxy-2-cyclohexenones and 2-acyloxy-5,6-epoxy-3-cyclohexenones. The reaction involves a rapid homolysis of the peroxy bond of peroxy esters transiently formed in the pre-existing slow step.

Following our previous interesting observations on the base- and acid- catalyzed reaction of 4-acyldioxy-4-alkyl-2,6-di-t-butyl-2,5-cyclohexadienones (1)[1-3] we have attempted to examine the chemical behavior of isomeric peroxy esters from 4-substituted 6-hydroperoxy-2,6-di-t-butyl-2,4-cyclohexadienones (2). Contrary to the succesful formation of 1 by the Schotten-Baumann acylation of 4-alkyl-4-hydroperoxy-2,6-di-t-butyl-2,5-cyclohexadienones, we now find that the hydroperoxides 2 do not give the corresponding thermally stable peroxy esters but products resulting from cleavage of the peroxy bond under the Schotten-Baumann acylation conditions even at -20 °C.

Reaction of 2[4] with acetyl chloride in pentane in the presence of an equimolar amount of pyridine at 0 °C was complete in 5 h and gave unexpected products, 4-acetoxy-2,6-di-t-butyl-5,6-epoxy-2-cyclohexenones (3) and 2-acetoxy-2,6-di-t-butyl-5,6-epoxy-3-cyclohexenones (4) together with a small amount of unidentified products (Table 1).[7] Similar results were obtained at -20 °C although the reaction took a long time. The products 3a and 3b were identical with authentic samples synthesized by acetylation of 2,4,6-tri-t-butyl-5,6-epoxy-4-hydroxy-2-cyclohexenone (5a)[5] and 2,6-di-t-butyl-5,6-epoxy-4-hydroxy-4-(4-methoxyphenyl)-2-cyclohexenone (5b).[6] Alkaline hydrolysis of 3a and 3b gave 5a and 5b, respectively, in quantitative yield. Spectral and analytical data of 4 were in good agreement with the structures (Table 2). The structures of 4a and 4b were further confirmed by alkaline hydrolysis (the corresponding epoxyols 6[8] were obtained quantitatively) followed by epoxidation with m-chloroperbenzoic acid giving the corresponding diepoxyols 7,[8] which were identical with epoxidation products from epoxy-o-quinols 8.[5,6] Hydroperoxides



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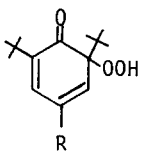
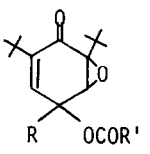


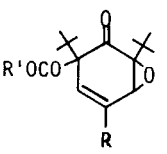
2

a; R = t-Bu
b; R = 4-MeOPh
c; R = 4-MePh
d; R = Ph



3

a; R = t-Bu, R' = Me
b; R = 4-MeOPh, R' = Me
c; R = 4-MePh, R' = Me
d; R = Ph, R' = Me
e; R = R' = t-Bu



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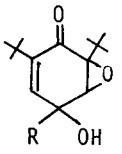

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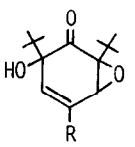
a; R = t-Bu
b; R = 4-MeOPh
c; R = 4-MePh
d; R = Ph

Table 1. Acylation of 2 with Acyl Chloride-Pyridine in Pentane.[a]

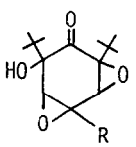
2	Acyl Chloride	Reaction Temp. (°C)	Reaction Time (h)	Conversion (%)	Product, Yield[b] 3	4	Others[c]
2a	MeCOCl	0	5	100	31	50	13
2a	MeCOCl	-20	8	100	21	58	13
2a	MeCOCl	20	5	100	16	35	38
2a	t-BuCOCl	0	5	30	0	60	-[d]
2a	t-BuCOCl	0	42	44	0	77	-[d]
2b	MeCOCl	0	5	100	35	57	8
2c	MeCOCl	0	5	100	24	53	23

[a] A solution of 2 (1 mmol) and acyl chloride (1 mmol) in pentane (5 ml) was added to a solution of pyridine (1 mmol) in pentane (5 ml) in 30 min. [b] Determined by ^{1}H-NMR. [c] Unidentified products containing 3-t-butyl-5-R-o-benzoquinone as judged by ^{1}H-NMR. [d] Not determined.



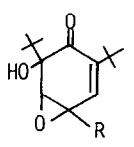
6

a; R = t-Bu
b; R = 4-MeOPh



7

a; R = t-Bu
b; R = 4-MeOPh



8

a; R = t-Bu
b; R = 4-MeOPh

2 are fairly stable in acetic anhydride containing pyridine at room temperature and did not give the corresponding acetates of 2. However, heating of solutions of 2 in the acetic anhydride -pyridine system at 80 °C gave also 3 and 4 (Table 3). Compounds 4 were formed in pref

erence to 3 under the acylation conditions with acyl chloride, but the reverse was found in the reaction of 2b-d with acetic anhydride - pyridine.

Table 2. Physical Data of 4

4	mp (°C)	IR(Nujol) ν_{CO} (cm^{-1})	^{1}H-NMR($CDCl_3$), δ t-Bu	R'	OC-H[b]	C=CH[b]	R
4a	91-93	1730, 1765	1.00, 1.12	2.01	3.63	5.42	1.20
4b	141-143	1730, 1755	1.15, 1.21	2.04	3.86	5.92	3.85,[c] 7.20[d]
4c	97-99	1730, 1755	1.13, 1.20	2.05	3.90	5.97	2.39,[c] 7.35[d]
4d	137-138	1730, 1755	1.12, 1.20	2.03	3.87	5.97	7.40[d]
4e	87-89	1725, 1745	1.03, 1.14	1.21	3.62	5.37	1.21

[a] Isolated by preparative tlc. [b] d, J = 2 Hz. [c] Me group. [d] Ar-H, m

Table 3. Acetylation of 2 by Acetic Anhydride-Pyridine System.[a]

2	Reaction Temp. (°C)	Reaction Time (h)	Conversion (%)	Product, Yield (%)[b] 3	4	Others[c]
2a	25	3	0	-	-	-
2a	80	3	100	14	68	9
2b	80	3	100	61[d]	39	0
2c	80	3	100	53[d]	46	1
2d	80	3	100	73[d]	25	2

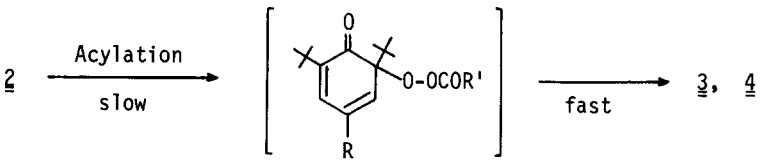
[a] A solution of 2 (3.4 mmol) in acetic anhydride (8 ml) and pyridine (2 ml) was heated. [b] Determined by ^{1}H-NMR. [c] Unidentified products. [d] Chromatographic separation gave only the corresponding epoxyquinols 5.

Detailed mechanism of the present reaction has not been clarified yet. It may be, however, noted that the peroxy bond cleavage does not occur prior to the formation of peroxy ester 9, because neither 5 nor 6 can be acetylated under the reaction conditions and they were not detectable in the reaction mixtures. Furthermore, in the acylation of 2a with pivaloyl chloride, 4e was partly formed and the remainder was recovered almost as 2a even in a long time reaction (Table 1).

From these findings the formation of 3 and 4 from 2 is reasonably considered to involve a rate-determining acylation step and a rapid decomposition of the resulting ester 9. The decomposition of 9 should involve homolysis of the peroxy bond, because heterolysis of the peroxy bond of 2 gives different products.[2,3,10]

Since p-quinoxy radicals from 1 do not form epoxy ring but undergo an expansion of the

dienone ring,[2] the present results provide a novel reaction of quinoxy radicals.



9

Reasons why the peroxy esters 9 are so unstable compared to 1 and why the product ratio (3 to 4) changes depending on the acylation conditions are still obscure.[11] These problems are currently investigated.

References and Notes

1. A. Nishinaga, K. Nakamura, and T. Matsuura, Chem. Lett., 303 (1977).
2. A. Nishinaga, K. Nakamura, and T. Matsuura, Tetrahedron Lett., 3557 (1978).
3. A. Nishinaga, K. Nakamura, T. Matsuura, A. Rieker, D. Koch, Tetrahedron Lett., 3597 (1978).
4. Hydroperoxides 2 were prepared from the corresponding 4-substituted 2,6-di-t-butylphenols.[5,6]
5. A. Nishinaga, T. Itahara, T. Shimizu, and T. Matsuura, J. Am. Chem. Soc., 100, 1820 (1978).
6. A. Nishinaga, T. Itahara, T. Matsuura, A. Rieker, D. Koch, K. Albert, and P. B. Hitchkock, J. Am. Chem. Soc., 100, 1826 (1978).
7. Following the reaction with 2a by ^{1}H-NMR spectroscopy at 0 °C, signals corresponding to 9 were temporarily observed.
8. Analytical and spectral data for 6 and 7 are in good agreement with the structures.
9. A. Nishinaga, K. Nishizawa, H. Tomita, and T. Matsuura, Synthesis, 270 (1977).
10. It is rather suspicious to consider o-quinolate anion or o-quinol intermediate because it undergoes always de-t-butylation or an acyloin rearrangement to give catechol derivatives.[6,12]
11. Heating of 4b in acetic anhydride - pyridine at 80 °C for 3 h resulted in the conversion of 4b to 3b in 14%, but this does not explain fully the results given in Tables 1 and 3.
12. o-Quinols derived from 2b by reduction with Me_2S gives 3,6-di-t-butyl-4-(4-methoxyphenyl)-catechol resulting from an acyloin rearrangement[13] in basic medium: A. Nishinaga, T. Shimizu, and T. Matsuura, J. Org. Chem., submitted.
13. A. Nishinaga, T. Itahara, T. Matsuura, S. Berger, G. Henes, and A. Rieker, Chem. Ber., 109, 1530 (1976).

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