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A NOVEL BASE-CATALYZED REARRANGEMENT OF p-PEROXYQUINOL ESTERS

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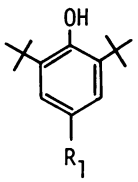
The p-peroxyquinol esters derived from the base-catalyzed oxygenation of 4-alkyl-2,6-di-t-butylphenols (alkyl=R_1) followed by the Schotten-Baumann acylation (R_2COCl) undergo a novel base-catalyzed rearrangement with t-BuOK in DMF to give p-quinoxyacetic acid derivatives in excellent yields. A mechanism involving the initiation by the homolysis of O-O bond is discussed.

The reactions of peroxy esters with bases have been demonstrated so far to result in the fragmentation through the ionic cleavage of the peroxy bond either by the direct attack of bases on the peroxy bond[1-4] or by the deprotonation at α-position to the peroxy group followed by a concerted ionic decomposition.[5] Hydroxy anion attacks the carbonyl group of peroxy esters leading to hydrolysis.[6] We report here a novel base-catalyzed rearrangement of peroxy esters (3) derived from 4-alkyl-2,6-di-t-butylphenols (1) to give p-quinoxyacetic acid derivatives (4) in excellent yields.

The Schotten-Baumann acylation of p-peroxyquinols (2) derived from the base-catalyzed oxygenation of 1[7] gives peroxy esters 3 in quantitative yields (Table 1). The peroxy esters obtained



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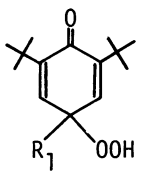

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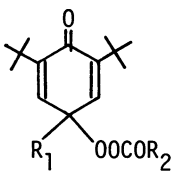

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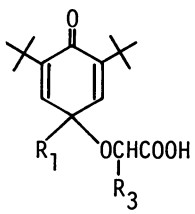

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	a	b	c	d	e	f	g	h
R_1	Me	Et	i-Pr	t-Bu	Me	Me	Me	Me
R_2	Me	Me	Me	Me	Et	CH_2Ph	i-Pr	Ph
R_3	H	H	H	H	Me	Ph	-	-

except 3b, 3f, and 3h are not crystalline but tlc and NMR spectra of these esters showed the quantitative formation of 3. The resulting solution after filtration of pyridine hydrochloride formed can normally be utilized for the next reaction step without further purification of 3.

Table 1. Physical Data of Peroxyquinol Esters (3)[a]

3	Mp (°C)	IR(Nujol) (cm^{-1})	NMR(CCl_4), δ(ppm) t-Bu	R_1	R_2	C=CH	Elemental Analysis	C(%)	H(%)
3a	bp. 105°/5mm	1780, 1630	1.22	1.43	1.83	6.49	Calc.	69.36	8.90
							Found	69.28	8.90
3b	46-48	1780, 1630	1.23	0.84(t)[b] 1.78(q)	1.84	6.41	Calc.	70.10	9.15
							Found	69.84	9.41
3c		1790, 1640	1.22	0.91(d)[b] 2.04(s)	1.81	6.50			
3d		1800, 1665	1.21	1.03	1.84	6.64			
3e		1790, 1650	1.24	1.44	1.08(t)[b] 2.09(q)	6.49			
3f	88-90	1785, 1645	1.17	1.41	3.39	6.48	Calc.	74.56	8.16
							Found	74.39	8.18
3g		1780, 1645	1.21	1.43	1.08(d)[b] 2.29(s)	6.55			
3h	121-123	1760, 1640	1.16	1.52	7.5	6.57	Calc.	74.13	7.92
							Found	74.37	8.10

[a]The acylation of 2 was carried out by addition of acyl chloride into a solution of 2 (4 mmol) and pyridine (4 mmol) in petroleum ether at 0°C. [b]J = 7.5 Hz.

The base-catalyzed rearrangement of 3 was carried out in the following manner: a solution of 3 (4 mmol) in petroleum ether (15 ml) was added to a stirred and cooled (-60 °C) solution of t-BuOK in dimethyl formamide (15 ml). After 2 h the reaction mixture was acidified (dil. HCl) and extracted with ether to give the migrated products 4 in crystalline forms. The results are summarized in Table 2.

Table 2. The Base-Catalyzed Rearrangement of 3 to 4.

4	Yield[a] (%)	Mp[b] (°C)	IR(Nujol) (cm^{-1})	NMR(CCl_4), δ(ppm) t-Bu	R_1	R_2	C=CH	λ_{max}(EtOH) nm (log ε)
4a	81	84-86	1730, 1650	1.22	1.45	3.79	6.43	235(4.53)
4b	92	93-95	1725, 1650	1.20	0.77(t)[c] 1.79(q)	3.82	6.35	
4c	94	94-96	1720, 1660	1.23	0.93(d)[c] 2.04(s)	3.94	6.47	
4d	53	110-112	1725, 1645	1.22	0.91	3.84	6.51	
4e	38	75-77	1720, 1660	1.13 1.21	1.39	1.28(d)[c] 3.66(q)	6.26(d)[d] 6.47(d)	235(4.52)
4f	34	114-116	1725, 1660	1.08 1.17	1.46	4.52(CH) 7.30(Ar)	6.13(d)[d] 6.53(d)	234(4.52)

[a]Yields were determined by NMR analysis. [b]The elemental analyses were in satisfactory agreement with theoretical values. [c]J = 7.5 Hz. [d]J = 3.0 Hz.

Elemental analyses and spectral data (Table 2) are in good agreement with the structure 4. The UV spectra of 4a, 4e, and 4f are quite similar to each other indicating that the same p-quinoid

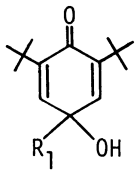
chromophore[8] exists in these products. Furthermore, the reduction of 4a and 4f with Zn/HCl in ethanol gave 1a and 1f nearly quantitatively.[9] Ethyl mandelate[11] was also isolated from the reduction of 4f in 70% yield. Methylation of 4a with diazomethane afforded the corresponding ester, mp 93-95°; NMR($CDCl_3$), δ 1.22 (t-Bu), 1.49 (Me), 3.76 (COOMe), 3.88 (CH_2), and 6.48 (C=CH); Anal. Calcd: for $C_{18}H_{28}O_4$, C 70.10, H 9.15; Found: C 70.30, H 9.15. From these results, the structure 4 is reasonably assigned. The ^1H NMR spectra of 4e and 4f show two signals for nonequivalent t-butyl groups and a pair of doublets (J = 3.0 Hz) in the olefinic region. This unexpected NMR spectrum may be attributed to an asymmetric interaction of these protons with the migrated group.

The rearrangement of 3 to 4 is affected by bulkiness of the groups R_1 and R_2 and by the nature of the base used. The strong steric interaction between R_1 and R_2 and the strong nucleophilicity of the base are unfavorable to the rearrangement (Table 3). No reaction takes place with amines (pyridine and diethylamine) or with sodium hydride.

Table 3. Effects of Substituents and Bases on the Base-Catalyzed Reaction of 3.

3	Base	Product, Yield (%)[a] 1	2	4	5	Others
3d	t-BuOK	2	-	53	15(5b)	17[b]
3e	t-BuOK	9	-	38	35(5a)	
3f	t-BuOK	7	-	34	-	13 (Unknown)
3g	t-BuOK	-	-	0	77(5a)	22 (Unknown)
3h	t-BuOK	54	12	0	-	32 ($PhCOOBu^t$ + PhCOOH)
3a	MeONa	21	-	19	60(5a)	

[a]Yields were determined by NMR analysis. [b]2,6-Di-t-butyl-p-benzoquinone.



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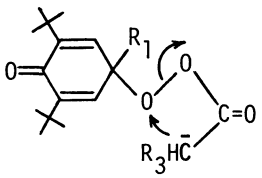
a; R_1 = Me, b; R_1 = t-Bu



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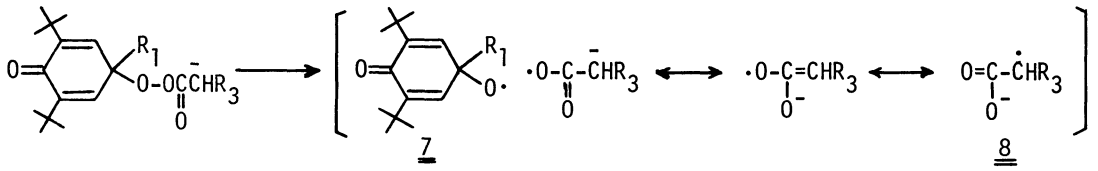
On the basis of the knowledge on the reactivity of peroxy esters towards bases,[1-5] an intramolecular concerted ionic mechanism (6) may be suggested for the rearrangement of 3 to 4, an alternative mechanism involving homolysis of the peroxy bond of 3 where the acyloxy radical moiety would give a carbon radical (8) by the resonance through enolic form is also probable.[12] The recombination of quinoxy radical (7) with the resulting carbon radical (8) in the cage can give the

migrated product (4). The substituent effect on the rearrangement can be interpreted by a steric repulsion between R_1 and R_3 in 6 (ionic mechanism) or in 7 and 8 (radical mechanism). In case of 3d, quinol (5b) and 2,6-di-t-butylbenzoquinone was obtained besides 4d. The larger steric interaction between R_1 and R_3 results in the increase of the formation of quinol 5 (compare the case of 3e with that of 3g)(Table 3). Since these quinols and the benzoqinone are considered to be formed from the



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quinoxy radical (7) which can abstract hydrogen from the environment,[13] the results may be better illustrated by the latter mechanism. The formation of phenols (1) is resulted from the liberation of O_2 from the peroxy anion[7] formed by the nucleophilic attack of the bases on the carbonyl group. The reaction of 3 with the bases, therefore,involves the competition between the nucleophilic addition of the bases to the carbonyl group in 3 and the deprotonation from the α-carbon of R_2. Since the nucleophilicity of methoxide anion is large, the deprotonation is preceded by the nucleophilic addition in the reaction with methoxide resulting in the predominant formation of 1 and 5. The decomposition path of the base addition intermediate giving rise to the formation of 1 or the cleavage of the peroxy bond depends on the stability of the intermediate, where sterically hindered intermediate may be expected to undergo rapid decomposition to form 1. Thus, 3h gives mainly 1a and t-butyl benzoate and the reaction of 3a with methoxide gives 5a as the main product (Table 3).

Since the peroxy esters 3 are thermally stable (even at 70°C),[14] the present results provide an interesting information that,if the group R_2 in 3 is negatively charged,the peroxy bond becomes quite susceptible to the homolysis even at -60°C.

References and Notes

1. R. E. Ball, J. O. Edwards, M. L. Haggett, and P. Jones, J. Am. Chem. Soc., 89, 2331 (1967).
2. E. Koukek and J. E. Welson, J. Org. Chem., 33, 445 (1968).
3. S. -O. Lawesson and N. C. Yang, J. Am. Chem. Soc., 81, 4231 (1959).
4. S. -O. Lawesson, C. Friesell, D. Z. Denney, and D. B. Denney, Tetrahedron, 19, 1229 (1963).
5. R. E. Pincock, J. Am. Chem. Soc., 86, 1820 (1964).
6. V. L. Anonovoski, M. M. Buzlanova, and Z. S. Frolova, Kinet. Katal., 8, 671 (1967).
7. A. Nishinaga, T. Itahara, and T. Matsuura, Chem. Lett., 667 (1974).
8. A. Rieker, W. Rundel, and H. Kessler, Z. Naturforsch., 24b, 547 (1969).
9. The reduction is analogous to that of p-quinols giving rise to the corresponding phenols reported in a literature.[10]
10. A. Rieker and K. Scheffler, Liebigs Ann. Chem., 689, 73 (1965).
11. F. Adickes, J. Prakt. Chem., 150, 81 (1938). The product was identified with that obtained by heating mandelic acid with conc. HCl in ethanol.
12. T. Koenig and R. Wielesek, J. Am. Chem. Soc., 91, 2551 (1969).
13. A. Nishinaga, K. Watanabe, and T. Matsuura, Tetrahedron Lett., 1921 (1974).
14. Compound 3a is stable under the distillation conditions (Table 1).

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