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REACTION OF PEROXY-p-QUINOL ACETATES WITH TRIFLUOROACETIC ANHYDRIDE. FORMATION OF NEW OXEPINONE DERIVATIVES.[1]

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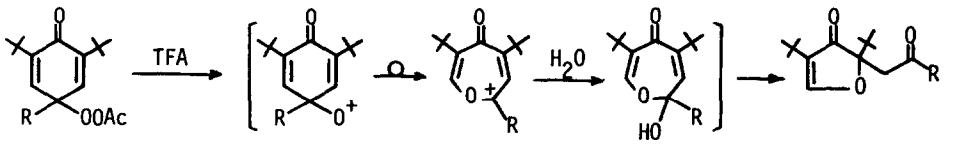
The reaction of peroxy-p-quinol acetates derived from 4-R-2,6-di-t-butylphenols (R = Me, Et, n-Pr, s-Bu) with trifluoroacetic anhydride gives the corresponding 2-trifluoroacetylmethylidene-5-oxepinone derivatives. A favoured mechanism involves efficient conversion of a quinoxy cation intermediate primarily formed into an oxepinone derivative to which a trifluoroacetyl group is incorporated.

The acid- and base-catalyzed reactions of peroxy esters derived from 4-substituted 2,6-di-t-butylphenols have provided new findings in the organic peroxide chemistry.[2-4] The trifluoroacetic acid-catalyzed reaction of peroxy-p-quinol acetates (1), easily available from the oxygenation of 4-alkyl-2,6-di-t-butylphenols followed by acetylation, has been shown to give 4-oxa-2-pentenone derivatives (4).[4] An oxepinium cation intermediate (3) resulting from the ring expansion of the quinoxy cation (2) primarily formed has been postulated for this reaction.



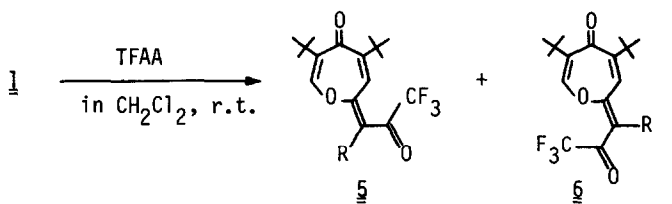
1 2 3 4

a; R = Me b; R = Et

c; R = n-Pr d; R = s-Bu

It is now found that oxepinone derivatives of type 5 are actually formed in good yield when the peroxy acetates 1a-d are treated with trifluoroacetic anhydride, providing a new oxepinone system.

The treatment of 1a with trifluoroacetic anhydride (TFAA) in CH_2Cl_2 at room temperature for 24 h gave a mixture of oxepinone derivatives in which a trifluoroacetyl group is incorporated, 5a,[5] mp 65-66 °C (71% yield) and its geometrical isomer 6a; liquid (29% yield), which were isolated by TLC. The analytical and spectral data of these products (Table 1) are in good agreement with the structures. The compound 6a is exclusively converted into 5a by heating, indicating



a; R = H b; R = Me c; R = Et d; R = i-Pr

that 5a is a stable form. The instability of 6a is probably due to an electronic repulsion between the CF_3CO group and the lone pair electrons of ring oxygen. The reduction of 5a and/or a mixture of 5a and 6a with Zn/HCl in ethanol gave 2,6-di-t-butyl-4-trifluoroacetylmethylphenol (7)[5]

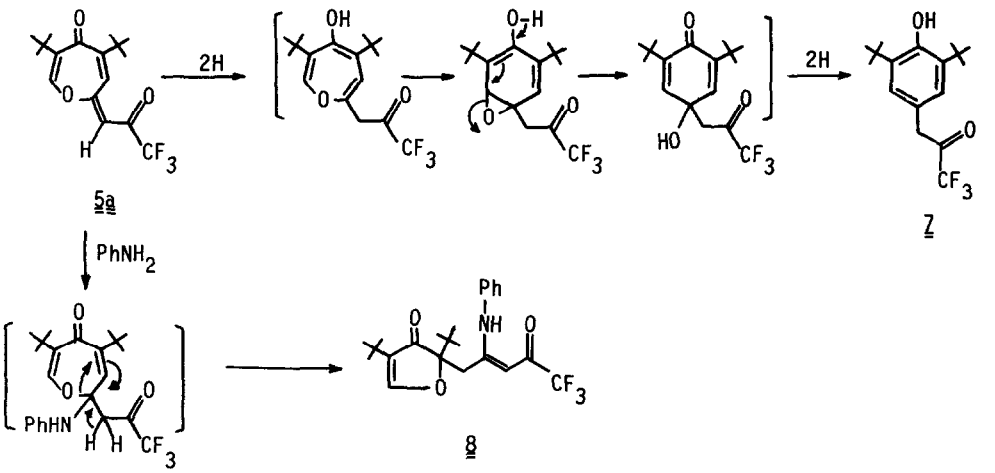
Table 1. ^{1}H NMR Data of the Oxepinone Derivatives 5, 6 and 10.[a]

Oxepinone	t-Bu	t-Bu	R	O=C-C=C-H	C=CH-O-
5a	1.26	1.35	6.05	7.79	6.73
6a	1.25	1.30	5.82	6.32	6.82
5b	1.26	1.30	2.06[b]	7.30[c]	6.86
5c	1.24	1.28	0.94(t)[d],2.41(q)[d]	7.16	6.86
6c	1.24	1.28	0.97(t)[d],2.52(q)[d]	7.12	6.78
5d	1.20	1.27	1.15(d)[d],2.76(sep)[d]	6.76	6.54
6d	1.18	1.23	1.20(d)[d],3.01(sep)[d]	6.60	6.49
10a	1.44	2.35[e]	6.21[f]	7.83[g]	6.84(s)
10b	1.53	2.03[h]	6.26[f]	7.88[i]	6.74(q)[j]

[a] The assignment is confirmed by decoupling technique with 10. [b] A doublet (J_{H-H}= 0.9 Hz) of quartets(J_{H-F}=2 Hz). [c] q; J=0.9 Hz. [d] Chemical shift values are tentatively assigned. [e] Me group: d,d; J_{Me-H_a}=1.4 Hz, J_{Me-H_b}=0.4 Hz. [f] multi. [g] A broad q; J_{Me-H_a}=1.4 Hz. [h] Me group: d; J=1.4 Hz. [i] A broad s. [j] J=1.4 Hz.

resulting quantitatively from a two-step reduction. A favoured mechanism involves conversion of the first reduction product, an oxepin analogue, into an arene oxide[6] which isomerizes to a quinol followed by further reduction to the phenol.[7] When 5a (1 mmol) was heated with aniline (2

mmol) in dioxane (10 ml) under reflux for 4 h, the compound 8,[8] a ring contracted product in which aniline is incorporated, was obtained in quantitative yield. This is analogous to the formation of 4 from 1. The structures 5a and 8 are confirmed by X-ray crystallographic analyses.[9]

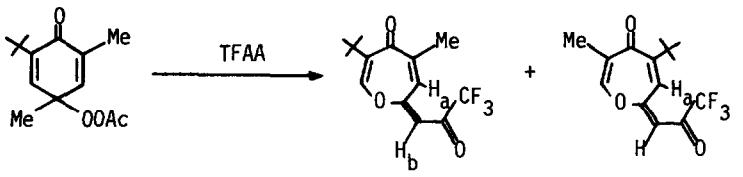


The reaction of 1b-d with TFAA similarly gave the corresponding oxepinone derivatives 5 and 6, whose ^{1}H NMR data are given in Table 1. The products in these cases were separated by TLC and purified by distillation. From 1b only the stable isomer 5b[5] (yellow liquid, 120-121 °C/1 mmHg) was obtained in 78% yield, whereas 1c and 1d gave nearly 1 : 1 mixtures of the corresponding 5 and 6.[10] The fact that the products from 1c and 1d are not converted into a single component by heating indicates that the steric character of the groups R and $COCF_3$ in 5c-d and 6c-d is similar to each other.

The reaction of 9 with TFAA at room temperature followed by distillation of the products gave a 1 : 1 mixture of 10a and 10b (yellow liquid, 100 °C/1 mmHg, 60% yield), which provides conclusive informations for the assignment of ^{1}H NMR data of the present oxepinone derivatives.

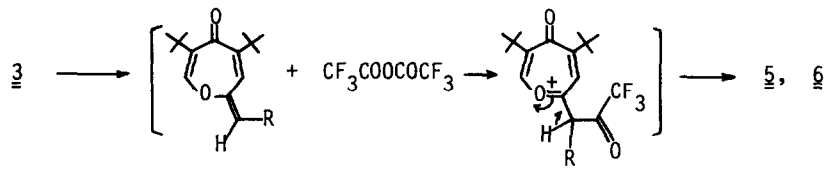
The peroxy acetates 1 (R = t-Bu, i-Pr, $PhCH_2$), upon treating with TFAA, gave only 2,6-di-t-butyl-p-benzoquinone (11), the results being the same as those in the reaction of these acetates with trifluoroacetic acid (TFA).[4] With 1 (R = $PhCH_2$) benzyl trifluoroacetate was isolated quantitatively along with 11. It may be, therefore, concluded that the reaction of 1 with TFAA is catalyzed by TFA formed *in situ* and involves the quinoxy cation intermediate 2.

The mechanism by which the $COCF_3$ group is incorporated into the products should involve a



9 10a 10b

nucleophilic attack by the enol ether part in the oxepinone 12 on the carbonyl group of TFAA. Analogous nucleophilic reactions of enol ethers have been reported.[11]



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References and Notes

(1) Peroxy Esters. V. Part IV, Ref. 2c; Part III, Ref. 4.

(2) (a) A. Nishinaga, K. Nakamura, and T. Matsuura, Chem. Lett., 303 (1977); (b) Tetrahedron Lett., 3557 (1978); (c) ibid., 2165 (1979).

(3) A. Nishinaga, K. Nakamura, T. Matsuura, A. Rieker, and D. Koch, Tetrahedron Lett., 3597 (1978).

(4) A. Nishinaga, K. Nakamura, T. Matsuura, A. Rieker, D. Koch, and R. Griesshammer, Tetrahedron, 35, 2493 (1979).

(5) 5a: C, ± 0.1%; H, ± 0.02%; F, ± 0.08 %. 7: bp, 106-108 °C/1.5 mmHg; IR(Nujol), 3665 (OH), 1765 (CO) cm^{-1}; ^1H NMR($CDCl_3$) δ 1.44 (s, 18 H, t-Bu), 3.90 (s, 2 H, CH_2), 5.19 (s, 1 H, OH), 6.95 (s, 2 H, ArH). 5b: C, ± 0.3%; H, ± 0.2%; F, ± 0.2%.

(6) E. Vogel and H. Gunther, Angew. CHem., 79, 429 (1967).

(7) A. Rieker and K. Scheffler, Liebigs Ann. Chem., 689, 78 (1963).

(8) Colorless prisms; mp, 125-126 °C; IR(Nujol) 3100 (NH), 1710 (CO) cm^{-1}; ^1H NMR($CDCl_3$) δ 0.75 (s, t-Bu), 1.17 (s, t-Bu), 2.95 (q, CH_2, J = 13 Hz), 5.38 (s, C=CH), 7.03-7.5 (Ar), 7.83 (s, C=CH-O-).

(9) A. Nishinaga, K. Nakamura, K. Hirotsu, and T. Matsuura, to be published.

(10) The TLC separation of the products from 1c gave a 1 : 1 mixture of 5c and 6c (61% yield) and the benzoquinone 11 (11% yield) and from 1d a 1 : 1 mixture of 5d and 6d (41% yield) and 11 (4% yield). For purification the mixture of 5c and 6c was distilled at 115 °C/3 mmHg and of 5d and 6d at 115 °C/3 mmHg. Attempts to isolate each component from the mixtures of 5c-d and 6c-d were not successful but the structures of these products are clearly distinguishable from their characteristic NMR signals.

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