The Cleavage of Ethers by Mixed Sulfonic–Carboxylic Anhydrides

Sir:

Mixed sulfonic–carboxylic anhydrides, first reported by Baroni[1] and recently made available by an improved method due to Overberger and Sarlo,[2] have received surprisingly little attention[3] in spite of their potential use, pointed out by the latter workers,[2] as active acylating agents.

As the first part of a program to examine the potentialities of mixed sulfonic–carboxylic anhydrides it has been found that a wide variety of aliphatic ethers, both simple and mixed, cyclic and noncyclic, undergo facile cleavage by these reagents. The yields obtained are high, particularly in cases where cleavage by more well-known reagents gives poor results. Catalysis by added Lewis acids is unnecessary, cleavage of the most unreactive ethers occurring after a few hours at reflux in acetonitrile. Furthermore, cleavage of unsymmetrical ethers occurs with a far higher specificity than with other reagents. The results obtained for some representative ethers are shown in Table I. The structures of the products were established by analysis and infrared and nmr spectroscopy.

acetic anhydride at 70° under high vacuum, gave the required mixed anhydride.

The product, containing 0–10% p-toluenesulfonic acid and 5–20% p-toluenesulfonic anhydride (whose proportion depended upon the reaction temperature[3b]), could be used without further purification. All other mixed anhydrides used could be prepared in like manner.

The advantage of this method of ether cleavage becomes clear by comparison of the results noted in Table I with analogous reactions recorded in the literature. Thus the cleavage of tetrahydrofuran to give butane-1,4-diol diacetate in 66% yield by reaction with acetic anhydride both requires the presence of zinc chloride as catalyst and necessitates 8 hr of heating at 230°.[4]

By comparison, tetrahydrofuran is cleaved by mixed anhydride to the appropriate diester in 3 hr at room temperature in yields approaching 100% (Table I). Again 1,4-dioxane, which gives on overnight reflux in acetonitrile with acetyl p-toluenesulfonate an 87% yield of diester, gives, with acetyl chloride and stannic chloride after 30 hr at 200°, only 16% 2-chloroethyl acetate[5] and an even poorer yield of a mixture of di-(2-acetoxyethyl) ether and glycol diacetate after prolonged heating with acetic anhydride and ferric chloride.[6]

Table I. Cleavage of Ethers with Mixed Sulfonic–Carboxylic Anhydrides

Ether	Mixed anhydride	Reaction conditions	Product(s)	Yield, %
$(n\text{-}C_4H_9)_2O$	$CH_3COOSO_2C_6H_4CH_3$	80°, 15 hr, CH_3CN	$n\text{-}C_4H_9OAc$ $n\text{-}C_4H_9OTs$	50[a]
$(i\text{-}C_3H_7)_2O$	$CH_3COOSO_2C_6H_4CH_3$	80°, 18 hr, CH_3CN	$i\text{-}C_3H_7OAc$ $i\text{-}C_3H_7OTs$	80[a]
$(C_6H_5CH_2)_2O$	$CH_3COOSO_2C_6H_4CH_3$	25°, 48 hr, CH_3CN	$C_6H_5CH_2OAc$ $C_6H_5CH_2OTs$	50[a]
Tetrahydrofuran	$CH_3COOSO_2C_6H_4CH_3$	25°, 12 hr[b]	$AcO(CH_2)_4OTs$	82
2-Methyltetrahydrofuran	$CH_3COOSO_2C_6H_4CH_3$	25°, 12 hr	$AcO(CH_2)_3CH(CH_3)OTs$[c]	95
1,4-Dioxane	$CH_3COOSO_2C_6H_4CH_2$	80°, 24 hr	$AcOCH_2CH_2OCH_2CH_2OTs$	87
$AcOCH_2CH_2OCH_2CH_2OTs$	$CH_3COOSO_2C_6H_4CH_3$	130°, 2 hr	$AcOCH_2CH_2OTs$[c]	45
Ethylene oxide	$CH_3COOSO_2C_6H_4CH_3$	25°, 2 hr, CH_3CN[d]	$AcOCH_2CH_2OTs$	80
2,5-Dihydrofuran	$CH_3COOSO_2C_6H_4CH_3$	80°, 16 hr, CH_3CN	$AcOCH_2CH=CHCH_2OTs$[c]	82
Tetrahydrofuran	$C_2H_5COOSO_2C_6H_4CH_3$	25°, 48 hr[d]	$C_2H_5COO(CH_2)_4OTs$	95
Tetrahydrofuran	$CH_3COOSO_2CH_3$	25°, 12 hr[d]	$CH_3COO(CH_2)_4OSO_2CH_3$	95
$(t\text{-}C_4H_9)OC_2H_5$	$CH_3COOSO_2CH_3$	25°, 30 min, CH_3CN	$CH_3COOC_2H_5$[c] $(CH_3)_2C=CH_2$	

[a] Based on recovery of the nonvolatile tosylate. [b] Following the reaction course by nmr spectroscopy showed cleavage to be essentially complete after 3 hr at 25°. [c] No trace of alternative products were observed showing cleavage to be specifically monodirectional. [d] Reaction immediate and exothermic.

The mixed sulfonic–carboxylic anhydrides were prepared in convenient large-scale batches by two methods, neither of which suffered the disadvantage of necessitating the use of silver salts.[1,2] Thus acetyl p-toluenesulfonate was prepared in quantitative yield by refluxing anhydrous p-toluenesulfonic acid in an excess of acetyl chloride until evolution of hydrogen chloride ceased (3–5 hr); this step was followed by removal of the excess acetyl chloride under reduced pressure, to yield the colorless crystalline anhydride. Alternatively, heating of an excess of acetic anhydride with anhydrous p-toluenesulfonic acid at 130° for 30 min, followed by removal of acetic acid and excess

The cleavage of unsymmetrical ethers with mixed sulfonic–carboxylic anhydrides also favors a greater specificity of cleavage than other methods. Thus 2-methyltetrahydrofuran is cleaved by acetyl bromide in the presence of zinc chloride after 1 hr at 80° to give a mixture of both possible bromo acetates.[7]

With acetyl p-toluenesulfonate, however, 2-methyltetrahydrofuran yields only 1-acetoxypentyl 4-p-toluenesulfonate in 95% yield (Table I). Similarly mixed acyclic aliphatic ethers in which the α carbon atoms were alkyl substituted to differing degrees cleaved in one direction only (*e.g.*, ethyl t-butyl ether, Table I). Such a finding supports the dominance of S_N1 reaction in the cleavage step.

(1) A. Baroni, *Atti Accad. Nazl. Lincei, Mem. Classe Sci. Fis., Mat. Nat., Sez. I*, **17**, 1081 (1933).
(2) C. G. Overberger and E. Sarlo, *J. Am. Chem. Soc.*, **85**, 2446 (1963).
(3) (a) G. A. Olah and S. J Kuhn, *J. Org. Chem.*, **27**, 2667 (1962); H. Boehme and K-H. Meyer-Dulheuer, *Ann.*, **688**, 78, (1965); W. H. Knoth, *J. Am. Chem. Soc.*, **86**, 3973 (1964); (b) W. Flavell and N. C. Ross, *J. Chem. Soc.*, 5474 (1964).

(4) R. Paul, *Bull. Soc. Chim. France*, **6**, 1162 (1939).
(5) Ya. L. Gol'dfarb and L. M. Smorgonskii, *J. Gen. Chem. USSR*, **8**, 1516 (1938).
(6) M. Macleod, *J. Chem. Soc.*, 3092 (1928).
(7) S. A. Morrell, *Chem. Abstr.*, **41**, 7411 (1947); D. Gagnier and A. Butt, *Bull. Soc. Chim. France*, 309 (1961).
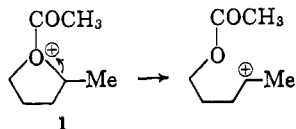
The weakness of tosylate anion as a nucleophile serves to inhibit the possibility of SN2-type cleavage of the acylated species 1, thus favoring cleavage of the alternative O–C bond to yield mixed products.[8]

The remarkably specific cleavage of 2-acetoxyethyl 2'-tosyloxyethyl ether, a diprimary ether which on cleavage with acetyl p-toluenesulfonate gives only ethylene glycol acetate tosylate (Table I), may be explained by the assistance to cleavage in this direction rendered by neighboring acetate participation.[9]
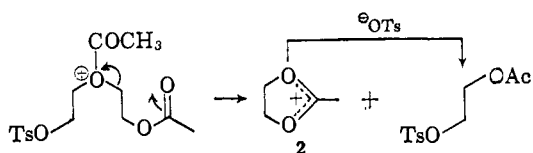
The preparation, from cyclic ethers, of mixed acetate sulfonate diesters by reaction with mixed sulfonic-carboxylic anhydrides promises to have useful synthetic applications. Subsequent nucleophilic displacement of the labile sulfonate group by nucleophiles such as halide or amine moieties has enabled high-yield syntheses of a number of novel substituted acetates to be achieved. Full details of these reactions together with further regions of application of these versatile mixed anhydrides will be discussed in forthcoming publications.

(8) The reluctance of ⁻OTs to engage in nucleophilic attack is shown by the preponderance of isobutylene formation in the cleavage of t-butyl ethyl ether with acetyl p-toluenesulfonate, such formation being a consequence of the longer lifetime of the t-butylcarbonium ion generated by cleavage. In contrast cleavage of t-butyl ethyl ether with acetyl chloride–zinc chloride is reported to give a quantitative yield of t-butyl chloride: J. F. Norris and G. W. Rigby, J. Am. Chem. Soc., 54, 2088 (1932).

(9) Such AcO-5 participation invoking formation of the stabilized 2-methyl-1,3-dioxolenium ion 2 is well known; cf. B. Capon, Quart. Rev. (London), 18, 45 (1964).

(10) Weizmann Fellow, 1967–1968.

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The Dicyanoethylene Anion Moiety.
A New Spin Label

Sir:

The number of spin labels in rigid, bridged polycyclic compounds is growing rapidly.[1–3] An important

(1) Semidiones: (a) G. A. Russell and K. Y. Chang, J. Am. Chem. Soc., 87, 4381 (1965); (b) G. A. Russell, K. Y. Chang, and C. W. Jefford, ibid., 87, 4383 (1965); (c) G. A. Russell, E. T. Strom, E. R. Talaty, K. Y. Chang, R. D. Stephens, and M. C. Young, Record. Chem. Progr. (Kresge-Hooker Sci. Lib.), 27, 3 (1966); (d) G. A. Russell, G. Holland, K. Y. Chang, and L. H. Zulkow, Tetrahedron Letters, 1955 (1967); (e) G. A. Russell, G. Holland, and K. Y. Chang, J. Am. Chem. Soc., 89, 6629 (1967).

(2 Semiquinones: (a) L. M. Stock and J. Suzuki, ibid., 87, 3909 (1965); (b) D. Kosman and L. M. Stock, ibid., 88, 843 (1966); (c) S.
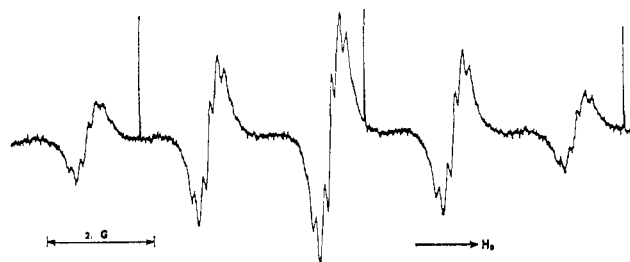
Figure 1. Anion radical from the reduction of compound I; 0.81 mM solution in acetonitrile.

new member of this class is the dicyanoethylene moiety. This communication presents preliminary results obtained with this useful spin-density probe in the anion radicals of two compounds, 2,3;5,6-dibenzo-7,8-dicyanobicyclo[2.2.2]oct-7-ene (I) and 2,3-dicyanobicyclo-[2.2.2]octa-2,7-diene (II).

I   II
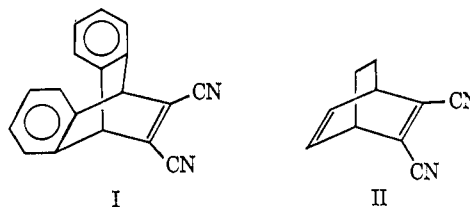
The parent compounds are easily synthesized by the facile Diels–Alder addition of dicyanoacetylene to anthracene and 1,3-cyclohexadiene, respectively.[4] Each compound is easily reduced electrochemically in acetonitrile. The half-wave potentials (vs. saturated calomel electrode) are -1.4 V for I and -1.59 V for II, and in each case the wave is polarographically reversible.

The electron spin resonance (esr) spectrum of the anion radical of I is shown in Figure 1. Its assignment is open to some question. The major splitting is due to coupling of the unpaired electron with two equivalent nitrogen nuclei; the nitrogen coupling constant is 2.30 G. The remaining hyperfine structure appears to be due to coupling with six equivalent protons. However, there are not six symmetrically equivalent hydrogen atoms present in the molecule, and so it was proposed that the two bridgehead protons had a coupling constant which was accidentally the same as that of four equivalent aromatic protons, 0.15 G.

In order to test this hypothesis, 9,10-dideuterioanthracene was prepared[5] and allowed to react with dicyanoacetylene. A spectrum of the 1,4-dideuterio anion of I shows coupling with two equivalent nitrogens and further quintet splitting, presumably due to coupling with four equivalent ring protons. At this time it is impossible to state which group of hydrogens, H_a or H_b, is responsible for this splitting. In all likelihood,
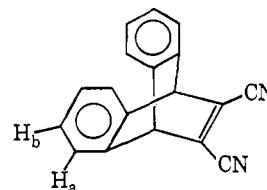
F. Nelson and B. M. Trost, Tetrahedron Letters, 5737 (1966); (d) D. Kosman and L. M. Stock, ibid., 1511 (1967).

(3) Semifuraquinones: S. F. Nelson and E. D. Seppanen, J. Am. Chem. Soc., 89, 5740 (1967).

(4) C. D. Weis, J. Org. Chem., 28, 74 (1963).

(5) Anthraquinone was reduced in the presence of D₂O according to the method of E. L. Martin, J. Am. Chem. Soc., 58, 1438 (1936).