Mixed Sulfonic-Carboxylic Anhydrides. II.[1] Reactions with Aliphatic Ethers and Amines

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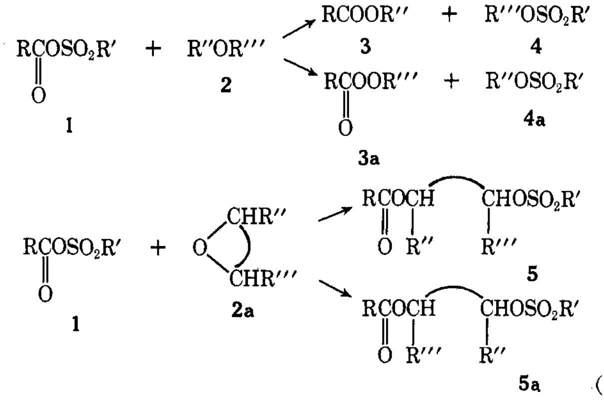
The powerful acylating ability of mixed sulfonic-carboxylic anhydrides is demonstrated by their facile cleavage of ethers. The nature of this cleavage process is discussed and its distinction and advantages over acyl halide cleavage indicated. Potential synthetic uses of this reaction are pointed out and a brief summary of the results with amines is included.

The chemistry of mixed sulfonic-carboxylic anhydrides has been but sporadically and sparsely investigated,[1-12] although it had already been pointed out in 1955 that mixed anhydrides should be "highly reactive acylating agents."[3] Following their general synthesis,[1,4-6] this surmise was confirmed, and the reagents were indeed observed to function as powerful acylating agents. Thus anilines, primary alcohols, and phenols were speedily acylated in good yield, and the reactivity of mixed anhydrides compared favorably with that of benzoyl chloride;[4] hydrogen fluoride reacted to give the relatively inaccessible acetyl fluoride. Acylation reactions on O and N with subsequent cleavage were observed with species which were readily cleavable with mild acid. Thus, such reactions were observed to proceed upon the epoxide ring[4] and with both 1,1-diamines and dialkylamino ethers, these latter both yielding immonium sulfonate salts.[6]

We wished to demonstrate the considerable acylating ability of mixed anhydrides and, to this end, have examined their reactions with aliphatic ethers, ordinarily inert to all but the most powerful electrophiles. Our results have shown the acylating ability of the system to be extremely high and we have developed from these experiments a general method for the cleavage of aliphatic ethers.

I. Reactions of Mixed Sulfonic-Carboxylic Anhydrides with Ethers.—Treatment of a wide variety of aliphatic ethers (simple or mixed, cyclic or acyclic) with mixed anhydrides effected cleavage represented in the general case by eq 1. An ether, R″OR‴, 2,



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should suffer cleavage by an acyl sulfonate, $RCOOSO_2R'$, 1, being converted in the process to a mixture of carboxylate 3 and 3a and sulfonate ester 4 and 4a or, if the initial ether were cyclic, to a cyclic diester or, in unsymmetrical cyclic ethers, 2a, to a potential mixture of two cyclic diesters 5 and 5a. Table I lists the ethers cleaved in this manner. The yields obtained are high, reaction occurring under mild conditions without the necessity for added Lewis acid catalyst. Thus the most unreactive ethers, the diprimary acyclic cases, are cleaved in 1 hr or so at 130°, or in several hours under reflux in acetonitrile. All other ethers require less drastic conditions. Cleavage of asymmetric ethers occurs with a higher specificity than observed with other reagents, and the products are clean and free of secondary products. We believe the reaction to proceed *via* initial acylation of the ether oxygen atom followed by cleavage of one of the two adjoining carbon-oxygen bonds.

The first step can be visualized in either of two ways. The acylation could take place *via* the highly reactive acylium ion, present in small concentrations and gener-

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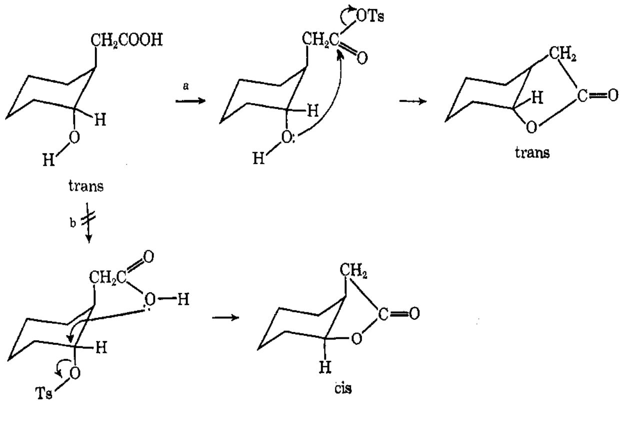
(1) Part I: M. H. Karger and Y. Mazur, *J. Org. Chem.* **36**, 528 (1971).

(2) A preliminary account of some of the work described in this paper has previously appeared: M. H. Karger and Y. Mazur, *J. Amer. Chem. Soc.*, **90**, 3878 (1968).

(3) J. H. Brewster and C. J. Ciotti, Jr., *ibid.*, **77**, 6214 (1955). In order to account for the observation that *trans*-2-hydroxycyclohexaneacetic acid is lactonized with *retention* of configuration on treatment with sulfonyl chlorides in pyridine, it was suggested that the reaction proceeded *via* a mixed anhydride intermediate (path a) rather than the expected sulfonate (path b); see J. B. Brewster and C. H. Kucera, *ibid.*, **77**, 4564 (1955).



(4) C. G. Overberger and E. Sarlo, *ibid.*, **85**, 2446 (1963).

(5) G. A. Olah and S. J. Kuhn, *J. Org. Chem.*, **27**, 2667 (1962).

(6) H. Boehme and K.-H. Meyer-Dulheuer, *Justus Liebigs Ann. Chem.* **688**, 78 (1965).

(7) M. S. Kharasch, T. H. Chao, and H. C. Brown, *J. Amer. Chem. Soc.*, **62**, 2393 (1940).

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(10) A. Baroni, *Atti Accad. Naz. Lincei, Mem., Cl. Sci. Fis. Mat. Natur.*, **17**, 1081 (1933).

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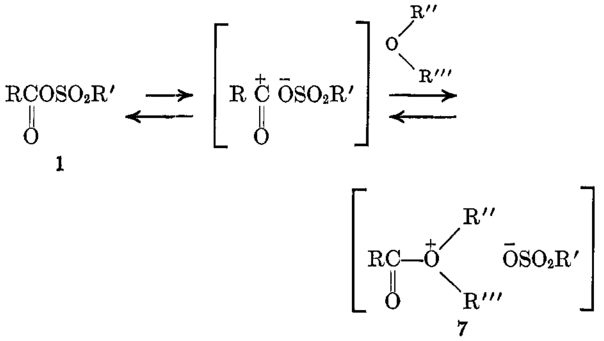
(12) W. J. Knoth, *J. Amer. Chem. Soc.*, **86**, 3973 (1964).

TABLE I

CLEAVAGE OF ALIPHATIC ETHERS WITH MIXED SULFONIC–CARBOXYLIC ANHYDRIDES

Ether	Mixed anhydride	Reaction conditions (°C, hr, solvent)	Product	Yield, %
$(n\text{-}C_3H_7)_2O$	$CH_3COOSO_2C_7H_7$	91, 15	$CH_3COOC_3H_7$	...[a]
			$C_3H_7OSO_2C_7H_7$	30
$(n\text{-}C_4H_9)_2O$	$CH_3COOSO_2C_7H_7$	80, 15, CH_3CN	$CH_3COOC_4H_9$	...[a]
			$C_4H_9OSO_2C_7H_7$	50
$C_2H_5O\text{–}n\text{-}C_4H_9$	$CH_3COOSO_2CH_3$	130, 2	$CH_3COOC_2H_5$	47 } 66 total
			$CH_3COOC_4H_9$	19
			$C_2H_5OSO_2CH_3$	...[a]
			$C_4H_9OSO_2CH_3$	...[a]
$(C_6H_5CH_2)_2O$	$CH_3COOSO_2C_7H_7$	25, 48, CH_3CN	$CH_3COOCH_2C_6H_5$	50
			$C_6H_5CH_2OSO_2C_7H_7$	76[b]
	$CH_3COOSO_2C_7H_7$	25, 2,[d] CH_3CN	$CH_3COOCH_2CH_2OSO_2C_7H_7$	80
	$CH_3COOSO_2CH_3$	25, 2,[d] CH_3CN	$CH_3COOCH_2CH_2OSO_2CH_3$	63
	$CH_3COOSO_2C_7H_7$	25, 12[c]	$CH_3COO(CH_2)_4OSO_2C_7H_7$	82
	$C_2H_5COOSO_2C_7H_7$	25, 48[d]	$C_2H_5COO(CH_2)_4OSO_2C_7H_7$	95
	$CH_3COOSO_2CH_3$	25, 12[d]	$CH_3COO(CH_2)_4OSO_2CH_3$	95
	$CH_3COOSO_2CH_3$	82, 48	$CH_3COO(CH_2)_5OSO_2CH_3$	80[e]
	$CH_3COOSO_2C_7H_7$	82, 48	$CH_3COO(CH_2)_5OSO_2C_7H_7$	95[e]
	$CH_3COOSO_2C_7H_7$	80, 24	$CH_3COOCH_2CH_2OCH_2CH_2OSO_2C_7H_7$	87
	$C_2H_5COOSO_2C_7H_7$	80, 48	$C_2H_5COOCH_2CH_2OCH_2CH_2OSO_2C_7H_7$	67
	$CH_3COOSO_2C_7H_7$	80, 16, CH_3CN	$CH_3COOCH_2CH{=}CHCH_2OSO_2C_7H_7$	82
	$CH_3COOSO_2C_7H_3$	80, 16, CH_3CN	$CH_3COOCH_2CH{=}CHCH_2OSO_2CH_3$	54
$i\text{-}(C_3H_7)_2O$	$CH_3COOSO_2C_7H_7$	80, 18, CH_3CN	$i\text{-}C_3H_7OCOCH_3$	...[a]
			$i\text{-}C_3H_7OSO_2C_7H_7$	80
$i\text{-}(C_3H_7)_2O$		80, 24	$i\text{-}C_3H_7OCOCH_2CH_2SO_2OiC_3H_7$	42
	$CH_3COOSO_2C_6H_4CH_3$	25, 12	$CH_3CO(CH_2)_3CH(CH_3)OSO_2C_7H_7$[f]	95
	$CH_3COOSO_2C_7H_7$	25, 2	$CH_3COOCH_2CH(CH_3)OSO_2C_7H_7$	88
			$CH_3COOCH(CH_3)CH_2OSO_2C_7H_7$	
	$CH_3COOSO_2CH_3$	25, 2	$CH_3COOCH_2CH(CH_3)OSO_2CH_3$	40
			$CH_3COOCH(CH_3)CH_2OSO_2CH_3$	
$(tert\text{-}C_4H_9)OC_2H_5$	$CH_3COOSO_2CH_3$	25, 0.5, CH_3CN	$CH_3COOC_2H_5$[f]	
			$(CH_3)_2C{=}CH_2$	
$CH_3COOCH_2CH_2O$ $C_7H_7SO_2OCH_2CH_2$	$CH_3COOSO_2C_7H_7$	130, 2	$CH_3COOCH_2CH_2OSO_2C_7H_7$[f]	45

[a] The ester was not separated from the excess of ether used. [b] Yield based on yield of polybenzyl after distillation of benzyl acetate. [c] Following the reaction course by nmr spectroscopy showed reaction to be complete after 3 hr. [d] Reaction immediate and exothermic. [e] Yield after 4 hr, reflux 35°. [f] No trace of alternative products were observed showing cleavage to be specifically unidirectional.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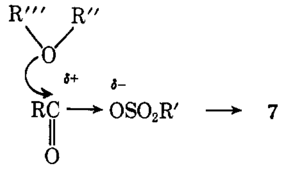
ated by the equilibrium outlined in eq 2.[13] Alternatively acylation could take place by attack of the ether on an un-ionized molecule of mixed anhydride (eq 3).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(3)

In either case, the reason for the high reactivity of mixed anhydrides is the powerful electron-withdrawing nature of the sulfonate group.

We could find no direct evidence for the presence of the complex 7.[14] Thus careful and continuous examination of mixtures of various concentrations of mixed anhydride in both easily cleaved (tetrahydrofuran), and less easily cleaved (n-butyl ether, 1,4-dioxane) ethers at ambient temperatures revealed neither a shift in the nmr frequencies of the $-CH_2O-$ group, nor any new peak (minimum shift observable 0.5 cps). This is in direct contrast to the equilibrium between ethyl ethers and boron halides where the nmr frequencies of the CH_2O group hydrogens shift downfield, the magnitude of the shift increasing with the molar ratio of boron trihalide.[15] The results indicate that in an ether–mixed anhydride solution the concentration of complex

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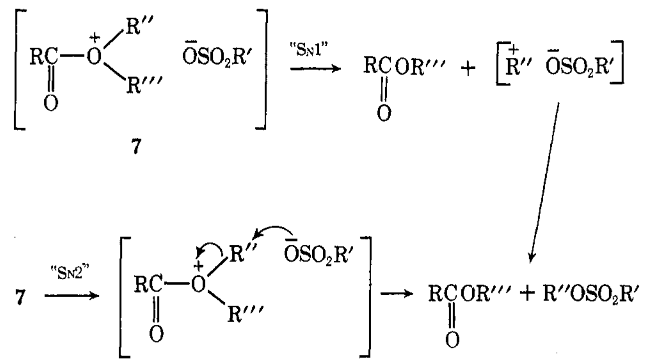
[13] Similar equilibria have been put forward to explain the mode of acylation of trifluoroacetic anhydride in carboxylic acids [E. J. Bourne, M. J. Stacey, J. C. Tatlow, and J. Randles, *J. Amer. Chem. Soc.*, **76**, 3206 (1954)], and of acyl halides in acetic anhydride [G. Jander, E. Rusberg, and H. Schmidt, *Z. Anorg. Chem.*, **255**, 238 (1948)].

[14] The compound $(CH_3CO^+)SbCl_6^-$ is thought, from conductivity measurements, to be present in mixtures of antimony pentachloride–acetyl chloride [F. Seel and H. Bauer, *Z. Naturforsch. B*, **2**, 397 (1947)], while the formation of a complex salt of structure $(CH_3COOEt_2^+)BF_4^-$ from acetyl fluoride and the ethyl ether complex of BF_3 has been reported at low temperatures [F. Seel *Z. Anorg. Chem.*, **250**, 331 (1943)].

[15] E. Gore and S. S. Danyluk, *J. Phys. Chem.*, **69**, 89 (1965); R. A. Craig and R. E. Richards, *Trans. Faraday Soc.*, **59**, 1962 (1963). The downfield shift at a 1:1 ratio of diethyl ether–boron trifluoride is *ca.* 25 Hz. Only one signal is observed in these mixtures indicating a rapid exchange of boron halide between ether molecules at room temperature.

7, in relation to unchanged ether, was too small to be observed by nmr (<2%).

The mechanism of cleavage of the complex **7** closely parallels that observed for the Lewis acid catalyzed cleavage of ethers by acyl halides, which have been extensively covered in two reviews.[16,17] For these reactions S_N1 mechanism is the rule for all but primary ethers which appear to undergo cleavage by an S_N2 mechanism (eq 4). Our cleavage reactions appear to follow a similar course. Thus we have observed the reactivity toward mixed anhydrides to be in the order tertiary ethers ≫ secondary ether > primary ethers, with benzylic ethers showing the expected enhanced reactivity (Table I). Mixed anhydrides do, however, exhibit one important mechanistic difference stemming from the fact that sulfonate ion is an exceptionally weak nucleophile.[18] Thus the tendency for reaction to follow the S_N2 path is less pronounced in any given case than for the corresponding acyl halide and, in cases where S_N1 cleavage is the rule, the lifetime of the generated carbonium ion will be greater than for acyl halide cleavage. Using the recent suggestion of Sneen and Larson,[19] we can say that mixed anhydride–ether cleavage will be displaced toward the S_N1 end of the mechanistic spectrum compared with acyl halide–ether cleavage. This has two important consequencies. Cleavage of mixed ethers will favor cleavage of the bond to the more substituted radical to a greater extent. In addition, the longer lifetime of a carbonium ion generated by mixed anhydride cleavage allows alternative pathways to that of immediate ion pair collapse which is suffered following cleavage by acyl halide. Reaction conditions, products, and yields are listed in Table I.



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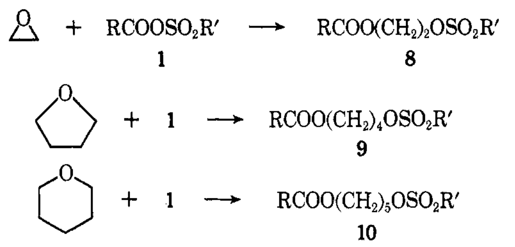
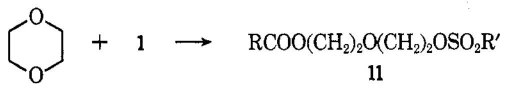
A. Primary Acyclic.—These were the most unreactive of the ethers examined. Overnight reflux of higher boiling diprimary ethers in acetonitrile, generally found to be the most effective solvent for mixed anhydride reactions, led to yields of 30–60% of the alkyl sulfonate based on the weight of mixed anhydride used. This yield is lowered somewhat from the maximum attainable since overnight reflux of mixed anhydride in acetonitrile has been found to effect up to 25% disproportionation.[1] With diprimary asymmetric ethers, cleavage was in both directions, giving all four possible products. Thus the cleavage of ethyl *n*-butyl ether with acetyl methanesulfonate at 130° led to 47% ethyl acetate and 19% butyl acetate.[20] With dibenzyl ether reaction proceeded rapidly, being complete within 48 hr at room temperature. Benzyl acetate was isolated by distillation in 50% yield but the benzyl sulfonate could not be isolated because it decomposed upon mild heating to a mixture of sulfonic acid and polybenzyl. This accords with the known tendency of benzyl sulfonates to polymerize on standing.[21]

B. Primary Cyclic.—With unstrained ring systems reaction proceeded at about the same rate as with the acyclic primary analogs. Thus tetrahydropyran (eq 5) gave the ring-opened diester **10** in 30% yield after 4-hr reflux, and in 80% yield after 48 hr reflux. Similarly, 1,4-dioxane gave an 87% yield of the diester **11** (eq 6) after 24-hr reflux without solvent.[22] In this case the product, a diprimary ether, was less reactive than the starting material and did not suffer cleavage as long as the dioxane remained in excess. When the isolated diester **11** was treated at 130° with a second



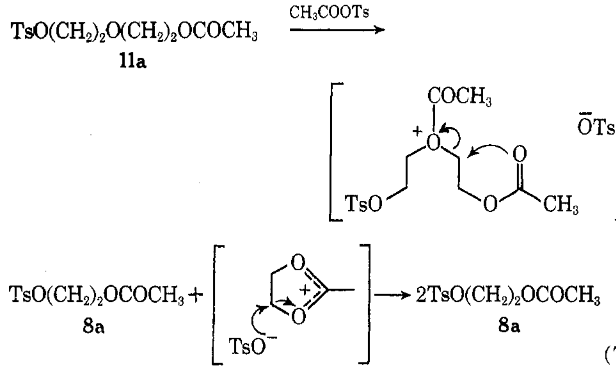
(5)

a, $R = CH_3$; $R' = C_6H_4CH_3$
b, $R = CH_3$; $R' = CH_3$
c, $R = C_2H_5$; $R' = C_6H_4CH_3$



(6)

a, $R = CH_3$; $R' = CH_3C_6H_4$
b, $R = CH_3$; $R' = CH_3$
c, $R = C_2H_5$; $R' = CH_3C_6H_4$



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[16] R. L. Burwell, Jr., *Chem. Rev.*, **54**, 615 (1954).

[17] Francis Johnson in "Friedel-Craft's and Related Reactions," Vol. IV, G. Olah, Ed., Interscience, New York, N. Y., 1965, p 1.

[18] E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, p 261.

[19] R. A. Sneen and J. W. Larsen, *J. Amer. Chem. Soc.*, **91**, 362 (1969).

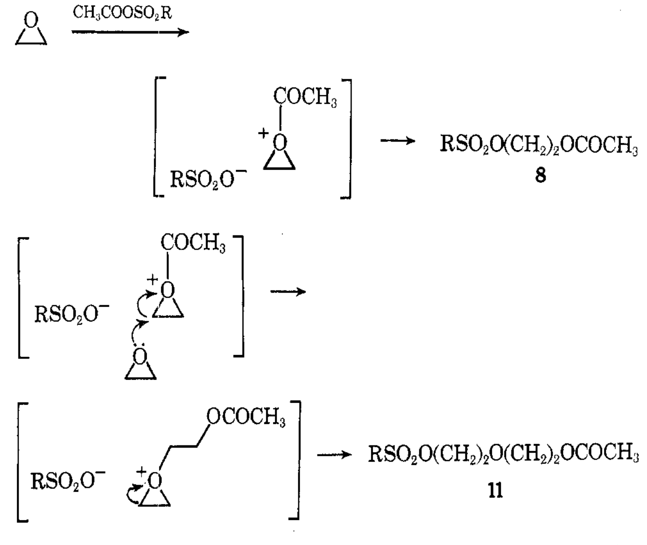
[20] Cleavage of the same ether with acetyl chloride gave 34% ethyl acetate and 58% *n*-butyl acetate at room temperature, and 23% ethyl acetate and 76% *n*-butyl acetate at 60° [J. F. Norris and G. W. Rigby, *ibid.*, **54**, 2088 (1932)]. At higher temperature in the reaction with acetyl chloride, cleavage of the bond to the ethyl group, favored by S_N2 cleavage, increasingly predominates at higher temperatures. With acetyl sulfonates this is less true and even at 80° ethyl acetate formation predominates by over 2:1, a consequence of the weakness of sulfonate nucleophile S_N2 cleavage.

[21] J. K. Kochi and G. S. Hammond, *ibid.*, **75**, 3443 (1953).

[22] The cleavage of 1,4-dioxane illustrates the advantages of the present method of ether cleavage over more conventional acylating systems. Thus with acetyl chloride and Lewis acid, 1,4-dioxane gives the 2-chloroethyl acetate in 16% yield after 30 hr at 200° [Ya. L. Gol'dfard and L. M. Smorgonskii, *J. Gen. Chem. USSR*, **8**, 1516 (1938)]; prolonged heating with acetic anhydride and ferric chloride gives an even smaller yield of a mixture of di(2-acetoxyethyl) ether and glycol diacetate [M. Macleod, *J. Chem. Soc.*, 3092 (1928)].

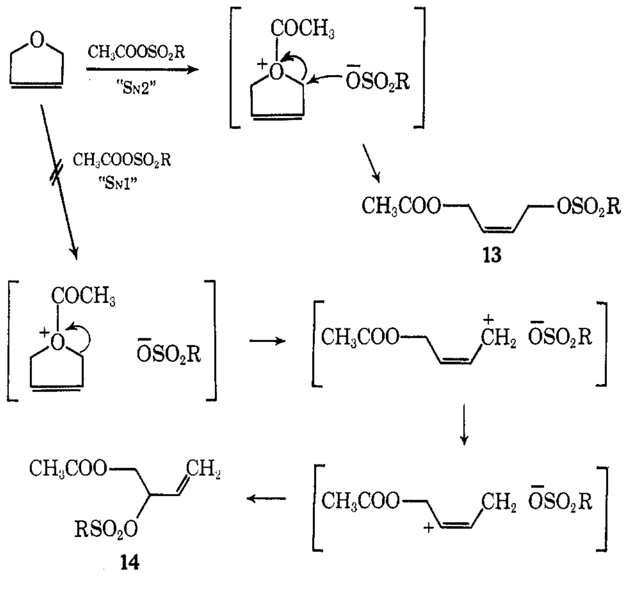
mole of mixed anhydride, it was speedily cleaved. Interestingly, only a single product, ethylene glycol acetate tosylate,[8a] was obtained, no trace of the alternative cleavage products being noted when the reaction was monitored by nmr. That only unidirectional cleavage, in fact, occurs may be explained by the nature of the two functional groups, the acetate group being capable of assisting cleavage in the direction indicated in eq 7 by participating in the formation of the stabilized intermediate 2-methyl-1,3-dioxolenium ion. Such AcO-5 neighboring-group participation, involving formation of this stabilized ion, is well known.[22]

With strained ring systems reaction was considerably faster. Ethylene oxide (eq 5) opened on contact at room temperature, the reaction, even in a solvent, being considerably exothermic. Yields were again around 80%. In addition, diesters of the same structural type as **11** were formed in small yield when excess ethylene oxide was taken, a consequence of an attack of a second molecule of ethylene oxide on the acylated intermediate, rather than simple ion-pair collapse (eq 8). Tetrahydrofuran was opened with exceptional ease, the diester **9** being isolated in 80–95% yield, upon treatment with mixed anhydride at room temperature for a few hours (eq 5).[23] 2,5-Dihydrofuran (**12**) requires several hours reflux to effect complete reaction, but the product is exclusively the terminal diester **13** with no trace of the product formed by allylic rearrangement, **14**, which might be anticipated from an SN1 cleavage process (eq 9).



a, R = $C_6H_4CH_3$ (8)
b, R = CH

The degree of acid catalysis in these mixed anhydride reactions was ambiguous due to the variable quantities of sulfonic acid initially present as impurity in most of the reactions conducted. When tetrahydrofuran was treated with acetyl methanesulfonate freshly prepared and containing a maximum of 0.5% free acid (as estimated from the low-field signal in the nmr) for 16 hr at room temperature, the yield of diester was 47.5%. Repetition of the reaction under identical conditions but with the prior addition of 5% methanesulfonic acid led to an increase in yield to 81%. This result leads one to suspect that reaction in the complete absence of acid, a condition experimentally difficult to attain, would considerably lower the rate of reaction. The presence of free acid probably serves to catalyze the reaction *via* carbonyl group protonation.[24]



a, R = $CH_3C_6H_4$ (9)
b, R = CH_3

Tetrahydrofuran could also be cleaved to the bissulfonate by reaction with sulfonic anhydride. The reaction was considerably slower than that of the mixed anhydride and the yield somewhat lower (30%).

C. Secondary and Tertiary Acyclic.—Although secondary ethers cleaved only slightly faster than primary ethers, tertiary ethers cleaved almost instantaneously at room temperature. Thus diisopropyl ether gave 80% of the two isopropyl esters after overnight reflux. Ethyl *tert*-butyl ether cleaved specifically in one direction giving, ethyl acetate, isobutylene (detected by its appearance in the nmr), and *p*-toluenesulfonic acid. *tert*-Butyl *p*-toluenesulfonate was a minor product[25] (eq 10).

D. Mixed Ethers.—The cleavage of unsymmetrical ethers was investigated in order to ascertain the specificity of mixed anhydride cleavage. 2-Methyltetrahydrofuran was most closely examined, since abundant documentation as to the specificity of cleavage with acyl halide existed.[26] Treatment of 2-methyltetrahydrofuran **15** with acetyl *p*-toluenesulfonate led, in 95% yield, to a single product, the diester **16** (eq 11). The structure was verified by conversion to the bromoacetate **17** with lithium bromide in near-quantitative yield. By comparison, 2-methyltetrahydrofuran was converted to a mixture of two isomeric bromoacetates, **17** and **18**, in a ratio of 3:1 in 80% yield when treated with acetyl bromide. Comparison by glc of the product

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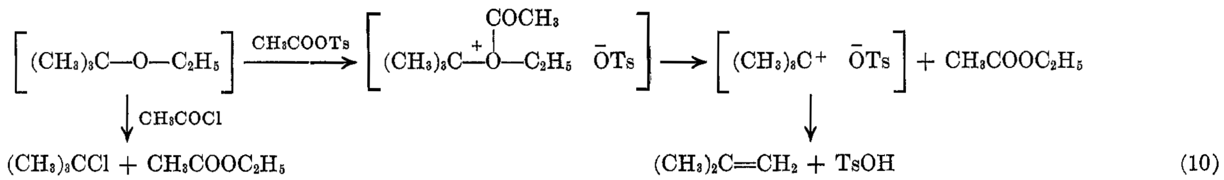
[23] This reaction is in marked contrast with the cleavage by acetic anhydride which requires both the presence of zinc chloride as catalyst and heating for 8 hr at 230° to give the diacetate in 66% yield [R. Paul, *Bull. Soc. Chim. Fr.*, **6**, 1162 (1939)].

[24] S. C. Datta, J. N. E. Day, and C. K. Ingold, *J. Chem. Soc.*, 838 (1939).

[25] This result is in marked contrast with the cleavage of this ether with acetyl chloride–zinc chloride which is reported (ref 20) to give a quantitative yield of *tert*-butyl chloride. This different result is a consequence of the more powerfully nucleophilic chloride ion attacking the *tert*-butyl carbonium ion as soon as its charge begins to develop. The weakly nucleophilic sulfonate ion on the other hand by allowing the carbonium ion a longer lifetime permits it to react by an alternative pathway losing a proton to give the olefin (eq 10).

[26] D. Ganaire and A. Butt, *Bull. Soc. Chim. Fr.*, 309 (1960).



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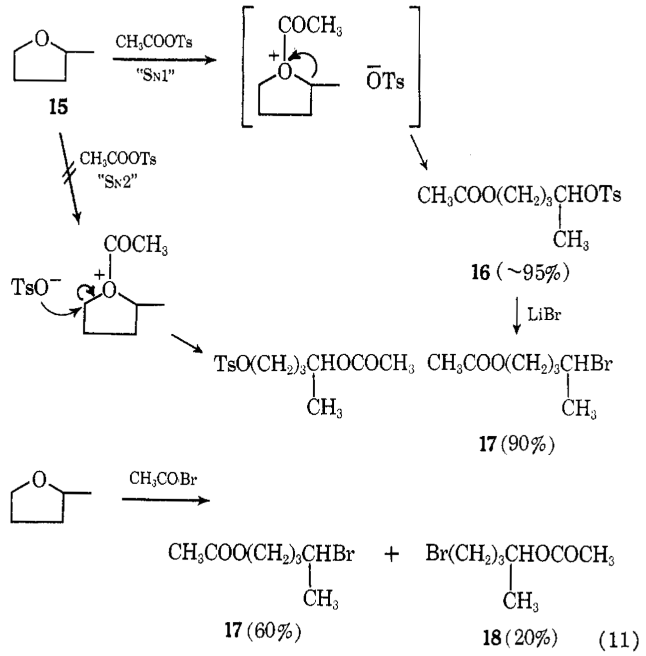
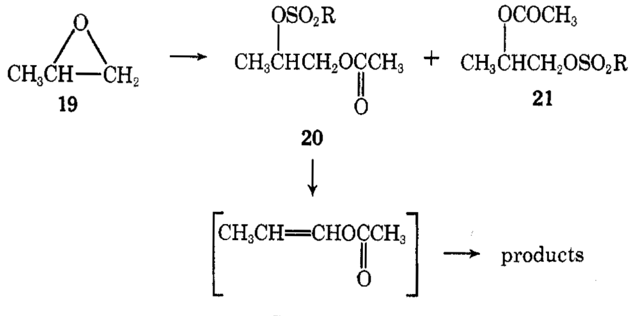


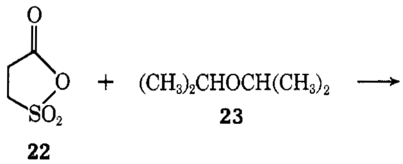
(11)

from the mixed anhydride cleavage with that from the acetyl bromide cleavage showed the former to contain none of the second isomer present in the latter. Thus in the former case, cleavage is exclusively from the most substituted carbon while in the latter 25% of cleavage is from the least substituted carbon.[27] Interestingly, the cleavage of propylene oxide (**19**) led to an almost equal proportion of the two isomers, **20** and **21**, in around 40% yield. In this cleavage of a highly strained ring, the ring opening could be so rapid as to admit to a measure of kinetic control as a factor determining the product distribution. Furthermore, the isomer **20** which would be expected to predominate is capable of a facile acid-catalyzed elimination to a vinyl ether which would not survive the work-up conditions (eq 12).



a, R = $C_6H_4CH_3$
b, R = CH_3 (12)

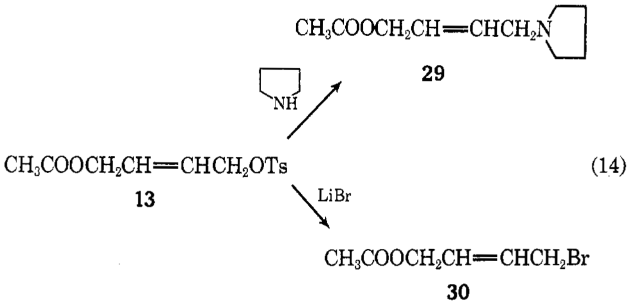
E. Ether Cleavage with Sulfopropionic Anhydride.—This cyclic mixed anhydride[28] **22** reacted with ethers in the anticipated fashion. Thus diisopropyl ether **23** gave, in high yield, the diester **24** on overnight reflux (eq 13).



$$(CH_3)_2CHOCOCH_2CH_2SO_2OCH(CH_3)_2 \quad (13)$$

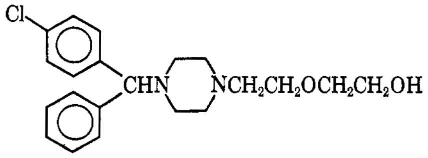
24

II. Synthetic Application of Mixed Anhydride Ether Cleavage—The cleavage of cyclic ethers to a mixed carboxylate–sulfonate diester would appear to have some use in synthesis. Such an operation effects the simultaneous introduction of two functional groups of widely differing reactivities. The sulfonate group is considerably more reactive toward nucleophiles and is readily displaced by such, but the carboxylate function is unaffected. Thus we have selectively displaced the sulfonate group with hydride, halide, and amine moieties (eq 14). As an illustration of the potential



(14)

utility of such procedures, we have synthesized an analog **32** of the pharmacologically active compound 1-(*p*-chloro-α-phenylbenzyl)-4-(2-hydroxyethoxyethyl)-piperazine (**25**)[29] in the manner shown (eq 15).



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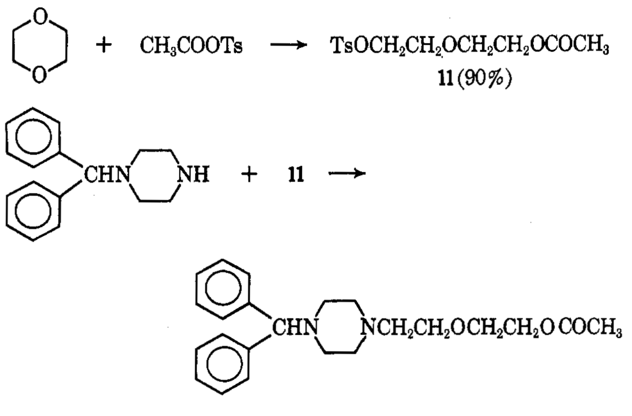

32 (70%) (15)

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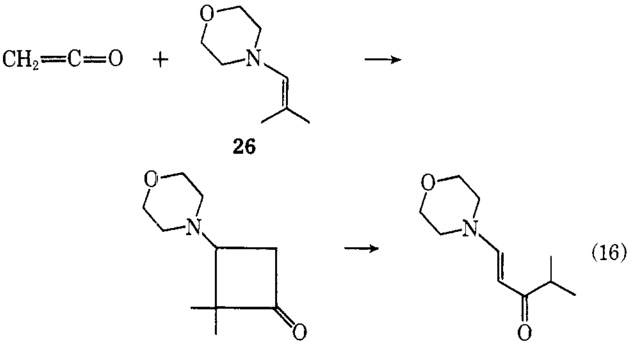
[27] This result confirms the greater tendency for mixed anhydride cleavage to proceed *via* SN1 mechanism and points to the possible advantages of mixed anhydride cleavage of unsymmetrical ethers in eliminating the presence of contaminating isomers (eq 11).

[28] M. S. Kharasch, T. H. Chao, and H. C. Brown, *J. Amer. Chem. Soc.*, **62**, 2393 (1940).

[29] U. S. Patent 2,899,436 (1959).

III. The Reaction of Mixed Anhydrides with Amines. A. Tertiary Amines.—Acetyl sulfonates, when treated with tertiary amines, yielded ketene and the amine sulfonate salt. This reaction was undergone by all those mixed anhydrides the acyl portion of which possessed a β hydrogen atom. The reaction proceeded at low temperature, below 0°, compared with the temperature of 130° required to generate ketene thermally from mixed anhydride.[1] The ketene was trapped by using it *in situ* to form a cycloadduct with an enamine.[30] Thus acetyl methanesulfonate treated with triethylamine in the presence of 1-(*N*-morpholino)-isobut-1-ene (**26**) gave a mixture of the cyclobutanone adduct **27** and its ring-opened degradation product **28** in 62% yield (eq 16).

$$CH_3COOSO_2CH_3 + (C_2H_5)_3N \longrightarrow [(C_2H_5)_3{}^{+}NH\ {}^{-}OSO_2CH_3] + CH_2{=}C{=}O$$



B. Primary and Secondary Amines.—Amines containing labile hydrogen gave moderate yields (20–40%) of the *N*-acyl salt. The yield of amine sulfonate salt was far higher (80–95%), testifying to the simultaneous base-induced formation of ketene observed to proceed with tertiary amines.

Experimental Section[31]

***n*-Butyl Ether and Acetyl *p*-Toluenesulfonate.**—Acetyl *p*-toluenesulfonate (6.0 g, 75% pure, 21 mmol) in acetonitrile (15 ml) was refluxed with a large excess of *n*-butyl ether (12.5 ml) for 15 hr. The reaction mixture was worked up in the usual manner and the crude product distilled at atmospheric pressure. The distillate, a mixture of excess ether and *n*-butyl acetate, was collected in three fractions, bp 120–126°, 126–135°, and 135–141°. Each fraction had ν_{max} 1750 cm^{-1} ($OCOCH_3$). The nonvolatile residue was distilled under reduced pressure, to afford *n*-butyl tosylate: bp 110° (10^{-2} mm); yield 2.6 g (50%); ν_{max} 1600 ($ArC{=}C$), 1380 cm^{-1} (OSO_2); nmr δ 0.85 (t, J = 6 Hz, 3 H, $C\mathbf{H}_3CH_2$), 1.5 (m, 4 H, $CH_3C\mathbf{H}_2C\mathbf{H}_2CH_2O$), 2.43 (s, 3 H, $ArC\mathbf{H}_3$), 4.04 (t, J = 7 Hz, 2 H, $OC\mathbf{H}_2$), and 7.57 (AB quartet, Δ_{AB} = 28 Hz, J_{AB} = 8 Hz, 4 H, *p*-$C_6\mathbf{H}_4$).

Anal. Calcd for $C_{11}H_{16}SO_3$: C, 57.87; H, 7.06; S, 14.04. Found: C, 57.95; H, 6.93; S, 14.15.

***n*-Propyl Ether and Acetyl *p*-Toluenesulfonate.**—Acetyl *p*-toluenesulfonate (6.0 g, 75% pure, 21 mmol) was refluxed in an excess of *n*-propyl ether (12.5 ml) for 15 hr. The reaction mixture was worked up in the usual way and the crude product distilled at atmospheric pressure. The distillate was a mixture of *n*-propyl ether and *n*-propyl acetate, bp 90–94°, ν_{max} 1750 cm^{-1}. The residue was distilled collecting *n*-propyl tosylate: bp 100° (0.01 mm); yield 1.4 g (30%); ν_{max} 1600 and 1360 cm^{-1}; nmr δ 0.86 (t, J = 7 Hz, 3 H, $CH_2C\mathbf{H}_3$), 1.65 (s, J = 7 Hz, 2 H, $CH_2C\mathbf{H}_2CH_2$), 2.42 (s, 3 H, $ArCH_3$), 4.0 (t, J = 7 Hz, 2 H, $OC\mathbf{H}_2CH_2$), and 7.60 (AB quartet Δ_{AB} = 27 Hz, J_{AB} = 8 Hz, 4 H, *p*-$C_6\mathbf{H}_4$).

Anal. Calcd for $C_{10}H_{14}SO_3$: C, 56.05; H, 6.59; S, 14.96. Found: C, 55.97; H, 6.53; S, 14.91.

Ethyl *n*-Butyl Ether and Acetyl Methanesulfonate.—Ethyl *n*-butyl ether (10.2 g, 0.1 mol) and acetyl methanesulfonate (13.8 g, 0.1 mol) were heated at 130° for 24 hr in a sealed evacuated tube. The dark liquid was distilled under atmospheric pressure collecting two fractions, bp 76–90 and bp 90–100°. Vpc (5% Carbowax, 160°) showed each fraction to consist of a mixture, in different proportions, of ethyl acetate, *n*-butyl ethyl ether, and *n*-butyl acetate. The total weights of product calculated from the vpc traces follow: ethyl acetate, 4.15 g (47%); *n*-butyl acetate, 2.21 g (19%); total yield, 66%. The distillate residue, a mixture of the two respective methanesulfonates was distilled under reduced pressure but speedily decomposed, the only product isolated in the distillate being methanesulfonic acid.

Benzyl Ether and Acetyl *p*-Toluenesulfonate.—To a solution of acetyl *p*-toluenesulfonate (11.0 g, 51.3 mmol) in acetonitrile (50 ml) was added dibenzyl ether (9.0 g, 45 mmol). The reaction mixture was kept at room temperature for 48 hr and then worked up in the usual manner to yield a pale yellow oil (14.0 g, 76%) which was distilled under reduced pressure collecting benzyl acetate: bp 53–56° (0.005 mm); yield 3.4 g (50%); ν_{max} 1740 cm^{-1} ($OCOCH_3$); nmr δ 2.0 (s, 3 H, $COC\mathbf{H}_3$), 5.05 (s, 2 H, $ArC\mathbf{H}_2O$), and 7.30 (s, 5 H, $C_6\mathbf{H}_5$).

Anal. Calcd for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 71.79; H, 6.67.

The distillate residue was extracted with methanol and the methanol evaporated under reduced pressure to yield an oil containing mostly *p*-toluenesulfonic acid, contaminated with traces of polybenzyl (4.0 g, 52%); nmr was superimposable upon that of authentic *p*-toluenesulfonic acid. The methanol-insoluble residue consisted of polybenzyl: yield 3.1 g (76%); nmr[32] δ 3.8 (m, 2 H, $ArC\mathbf{H}_2$), 7.1 (m, 5 H, C_6H_4).

Ethylene Oxide and Acetyl *p*-Toluenesulfonate.—Ethylene oxide (2.1 g, 47.7 mmol) was added to a solution of acetyl *p*-toluenesulfonate (12.0 g, 75% pure, 47.2 mmol) in acetonitrile (50 ml). A rapid exothermic reaction ensued, the temperature reaching 75°. After cooling to room temperature and keeping for 24 hr, the reaction mixture was worked up in the usual manner to give the pure ethylene glycol acetate tosylate (**8a**): yield 8.2 g (80%); ν_{max} 1760 ($OCOCH_3$), 1600 ($ArC{=}C$), and 1360 cm^{-1} (OSO_2); nmr δ 1.96 (s, 3 H, $OCOC\mathbf{H}_3$), 2.42 (s, 3 H, $ArC\mathbf{H}_3$), 4.21 (s, 4 H, $OC\mathbf{H}_2$), and 7.56 (AB quartet, Δ_{AB} = 27 Hz, J_{AB} = 8 Hz, 4 H, *p*-$C_6\mathbf{H}_4$). Attempted distillation of the oil at reduced pressure (10^{-3} mm) led to decomposition.

Repetition of the reaction using a threefold excess of ethylene oxide gave a crude product containing, in addition to an estimated 66% of the expected diester, 33% of 2-acetoxyethyl-2′-tosyloxyethyl ether (**11a**), the nmr of which could be superimposed over that of an authentic sample (*vide infra*) and the proportion of which was readily estimated by comparison of the nmr integrated intensities.

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(30) G. Optiz and M. Kleeman, *Justus Liebigs Ann. Chem.*, **665**, 114 (1963).

(31) Melting points are uncorrected. All ir spectra were carried out on a Perkin-Elmer Infracord double beam spectrophotometer, all nmr spectra on a Varian A-60A instrument. Vpc analyses were done on an Aerograph A-90P. All spectra unless otherwise stated were done on liquid films (ir) or in $CDCl_3$ solution (nmr). In cases where the compounds were unstable and the analytical data were unobtainable, their characterizations were based mainly on the nmr data. All abbreviations used were standard except q^4 = quartet, q^5 = quintet, and s^7 = septet. All solvents as well as the ethers used were obtained commercially and were scrupulously dried and distilled prior to use. The mixed anhydrides were prepared as described previously.[1] Reactions were carried out under anhydrous conditions prior to aqueous work-up. To save unnecessary repetition the phrase, "the reaction mixture was worked up in the usual manner" denotes the following procedure. The reaction mixture was cooled to room temperature and poured into water. A double volume of ether was added, the mixture thoroughly shaken and allowed to settle, and the lower aqueous layer withdrawn. The remaining ether solution was thrice successively extracted with half volumes of a 5% solution of sodium bicarbonate and finally extracted with an equal volume of water. The ether solution was dried by standing over anhydrous magnesium sulfate for at least 1 hr, filtered, and, if colored, decolorized by standing over active charcoal for 1 hr. After filtration, the ether solution was cooled to 0°, any crystals of sulfonic anhydride crystallizing at this stage being filtered off. The ether solution was evaporated under reduced pressure at room temperature and the residual oil was submitted to high vacuum for 1 hr leaving the crude product. The yields, where based on the weight of mixed anhydride taken, make allowance for the purity of the mixed anhydride when stated but are based on the weight taken when this latter is not stated.

(32) J. P. Kennedy and R. B. Isaacson, *J. Macromol. Chem.*, **1**, 541 (1966).

Ethylene Oxide and Acetyl Methanesulfonate.—Ethylene oxide (2.1 g, 47.2 mmol) in acetonitrile (25 ml) was added to acetyl methanesulfonate (3.4 g, 25 mmol) in acetonitrile (25 ml) at room temperature. Work-up in the usual manner left an oil, essentially pure ethylene glycol acetate methanesulfonate (**8b**); yield, 2.8 g (63%); bp 125° (0.01 mm); ν_{max} 1760 and 1360 cm^{-1}; nmr δ 2.10 (s, 3 H, CH_3CO), 3.10 (s, 3 H, CH_3SO_2), 4.40 (s, 4 H, OCH_2).

Anal. Calcd for $C_5H_{10}O_5S$: C, 32.96; H, 5.53; S, 17.60. Found: C, 32.50; H, 5.53; S, 17.28.

Propylene Oxide and Acetyl *p*-Toluenesulfonate.—To a solution of acetyl *p*-toluenesulfonate (6.0 g, 75% pure, 21 mmol) in acetonitrile (25 ml) was added at room temperature propylene oxide (2.75 g, 47.2 mmol). An exothermic reaction ensued and was allowed to proceed, the reaction mixture being kept for a further 2 hr at room temperature. Work-up in the usual manner gave, as a colorless oil, an almost 1:1 mixture of propane-1,2-diol acetate tosylate (**20a**), and propane-1,1-diol tosylate acetate (**21a**) which was not separated: yield, 5.0 g (88%); ir ν_{max} 1760, 1600, and 1360 cm^{-1}; nmr δ 1.20, 1.29 (two overlapping doublets, $J = 7$ Hz, $CHCH_3$), 1.83, 1.90 (two singlets, ratio *ca.* 5:4, $OCOCH_3$), 2.45 (s, $ArCH_3$), 4.05, 4.07 (two overlapping doublets, $J = 7$ Hz, OCH_2CH), 4.90 (m = two overlapping sextets, $J = 7$ Hz, CH_3CHCH_2), and 7.73 (A_2B_2 system, $\Delta_{AB} = 27$ Hz, $J_{AB} = 8$ Hz, p-C_6H_4). Attempted distillation led to decomposition; thus no analytical samples could be prepared.

Propylene Oxide and Acetyl Methanesulfonate.—Acetyl methanesulfonate (6.5 g, 47.2 mmol) was dissolved in acetonitrile (25 ml) and propylene oxide (2.75 g, 47.2 mmol) in acetonitrile (25 ml) added at room temperature. An exothermic reaction ensued and after keeping the reaction mixture at room temperature for 24 hr it was worked up in the usual way to yield an oil, **20b** and **21b**: yield, 3.7 g (40%); ir ν_{max} 1760, 1360 cm^{-1}; nmr δ 1.33, 1.45 (two overlapping doublets, $J = 8$ Hz, $CHCH_3$), 2.07, 2.10 (two singlets, ratio 1:1, $OCOCH_3$), 3.08 (s, OSO_2CH_3), 4.18, 4.25 (two overlapping doublets, $J = 8$ Hz, CCH_2CH), 5.05 (m, two overlapping sextets, $J = 8$ Hz, CH_3CHCH_2).

Anal. Calcd for $C_6H_{12}O_5S$: C, 36.72; H, 6.16; S, 16.34. Found: C, 37.01; H, 6.16; S, 16.86.

Tetrahydrofuran and Acetyl *p*-Toluenesulfonate.—Acetyl *p*-toluenesulfonate (11.0 g, 51.4 mmol) was dissolved in a large excess of tetrahydrofuran (25 ml) and the mixture kept at room temperature for 12 hr. The reaction mixture was worked up in the usual manner yielding an essentially pure yellow oil, yield 12.0 g (82%). The oil was distilled under reduced pressure to afford a single component, butane-1,4-diol acetate tosylate (**9a**): yield, 73%; bp 164–172° (0.005 mm); ν_{max} 1740 ($OCOCH_3$), 1600 (Ar C═C), and 1360 cm^{-1} (OSO_2); nmr δ 1.70 (q, 4 H, $CH_2CH_2CH_2CH_2$), 2.02 (s, 3 H, $OCOCH_3$), 2.44 (s, 3 H, $ArCH_3$), 4.05 (m, 4 H, $CH_2CH_2CH_2CH_2$), and 7.59 (AB quartet $\Delta_{AB} = 28$ Hz, $J_{AB} = 8$ Hz, 4 H, p-C_6H_4).

Anal. Calcd for $C_{13}H_{18}SO_5$: C, 54.53; H, 6.34; S, 11.20. Found: C, 54.59; H, 6.28; S, 10.97.

In a separate small scale reaction, periodically monitored by nmr, the reaction was found to be complete after 3 hr at room temperature.

Tetrahydrofuran and Propionyl *p*-Toluenesulfonate.—Propionyl *p*-toluenesulfonate (18 g, 60% pure, 4.75 mmol) was dissolved in an excess of tetrahydrofuran (15 ml). An immediate exothermic reaction ensued which was complete within minutes. The reaction mixture was kept at room temperature for a further 48 hr and worked up in the usual manner to give an oil which was distilled at reduced pressure to afford a single component, butane-1,4-diol propionate tosylate (**9c**): bp 185–187° (0.001 mm); yield 13.5 g (95%); ν_{max} 1750, 1600, and 1360 cm^{-1}; nmr δ 1.09 (t, $J = 7.5$ Hz, 3 H, CH_2CH_3), 1.70 (q^5, $J = 3$ Hz, 4 H, $CH_2CH_2CH_2CH_2$), 2.27 (q^4, $J = 7.5$ Hz, 2 H, CH_2CH_3), 4.04, (t, $J = 7$ Hz, 2 H, OCH_2), 4.07 (t, $J = 7$ Hz, 2 H, OCH_2), and 7.60 (AB quartet, $\Delta_{AB} = 28$ Hz, $J_{AB} = 8$ Hz, 4 H, p-C_6H_4).

Anal. Calcd for $C_{14}H_{20}SO_5$: C, 55.98; H, 6.71; S, 10.67. Found: C, 55.43; H, 6.36; S, 10.87.

Tetrahydrofuran and Acetyl Methanesulfonate.—Acetyl methanesulfonate (6.7 g, 48.6 mmol) was dissolved in an excess of tetrahydrofuran (12 ml). An immediate exothermic reaction ensued. The reaction mixture was kept overnight at room temperature and worked up in the usual manner to give an oil, essentially pure butane-1,4-diol acetate methanesulfonate (**9b**), yield 9.7 g (95%). On attempted distillation under reduced pressure at 130° the distillate was found to contain tetrahydrofuran, formed by thermal cyclization of the diester. An analytical sample could not, thus, be obtained: ν_{max} 1750 and 1360 cm^{-1}; nmr δ 1.7 (m, 4 H, $CH_2CH_2CH_2CH_2$), 2.03 (s, 3 H, $OCOCH_3$), 3.04 (s, 3 H, CH_3SO_2O), 3.45 (m, 2 H, OCH_2) and 4.15 (s, 2 H, OCH_2).

Catalytic Effect of Acid.—The above reaction was repeated using twice distilled acetyl methanesulfonate (>99.5%). After 16 hr at room temperature careful work-up yielded 47.5% of the pure diester. It was noted that no warming was observed when the two reagents were mixed. When the same sample of acetyl methanesulfonate to which 5% of methanesulfonic acid had been added was treated with tetrahydrofuran under identical conditions 81% of the pure diester was isolated. It was noted that the reagents became warm on mixing.

Tetrahydropyran and Acetyl *p*-Toluenesulfonate.—Acetyl *p*-toluenesulfonate (5.0 g, 90% pure, 21 mmol) was refluxed for 48 hr in tetrahydropyran (25 ml). Work-up in the usual manner gave as an oil, pentane-1,5-diol acetate tosylate (**10a**), yield 6.0 g (95%). Attempted distillation at reduced pressure led to decomposition: ν_{max} 1740, 1600, and 1360 cm^{-1}; nmr δ 1.5 [m, 6 H, $CH_2(CH_2)_3CH_3$], 2.03 (s, 3 H, $OCOCH_3$), 2.43 (s, 3 H, $ArCH_3$), 4.1 (m, 4 H, OCH_2), and 7.64 (AB quartet, $\Delta_{AB} = 27$ Hz, $J_{AB} = 8$ Hz, 4 H, p-C_6H_4).

Anal. Calcd for $C_{14}H_{20}O_5S$ (unpurified material): C, 55.99; H, 6.71; S, 10.65. Found: C, 55.77; H, 6.85; S, 11.05.

Tetrahydropyran and Acetyl Methanesulfonate.—Acetyl methanesulfonate (2.6 g, 18.8 mmol) was refluxed in an excess of tetrahydropyran (25 ml) for 48 hr. Work-up in the usual manner gave, as an oil, pentane-1,5-diol acetate methanesulfonate (**10b**), yield 3.4 g (80%). The product distilled under reduced pressure without decomposition: bp 138–139° (0.005 mm); ν_{max} 1740, 1360 cm^{-1}; nmr δ 1.6 [m, 6 H, $CH_2(CH_2)_3CH_2$], 2.04 (s, 3 H, CH_3CO_2), 3.02 (s, 3 H, CH_3SO_2O), and 4.15 (m, 4 H, OCH_2).

Anal. Calcd for $C_8H_{16}O_5S$: C, 42.85; H, 7.19; S, 14.27. Found: C, 42.80; H, 7.31; S, 14.54.

1,4-Dioxane and Acetyl *p*-Toluenesulfonate.—Acetyl *p*-toluenesulfonate (12.0 g, 5.6 mmol) was refluxed in an excess of dioxane (25 ml) for 24 hr and worked up in the usual manner to yield 2-acetoxyethyl 2′-tosyloxyethyl ether (**11a**), yield 14.8 g (87%). The oil was distilled under reduced pressure to afford the pure diester with near-quantitative recovery: bp 175–180° (0.002 mm); ν_{max} 1750, 1600, and 1360 cm^{-1}; nmr δ 2.05 (s, 3 H, CH_3CO), 2.45 (s, 3 H, $ArCH_3$), 3.65 (m, 4 H, CH_2OCH_2), 4.16 (m, 4 H, CH_2OCO, CH_2OSO_2), and 7.6 (AB quartet, $\Delta_{AB} = 28$ Hz, $J_{AB} = 8$ Hz, 4 H, p-C_6H_4).

Anal. Calcd for $C_{13}H_{18}O_6S$: C, 51.65; H, 6.00; S, 10.59. Found: C, 51.73; H, 5.96; S, 10.81.

1,4-Dioxane and Propionyl *p*-Toluenesulfonate.—Propionyl *p*-toluenesulfonate (18 g, 60% pure, 4.75 mmol) was refluxed in an excess of dioxane (25 ml) for 48 hr. The reaction mixture was worked up in the usual manner to yield an oil which was distilled collecting 2-propionoxyethyl 2′-tosyloxyethyl ether (**11c**): bp 190–200° (0.001 mm); yield 10.0 g (67%); ν_{max} 1755, 1600, and 1360 cm^{-1}; nmr δ 1.08 (t, $J = 8$ Hz, 3 H, CH_2CH_3), 2.34 (q^4, $J = 8$ Hz, 2 H, CH_2CH_3), 2.44 (s, 3 H, $ArCH_3$), 3.70 (m, 4 H, CH_2OCH_2), 4.15 (m, 4 H, CH_2OCO, CH_2OSO_2), and 7.60 (AB quartet, $\Delta_{AB} = 27$ Hz, $J_{AB} = 8$ Hz, 4 H, p-C_6H_4).

Anal. Calcd for $C_{14}H_{20}O_6S$: C, 53.16; H, 6.37; S, 10.13. Found: C, 53.24; H, 6.22; S, 10.29.

2-Acetoxyethyl 2′-Tosyloxyethyl Ether (11) and Acetyl *p*-Toluenesulfonate.—The diester **11a** (2.0 g, 6.6 mmol) was heated with an excess of acetyl *p*-toluenesulfonate (6.0 g, 75% pure, 21 mmol) at 130° for 2 hr. The nmr of the crude reaction mixture showed total disappearance of starting ether. The only peak in the region δ 3.0–6.0 was a sharp singlet at 4.21 ppm. Work-up in the usual manner gave pure ethylene glycol acetate tosylate **8a** identified as such by the identity of its ir and nmr spectra with an authentic sample prepared from ethylene oxide and acetyl *p*-toluenesulfonate, yield 1.5 g (45%).

Repetition of the reaction in acetonitrile after 48-hr reflux gave only complete recovery of starting material.

2,5-Dihydrofuran and Acetyl *p*-Toluenesulfonate.—Acetyl *p*-toluenesulfonate (13.0 g, 60 mmol) and an excess of 2,5-dihydrofuran (10 ml) was refluxed in acetonitrile (15 ml) for 16 hr. The reaction mixture was worked up in the usual manner to yield as an oil, but-2-ene-1,4-diol acetate tosylate (**13a**): yield, 13.3 g (81%); ν_{max} 1750, 1600, and 1360 cm^{-1}; nmr δ 2.02 (s, broad 3 H, CH_3CO), 2.42 (s, 3 H, $ArCH_3$), 4.60 (m, 4 H, CH_2), 5.73 (m, 2 H, CH═CH), and at 7.60 (AB quartet, $\Delta_{AB} = 26$ Hz, $J_{AB} = 8$ Hz, 4 H, p-C_6H_4).

On standing for 4 days at room temperature, the oil turned black and deposited a crystalline material identified as *p*-toluenesulfonic acid. The rest of the material had undergone extensive decomposition as revealed by a second examination of the nmr spectrum. Preparation of an analytical sample by distillation under reduced pressure failed due to extensive decomposition.

2,5-Dihydrofuran and Acetyl Methanesulfonate.—Acetyl methanesulfonate (6.5 g, 47 mmol) and an excess of 2,5-dihydrofuran (10 ml) in acetonitrile (15 ml) were refluxed for 16 hr. The reaction mixture was worked up in the usual manner to yield, as an oil, but-2-ene-1,4-diol acetate methanesulfonate (**13b**): yield, 5.3 g (54%); ν_{max} 1730 and 1360 cm^{-1}; nmr δ 2.05 (s, 3 H, CH_3CO), 3.05 (s, 3 H, CH_3SO_2), 4.70 (d, J = 5 Hz, 2 H, CH_2CH), 4.88 (d, J = 5 Hz, 2 H, CH_2CH), and 5.88 (m, 2 H, $CH{=}CH$). No analytical sample could be obtained; the compound decomposed on attempted distillation.

Isopropyl Ether and Acetyl *p*-Toluenesulfonate.—Acetyl *p*-toluenesulfonate (13.0 g, 75% pure, 61 mmol) in acetonitrile (25 ml) was refluxed for 18 hr with isopropyl ether (15 ml) in excess. After working up in the usual manner the excess ether and isopropyl acetate formed in the reaction were evaporated under reduced pressure to leave an oil which was distilled collecting isopropyl tosylate: bp 110° (0.01 mm); yield, 8.0 g (80%); ν_{max} 1600 and 1360 cm^{-1}; nmr δ 1.30 [d, J = 7 Hz, 6 H, $CH(CH_3)_2$], 2.46 (s, 3 H, $ArCH_3$) 4.77 [s^7, J = 7 Hz, 1 H, $CH(CH_3)_2$], and 7.61 (AB quartet, Δ_{AB} = 28 Hz, J_{AB} = 8 Hz, 4 H, *p*-C_6H_4).

Anal. Calcd for $C_{10}H_{14}O_3S$: C, 56.05; H, 6.59. Found: C, 56.26; H, 6.39.

Isopropyl Ether and β-Sulfopropionic Anhydride[28] (**22**).—β-Sulfopropionic anhydride (1.5 g, 9.1 mmol) was refluxed in an excess of isopropyl ether (10 ml) for 24 hr. The excess ether was evaporated to yield a colorless oil (2.36 g) which was worked up in the usual manner and distilled collecting diisopropyl β-sulfopropionate (**24**, colorless liquid): bp 120° (0.05 mm); ν_{max} 1740 and 1360 cm^{-1}; nmr δ 1.27 [d, J = 7 Hz, 6 H, $CH(CH_3)_2$], 1.43 [d, J = 7 Hz, 6 H, $CH(CH_3)_2$], 3.12 (A_2B_2 symmetrical 16-line system, 4 H, $SO_2CH_2CH_2CO$), 5.00 [s^7, J = 7 Hz, 1 H, $CH(CH_3)_2$], and 5.09 [s^7, J = 7 Hz, 1 H, $CH(CH_3)_2$].

Anal. Calcd for $C_8H_{18}O_5S$: C, 45.37; H, 7.62; S, 13.43. Found: C, 45.60; H, 7.48; S, 13.65.

2-Methyltetrahydrofuran (15) and Acetyl *p*-Toluenesulfonate.—Acetyl *p*-toluenesulfonate (6.0 g, 75% pure, 21 mmol) was dissolved in an excess of 2-methyl tetrahydrofuran (10 ml) and the mixture kept at room temperature for 12 hr. The reaction mixture was worked up in the usual manner to give an oil whose nmr spectrum showed as essentially pure pentane-1,4-diol 1-acetate tosylate (**16**). On standing the diester gradually reverted to 2-methyl tetrahydrofuran. Attempted distillation of **16** under reduced pressure gave no distillate, and thus no analytical sample could be prepared, the residue being identified as pure *p*-toluenesulfonic acid formed from the intramolecular cyclization reaction: yield (**16**), 6.0 g (95%); ν_{max} 1750, 1600, and 1360 cm^{-1}; nmr δ 1.25 [d, J = 7 Hz, 3 H, $CH(CH_3)$], 1.60 (m, 4 H, CH_2CH_2), 2.02 (s, 3 H, CH_3CO), 2.43 (s, 3 H, $ArCH_3$), 3.99 (t, J = 7 Hz, 2 H, OCH_2) 4.7 [m, 1 H, $CH_2CH(CH_3)$] and 7.63 (AB quartet, Δ_{AB} = 28 Hz, J_{AB} = 8 Hz, 4 H, *p*-C_6H_4).

Reaction of Pentane-1,4-diol 1-Acetate 4-Tosylate (16) with Lithium Bromide.—The diester (**16**) prepared as above (6.0 g, 20 mmol) in acetone (50 ml) was treated with lithium bromide (2.5 g, 29 mmol) and the solution maintained at room temperature for 24 hr. The mixture was cooled to 0°, the lithium tosylate and excess lithium bromide were filtered off, and the residual solution was evaporated to dryness under reduced pressure. Extraction of this residue with cold ether followed by removal of the ether under reduced pressure gave 1-acetoxy-4-bromopentane (**17**) as an oil, yield 3.8 g (90%). A sample was distilled, bp 60° (0.01 mm). The crude oil as isolated above contained only one spot on tlc (silica gel) and a single peak on vpc (5% Carbowax) with no trace of the isomer (see below): ν_{max} 1760 cm^{-1}; nmr 1.75 (d, J = 7 Hz, 3 H, $CHBrCH_3$), 1.83 (m, 4 H, CH_2CH_2), 2.06 (s, 3 H, CH_3CO), and 4.13 m, 3 H, CHBr, CH_2OCOCH_3).

Anal. Calcd for $C_7H_{13}O_2Br$: C, 40.21; H, 6.27; Br, 38.22. Found: C, 39.95; H, 6.26; Br, 37.28.

Reaction of 2-Methyltetrahydrofuran with Acetyl Bromide.—To a sample of 2-methyltetrahydrofuran (15.6 g, 0.18 mmol), maintained at reflux and containing a few milligrams of zinc chloride, was added dropwise acetyl bromide (25 g, 0.2 mol). The reaction mixture was heated under reflux for 1 hr. This was then worked up in the usual manner to yield the product, an oil, yield 30 g (80%). The crude oil thus isolated was observed to comprise two components, one minor; the major component has the same retention time as 1-acetoxy-4-bromopentane. Vpc analysis revealed this latter to comprise some 70–80% of the material. The two components could not be separated by distillation and only the major component was isolated and identified by comparison with an authentic sample.[26] The minor component was readily identified, and its proportion precisely defined, from the nmr spectrum which, in addition to the peaks assigned to 1-acetoxy-4-bromopentane (**17**), showed the second component to be 4-acetoxy-1-bromopentane (**18**) present in a ratio of 1:3: nmr (minor component) δ 1.25 (d, J = 7 Hz, 3 H, $CHOAcCH_3$), 1.85 (m, 4 H, CH_2CH_2), 3.48 (t, J = 7 Hz, 2 H, CH_2Br), and 4.95 (s^6, J = 7 Hz, 1H, CH_2CH-$OAcCH_3$).

Reaction of But-2-ene-1,4-diol Acetate Tosylate (13) with Lithium Bromide.—The diester (5.68 g, 20 mmol) and lithium dibromide (3.5 g, 40 mmol) in acetone (50 ml) were maintained at room temperature for 24 hr. The reaction mixture was then cooled to 0°, the lithium tosylate and excess lithium bromide were filtered off, and the residue was evaporated to dryness at reduced pressure. This residue was extracted with cold ether and the ether removed under vacuum leaving the pure bromoacetate (**30**): yield, 3.8 g (98%); ν_{max} 1740 cm^{-1}; nmr δ 2.11 (s, 3 H, CH_3CO), 4.08 (d, J = 8 Hz, 2 H, $=CHCH_2Br$), 4.75 (d, J = 8 Hz, 2 H, $CHCH_2OCOCH_3$), and 5.88 (m, 2 H, $-CH{=}CH-$).

Anal. Calcd for $C_6H_9O_2Br$: C, 37.33; H, 4.70; Br, 41.40. Found: C, 37.01; H, 4.50; Br, 40.30.

Reaction of But-2-ene-1,4-diol Acetate Tosylate (13) with Pyrrolidine.—The diester (2.0 g, 7.3 mmol) was dissolved in ether and a large excess of pyrrolidine (2 ml) was added at room temperature. An immediate precipitate of amine sulfonate salt was observed. The ether was decanted and worked up in the usual way to give a yellow oil, 1-acetoxy-4-*N*-pyrrolidinebut-2-ene (**29**): yield, 550 mg (41%); ν_{max} 1740 cm^{-1}; nmr δ 1.75 (m, 4 H, CH_2CH_2) 2.03 (s, 3 H, CH_3CO), 2.50 (m, 4 H, NCH_3), 3.18 (d, J = 7 Hz, $=CCH_2N$), 4.68 (d, J = 7 Hz, $=CHCH_2O$-$COCH_3$), and 5.72 (m, 2 H, $-CHCH-$).

Anal. Calcd for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35; N, 7.64. Found: C, 56.90; H, 10.00; N, 6.74.

***tert*-Butyl Ethyl Ether and Acetyl Methanesulfonate.**—To a solution of acetyl methanesulfonate (0.94 g, 6.75 mmol) in acetonitrile (2 ml) was added, at room temperature, *tert*-butyl ethyl ether (750 mg, 7.5 mmol) and the reaction was periodically monitored by nmr. After 30 min no trace of the starting ether was observed to be present as shown by the complete disappearance of the CH_2 quartet at δ 3.40. Quantitative formation of ethyl acetate was observed, evidenced by the appearance of a new CH_2 quartet at δ 4.15. In addition the presence of methanesulfonic acid was confirmed by the peaks at δ 3.00 (SO_2CH_3) and at δ 12.7 (SO_3H), to an extent no less than 75%, as estimated from intergration measurements. The presence of isobutene was inferred from the terminal olefinic proton multiplet (J = 1.5 Hz) at 4.70 and the corresponding finely split singlet (J = 1.5 Hz) at 1.7 [$C{=}C(CH_3)_2$]. Both these latter signals progressively diminished in intensity on standing at room temperature, having disappeared after 22 hr. The simultaneous growth of a singlet at δ 1.22 appeared to indicate the probable fate of the olefin as acid-catalyzed polymerization.

Synthesis of 1-(α,α′-Diphenylmethyl)-4-(2′-acetoxyethoxyethyl)piperazine (32).—A solution of 1-(α,α′-diphenylmethyl)-piperazine (**31**) (1.26 g, 5 mmol) and 2-acetoxyethyl-2′-tosyloxyethyl ether (**11**) (850 mg, 2.8 mmol) in tetrahydrofuran (20 ml) was refluxed for 18 hr. The solution was evaporated to dryness under reduced pressure, ether was added, and the precipitated salt was collected, dried, and weighed, yield 1.05 g (100%). The filtrate was extracted with 2 *N* HCl which extract was made alkaline with NaOH and reextracted with ether to yield, after drying and evaporation to dryness under reduced pressure, the required amino acetate (**32**), a colorless oil, which gave only a single spot on silica gel tlc: yield, 650 mg (63%); ν_{max} 1760 ($COCH_3$), 1600, 705, 745, and 755 cm^{-1} (Ar 5 H); nmr δ 1.95 (s, 3 H, $COCH_3$), 2.5 (m, 10 H, NCH_2), 3.6 (m, 4 H, OCH_2), 4.25 [s, 1 H, $(Ar)_2CH$], 4.2 (t, J = 6 Hz, 2 H, OCH_2), and 7.2 (m, 10 H, C_6H_5).

Tetrahydrofuran and *p*-Toluenesulfonic Anhydride.—*p*-Toluenesulfonic anhydride was refluxed for 18 hr in an excess of tetrahydrofuran (25 ml). The solution was evaporated to dryness and worked up in the usual manner to yield, as a pure oil, butane-1,4-diol bistosylate: ν_{max} 1600 and 1360 cm^{-1}; nmr (identical with an authentic specimen[33]) δ 1.7 (m, 4 H, CH_2CH_2), 2.45 (s, 6 H, $ArCH_3$), 4.0 (m, 4 H, OCH_2), and 7.60 (AB quartet, Δ_{AB} = 29 Hz, J_{AB} = 8 Hz, 8 H, p-C_6H_4).

Tribenzylamine and Acetyl p-Toluenesulfonate.—Solutions of acetyl p-toluenesulfonate (8.7 g, 75% pure, 30 mmol) in ether (100 ml) and tribenzylamine (11.7 g, 40 mmol) in ether were mixed at room temperature. An immediate white precipitate was deposited and the reaction mixture left at room temperature for 24 hr. The crystalline material was filtered and dried, mp 202–203°. It was identified as the tosylate salt of tribenzylamine: yield, 13.2 g (96%); ν_{max} 1600, 750, 700, and 690 cm^{-1}; nmr δ 2.40 (s, 3 H $ArCH_3$), 4.31 (d, J = 5 Hz, 6 H, $ArCH_2N$), 7.3 (m, 15 H, Ar), and 7.70 (AB quartet J_{AB} = 8 Hz, 4 H, p-C_6H_4).

Anal. Calcd for $C_{28}H_{29}NO_3S$: C, 73.5; H, 5.95; N, 3.06; S, 6.99. Found: C, 73.41; H, 6.20; N, 2.78; S, 6.72.

The identity was confirmed by synthesis of the salt from p-toluenesulfonic acid and tribenzylamine, mp 204–205°, mmp (with product) 202–203°.

Trimethylamine and Acetyl Methanesulfonate.—To a solution of acetyl methanesulfonate (3.32 g, 24 mmol) in ether (100 ml) was added at room temperature an excess of trimethylamine (5 ml). After standing for some minutes the resulting white precipitate was filtered off and recrystallized from acetonitrile, mp 204–205°. It was identified as the methanesulfonate salt of trimethylamine by comparison with an authentic sample prepare from methanesulfonic acid, mp 204–206°, mmp 204°, yield 3.8 g (97%).

The residual ether solution was now evaporated to dryness under high vacuum. The resulting oil appeared to be polymerized ketene: yield, 800 mg (79%); ν_{max} 1790, and 1830 cm^{-1} [(C=O (saturated), C=O (anhydride)]; nmr δ 2.25 (s, CH_2).

Triethylamine and Acetyl Methanesulfonate in the Presence of 1-(N-Morpholino)isobut-1-ene (26).—A solution of acetyl methanesulfonate (4.14 g, 30 mmol) in ether (25 ml) was added dropwise at room temperature to a solution of triethylamine (3.0 g, 30 mmol) and 1-(N-morpholino)isobut-1-ene (26) (4.2 g, 30 mmol) in 50 ml of ether. The reaction mixture was kept at room temperature for 2 hr and the precipitated sulfonate salt of triethylamine was filtered off. The solution was evaporated to dryness under reduced pressure leaving a colorless oil, yield 3.43 g (62%). The oil was distilled under reduced pressure collecting two compounds: 3-morpholino-2,2-dimethylcyclobutanone[30] (**27**) [bp 64° (0.1 mm); ν_{max} 1780 cm^{-1} (cyclobutane C=O); nmr δ 1.17, 1.21, (s, 6 H, CH_3), 2.12 (s, 2 H, $COCH_2$), 2.45 (m, 4 H, NCH_2), 2.92 (s, 1 H, NCH), and 3.70 (m, 4 H, OCH_2)] and 1-morpholino-4-methylpent-1-ene-3-one[30] (**28**) {bp 110–112° (0.1 mm); ν_{max} 1640 cm^{-1} (N–C=C); nmr δ 1.08 [d, J = 7 Hz, 6 H, $CH(CH_3)_2$], 2.5 (s,[7] J = 7 Hz, 1 H, $CH(CH_3)_2$], 3.32 (m, 4 H, NCH_2), 3.70 (m, 4 H, OCH_2), and 6.38 (AB quartet, Δ_{AB} = 136.5 Hz, J_{AB} = 13 Hz, 2 H, NCH=CH)}.

Registry No.—**8a**, 19859-09-7; **8b**, 26923-81-9; **9a**, 19859-06-4; **9b**, 19859-00-8; **9c**, 19859-11-1; **10a**, 26923-85-3; **10b**, 26923-86-4; **11a**, 26923-87-5; **11c**, 26923-88-6; **13a**, 19859-10-0; **13b**, 26923-90-0; **16**, 19859-07-5; **17**, 26923-92-2; **18**, 26923-93-3; **20a**, 26923-94-4; **20b**, 26923-95-5; **21a**, 26923-96-6; **21b**, 26923-97-7; **24**, 26923-98-9; **27**, 2618-48-6; **28**, 2618-47-5; **29**, 26924-01-6; **30**, 26924-02-7; **32**, 26924-03-8; n-butyl tosylate, 778-28-9; n-propyl tosylate, 599-91-7; benzyl acetate, 140-11-4; isopropyl tosylate, 2307-69-9; butane-1,4-diol bistosylate, 4724-56-5; tribenzylamine (tosylate salt), 26924-09-4.

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[33] N. Frydmann and Y. Mazur, unpublished results.

Mixed Sulfonic–Carboxylic Anhydrides. III.[1]
Reactions with Aromatic Ethers and Aromatic Hydrocarbons

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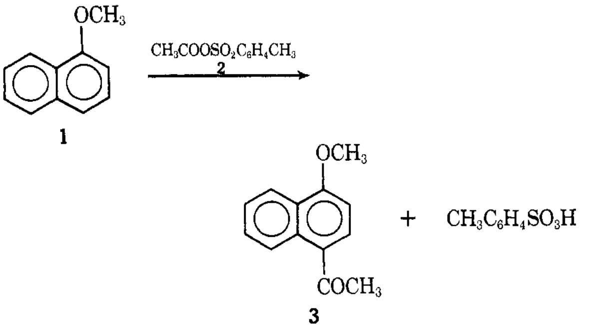
Mixed sulfonic–carboxylic anhydrides are shown to react with aromatic ethers. The products isolated depend upon the reaction conditions. When these are mild, the monoacylated aromatic ethers are formed but under more vigorous conditions these latter undergo self-condensation to the respective dypnones or triphenylbenzenes. Reaction with aromatic hydrocarbons is slow but the reaction with 9,10-dihydroanthracene effects aromatization in good yield, a reaction shown not to be of the ionic type of mechanisms usually associated with mixed anhydride reactions.

Previous publications in this series have demonstrated the reactive nature of mixed sulfonic–carboxylic anhydrides[1,2] as acylating agents. Aliphatic ethers were shown to undergo facile cleavage following initial acylation of the ether oxygen atom,[1] and thus it was of interest to examine the behavior of these reagents toward aromatic ethers.

With aromatic ethers the reaction was swift and comparatively clean. Thus reaction at room temperature of 1-methoxynaphthalene (**1**) with acetyl p-toluenesulfonate (**2**) in acetonitrile gave exclusively the 4-acetyl isomer **3** in 82% yield (eq 1), while under similar conditions 2-methoxynaphthalene (**4**) gave a 65% yield of the 1-acetyl isomer **5** (eq 2).

With the smaller, less hindered molecules, anisole and phenetole, reaction could be made to proceed further. Thus anisole **6** refluxed in acetonitrile with acetyl p-toluenesulfonate (**2**) gave, in addition to the expected p-methoxyacetophenone (**7**), a yellow crystalline material



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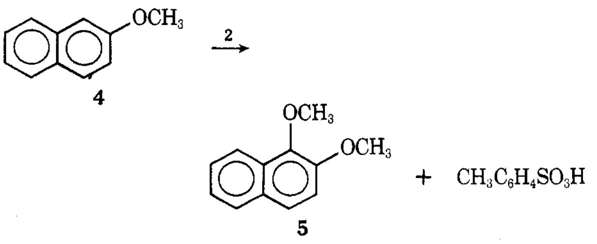

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[1] Paper II in this series: M. H. Karger and Y. Mazur, J. Org. Chem., **36**, 532 (1971).

[2] M. H. Karger and Y. Mazur, J. Amer. Chem. Soc., **90**, 3878 (1968); cf. C. G. Overberger and E. Sarlo, ibid., **85**, 2446 (1963).