1251. *The Preparation of Unstable Toluene*-p-*sulphonates*

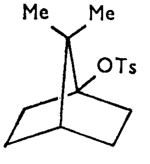
By H. M. R. Hoffmann

The methods for preparing toluene-*p*-sulphonates (and generally applicable to the preparation of other esters) are summarised and discussed briefly. A number of unstable toluene-*p*-sulphonates have been prepared, including 1-phenylethyl and t-butyl toluene-*p*-sulphonate, the latter being the first reported example of an arenesulphonic ester derived from a simple tertiary alcohol.

Toluene-*p*-sulphonates have been prepared by various methods. The most common,[1] formulated by equation (1),

$$\mathrm{ROH} + \mathrm{TsCl} \xrightarrow[\text{pyridine}]{0-20^\circ} \mathrm{ROTs} \quad (\mathrm{Ts} = p\text{-}\mathrm{CH_3{\cdot}C_6H_4{\cdot}SO_2}) \tag{1}$$

has been applied successfully to numerous primary alcohols, although the yields generally decrease with increasing chain-length.[2] Secondary alcohols tend to react less readily in the cold, whilst tertiary alcohols do not react at all under these conditions: an exception, and as yet the only example,* has been apocamphyl toluene-*p*-sulphonate[3] (I), which was formed in 34% yield, but only after the mixture had been kept for 20 hours at 100°. This general pattern of reactivity can be explained by the decreasing acidity of the hydroxylic proton together with the incursion of a steric effect.† A steric effect appears to be largely responsible for the very low reactivity of the bicyclic alcohol, although the rate of sulphonylation can be expected to increase with a change to a stronger base than pyridine. In the limiting case, the conjugate base of the alcohol itself, *i.e.*, the alkoxide (or phenoxide[4]) may be employed. Thus, a series of extremely unstable benzyl toluene-*p*-sulphonates has been prepared, including the *p*-methoxybenzyl ester[5] which could be handled only at −70°. It seems likely, that with this method, when applied to the sulphonylation of, *e.g.*, t-butyl alcohol, the strong base t-butoxide (particularly since it is not hydrogen-bonded[6]) will promote a fast *E*2 reaction from the transiently formed ester.



(I)

Alternative routes to unstable sulphonic acid esters are based upon the alkylation of toluene-*p*-sulphonic acid and its salts. Two unstable secondary sulphonates have been prepared in high yield by way of the diazoalkane:[7]

$$\mathrm{R_2CN_2} + \mathrm{HOTs} \xrightarrow{-\mathrm{N_2}} \mathrm{R_2CHOTs} \tag{2}$$

Finally, there is the silver-salt method:

$$\mathrm{RX} + \mathrm{AgOTs} \longrightarrow \mathrm{ROTs} + \mathrm{AgX} \quad (\mathrm{X} = \mathrm{Cl,\ Br,\ or\ I}), \tag{3}$$

for which acetonitrile is the best solvent,[8] since it allows the reaction to be carried out in a homogeneous medium. Thus, a number of the more stable toluene-*p*-sulphonates (and methanesulphonates) have been prepared in excellent yields, although on interaction of

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* *Added in proof*.—P. Carter, R. Howe, and S. Winstein (*J. Amer. Chem. Soc.*, 1965, **87**, 914) have recently prepared a "birdcage" toluene-*p*-sulphonate, having properties similar to that of (I); cf. also C. J. Norton, Ph.D. Thesis, Harvard, 1955.

† Sulphonylation can be seen in perspective with the mechanistically related base-catalysed acylation of alcohols. For the acetylation with, *e.g.*, acetic anhydride and pyridine, a similar sequence of reactivity is observed. All these reactions are related to the ester hydrolysis *via* mechanism $B_{\mathrm{Ac}}2$, for which both polar and steric factors have been established (C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, pp. 757, 778).

[1] (*a*) R. S. Tipson, *J. Org. Chem.*, 1944, **9**, 235; (*b*) F. Muth in "Methoden der Organischen Chemie," Houben-Weyl, Vol. **9**, 659, Thieme, Stuttgart, 1955.

[2] H. M. R. Hoffmann, following Paper.

[3] P. D. Bartlett and L. H. Knox, *J. Amer. Chem. Soc.*, 1939, **61**, 3184.

[4] J. F. Bunnett and J. Y. Bassett, *J. Amer. Chem. Soc.*, 1959, **81**, 2104.

[5] J. K. Kochi and G. S. Hammond, *J. Amer. Chem. Soc.*, 1953, **75**, 3443.

[6] D. J. Cram, B. Rickborn, C. A. Kingsbury, and P. Haberfield, *J. Amer. Chem. Soc.*, 1961, **83**, 3678.

[7] A. Ledwith and D. G. Morris, *J.*, 1964, 508.

[8] W. D. Emmons and A. F. Ferris, *J. Amer. Chem. Soc.*, 1953, **75**, 2257.

secondary and tertiary alkyl halides with silver toluene-*p*-sulphonate only the products resulting from elimination could be isolated.[8]

We now find that elimination can be cut down appreciably by working at low temperatures and by careful isolation of the products, and we report [9] the preparation of 1-phenylethyl,* diphenylmethyl,† and t-butyl toluene-*p*-sulphonate.‡ Furthermore, we have prepared the known *p*-methylbenzyl toluene-*p*-sulphonate [5] by this method and have evidence for the formation of *p*-methoxybenzyl toluene-*p*-sulphonate.[5]

t-Butyl toluene-*p*-sulphonate (and the *p*-methoxybenzyl ester), was obtained most conveniently *in situ*, since it proved far too unstable for an elemental analysis and even for being handled at 0° (the half-life in acetonitrile at 0° is 63 min.). Therefore, the existence of this compound required indirect proof which, however, has been made compelling; on mixing a solution of silver toluene-*p*-sulphonate in acetonitrile with an excess of t-butyl bromide at −35°, silver ion was precipitated in the theoretical amount. The reaction was very fast, if both solutions were sufficiently concentrated and one component, here t-butyl bromide, was in excess. The end of the reaction could be recognised by a sudden clearing of the supernatant liquor, or more quantitatively, by testing a small aliquot portion of the solution with an aqueous solution of bromide ion. After complete precipitation of silver bromide, the mixture contained a compound whose decomposition by way of an *E*1 reaction was followed at 0° and at 10°. This was possible by a non-aqueous titration after individual samples had been quenched to −40°. Sharp end-points were obtained. Since the liberated toluene-*p*-sulphonic acid catalysed the *E*1 reaction and, on the other hand, added back [10] to the isobutene formed, triethylamine or 2,6-lutidine ($<$0·05M) were added; the concentration of t-butyl toluene-*p*-sulphonate could now be calculated from the initial concentration of silver ion minus the concentration of protonated amine (which is identical to the concentration of olefin liberated). The observed rates remained constant and independent of the base, and all first-order plots gave excellent straight lines up to 75% reaction (referred to the total amount of silver ion used). A typical run is shown in Table 1. Addition of free toluene-*p*-sulphonate (as tetraethylammonium salt) increased the rate moderately (cf. Table 2), probably as a result of a medium effect (accelerating) which might be superseded at these low temperatures by a common-ion effect (decelerating).

TABLE 1

The first-order elimination of t-butyl toluene-*p*-sulphonate in acetonitrile at 0°

Initially $[\mathrm{AgOTs}]_0 = 0{\cdot}0514$M $[2,6\text{-lutidine}]_0 = 0{\cdot}0508$M and $[\mathrm{Bu^tBr}]_0 = 0{\cdot}556$M

Time (min.)	0	6	12	18	27	34	42	51	59	72
Ml. 0·0203M-acid per 5·0 ml. soln.	8·82	8·30	7·74	7·18	6·50	5·98	5·43	4·98	4·65	3·90
10^4k_1 (sec.$^{-1}$)	—	1·66	1·79	1·87	1·85	1·87	1·88	1·83	1·77	1·84

Independently, runs were followed conductometrically. For all experiments the conductivity increased steadily with time, indicating the decomposition of a reactive species with the formation of ions. A quantitative evaluation of this conductivity increase is difficult; however, one may expect a linear dependence of conductivity on the concentration of protonated amine in *dilute* solutions. A Guggenheim plot [11] (which, strictly

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* This compound was assumed as an intermediate in the oxidation of 1-phenylethyl toluene-*p*-sulphinate by hydrogen peroxide, but found too reactive for isolation (J. Kenyon, H. Phillips, and F. M. H. Taylor, *J.*, 1933, 173).

† Independently, this compound was prepared from diphenylmethyl chloride and silver toluene-*p*-sulphonate in ether solvent (G. W. H. Cheeseman and R. C. Poller, *J.*, 1962, 5277), and according to equation (2).[7]

‡ Various attempts to prepare this compound have failed. Cf., *e.g.*, (*a*) E. Tommila and J. Jutila, *Acta Chem. Scand.*, 1952, **6**, 844; (*b*) B. L. Emling, *J. Amer. Chem. Soc.*, 1952, **74**, 4702; (*c*) ref. 8; (*d*) P. M. Laughton and R. E. Robertson, *Canad. J. Chem.*, 1955, **33**, 1208.

[9] Preliminary account, H. M. R. Hoffmann, *Chem. and Ind.*, 1963, 336.

[10] P. B. D. de la Mare, E. D. Hughes, C. K. Ingold, and Y. Pocker, *J.*, 1954, 2930,

[11] E. A. Guggenheim, *Phil. Mag.*, 1926, **2**, 538.

TABLE 2

First-order rate constants for the elimination of t-butyl toluene-*p*-sulphonate in acetonitrile [a, b]

$[Ag^+]_0$ (mmoles $l.^{-1}$)	78·8	73·2	57·0	51·4	51·4	54·2	56·8	48·5
$[OTs^-]_0$,,	78·8	73·2	57·0	51·4	82·5	90·6	56·8	48·5
$[NEt_3]_0$,,	101	48·1	46·0	50·8 [c]	49·2 [c]	49·2 [c]	46·6	41·5
Temp.	0°	0°	0°	0°	0°	0°	9·9°	10·04°
10^4k_1 (sec.$^{-1}$)	1·92	1·73	1·85	1·84	2·13	2·10	6·28	6·40

[a] A 10-fold excess of t-butyl bromide over silver ion was used. [b] $\Delta H^\ddagger = 19$ kcal.; $\Delta S^\ddagger = -5$ e.u. at 273°K. [c] 2,6-Lutidine used as base.

speaking, should only be applied to a reaction which can be followed over several half-lives) gave an initial rate constant of $k_1 = 1{\cdot}84 \times 10^{-4}$ sec.$^{-1}$ (cf. Table 3). In view of the assumptions made, the agreement with the more reliable titrimetric value is excellent, but probably to some extent fortuitous.

TABLE 3

The elimination of t-butyl toluene-*p*-sulphonate in acetonitrile at 0°, followed conductometrically

Initially, $[AgOTs]_0 = 0{\cdot}0395$M, $[t\text{-}Bu^tBr]_0 = 0{\cdot}81$M and $[NEt_3]_0 = 0{\cdot}0422$M

Time *t* (min.)	22	24	25	30	32	33	34	35	40	45	50
Conductivity [μmho]											
At *t* min.	660	687	700	768	791	803	815	827	885	940	992
At *t* + 20 min. ...	907	929	940	992	1012	1022	1032	1042	1085	1124	1159
10^4k_1 (sec.$^{-1}$)	—	1·73	1·66	2·06	1·88	1·85	1·82	1·80	1·96	2·14	2·33

Mean k_1 (neglecting the last two values): $1{\cdot}84 \times 10^{-4}$ sec.$^{-1}$.

The nitrilium salt $[MeCNBu^t]^+$ OTs^-, which might be regarded as an alternative to the formation of t-butyl toluene-*p*-sulphonate under our conditions, can be ruled out on several grounds.

(*a*) The decomposition of an ionic salt should not give a clear increase in conductivity (cf. Table 3).

(*b*) The reaction of t-butyl bromide with silver tetrafluoroborate liberated acid only, under our conditions.

(*c*) The decomposition of t-butyl toluene-*p*-sulphonate in acetonitrile was acid-catalysed, since initial rates in the absence of base [9] were about twice as fast as those measured in the presence of base. No acid catalysis would be expected for the decomposition of a nitrilium salt.

(*d*) The toluene-*p*-sulphonate anion, if at all present in a nitrilium salt, should be precipitated by an equivalent amount of lithium ion as lithium toluene-*p*-sulphonate, which is virtually insoluble in acetonitrile. After adding a solution of lithium chloride in acetonitrile to the reaction solution we observed the precipitation of only a small amount of lithium toluene-*p*-sulphonate, indicating some decomposition of the product. The precipitate could be centrifuged off at —20° and then the reaction solution remained clear at this temperature. Warming the solution, however, to above 0° rapidly precipitated a further crop of lithium salt, which was again separated at low temperature. The precipitate could be made to reappear a number of times until all the t-butyl toluene-*p*-sulphonate had decomposed.

(*e*) Acetonitrile is only weakly nucleophilic, *i.e.*, nitrilium salts are very strong alkylating agents, second only to oxonium salt, and therefore require an anion such as BF_4^-, $SbCl_6^-$, or $AlCl_4^-$ for their stabilisation.[12]

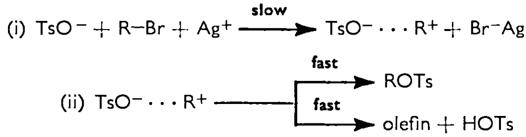
(*f*) The *E*1 reaction of t-butyl toluene-*p*-sulphonate in acetonitrile at 0° is 5000 times faster than that of t-butyl bromide. For the 1-phenylethyl system this ratio is *ca.* 500, which is reasonable.[2]

With regard to (*b*), and more generally to the mechanism of the reaction, it is interesting that silver toluene-*p*-sulphonate actually reacts *faster* with t-butyl bromide in acetonitrile than silver tetrafluoroborate does. Typically, in two experiments, one involving equimolar

[12] H. Meerwein, P. Laasch, R. Mersch, and J. Spille, *Chem. Ber.*, 1956, **89**, 209.

concentrations (0·035M) of t-butyl bromide and silver toluene-*p*-sulphonate, another the same concentrations of t-butyl bromide and silver tetrafluoroborate, the first half-life for the formation of silver bromide at 25° was about 10 times shorter for the reaction with silver toluene-*p*-sulphonate. This suggests that, even in the formation of t-butyl toluene-*p*-sulphonate, the rate-determining step has some S_N2 character,* in accord with the mechanism proposed[13] for the related reactions of alkyl bromides with silver nitrate.

For these and similar reactions all the experimental evidence available is consistent with a two-stage reaction,[13,14] in which the rate-controlling step (i) involves the formation of an ion-pair intermediate, which collapses in the product-determining steps (ii) to give the observed ester and olefin:



$$\text{(i) } TsO^- + R{-}Br + Ag^+ \xrightarrow{\text{slow}} TsO^- \cdots R^+ + Br^-Ag^+$$

$$\text{(ii) } TsO^- \cdots R^+ \begin{cases} \xrightarrow{\text{fast}} ROTs \\ \xrightarrow{\text{fast}} \text{olefin} + HOTs \end{cases}$$

Since, on this mechanism, one and the same toluene-*p*-sulphonate group is involved in steps (i) and (ii), the only molecule which could conceivably intervene in the product-determining stage is a solvent molecule.[13] However, this would lead to a nitrilium salt which can have at best a transient existence (see above). Adding free toluene-*p*-sulphonate ions, we have found for two runs by extrapolating to zero time that the rate is accelerated [in accord with step (i)] but that the product distribution is virtually unchanged, as demanded by step (ii).

t-Butyl toluene-*p*-sulphonate is the first example of a sulphonic acid ester derived from a simple tertiary alcohol; 1-phenylethanol, known to be comparable to t-butyl alcohol in its reactivity, forms an ester which is slightly more stable.[2] Clearly, the silver-salt method as described is a useful complement to the other methods for preparing unstable sulphonic and other esters in general, since the low reaction temperature and the initially neutral medium ensure a maximum of protection to the products. A possible limitation of the method may arise whenever the carbonium ion derived from the alkyl halide is capable of undergoing a rearrangement, although more work needs to be done here.

EXPERIMENTAL

Materials.—Acetonitrile was purified as described.[15] The alkyl bromides were purified commercial materials or obtained by conventional methods. Silver toluene-*p*-sulphonate was most readily prepared by rapidly mixing equimolar solutions of silver nitrate and sodium toluene-*p*-sulphonate in water; the product came down quickly. In order to avoid coprecipitation of sodium nitrate, 0·3 moles of the silver salt were prepared in 400 ml. of water. The mother-liquor was cooled to 5°, the product (50 g.) filtered off, and washed successively with ice-cold water, acetone, and ether. The combined aqueous washings and the mother-liquor gave three further fractions of 40 g. (total yield 97%). All operations were carried out swiftly in diffuse daylight, since silver toluene-*p*-sulphonate turned brownish on prolonged exposure to light.

*Preparation of Toluene-*p*-sulphonates.—General technique.* With the exception of the t-butyl ester, equimolar quantities of the alkyl bromide and silver toluene-*p*-sulphonate were used. The compounds were dissolved in the minimum amount of acetonitrile, and then introduced separately into the two arms of an inverted Y-tube equipped with a low-temperature

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* In contrast, an S_N2 attack on t-butyl bromide *without* electrophilic assistance appears to be of little importance (cf. S. Winstein, S. Smith, and D. Darwish, *Tetrahedron Letters*, 1959, No. 16, 24).

[13] See D. N. Kevill, Ph.D. Thesis, University of London, 1960, for an excellent discussion.

[14] (*a*) G. S. Hammond, M. F. Hawthorne, J. H. Waters, and B. M. Graybill, *J. Amer. Chem. Soc.*, 1960, **82**, 704; (*b*) J. Landais, *Ann. Chim. (France)*, 1963, **8**, 575; (*c*) The push-pull character of these reactions has been stressed by N. Kornblum. Cf., *e.g.*, *Org. Reactions*, 1962, **12**, 101.

[15] H. M. R. Hoffmann and E. D. Hughes, *J.*, 1964, 1252.

thermometer. The solutions were mixed below −25° and left until precipitation of silver bromide was complete. The product was isolated in one of two ways.

(i) It was frozen out, collected with the silver halide, then extracted with a suitable solvent and reprecipitated by cooling and/or adding light petroleum. Some losses occurred owing to the solubility of product in acetonitrile, but this method ensured a rapid work-up with practically no decomposition of the product.

(ii) Alternatively, the silver bromide was separated by filtration or centrifugation, and the mother liquor evaporated below 0°.

The compounds were analysed immediately by complete hydrolysis, since C and H analyses tended to be irreproducible owing to decomposition. The melting points, determined on a Kofler bench, were not characterstic.

1-*Phenylethyl toluene*-p-*sulphonate*. Silver toluene-*p*-sulphonate (7·0 g.) dissolved in acetonitrile (35 ml.) and 1-phenylethyl bromide (4·7 g.) in acetonitrile (10 ml.) were transferred into the two arms of the reaction vessel and then mixed with vigorous shaking at −30°. The resulting suspension was kept for 10 min. at −30°, warmed briefly to 0° and checked for the absence of silver ion. Cooling the solvent to near freezing precipitated the bulk of the product together with silver bromide. The solid was filtered off rapidly and extracted with acetone (2 × 10 ml.) at 0°. On cooling the combined clear acetone solution to −80°, 1-phenylethyl toluene-*p*-sulphonate crystallised. It was filtered, twice washed with light petroleum (b. p. below 40°) at 0°, dried rapidly at 0°/0·05 mm., and stored at −80° (2·9 g., 42%; or 90% based upon titration of liberated acid in the mother-liquor). The compound turned brick red on decomposition which was rapidly induced at room temperature. For the kinetic experiments [2] product from three different preparations was used. All samples gave theoretical infinity values in the ethanolysis, and two samples of different origin gave identical rate constants for runs at the same temperature.

Diphenylmethyl toluene-*p*-sulphonate was prepared analogously, diphenylmethyl bromide (6·3 g.) being used. After 4 min. at −30°, the reaction was complete. The mixture was then cooled further, filtered, and the solid immediately extracted with acetone (3 × 10 ml.) at −20°, which, on cooling to −80°, yielded diphenylmethyl toluene-*p*-sulphonate (4·75 g., 55%). Saponification equivalent: Found 342. Calc. 338.

t-Butyl toluene-p-*sulphonate*. Silver toluene-*p*-sulphonate (3·0 g.), suspended in acetonitrile (5 ml.), and t-butyl bromide (5·0 ml.) were mixed for 3 min. with vigorous shaking at −30°. The precipitated silver bromide was centrifuged off below 0° and the supernatant mother-liquor evaporated rapidly at −35° using a bath of melting 1,2-dichloroethane as a coolant. A copious precipitate remained behind decomposing rapidly at 0° with liberation of a gas.

Kinetic experiments. A solution (20 ml.) at 0° of silver toluene-*p*-sulphonate (0·2061M) in acetonitrile was mixed with a solution (10 ml.) at 0° of t-butyl bromide (4·45M) in acetonitrile for 3 min. at −30° and shaken vigorously for a further 5 min. at 0° to ensure complete reaction and temperature equilibration. After adding a solution (50 ml.) of 2,6-lutidine (0·0508M) in acetonitrile at 0° and further shaking for 3 min., the first sample was withdrawn and quenched to −40° in a solution (40 ml.) of 10% v/v acetic acid in chloroform. The free base present was then titrated immediately with standard anhydrous perchloric acid in glacial acetic acid to the first pink colour of the indicator (Oracet Blue B). The concentration of t-butyl toluene-*p*-sulphonate was calculated as stated above, *i.e.*, from the total concentration of silver ion (0·0514M) minus the concentration of protonated 2,6-lutidine (cf. Table 1). The reaction was also followed conductometrically (Table 3): a solution (10 ml.) at 0° of silver toluene-*p*-sulphonate (0·2170M) in acetonitrile was mixed with t-butyl bromide (6·12 g.) at −30° for 8 min. and warmed quickly to −10°. A solution (40 ml.) at 0° of triethylamine (0·0580M) in acetonitrile was added with shaking, silver bromide filtered off with suction, and the filtrate measured for its conductivity at 0°, using a Wayne Kerr Universal Bridge type B 221.

p-*Methylbenzyl toluene*-p-*sulphonate*. The preparation of this compound by way of the alcohol has been described.[5] Silver toluene-*p*-sulphonate (5·16 g.) dissolved in acetonitrile (20 ml.) was mixed with a solution (10 ml.) of *p*-methylbenzyl bromide (3·42 g.) in acetonitrile at 0°, and the mixture shaken occasionally. After 1 hr. at 0° the reaction was practically complete; the silver bromide was centrifuged off and the mother-liquor evaporated at 0°. The residue was dissolved in the minimum amount of dry ether and the resulting solution centrifuged to remove an additional small quantity of silver bromide. On pouring the ethereal solution into an excess of light petroleum (b. p. below 40°) and cooling to $-80°$, *p*-methylbenzyl toluene-*p*-sulphonate crystallised (3·93 g., 77%, after recrystallisation from ether–light petroleum). Saponification equivalent: Found 278. Calc. 276. The compound decomposed after about 2 hr. at room temperature or 3 days at 0°, assuming a red coloration. In contrast, *p*-methylbenzyl bromide can be kept at room temperature without any decomposition.

p-Methoxybenzyl toluene-*p*-sulphonate[5] was prepared *in situ* using a 1·2-fold excess of *p*-methoxybenzyl bromide. The kinetic technique was the same as described for t-butyl toluene-*p*-sulphonate, the disappearance of 2,6-lutidine being titrated. The rate of dissociation at 0° was found to be in the same order of magnitude as that of t-butyl toluene-*p*-sulphonate. However, the results were not fully reproducible and it might be that the added base, although sterically hindered, reacts with the ester in an S_N2 reaction and/or reversible ionisation interferes.

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