Synthesis of Enol Sulphonates from Carbonyl Compounds

By NORBERT FRYDMAN, RUTH BIXON, MILON SPRECHER, and YEHUDA MAZUR*
(*Department of Chemistry, The Weizmann Institute of Science, Rehovoth, Israel*)

Summary Sulphonic anhydrides and dimethylformamide convert ketones and aldehydes into enol sulphonates, which are generally relatively stable towards acids and bases but regenerate the carbonyl compounds by O–S bond cleavage on more vigorous treatment.

No general method for the synthesis of enol sulphonates has been available until recently.[1]

We report a general method for converting carbonyl compounds into the corresponding enol sulphonates, by heating a solution of the carbonyl compound and sulphonic anhydride in dimethylformamide. Enol tosylates were prepared by heating *ca.* 15% dimethylformamide solutions of ketones or aldehydes with 1—2 mol. equiv. of toluene-*p*-sulphonic anhydride at 120—140° for 0·5—2 hr. This reaction was applicable to acyclic, alicyclic, and aromatic

ketones and aldehydes.† Among others, pentan-3-one, cyclohexanone, 17β-acetoxyandrostan-3-one, acetophenone, deoxybenzoin, benzyl methyl ketone, decanal, cyclohexanecarbaldehyde, phenylacetaldehyde, and diphenylacetaldehyde have been converted into the corresponding enol tosylates. The yields obtained varied between 5 and 40%; yields based on recovered starting materials were considerably higher. Whenever more than one isomeric enol toluene-*p*-sulphonate was formed they were separated by column chromatography; stereochemical assignment was based on the n.m.r. spectra.

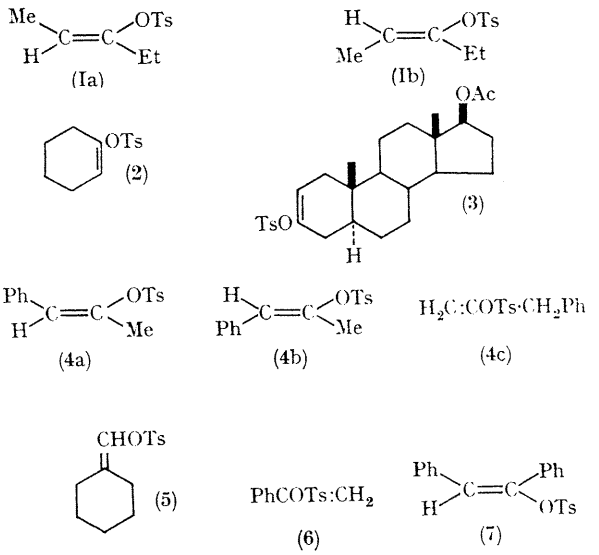
We have also treated some of the ketones with methanesulphonic anhydride and dimethylformamide, and isolated the corresponding enol methanesulphonates.

In an alternative procedure ketones were converted into enol sulphonates by heating their carbon tetrachloride solutions under reflux with sulphonic anhydrides and sulphonic acids. Generally, 1% solutions of ketones containing 1 mol. equiv. of the acid, and 2 mol. equiv. of the anhydride were used. Thus cyclohexanone and pentan-3-one yielded the respective enol tosylates (2) (16%) (1a) and (1b) (17 and 10%) after reflux for 1 hr., the rest of the material consisting mainly of aldol-condensation products. However, this method proved to be less general than the former, since the acid-sensitive aldehydes and the less reactive aromatic ketones could not be converted into their enol sulphonates.

The enol sulphonates were relatively stable towards alcoholic solutions of mineral acids and bases which only slowly regenerated the parent carbonyl compounds.‡ This lack of reactivity is exemplified by the almost quantitative solvolysis of acetoxy-enol sulphonate (3) to the respective hydroxy-derivative (3; 17β-OH) with either 2% sodium hydroxide or 4% sulphuric acid in 50% aqueous methanol after 2 and 12 hr. reflux, respectively, the enol sulphonate function remaining unchanged. The solvolysis of the latter function to give the corresponding 17β-hydroxy-3-ketone necessitates reflux either with 4% sodium hydroxide for 8 hr. (complete conversion) or with 4% sulphuric acid for 24 hr. (30% conversion).§

The solvolysis of enol sulphonate (3) with 97% ^{18}O-labelled sodium methoxide and methanol resulted in the hydroxy-ketone having 15% ^{18}O in the keto-group. This enrichment was due to the exchange of carbonyl oxygen of the product with reagent, as proved by control experiments. These findings show that the attack of the base occured at the sulphur atom, and not at the double bond, by analogy with the behaviour of phenyl sulphonates.[2]

Treatment of the three enol sulphonates derived from benzyl methyl ketone (4a), (4b), and (4c) with potassium t-butoxide in t-butyl alcohol at room temperature gave phenylallene in high yield. However, other enol sulphonates on similar treatment gave neither allenes nor acetylenes¶ but rather the parent ketones or products derived from aldehydes. A single exception was the case of compound (5), in which the OTs group was replaced by t-butoxide.



Accordingly, base-catalysed elimination of the toluene-*p*-sulphonyloxy-group is observed only when allylic proton abstraction gives rise to a delocalisation of the incipient negative charge.[3]

Hydride reduction of aliphatic enol sulphonates derived from ketones demonstrates their lack of susceptibility to nucleophilic attack at the vinylic carbon atom; thus lithium aluminium hydride reduction of (3) gave androstane-3β, 17β-diol (78%) accompanied by the 17β-hydroxy-3-ketone (7%). Neither androst-2-en-17β-ol nor androstan-17β-ol was formed.

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† Satisfactory analyses and i.r., n.m.r., and mass spectra were obtained for all new compounds reported.

‡ The regeneration of carbonyl compounds from aliphatic enol sulphonates with formic acid was reported previously: ref. 1.

§ The pseudo-first-order rate constants for conversion of (3) (0·007M) into the 17β-hydroxy-3-ketone in 50% MeOH and 56° were with NaOH (1M) $3{\cdot}17 \times 10^{-4}$ sec.$^{-1}$ and with H_2SO_4 (0·4M) $3{\cdot}4 \times 10^{-6}$ sec.$^{-1}$.

¶ In this respect, the vinyl sulphonates (6) and (7) differ from the corresponding enol phosphates which, under base treatment, are converted into mono- and di-phenylacetylenes, respectively [J. Cymerman Craig and M. Moyle, *J. Chem. Soc.*, 1963, 3712).

[1] P. E. Peterson and J. M. Indelicato, *J. Amer. Chem. Soc.*, 1968, **90**, 6515; this report deals with preparation of double, substituted aliphatic enol toluene-*p*-sulphonates and bromobenzenesulphonates. For other methods see ref. 1 of this paper.

[2] C. A. Bunton and Y. H. Frei, *J. Chem. Soc.*, 1951, 1872.

[3] For other examples of elimination reaction of enol sulphonates see I. Fleming and J. Harley-Mason, *J. Chem. Soc.*, 1963, 4771, 4778; E. J. D. Brown and J. Harley-Mason, *J. Chem. Soc.* (*C*), 1966, 1390; G. Nakaminami, *Bull. Chem. Soc. Japan*, 1962, **35**, 1629.