Preparation of 1-Arenesulfonyloxyalkyl Ketones

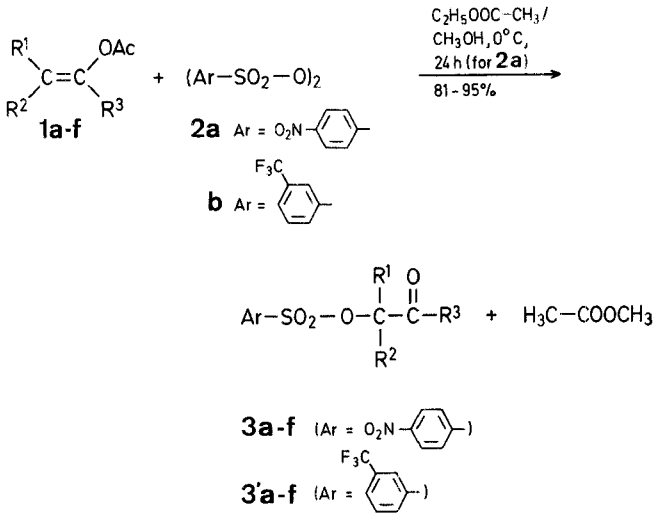
Robert V. HOFFMAN

Department of Chemistry, Box 3C, New Mexico State University, Las Cruces, New Mexico 88003, U.S.A.

While the preparation and reactions of 1-haloalkyl ketones have been well-studied for many years[1,2,3] it has been only recently that the chemistry of 1-sulfonyloxyalkyl ketones has been investigated to any exent[4-10]. They have been used as precursors to α-keto cations[4-7], as Favorski ring contraction substrates[9], and as thiol specific electrophiles[8].

The most common method of preparation is to condense a 1-hydroxyalkylketone with a sulfonyl chloride. This method is extremely erratic[6,7], and often it is necessary to first prepare the corresponding sulfinate ester which is then oxidized to the sulfonate ester. A recent paper[10] describes the preparation of 1-tosylalkyl ketones by the reaction of ketones with [hydroxy-(tosyloxy)-iodo]benzene. This method is not regiospecific for unsymmetrical ketones, although good yields are obtained.

In connection with our interest in the additions of arenesulfonyl peroxides to olefins[11], and particularly electron-rich olefins[12], we now report that the reaction of arenesulfonyl peroxides **(2)** with enol acetates **(1)** gives high yields of 1-arenesulfonyloxyalkyl ketones **(3)** (Scheme **A**).



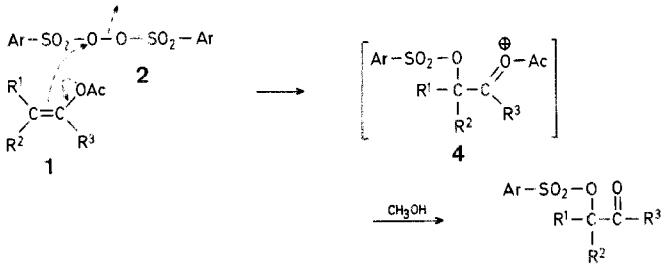
1,3	R¹	R²	R³
a	H	H	CH_3
b	CH_3	H	C_2H_5
c	H	$-(CH_2)_4-$	
d	H	H	C_6H_5
e	CH_3	H	C_6H_5
f	H		

Scheme **A**

A number of aliphatic, alicyclic, and aromatic enol acetates **1a–f**, prepared from the ketones with isopropenyl acetate and sulfuric acid[13], were treated with *p*-nitrobenzenesulfonyl peroxide (**2a**; 1 equiv) in ethyl acetate: methanol (10:1) at 0 °C. The mixture was stirred until the peroxide **2a** had dissolved (20 min) and stored at 0 °C overnight. Assay with potassium iodide/acetic acid was used to confirm the disappearance of the peroxide. Aqueous washing followed by solvent removal gave excellent yields of the 1-nosylalkyl ketones **3a–f** which crystallized in the receiver and showed no other components by either T. L. C. or ^{1}H-N.M.R. analysis. They could be purified further by recrystallization (Table). The most telling spectral information is the shift to higher frequency of the carbonyl stretch in the I. R. spectrum and the methine C—H proton chemical shift in the ^{1}H-N.M.R. spectrum. The 1-nosylalkyl ketones **3a** and **3d** can be stored for long periods at room temperature, but those with β-hydrogen atoms, **3b, 3c, 3e,** and **3f**, decompose over several months at room temperature, but can be kept indefinitely at 0 °C.

If *m*-trifluoromethylbenzenesulfonyl peroxide **(2b)** is used, high yields of clean products **3'** were obtained which had virtually identical ^{1}H-N.M.R. spectra, except for the aromatic region where the *m*-trifluoromethylbenzenesulfonyloxy multiplet replaced the *p*-nitrobenzenesulfonyloxy quartet. The I. R. spectra showed the same shift of the carbonyl stretch. These products were oils and thus were difficult to purify and are not discussed further here; they are acceptable for most purposes, however.

By mechanistic analogy to other sulfonyl peroxide reactions[11,12], it is likely that electrophilic addition to the double bond gives oxonium ion **4** (Scheme **B**). Interestingly, the methanol present in solution adds to the acetate carbonyl, no evidence of acetal formation was seen.



Scheme **B**

Table. 1-(*p*-Nitrobenzenesulfonyloxy)-alkyl Ketones **3a–f** prepared from Enol Acetates **1a–f** and *p*-Nitrobenzenesulfonyl Peroxide **(2a)**

Product	Yield [%][a]	m.p. [°C]	Molecular Formula[b]	I. R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
3a	86	120–121°	$C_9H_9NO_6S$ (259.2)	1733 (C=O); 1510 (NO_2); 1360, 1185 (SO_2—O)	2.21 (s, 3H, CH_3); 4.70 (s, 2H, CH_2O); 8.28 (AA'BB'-system, $4H_{arom}$)
3b	95	67.5–69°	$C_{11}H_{13}NO_6S$ (287.3)	1729 (C=O); 1520 (NO_2); 1360, 1180 (SO_2—O)	1.05 (t, 3H, J = 7 Hz, CH_2CH_3); 1.45 (d, 3H, J = 6 Hz, $CHCH_3$); 2.58 (q, 2H, J = 7 Hz, CH_2CH_3); 5.02 (q, 1H, J = 6 Hz, $CHCH_3$); 8.28 (AA'BB'-system, $4H_{arom}$)
3c	92	84–86° (dec.)	$C_{12}H_{13}NO_6S$ (299.3)	1725 (C=O); 1520 (NO_2); 1360, 1180 (SO_2—O)	1.98–2.45 [m, 8H, —$(CH_2)_4$—]; 5.05 (dd, 1H, J = 6 Hz, 11 Hz, CHO); 8.28 (AA'BB'-system, $4H_{arom}$)
3d	90	129–131°	$C_{14}H_{11}NO_6S$ (321.3)	1700 (C=O); 1520 (NO_2); 1360, 1180 (SO_2—O)	5.49 (s, 2H, CH_2O); 7.55 (m, $3H_{arom}$); 7.83 (dd, 2H, J = 2 Hz, 8 Hz, o-H_{arom}); 8.28 (AA'BB'-system, $4H_{arom}$)
3e	95	156–158°	$C_{15}H_{13}NO_6S$ (335.3)	1699 (C=O); 1520 (NO_2); 1360, 1180 (SO_2—O)	1.86 (d, 3H, J = 7 Hz, CH_3); 6.03 (q, 1H, J = 7 Hz, CHO); 7.55 (m, $3H_{arom}$); 7.87 (dd, 2H, J = 2 Hz, 8 Hz, o-H_{arom}); 8.29 (AA'BB'-system, $4H_{arom}$)
3f	81	135–137°	$C_{16}H_{13}NO_6S$ (347.3)	1708 (C=O); 1520 (NO_2); 1360, 1180 (SO_2—O)	2.6 (m, 2H, CH_2); 3.17 (m, 2H, CH_2); 5.32 (dd, 1H, J = 5 Hz, 12 Hz, CHO); 7.1–7.6 (m, $3H_{arom}$); 7.91 (dd, 1H, J = 1.5 Hz, 8 Hz, o-H_{arom}); 8.29 (AA'BB'-system, $4H_{arom}$)

[a] Yield of isolated product, averaged from two or more experiments.

[b] Satisfactory microanalyses obtained: C ±0.30, H ±0.20, N ±0.17.

This method for the preparation of 1-arenesulfonyloxyalkyl ketones **3** offers several advantages over existing methods. In the first place the reaction is mild, general, and gives uniformly high yields. Different arenesulfonyloxy groups can be attached by using different sulfonyl peroxides **2**. In the second place there is no need to prepare the 1-hydroxyalkyl ketone precursors. In the third place enol acetates **1** are widely available and can be produced regiospecifically[14], thus the ketones **3** can be made easily and are isomerically pure.

Preliminary studies indicate that ketones **3** have interesting and, in some cases, unique chemistry that complements the known chemistry of 1-haloalkylketones.

2-(*p*-Nitrobenzenesulfonyloxy)-cyclohexanone (3c); Typical Procedure:

To a cooled (0°C) solution of 1-acetoxycyclohexene (**1c**; 280 mg, 2 mmol) in ethyl acetate (50 ml)/methanol (5 ml) is added *p*-nitrobenzenesulfonyl peroxide (**2a**; 808 mg, 2 mmol). The mixture is stirred at 0°C for 20 min until homogenous and then placed in the refrigerator. After 4.5 h assay of a small portion with potassium iodide (10%) and glacial acetic acid shows only a small amount of the peroxide remaining. The mixture is allowed to stand in the refrigerator overnight and is then extracted with water (2 × 25 ml) and saturated sodium chloride (10 ml), dried with magnesium sulfate, and evaporated to give a clear oil which slowly solidifies; yield: 540 mg (90%).

Only a single component is detected by T.L.C. and the ^{1}H-N.M.R. spectrum contains no other peaks than those for the α-nosyl ketone **3c**. An analytical sample is recrystallized from 1:3 ethyl acetate/hexane to give white plates; m.p. 84–86°C (dec.).

$C_{12}H_{13}NO_6S$	calc.	C 48.16	H 4.38	N 4.68
(299.3)	found	48.05	4.30	4.59

This work was supported in part by the Donors of the Petroleum Research Fund, administered by the American Chemical Society, and by the National Science Foundation to whom we are indebted.

Received: December 10, 1984

[1] Rappe, C. in: *The Chemistry of the Carbon-Halogen Bond*, Part 2, Patai, S., Ed., Interscience, London, 1973, pp. 1071–1105.
[2] March, J.A. *Advanced Organic Chemistry*, 2nd Edn., McGraw-Hill, New York, 1977, pp. 991–995.
[3] House, H.O. *Modern Synthetic Reactions*, 2nd Edn., W.A. Benjamin New York, 1972.
[4] Creary, X. *J. Am. Chem. Soc.* **1984**, *106*, 5568.
[5] Creary, X., Geiger, C.C. *J. Am. Chem. Soc.* **1983**, *105*, 7123.
[6] Creary, X., Geiger, C.C. *J. Am. Chem. Soc.* **1982**, *104*, 4151.
[7] Creary, Y., Rollin, A. *J. Org. Chem.* **1977**, *42*, 4226, 4231.
[8] Simons, Jr., S.S., Pons, M., Johnson, D.F. *J. Org. Chem.* **1980**, *45*, 3084, and references therein.
[9] Conia, J.M., Salaun, J.R. *Acc. Chem. Res.* **1972**, *5*, 33.
[10] Koser, G.F., Relenyi, A.G., Kalos, A.N., Rebrovic, L., Wettach, R.H. *J. Org. Chem.* **1982**, *47*, 2487, and references therein.
[11] Hoffman, R.V., Bishop, R.D. *Tetrahedron Lett.* **1976**, 33.
[12] Hoffman, R.V., Buntain, G.A. *J. Org. Chem.* **1983**, *48*, 3308.
[13] House, H.O., Kramar, V. *J. Org. Chem.* **1963**, *28*, 3362.
[14] Larock, R.C., Oertle, K., Beatty, K.M. *J. Am. Chem. Soc.* **1980**, *102*, 1966, provides an excellent summary of preparations.
[15] *p*-Nitrobenzenesulfonyl peroxide (**2a**) was prepared according to: Dannley R.L., Gagen, J.E., Stewart, O.J. *J. Org. Chem.* **1970**, *25*, 3976.
m-Trifluoromethylbenzenesulfonyl peroxide (**2b**) was prepared according to: Dannley, R.L., Tornstrom, P.K. *J. Org. Chem.* **1975**, *40*, 2278.