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REGIOSPECIFIC SYNTHESIS OF α-ARYLSULFONOXY KETONES FROM KETONE DERIVATIVES

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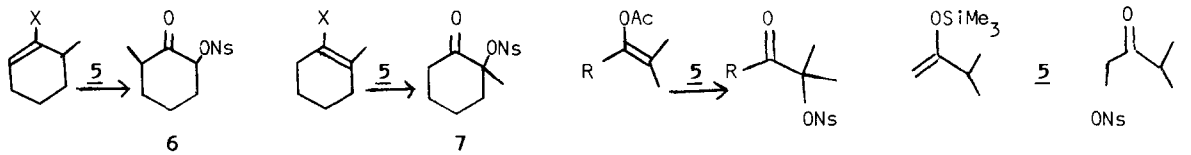
Summary Isomeric enol ester, enamine, and silyl enol ether derivatives of unsymmetrical ketones are converted regiospecifically to α-arylsulfonoxy ketones with arylsulfonyl peroxides.

It was previously shown that electron-rich ketone derivatives such as enol esters, silyl enol ethers, and enamines react with arylsulfonyl peroxides to give α-arylsulfonoxy ketones. (Eq. 1)[1] These compounds exhibit high selectivity in their reactions with nucleophiles and bases, and thus have good potential as synthetic intermediates.[2] Alternate procedures are known for the preparation of these materials, but these methods remain problematic in terms of generality and/or regioselectivity.[1b] The ability to produce enol and enamine derivatives of unsymmetrical ketones regiospecifically (or regioselectively), and the efficiency of their reactions with arylsulfonyl peroxides suggested a general and regiospecific route to α-arylsulfonoxy ketones. We wish to report that unsymmetrical ketones can, in fact, be converted efficiently to α-arylsulfonoxy derivatives regiospecifically.

Enol acetates **1-4** were prepared from the corresponding ketones. Thermodynamic isomers **2, 3,** and **4** were prepared using acetic anhydride and perchloric acid.[3] Kinetic isomer **1** was prepared by quenching the kinetic enolate in acetic anhydride.[4] Attempts to prepare kinetic enol esters from acyclic ketones were unsuccessful as previously reported.[5] Reaction of **1-4** with p-nitrobenzenesulfonyl peroxide (NsO_2, Ns= $p\text{-}NO_2C_6H_4SO_2$-), **5**, in ethyl acetate: 5% methanol at 0° C gave the α-arylsulfonoxy ketones **6-9** in high yields. The purity of the crude products was also very high. (> 95%) Recrystallization from ethyl acetate: hexane gave products of analytical purity.[6] Structures were determined by IR and pmr spectroscopy.[7] Examination of the reaction mixtures revealed only one regioisomer was produced from each substrate. Thus isomerically pure enol esters yield α-arylsulfonoxy ketones regiospecifically.



1 X=OAc
10a X=morpholino
10b X=pyrrolidino
12 X=$OSiMe_3$

2 X=OAc
11a X=morpholino
11b X=pyrrolidino
13 X=$OSiMe_3$

3 R=Me
4 R=Et

8 R=Me
9 R=Et

Enamine derivatives of 2-methylcyclohexanone were prepared using both morpholine and pyrrolidine.[8] The former gave a 1:1 mixture of regioisomers **10a** and **11a**, while the latter gave a 70:30 mixture of **10b** and **11b**. Each enamine mixture was reacted with **5** in ethyl acetate at -78° C. Acidic hydrolysis gave high yields of α-sulfonoxy ketones **6** and **7**. Enamine mixture **10a-11a** gave a 1:1 mixture of **6** and **7** (88%), and enamine mixture **10b-11b** gave **6** and **7** (94%) in a 70:30 ratio. These data indicate that enamines are also converted to α-arylsulfonoxy ketones regiospecifically.

Silyl enol ethers **12**[9] and **13**[10] gave only **6** and **7** respectively when treated with **5**, however the yields were somewhat lower yields, and the product mixtures were more complex. This is consistent with earlier observations. Only one regioisomer was found in the α-sulfonoxy ketone fraction, indicating regiospecific conversion. The kinetic silyl enol ether **14**[10] produced only **15**[6,7] in 35% yield, but it was difficult to separate **15** from reaction by-products, even using column chromatography on silica gel. Regioisomer **9** was not detected in the reaction mixture supportive of the regiospecificity of the reaction.

These results indicate that isomeric carbonyl derivatives of unsymmetric ketones can be converted regiospecifically to α-sulfonoxy ketones. Enol esters and enamines give the highest yields and cleanest products, however, silyl enol ethers have been shown to be excellent substrates in many instances.[1b]

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6. All new compounds **6-10, 15** gave satisfactory microanalysis (C,H,N).

7. **6**: IR (KBr) 3100, 2940, 2870 (C-H); 1721 (C=O); 1608 (arom.C=C); 1530 (NO_2); 1374, 1349, 1309, 1182 (SO_2); 976 cm^{-1}; pmr ($CHCl_3$) 8.4-8.1 (q, 4H, arom. H's), 5.17 (dd, 1H, CH-ONs), 2.5 (br. m, 3H, ring H's), 1.94 (br. m, 4H, ring H's), 1.05 (d, 3H, $CH-CH_3$). **7**: IR (KBr) 3100, 2915, 1722, 1601, 1527, 1352, 1185, 985; pmr ($CHCl_3$) 8.4-8.1 (q, 4H, arom. H's), 2.80 (q, 2H, $C(O)-CH_2$), 2.52 (m, 2H, ring H's), 2.1-1.8 (m, 4H, ring H's), 1.78 (s, 3H, $-CH_3$. **8**: (KBr) 3100, 2920, 1722, 1607, 1532, 1351, 1185, 890 cm^{-1}; pmr ($CHCl_3$) 8.4-8.1 (q, 4H, aromatic H's), 2.36 (s,3H, $C(O)-CH_3$), 1.68 (s, 6H, $-CH_3$). **9**: IR (KBr) 3121, 2982, 2940, 1724, 1605, 1528, 1342, 1182, 891 cm^{-1}; pmr ($CHCl_3$) 8.4-8.1 (q, 4H, aromatic H's), 2.70 (q, 2H, J=7Hz, $-CH_2-$), 1.67 (s, 6H, $-CH_3$), 1.12 (t, 3H, J=7Hz, $-CH_2CH_3$). **15**: IR (KBr) 3100, 2952, 1723, 1607, 1531, 1350, 1186, 850 cm^{-1}; pmr ($CHCl_3$) 8.4-8.1 (q, 4H, aromatic H's), 5.2 (s, 2H, $-CH_2-$), 2.25 (septet, 1H, -CH-), 1.16 (d, 6H, $-CH_3$).

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