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FLUORIDE ANION INDUCED NOVEL REACTION OF α-(SULFONIO)KETONE TRIFLATE

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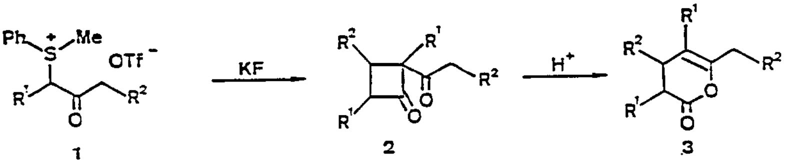
Abstract: α-(Phenylmethylsulfonio)ketone triflates (1) are treated with a suspension of KF in aprotic polar solvent to give dimeric 2-acylcyclobutanones (2), which are rearranged to γ,δ-unsaturated δ-valerolactones (3) by acid catalyst.

Basic character of fluoride anion endowed in aprotic polar solvent has been utilized in organic synthetic reactions.$^{1)}$ The mild base offers sometimes advantages over classical conditions and unique functions which are not otherwise accessible. Herein, we wish to report a potassium fluoride induced reaction of α-(sulfonio)ketone triflates (1) producing 2-acylcyclobutanones (2). The product 2 is derived from two molecules of α-(sulfonio)ketone triflate (1) with concurrent rearrangement of the carbon skeleton, as shown below.



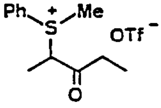
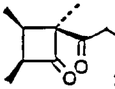
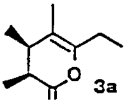
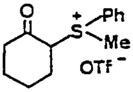
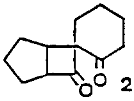
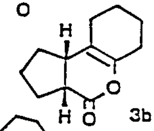
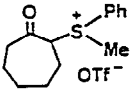
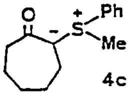
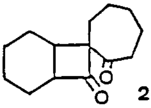
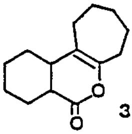
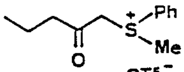
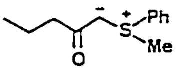
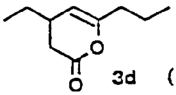
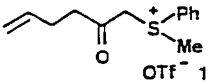
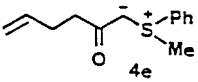
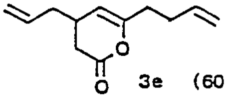
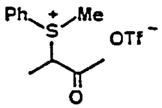
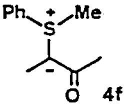
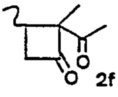
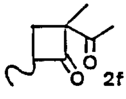
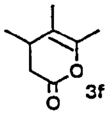
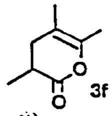
Some results of the KF induced dimerization of α-(sulfonio)ketone triflates (1) are summarized in Table 1. 2-(Phenylmethylsulfonio)-3-pentanone triflate (1a)$^{2)}$ (3 mmol), which is prepared by quaternization of 2-(phenylthio)-3-pentanone with methyl trifluoromethanesulfonate, was treated with a suspension of KF (9 mmol) in acetonitrile (6 mL) at 0°C overnight to afford 2-propionyl-2,3,4-trimethylcyclobutanone (2a) in 86% yield as a single stereoisomer [TLC on silica gel (3 : 1 C_6H_{14}/EtOAc) Rf=0.49], which was identified by 400 MHz ^{1}H NMR and ^{13}C NMR spectra. An NOE difference spectrum established the indicated stereochemistry of 2a. [2a : IR(neat) 1765, 1706 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.02 (t, 3H, J=7.4 Hz), 1.03 (d, 3H, J=7.2 Hz), 1.06 (d, 3H, J=7.2 Hz), 1.52 (s, 3H), 2.44 (dq, 1H, J=19.0 and 7.4 Hz), 2.48 (dq, 1H, J=10.1 and 7.2 Hz), 2.70 (dq, 1H, J=19.0 and 7.4 Hz), 3.53 (dq, 1H, J=10.1 and 7.2 Hz); ^{13}C NMR δ 5.72(q), 6.35(q), 10.53(q), 21.09(q), 33.63(t), 34.13(d), 50.04(d), 73.55(s), 206.96(s), 210.3(s).] The product 2a was isomerized quantitatively to γ,δ-unsaturated δ-valerolactone (3a)$^{3)}$ on heating at reflux in benzene for 2 hrs with a catalytic amount of p-toluenesulfonic acid.

The similar treatment of 2-(phenylmethylsulfonio)cyclohexanone triflate (1b) with KF gave the corresponding dimeric 2-acylcyclobutanone derivative (**2b**)$^{4)}$, which was then isomerized to 3b$^{4)}$ in 75% overall yield.

On the other hand, α-(sulfonio)ketone triflates (1c)-(1f) afforded neither the expected 2-acylcyclobutanones (2) nor δ-valerolactones (3) under the similar reaction conditions and even at higher temperature up to 80°C. However, sulfonium ylides (**4c**)-(**4e**)$^{5)}$, which are obtained by treatment of α-(sulfonio)ketone triflates (1c)-(1e) with aqueous K_2CO_3, were heated at 80°C for

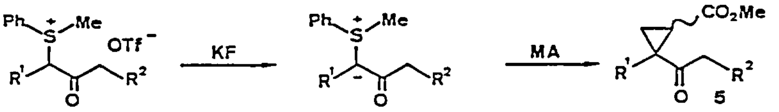
2 hrs with a suspension of KF in DMF to furnish 2-acylcyclobutanones (2c)-(2e), of which acid treatment gave the respective γ,δ-unsaturated δ-valerolactones (3c)-(3e) in moderate overall yields. Of note is that sulfonium ylide, α-acetylethylidene sulforane (4f) gave a 2 : 1 mixture of two isomeric γ,δ-unsaturated δ-valerolactones (3f) and (3f')[6] after acid treatment.

Table 1.

No.	Sulfonium Triflate	Sulfonium Ylide	2-Acylcyclobutanone	Unsaturated δ-Valerolactone(%)[a]
1.	 1a	——	 2a	 3a (86%)
2.	 1b	——	 2b	 3b (75%)
3.	 1c	 4c	 2c	 3c (45%)
4.	 1d	 4d	——	 3d (45%)
5.	 1e	 4e	——	 3e (60%)
6.	 1f	 4f	 2f  2f'	 3f  3f' (60%)

a) Isolated overall yield based on **1** or **4**.

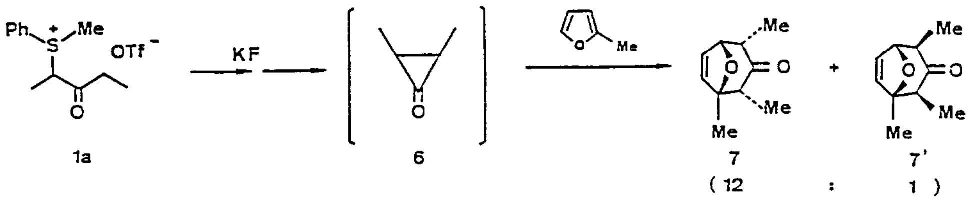
Intermediacy of sulfonium ylide (4) in the reaction of α-(sulfonio)ketone triflate (1) with KF was in accord with the following trapping experiment, in which α-(sulfonio)ketone triflate (1) was stirred at 0°C with a suspension of KF in acetonitrile in the presence of a large excess of methyl acrylate (MA) to give cyclopropane carboxylate derivative (5)[5].



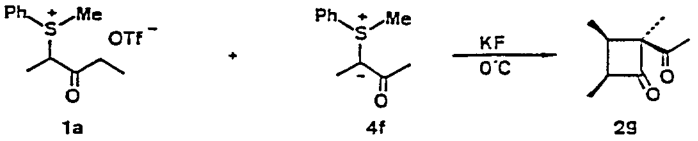
1 4 5

a: R^1=Me, R^2=Me (55%)
b: R^1-R^2= -$(CH_2)_3$- (40%)
c: R^1=Me, R^2=H (35%)

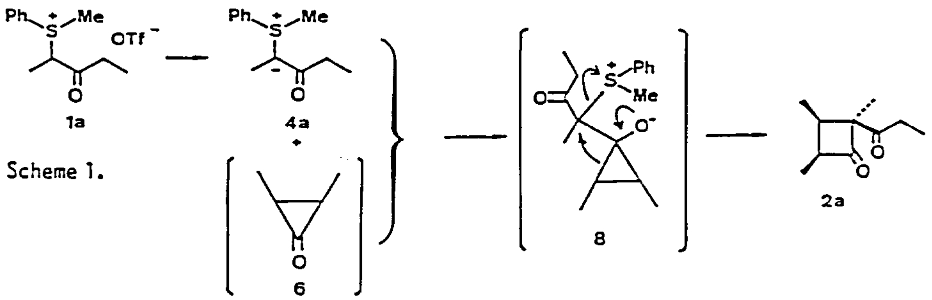
The following two trapping experiments give further mechanistic implications for the present dimerization of α-(sulfonio)ketone triflates (1). When 2-(phenylmethylsulfonio)-3-pentanone triflate (1a) in acetonitrile was dropwise added to a suspension of KF and ca. twenty fold excess of 2-methylfuran in acetonitrile at 80°C over 12 hrs and stirred overnight, 1,2,4-trimethyl-3-oxo-8-oxabicyclo[3.2.1]octene-6 was produced as a mixture of endo, cis- (7) and exo, cis-isomers (7') (12 : 1) in 45% total yield7). This finding is reasonably explained by assuming an intervension of 2,3-dimethylcyclopropanone (6)8), which might be generated via a penultimate intermediate (4a) from 1a.



Next, 2-(phenylmethylsulfonio)-3-pentanone triflate (1a) was reacted at 0°C with KF in acetonitrile in the presence of α-acetylethylidene sulforane (4f) to give 2-acetyl-2,3,4-trimethylcyclobutanone (2g)9) (40% yield) together with a small amount of 2a. In the cross dimeric product of 2g, the carbon skeleton of the sulfonium ylide (4f) was incorporated without its rearrangement.



Based upon these findings, a possible reaction mechanism for the KF induced dimerization of α-(sulfonio)ketone triflate (1) is presented in the Scheme 1. Reactive cyclopropanone intermediate (6) generated via the sulfonium ylide (4) from α-(sulfonio)ketone triflate (1) reacts rapidly with 4 to give a betaine intermediate (8), which rearranges to cyclobutanone (2).



Scheme 1.

α-(Trimethylammonio)ketone triflate or bromide was also treated with KF or CsF in DMF at 120°C for 5 hrs to directly afford δ-valerolactone (3) in moderate yield, e.g., 2-(trimethylammonio)cyclohexanone triflate gives **3b** in 65% yield.

References and Notes

1) a) B. Simoneau and P. Brassard, J.C.S. Perkin I, 1507 (1984). b) T. Ando, J. Yamawaki, T. Kawata, S. Sumi, and T. Hanafusa, Bull. Chem. Soc. Japan, 55, 2504 (1982). c) J. Yamawaki, T. Kawata, T. Ando, and T. Hanafusa, Bull. Chem. Soc. Japan, 56, 1885 (1983). d) J. H. Clark and J. M. Millar, Tetrahedron Lett., 599 (1977). e) J. H. Clark and J. M. Millar, J. Chem. Soc. Perkin I, 1977, 2063. e) W. G. Dauben and D. J. Hart, J. Org. Chem., 42, 3787 (1977).

2) 1a (a 1 : 1.8 mixture of two diastereomers) : IR(neat) 1716 cm^{-1}; NMR ($CDCl_3$) δ 1.15 (t, 3H) and 0.98 (t, 3H), 1.49 (d, 3H) and 1.80 (d, 3H), 2.76 (q, 2H) and 2.61 (q, 2H), 3.33 (s, 3H) and 3.33 (s, 3H), 5.24 (q, 1H) and 5.28 (q, 1H), 7.57-8.30 (m, 5H) and 7.57-8.30 (m, 5H).

3) The structure of **3a** was confirmed by IR and NMR spectra. **3a** : IR(neat) 1752, 1698 cm^{-1}; 400 MHz ^{1}H NMR ($CDCl_3$) δ 1.052 (d, 3H, J=7.20 Hz), 1.076 (t, 3H, J=7.50 Hz), 1.213 (d, 3H, J=7.20 Hz), 1.712 (s, 3H), 1.939 (dq, 1H, J=7.20 and 3.20 Hz), 2.195 (dq, 1H, J=10.13 and 7.50 Hz), 2.220 (dq, 1H, J=10.13 and 7.50 Hz), 2.479 (dq, 1H, J=3.20 and 7.20 Hz).

4) 2b : IR(neat) 1760 and 1700 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 21.46(t), 25.27(t), 25.58(t), 26.27(t), 27.55(t), 28.62(t), 33.56(d), 39.57(t), 61.99(d), 79.55(s), 202.33(s), 210.77(s). **3b**: IR(neat) 1756, 1712 cm^{-1}; 400 MHz ^{1}H NMR ($CDCl_3$) δ 2.50 (ddd, 1H, J=8.5, 8.0 and 8.0 Hz) and 2.93 (ddd, 1H, J=8.5, 6.1 and 8.9 Hz) for two bridgehead protons;

5) a) B. M. Trost and L. S. Melvin, Jr., "Sulfur Ylides", Academic Press, New York, 1975. b) G. B. Payne, J. Org. Chem., 32, 3351 (1967).

6) 3f : IR(neat) 1760, 1702 cm^{-1}; 400 MHz ^{1}H NMR ($CDCl_3$) δ 1.055 (d, 3H, J=7.09 Hz), 1.706 (q, 3H, J=0.49 Hz), 1.863 (t, 3H, J=1.10 Hz), 2.25-2.34 (m, 1H), 2.423 (dd, 1H, J=15.75 and 3.54 Hz), 2.662 (dd, 1H, J=15.75 and 6.59 Hz). **3f'** : IR(neat) 1752, 1706 cm^{-1}; 400 MHz ^{1}H NMR ($CDCl_3$) δ 1.262 (d, 3H, J=6.83 Hz), 1.698 (q, 3H, J=0.98 Hz), 1.862 (dq, 3H, J=1.59 and 0.98 Hz), 2.145 (broad d, 2H, J=9.52 Hz), 2.618 (ddq, 1H, J=8.66, 10.87 and 6.84 Hz).

7) **7** : Exact mass. Calcd for $C_{10}H_{14}O_2$ 166.0994 Found 166.1000. IR(neat) 1725, 1615 cm^{-1}; 400 MHz ^{1}H NMR ($CDCl_3$) δ 0.963 (d, 3H, J=7.08 Hz), 1.011 (d, 3H, J=6.96 Hz), 1.502 (s, 3H), 2.562 (q, 1H, J=6.96 Hz), 2.768 (dq, 1H, J=6.96 and 4.64 Hz), 4.837 (dd, 1H, J=4.64 and 1.71 Hz), 6.119 (d, 1H, J=5.98 Hz), 6.242 (dd, 1H, J=5.98 and 1.71 Hz).

8) a) N. J. Turro, Acc. Chem. Res., 2, 25 (1969). b) N. J. Turro, S. S. Edelson, J. R. Williams, J. R. Darling, and W. B. Hammond, J. Am. Chem. Soc., 91, 2283 (1969).

9) The stereochemistry of **2g** was confirmed by an NOE difference spectrum. **2g** : IR(neat) 1768, 1710 cm^{-1}; 400 MHz ^{1}H NMR ($CDCl_3$) δ 1.060 (d, 3H, J=7.44 Hz), 1.064 (d, 3H, J=7.57 Hz), 1.529 (s, 3H), 2.220 (s, 3H), 2.493 (dq, 1H, J=7.44 and 10.14 Hz), 3.543 (dq, 1H, J=7.57 and 10.14 Hz).

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