Tetrahedron, 1965, Vol. 21, pp. 1 to 4. Pergamon Press Ltd. Printed in Northern Ireland

TRIFLUOROMETHANESULPHONATE ESTERS AND THEIR ALKYLATING PROPERTIES

J. BURDON and V. C. R. MCLOUGHLIN
Chemistry Department, University of Birmingham

(*Received* 14 *September* 1964)

Abstract—Trifluoromethanesulphonate esters, even the 2,2,2-trifluoroethyl, will alkylate pyridine and alkoxides to give pyridinium salts and ethers, respectively. These esters are probably the most powerful alkylating agents of this type.

GRAMSTAD and Haszeldine,[1] in 1956, reported the preparation of the methyl and ethyl esters of trifluoromethanesulphonic acid from the alkyl iodides and the silver salt of the acid. They were unable to obtain an ester from the following reaction:

$$CF_3SO_2F + C_2H_5O^- \rightarrow CF_3SO_3C_2H_5$$

Instead, only diethyl ether was produced by O-ethylation of the ethoxide ion:

$$CF_3SO_3C_2H_5 + C_2H_5O^- \rightarrow (C_2H_5)_2O + CF_3SO_3^-$$

Ethyl trifluoromethanesulphonate must therefore ethylate ethoxide ion more rapidly than this ion reacts with the acid fluoride.

The same authors[2] showed that methyl trifluoromethanesulphonate would O-alkylate diethyl ether to give methyl ethyl ether and that the ethyl ester reacted with benzene to give ethyl- and diethyl-benzene, and with diethylamine and aniline to give N-ethylated products. Related to this, Brown[3] found that ethyl iodide and silver perfluoro-n-octanesulphonate reacted in benzene to give a 75% yield of ethylbenzene; this reaction is an alkylation of benzene with ethyl perfluoro-n-octanesulphonate.

We now report some further observations on the preparation of trifluoromethanesulphonate esters and their alkylating properties.

The most readily accessible starting material for the preparation of these esters is trifluoromethanesulphonyl fluoride, as it is the product (in high yield[1,4,5]) of electrochemical fluorination of methanesulphonyl chloride. Trifluoromethanesulphonyl chloride, which should react in a similar way to the fluoride, should now be accessible from trichloromethanesulphenyl chloride.[6]

Reaction of the acid fluoride with alcohols in pyridine gave an ester in only two cases; 2-naphthyl trifluoromethanesulphonate (54%) and the 2,2,2-trifluoroethyl ester (25%). With ethanol and *p*-nitrobenzyl alcohol, only ethyl- and *p*-nitrobenzylpyridinium trifluoromethanesulphonates were formed, and in good yield. Indeed, in the case of 2,2,2-trifluoroethanol the ester was only obtained when one equivalent of pyridine was employed; when five equivalents were used, none of the ester was

---

[1] T. Gramstad and R. N. Haszeldine, *J. Chem. Soc.* 173 (1956).

[2] T. Gramstad and R. N. Haszeldine, *J. Chem. Soc.* 4069 (1957).

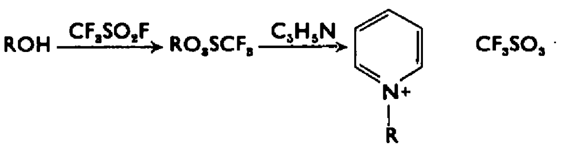
[3] H. C. Brown; presented at the 128*th Meeting of the American Chemical Society*, Minneapolis, Sept. (1955);

[4] J. Burdon, I. Farazmand, M. Stacey and J. C. Tatlow, *J. Chem. Soc.* 2574 (1957).

[5] T. J. Brice and P. W. Trott, U.S. Pat. 2,732,398 (1956); B. Pat. 758,467 (1956).

[6] C. W. Tullock and D. D. Coffman, *J. Org. Chem.* **25**, 2016 (1960).

detectable, the only product being an involatile oil which could have been 2,2,2-trifluoroethylpyridinium trifluoromethanesulphonate. Thus N-alkylation readily occurs with these esters.



Even the sterically hindered base 2,6-lutidine was rapidly N-alkylated at room temperature by *p*-nitrobenzyl alcohol and trifluoromethanesulphonyl fluoride.

As mentioned above, Gramstad and Haszeldine[1] were unable to prepare ethyl trifluoromethanesulphonate from sodium ethoxide and the acid fluoride. We have found that even with a considerable excess of acid fluoride over ethoxide, diethyl ether was the only product.

We have been able, however, to use this alkoxide method successfully to prepare 2,2,2-trifluoroethyl trifluoromethanesulphonate. Even in this case, where O-alkylation with the trifluoroethyl group should be far more difficult than with the ethyl, about 9% of bis(2,2,2-trifluoroethyl) ether was formed as well as the ester. In fact, when an excess of sodium 2,2,2-trifluoroethoxide over the acid fluoride was used, the ether and ester were produced in comparable amounts.

$$CF_3CH_2O^- \xrightarrow{CF_3SO_2F} CF_3CH_2OSCF_3 \xrightarrow{CF_3CH_2O^-} (CF_3CH_2)_2O.$$

We have confirmed that the ether is, in fact, formed from the ester by treating the latter with sodium trifluoroethoxide, when the ether was produced in excellent yield. No bis(2,2,2-trifluoroethyl) ether was obtained when trifluoroethyl *p*-toluenesulphonate was used instead of the trifluoromethanesulphonate; the perchlorate ester is known[7] to be similarly unsuccessful. Although bis(2,2,2-trifluoroethyl) ether itself is known,[8] the method used for its preparation is not general. It seems probable that the reaction sequence described in this paper, however, should be applicable to any ether of the type $R_fCH_2OCH_2R'_f[R_f,R'_f =$ polyfluoroalkyl groups].

It would seem then that, of their type, trifluoromethanesulphonate esters are the most powerful alkylating agents known. This is hardly surprising since trifluoromethanesulphonic acid is an extremely strong acid[1,9] and its anion should therefore be an excellent leaving group. The esters themselves can only be prepared with difficulty because of this. Only aryl and perhaps polyfluoroalkylmethyl $[R_fCH_2]$ esters can be prepared by the pyridine method and for other esters the silver salt–alkyl iodide procedure[1] will only be satisfactory if a non-alkylatable solvent can be used. The only general method appears to be the alcohol–anhydride reaction, but this has the disadvantage that the anhydride is not so easily available as the acid fluoride and is unstable in the presence of organic impurities.[4] From the alkylation stand-point, this lack of availability of the esters does not necessarily matter, as alcohol–acid fluoride and alcohol or olefin[1]–trifluoromethanesulphonic acid mixtures can be used directly.

---

[7] *Perchloryl Fluoride* (Booklet DC-1819), p. 8, Pennsalt Chemicals Corp., Philadelphia, U.S.A. (1957).

[8] W. R. Hasek, W. C. Smith and V. A. Engelhardt, *J. Amer. Chem. Soc.* **82**, 543 (1960).

[9] R. N. Haszeldine and J. M. Kidd, *J. Chem. Soc.* 4228 (1954).

EXPERIMENTAL

2,2,2-*Trifluoroethyl trifluoromethanesulphonate*

2,2,2-Trifluoroethanol (2·3 g) and trifluoromethanesulphonic anhydride (3·8 ml) were heated under reflux for 30 min and then poured into $NaHCO_3$ aq. Ether extraction (3 × 5 ml), evaporation of about 10 ml of the ether, and then separation of the residue by preparative-scale gas chromatography (column 35 mm dia × 4·8 m, packed with dinonyl phthalate on kieselguhr) gave, besides ether, 2,2,2-trifluoroethanol (1·1 g) and 2,2,2-*trifluoroethyl trifluoromethanesulphonate* (1·1 g), b.p. 90·5–91°, n_D^{20} 1·3051 (Found: C, 15·8; H, 1·0. $C_3H_2F_6O_3S$ requires: C, 15·6; H, 0·9%).

Reaction of trifluoromethanesulphonyl fluoride with alcohols in the presence of pyridine

(a) 2-*Naphthol.* The fluoride (2·7 g), 2-naphthol (2·0 g) and pyridine (4·1 g) were heated at 55° in a sealed tube for 30 min. The reaction mixture was taken up in ether, and the ethereal solution washed with 2N HCl and water and dried ($MgSO_4$) and evaporated to leave a residue which was triturated with light petroleum (b.p. 60–80°). The solid which formed was crystallized from the same solvent to give 2-naphthol (0·4 g), m.p. and mixed m.p. with authentic 2-naphthol, 122°.

The light petroleum washings and mother-liquors were distilled to give 2-*naphthyl trifluoromethanesulphonate* (2·1 g), b.p. 86–87°/0·2 mm, m.p. 27·5–28° from aqueous ethanol (Found: C, 48·2; H, 2·4. $C_{11}H_7F_3O_3S$ requires: C, 47·9; H, 2·5%).

(b) 2,2,2-*Trifluoroethanol.* The fluoride (3·3 g), pyridine (1·5 g) and the alcohol (2·2 g) were kept, in a sealed tube, at room temp for 48 hr and then at 110° for 2·5 hr. The reaction mixture was extracted with ether (2 × 5 ml); gas-phase chromatography indicated that the extracts contained, besides ether, only 2,2,2-trifluoroethyl trifluoromethanesulphonate. The last compound (0·9 g) was isolated by preparative-scale gas chromatography from these extracts.

When this experiment was repeated on fluoride (1·5 g), pyridine (4·0 g) and 2,2,2-trifluoroethanol (1·0 g), no trifluoroethanol or 2,2,2-trifluoroethyl trifluoromethanesulphonate could be detected. The only product was an involatile, ether-soluble, oil which would not crystallize.

(c) *Ethanol.* The fluoride (7.8 g), ethanol (2.35 g) and pyridine (12·3 g) reacted exothermically in a sealed tube. After 14 hr at room temp, the reaction mixture was distilled to leave a residue which would not distill at 275°/0·01 mm. This residue was taken up in ethanol and ether was added; an oil precipitated and solidified on being kept at 10 mm over P_2O_5. Purification by the same precipitation technique from ethanol–ether gave *ethylpyridinium trifluoromethanesulphonate* (12·3 g), m.p. ca. 38° (Found: C, 37·3; H, 4·0. $C_8H_8F_3NO_3S$ requires: C, 37·4; H, 3·9%).

(d) p-*Nitrobenzyl alcohol.* The fluoride (1·5 g), *p*-nitrobenzyl alcohol (1·35 g) and pyridine (2·4 g) reacted exothermically in a sealed tube at room temp. After 1 hr, the reaction mixture was shaken with water–chloroform and a solid separated at the liquid interface. It was p-*nitrobenzylpyridinium trifluoromethanesulphonate* (2·8 g), m.p. 187° from acetone–chloroform. (Found: C, 42·7; H, 3·0. $C_{13}H_{11}F_3N_2O_5S$ requires: C, 42·8; H, 3·0%). Evaporation of the chloroform used to wash the reaction mixture left no residue.

The same pyridinium salt was isolated in 57% and 77% yields, respectively, when trifluoromethanesulphonyl chloride and trifluoromethanesulphonic anhydride were used instead of the acid fluoride.

p-*Nitrobenzylpyridinium iodide*

p-Nitrobenzylpyridinium trifluoromethanesulphonate (0·20 g), NaI (0·50 g) and acetone (20 ml) were refluxed for 30 min. The yellow solution was evaporated, the residue was washed with water and crystallized from ethanol to give the yellow p-*nitrobenzylpyridinium iodide* (0·17 g), m.p. ca. 200° (dec). (Found: C, 42·0; H, 3·7. $C_{12}H_{12}IN_2O_2$ requires: C, 42·0; H, 3·5%).

p-*Nitrobenzyl-2,6-lutidinium trifluoromethanesulphonate*

p-Nitrobenzyl alcohol (1·4 g), trifluoromethanesulphonyl fluoride (1·5 g) and 2,6-lutidine (4·8 g) were allowed to react as in (d), above. Crystallization of the solid product from acetone–ether gave p-*nitrobenzyl-2,6-lutidinium trifluoromethanesulphonate* (1·3 g), m.p. 141–142° (Found: C, 46·0; H, 3·8. $C_{15}H_{15}F_3NO_5S$ requires C, 45·9; H, 3·8%).

Sodium ethoxide and trifluoromethanesulphonyl fluoride

Sodium ethoxide (from NaH (0·25 g) and dry ethanol (2 ml), followed by evaporation *in vacuo*) and the fluoride (10 g) were heated at 120° for 2·5 hr in a sealed tube. Gas-chromatography showed that the only volatile product was diethyl ether.

Sodium trifluoroethoxide and trifluoromethanesulphonyl fluoride

Sodium hydride (1·25 g) and 2,2,2-trifluoroethanol (15 g) were allowed to react in a glass tube before the acid fluoride (10 g) was distilled into them, *in vacuo*, the tube sealed and heated at 120° for 2·5 hr. The reaction mixture was distilled and the crude product (20 g) separated by gas-chromatography to give (i) bis(2,2,2-trifluoroethyl) ether (0·5 g), b.p. 63° (lit.,[8] 58–59°) n_D^{22}1·3010 (Found: C, 26·0; H, 2·3. Calc for $C_4H_4F_6O$: C, 26·4; H, 2·2%) (ii) 2,2,2-trifluoroethyl trifluoromethanesulphonate (8·0 g), identified by IR spectroscopy, and (iii) 2,2,2-trifluoroethanol (6·4 g).

When this reaction was repeated with sodium hydride (1·0 g), trifluoroethanol (7·0 g) and acid fluoride (2·5 g), gas-chromatography indicated that the product contained approximately equal amounts of the ether and the ester.

Bis(2,2,2-trifluoroethyl) ether

2,2,2-Trifluoroethanol (6·4 g), NaH (0·5 g) and 2,2,2-trifluoroethyl trifluoromethanesulphonate (4·0 g) were refluxed for 5 hr. Distillation *in vacuo*, followed by separation by gas-chromatography afforded bis(2,2,2-trifluoroethyl) ether (2·0 g) and unchanged ester (0·65 g), both identified by IR spectroscopy.

When this reaction was repeated on NaH (4·5 g), 2,2,2-trifluoroethanol (82·5 g) and 2,2,2-trifluoroethyl *p*-toluenesulphonate[10] (46 g) no bis(2,2,2-trifluoroethyl) ether could be detected in the product by gas-phase chromatography. Trifluoroethanol (75 g) and trifluoroethyl *p*-toluenesulphonate (30 g) were recovered.

Acknowledgements—We thank Professor J. C. Tatlow for his interest and advice, and the University of Birmingham for the award of a Research Scholarship (to VCRM).

[10] G. V. D. Tiers, H. A. Brown and T. S. Reid, *J. Amer. Chem. Soc.* **75**, 5978 (1953).