Rearrangement Studies with ^{14}C. XXXVIII. Isotopic Scrambling in the Synthesis of Labeled 2-Phenylethyl Triflate

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Received November 27, 1972

2-Phenylethyl triflate (**1**-OTf) was synthesized by the reaction of AgOTf with 2-phenylethyl iodide (**1**-I) in cyclohexane as solvent. However, when 1-^{14}C-2-phenylethyl iodide (**1**-I-1-^{14}C) was used as a reactant, the resulting **1**-OTf-^{14}C showed an essentially complete scrambling of the ^{14}C-label over the C-1 and -2 positions. Similar reactions of **1**-I-1-^{14}C with AgOTs and with AgOAc gave **1**-OTs-^{14}C and **1**-OAc-^{14}C with, respectively, about 49 and 11% rearrangement of the label from C-1 and -2.

Le triflate de phényl-2 éthyle (**1**-OTf) a été synthétisé par réaction du AgOTf avec l'iodure de phényl-2 éthyl (**1**-I) dans le cyclohexane comme solvant. Cependant, lorsque l'iodure de ^{14}C-1 phényl-2 éthyl a été utilisé comme réactif, le produit **1**-OTf-^{14}C résultant s'est révélé être un mélange pratiquement complet en ce qui a trait à la distribution du ^{14}C sur les positions C-1 et -2. Des réactions semblables du **1**-I-^{14}C-1 avec du AgOTs et avec du AgOAc ont donné le **1**-OTs-^{14}C et le **1**-OAc-^{14}C avec, respectivement, un réarrangement de la distribution du ^{14}C de C-1 à -2 d'environ 49 et 11%.

[Traduit par le journal]

Can. J. Chem., **51**, 1494 (1973)

The trifluoromethanesulfonate (triflate) anion is a facile leaving group in solvolytic reactions (1). Studies on the kinetics and deuterium isotope effects for the ethyl and propyl systems, however, have led to the conclusion that solvolyses of such primary alkyl triflates and tosylates are mechanistically similar, the reaction of the triflate being no more limiting than the tosylate (2, 3).

Since a great deal of work has been done on the isotopic scrambling that occurs in the solvolyses of 1-^{14}C-2-phenylethyl tosylate (**1**-OTs-1-^{14}C) (4–7), it would be of interest to have another comparison of the behaviors of triflates and tosylates by an investigation on the analogous solvolyses of 1-^{14}C-2-phenylethyl triflate (**1**-OTf-1-^{14}C). Hence attempts were made to synthesize **1**-OTf-1-^{14}C.

1-OTf was prepared from the reaction of 2-phenylethyl iodide (**1**-I) with silver triflate by the method of Gramstad and Haszeldine (8) as used in the synthesis of ethyl triflate, except that cyclohexane instead of ether was employed as solvent. When the reaction was carried out in ether, the product was highly contaminated by ethyl 2-phenylethyl ether and di-2-phenylethyl ether, apparently derived from *O*-alkylation of ethers by the triflate ester (9). When the synthesis was attempted by reacting **1**-I-1-^{14}C with AgOTf, the product obtained, however, showed an essentially complete scrambling of the ^{14}C-label over the C-1 and -2 positions (Table 1). The method thus failed to give the desired **1**-OTf-1-^{14}C.

Alternative syntheses of triflate esters were considered, but they too failed to give the desired result. Schleyer and coworkers (1) prepared a number of triflates of relatively inert systems by treatment of the alcohol with trifluoromethanesulfonic acid anhydride in the presence of pyridine. This method was not attempted in the present work since **1**-OTf was found to react readily with pyridine to give a solid product, presumably the result of *N*-alkylation, giving rise to the pyridinium salt (9, 10). Hansen (11) has prepared a series of 1,1-dihydroperfluoroalkyl triflates by treating the appropriate alcohol with trifluoromethanesulfonyl fluoride in the presence of triethylamine at −30°. When **1**-OH was treated in an analogous way using commercially purchased trifluoromethanesulfonyl chloride, no **1**-OTf could be obtained. A number of phenols have been converted to the corresponding aryl triflates by reaction with trifluoromethanesulfonic imidazolide at 80–90° (12). When the reaction was tried with **1**-OH, extensive decomposition occurred at 80–90°, while at room temperature or 50°, much of the **1**-OH remained unreacted. Thus **1**-OTf was successfully synthesized only by the treatment of **1**-I with AgOTf, and this reaction led to a complete scrambling of the ^{14}C-label when **1**-I-1-^{14}C was used as a reactant.

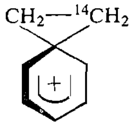
The isotopic scrambling in the **1**-OTf-^{14}C

TABLE 1. Data from the reaction of 1-^{14}C-2-phenylethyl iodide (**1**-I-1-^{14}C) with silver salts

Salt	Compound	Specific activity* (d.p.m./mmol)		Rearrangement to C-2(%)	
		Run 1	Run 2	Run 1	Run 2
AgOTf	$PhCH_2CH_2OTf$†	1 290 000	364 000	51.0	50.8
	PhCOOH	659 000	185 000		
AgOTs	$PhCH_2CH_2OTs$	974 000	358 000	48.5	49.2
	PhCOOH	472 000	176 000		
AgOAc	$PhCH_2CH_2OAc$†	481 000	444 000	11.2	10.6
	PhCOOH	54 100	46 900		

*Measured by a liquid scintillation counter.
†Converted to $PhCH_2CH_2OH$ and then assayed as the solid α-naphthylurethane.

could be most reasonably explained by the intervention of the ethylenebenzenium ion[1] (**2**) formed in the reaction of **1**-I-1-^{14}C with Ag^+ ion. Support for this interpretation was obtained



2

from the isotopic scramblings observed when **1**-I-1-^{14}C was treated with silver tosylate or silver acetate. As can be seen from Table 1, reaction with AgOTs also gave a product, **1**-OTs-^{14}C, with nearly complete scrambling of the label over C-1 and -2, while the **1**-OAc-^{14}C from the reaction of **1**-I-1-^{14}C with AgOAc showed about 11% rearrangement of the label from C-1 to -2. The lesser amount of scrambling in the **1**-OAc-^{14}C could be explained on the basis of concurrent S_N1–S_N2 processes (7). The more nucleophilic acetate ion could take part in a non-scrambling direct displacement and effectively compete with phenyl participation in the formation of **2**, thus giving rise to a net result of 11% rearrangement, much less than the 50% rearrangement expected in a product formed solely via **2**.

Experimental

Reaction of 1-^{14}C-2-Phenylethyl Iodide (1-I-1-^{14}C) with Silver Salts

A solution of 18.6 g (0.08 mol) of **1**-I-1-^{14}C, obtained from treatment of **1**-OTs-1-^{14}C with NaI in acetone (4), in 50 ml of cyclohexane, was added dropwise to a stirred suspension of 25.7 g (0.10 mol) of AgOTf in 150 ml of cyclohexane. The resulting mixture was stirred at room temperature for 4 h. The AgI was then removed by filtration through Celite and the cyclohexane was distilled off under reduced pressure to give 16.2 g (80%) of residual ^{14}C-2-phenylethyl triflate (**1**-OTf-^{14}C) as a colorless liquid. (In the second run, the yield of **1**-OTf-^{14}C calculated from isotope dilution was 87%). The product so obtained decomposed readily at elevated temperatures, but purification was effected by distillation at 65–70° and 1 Torr using an apparatus with a short condensation column jointed directly to the receiver to minimize any refluxing of the condensate into the distillation flask. The distilled **1**-OTf obtained from inactive trials gave the following data.

Anal. Calcd. for $C_9H_9O_3SF_3$: C, 42.52; H, 3.56. Found: C, 42.67; H, 3.51.

N.m.r. (CCl_4) δ 7.2 (m, 5, aromatic H), 4.60 (t, 2, J = 7 Hz, CH_2OTf), 3.08 (t, 2, J = 7 Hz, $PhCH_2$); mass spectrum m/e 254 (M^+) and major peaks at m/e 105 $(M - OTf)^+$, 104 $(M - HOTf)^+$, 91 $(C_7H_7{}^+)$. The titrimetric rate constant for the acetolysis of 0.5 M **1**-OTf at 30° was found to be $9.44 \times 10^{-5}\ s^{-1}$. Comparison with data extrapolated from Coke's results (6) indicated that at 30°, the acetolysis of **1**-OTf is faster than the acetolysis of **1**-OTs by a factor of about $10^{4.9}$.

The reaction of **1**-I-1-^{14}C with AgOTs or AgOAc was carried out in a similar way with only minor modifications. In the reaction with AgOTs, the mixture was refluxed for 4 and 10 h in the two runs, giving yields of **1**-OTs-^{14}C, based on isotope dilution, of 67 and 90%, respectively. The reaction mixture between **1**-I-1-^{14}C and AgOAc was refluxed for 20 h and the yields of **1**-OAc-^{14}C, based on isotope dilution, were 94 and 96% for the two runs.

Degradation

1-OTf-^{14}C and **1**-OAc-^{14}C were oxidized directly with alkaline $KMnO_4$ to give PhCOOH, while the **1**-OTs-^{14}C was converted to **1**-I-^{14}C by treatment with NaI in acetone before being oxidized to PhCOOH (4). The ^{14}C activity in the PhCOOH gave the extent of rearrangement of the label from C-1 to -2.

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[1] Previously, **2** has been commonly referred to as the ethylenephenonium ion. In accordance with the nomenclature recently suggested by Olah (13), **2** should be named as the ethylenebenzenium ion.

The financial support given by the National Research Council of Canada is gratefully acknowledged.

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