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Facile synthesis and rearrangement of propargylic trifluoromethanesulfinates

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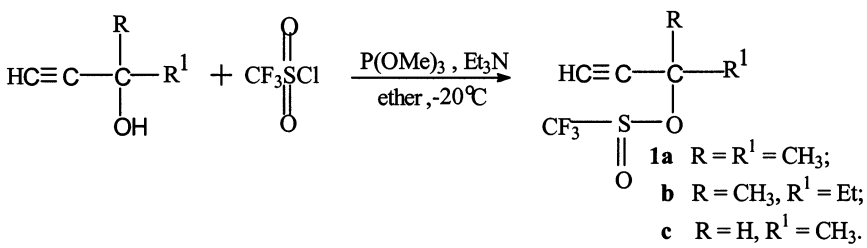
Abstract—The synthesis and reactivity of propargylic trifluoromethanesulfinates under various conditions have been investigated. These esters readily undergo [2,3]-sigmatropic rearrangement to the corresponding allenyl trifluoromethyl sulfones, even under solvolytic conditions. An unusually facile nucleophilic addition of the solvent to the allenyl sulfone under the latter conditions has also been observed.

The rearrangement and solvolysis of esters of sulfinic acids is well documented and reviewed.[1] The rearrangements of allylic and propargylic arenesulfinates to sulfones, demonstrated by us more than three decades ago[2] to proceed by a concerted mechanism is of particular interest, since these rearrangements have served as models for the well-known [2,3]-sigmatropic rearrangements of the corresponding sulfenates to sulfoxides.[3] More recently, we have shown that benzylic trichloro[4a] and trifluoromethanesulfinates[4b] exhibit some unique features. Thus, in contrast to benzyl arenesulfinates which undergo solvolysis with exclusive S–O bond fission, these esters undergo solvolysis with exclusive C–O bond fission, and with a rate enhancement by a factor of 10^6, comparable with benzyl tosylates. Similarly, unlike benzyl arenesulfinates,[4c] these esters undergo a facile rearrangement to sulfones on heating in polar nonhydroxylic solvents. The unusually high reactivity of these trihalomethanesulfinates has been explained by the enhanced leaving group ability of the corresponding anion, which in turn can be explained by the considerable difference in pK_a values of $ArSO_2H$ ($pK_a = 2.7$) and CF_3SO_2H ($pK_a = -0.6$).[4d] Prompted by these results, we became interested in the behavior of propargylic trifluoromethanesulfinates (triflinates) in order to test the effect of the CF_3 group on the mechanism of rearrangement. In addition, we were interested in the preparation of some allenic trifluoromethyl sulfones (triflones) which might exhibit high reactivity in nucleophilic addition. The latter is of considerable interest with regard to recent studies on the DNA-cleaving ability of various enediyne models.[5]

Although benzylic trihalomethanesulfinates have been originally prepared by us by oxidation of the corresponding sulfenates,[4a,b] this method is not applicable for the preparation of propargylic triflinates due to their potential [2,3]-sigmatropic rearrangement to allenic sulfoxides.[3] Therefore, we decided to use an alternative method recently reported by us for the preparation of *p*-anisyl triflinate.[6] This method, adopted from that reported by Klunder and Sharpless[7] for the preparation of various menthyl sulfinates, involves the reaction of alcohols with $CF_3S(O)Cl$ generated in situ by reduction of the corresponding sulfonyl chloride with trimethyl phosphite (Eq. (1)). However, in our hands, this method was only successful after several



(1)

Keywords: acetylenes; allenes; fluorine and sulfur compounds; rearrangements.

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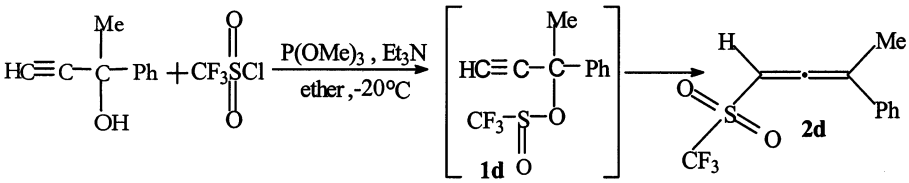
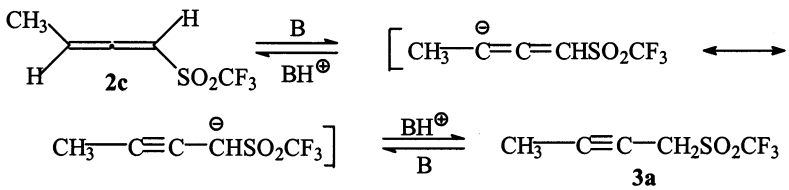
modifications, such as lowering the temperature to −20°C, shortening the time to minimum and reducing the amount of $(MeO)_3P$ from two to one equivalent. This method appears to be superior to the one used before for the preparation of $CF_3S(O)Cl$ in situ.[8] Recently, the formation of triflinates during the attempted preparation of triflates by using triflic anhydride in the presence of amines has also been reported.[9] However, this method is limited to sterically congested alcohols, the use of a suitable base and reaction conditions. Using our method, propargylic triflinates **1a–c** have been prepared in good yields (70–78%). Interestingly, and unlike the other triflinates prepared, α-methyl-α-phenylpropargyl triflinate could not be isolated because of spontaneous rearrangement to γ-methyl-γ-phenylallenyl triflone, indicating a full acetylene–allene isomerization, as expected from a concerted [2,3]-sigmatropic shift (Eq. (2)).



(2)



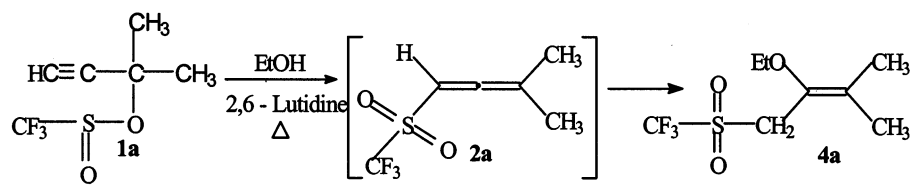
(3)

To study the reactivity of the new triflinates, we first examined their behavior under nonsolvolytic conditions. We have thus found that similar to the previous case, α,α-dimethyl and α-ethyl-α-methylpropargyl triflinates also readily and exclusively undergo rearrangement to the corresponding γ,γ-dialkylallenyl triflones.[10] Interestingly, the rate of rearrangement of α,α-dimethylpropargyl triflinate in acetonitrile at 40°C ($k=2\times10^{-5}$ s^{-1}) is twice as rapid as in chloroform ($k=9\times10^{-6}$ s^{-1}). This result is similar to the one found for propargyl arenesulfinates.[2c] The low sensitivity to solvent ionizing power may be used as evidence for a concerted [2,3]-sigmatropic shift for the rearrangement. Similarly, the exclusive rearrangement of these esters to allenic products may also be used as evidence for such a mechanism. Interestingly, a comparison of the reactivity of α,α-dimethylpropargyl triflinate and benzenesulfinate[2c] shows that the former is faster by a factor of ca. 5. In fact, the decreased nucleophilicity of the sulfur atom in the triflinate might be expected to decrease the rate of a concerted rearrangement. However, since precisely the same shift also involves cleavage of a better leaving group in the transition state, this may compensate in the opposite direction. For comparison, substitution of the aryl group by a trichloromethyl group in the case of benzylic sulfinates results in a much higher rate enhancement, for both solvolysis and rearrangement to sulfone, which proceed by an ionic mechanism.[4a–c]

A different behavior has been observed with the secondary α-methylpropargyl triflinate. We have found that heating this ester in acetonitrile for 2 months at 60°C over $CaCO_3$ afforded a mixture of γ-methylallenyl and γ-methylpropargyl triflones in a 1:2 ratio. In contrast to this result, in the absence of the base, only the first product was obtained. The conversion of the latter to the other isomer can be explained by a base-catalyzed prototropic shift, as shown in Eq. (3).

This result is quite similar to the one observed before with γ-methylallenyl phenyl sulfone in the presence of 2,6-lutidine, but not with $CaCO_3$, indicating that the latter is not basic enough to deprotonate the allenyl phenyl sulfone. This observation reflects the relative acidities of the two allenyl sulfones. Our observations are also consistent with the thermodynamic data, which indicate that a nonterminal acetylene is more stable than an isomeric nonterminal allene by 1.0 Kcal mol^{-1}.[2c] Formation of γ-methylallenyl triflone as the sole product is consistent with the results obtained with the α,α-disubstituted propargylic triflinates described above.

Prompted by these results, we decided to investigate the behavior of the new esters under solvolytic conditions. Surprisingly, heating of **1a** for 5 h at 60°C in ethanol yielded β-ethoxy-γ,γ-dimethylallyl triflone (Eq. (4)).



(4)

Similarly, reaction of **1b** under the same conditions yielded β-ethoxy-γ-ethyl-γ-methylallyl triflone. The latter product was obtained as a mixture of two

diastereoisomers, *Z* and *E* in the ratio of 1:1.1. The formation of these unexpected products can be explained by rearrangement of the propargylic triflinates to allenic triflones and subsequent nucleophilic addition of ethanol to the allenic β-carbon. This explanation is supported by the observation that when γ-methyl-γ-phenylallenyl triflone was tested under the same conditions, the corresponding product of nucleophilic addition was obtained, again as a mixture of *Z* and *E* diastereoisomers in the ratio of 1:1.5.

The data presented in this report are similar to those reported on the rearrangement of propargylic arenesulfinates. These esters rearranged to the corresponding allenic aryl sulfones almost exclusively even under solvolytic conditions. The unusual nucleophilic addition of ethanol to allenyl triflones can be explained by a higher electrophilicity of the allenic group in triflones comparable to aryl sulfones. It is interesting to note that addition of alcohols to allenyl aryl sulfones occurs only under more drastic conditions such as in the presence of NaH.[11] Our results are of particular significance with regard to the recent interest in the DNA-cleaving ability of allenyl sulfones.[5]

In conclusion, and in light of the evidence presented above, we suggest that the rearrangement of propargylic triflinates proceeds by a concerted [2,3]-sigmatropic mechanism.

General procedure and selected spectral data

To a cooled (−20°C) solution of the appropriate alcohol (1 mmol) and trifluoromethanesulfonyl chloride (1.25 mmol) in dry ether, under a nitrogen atmosphere, were added triethylamine (1.25 mmol) and trimethyl phosphite (1.25 mmol) simultaneously with stirring. After further stirring for 2 h at this temperature and another 20 min at room temperature the reaction mixture was washed consecutively with water, 3% aqueous HCl, 5% aqueous $NaHCO_3$ and water again. After drying over anhydrous $MgSO_4$ and removal of the solvent, the product was obtained as a viscous liquid. The rearrangement to sulfone was carried out by heating of a solution of the appropriate ester in acetonitrile followed by removal of the solvent and purification of the product by chromatography.

α,α-Dimethylpropargyl triflinate (1a) was obtained in 78% yield: ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.90 (s, 1H), 1.79 (s, 3H), 1.71 (s, 3H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 122.9 (q, $J=334.3$ Hz, **C**F_3), 82.21 (≡**C**-), 78.79 (-**C**-O), 78.38 (**C**H≡), 30.63 (-**C**-), 30.48 (-**C**H_3). ^{19}F NMR (200 MHz, $CDCl_3$): δ −80.96 (s, CF_3). IR (neat): 788.6, 851.8, 1126.9, 1201.5, 1372.0, 2358.0 cm^{-1}. MS (CI/CH_4): m/z 201.0 (MH^+, 100%), 149.0 (64.09%), 125.0 (61.2%), 124.0 (66.5%); HRMS (elemental composition): calc. ($C_6H_8O_2F_3S$) 201.019; found 201.021.

γ-Methyl-γ-phenylallenyl triflone (2d) was obtained in 70% yield: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 (m, 5H), 6.42 (q, $J=2.8$ Hz, 1H), 2.31 (d, $J=2.8$ Hz, 3H). ^{13}C NMR (200 MHz, $CDCl_3$): δ 214.70 (=**C**=), 131.27, 129.67, 129.06, 126.64 (**Ar**), 119.78 (q, $J=326.5$ Hz, CF_3), 113.18 (CH_3-**C**=), 93.33 (=**C**H-), 16.21 (-**C**H_3). ^{19}F NMR (200 MHz, $CDCl_3$): δ −79.78 (s, CF_3). IR (neat): 1119.2, 1202.7, 1219.7, 1374.3, 2253.7. MS (EI/HR): m/z 262.0 (MH^+, 2.5%), 129.1 ($MH^+-SO_2CF_3$, 100%), 128.1 (33.1%); HRMS (elemental composition): calc. ($C_{11}H_9O_2F_3S$) 262.027; found 262.024.

β-Ethoxydimethylallenyl triflone (4a) was obtained in 65% yield: ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.14 (s, 2H), 3.74 (q, $J=7.0$ Hz, 2H), 1.82 (s, 3H), 1.77 (s, 3H), 1.28 (t, $J=7.0$ Hz, 3H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 133.63 (-**C**=)*, 128.98 (-**C**=)*, 119.6 (q, $J=327.5$ Hz, CF_3), 66.20 (O-**C**H_2-), 50.61 (-**C**$H_2SO_2CF_3$), 19.44 (-**C**H_3), 18.05 (-**C**H_3), 15.06 (-CH_2-**C**H_3). ^{19}F NMR (200 MHz, $CDCl_3$): δ −79.03 (s, CF_3). IR (neat): 1121.0, 1642.6, 1685.1, 1198.7, 1218.8, 1364.9 cm^{-1}. MS (CI/CH_4): m/z 247.1 (MH^+, 50.9%), 114.1 ($MH^+-SO_2CF_3$, 11.4%), 113.1 (44.0%), 113.1 ($M^+-SO_2CF_3$, 100%); HRMS (elemental composition): calc. ($C_8H_{14}O_3F_3S$) 247.062; found 247.060.

Acknowledgements

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