Pergamon

Tetrahedron Letters, Vol. 37, No. 19, pp. 3371-3374, 1996

0040-4039/96 $15.00 + 0.00

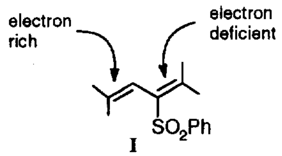
S0040-4039(96)00549-7

BF_3-Induced Rearrangement of Aziridinocyclopropanes Derived from 2-Phenylsulfonyl-1,3-Dienes. A New Approach to the Tropane Alkaloid Skeleton

Claes M. G. Löfström and Jan-E. Bäckvall*
Department of Organic Chemistry, University of Uppsala, Box 531
S-751 21 Uppsala, Sweden

Abstract. Five *N*-substituted derivatives of 1,2-methylene-3,4-aziridino 2-phenylsulfonyl cycloalkanes (**3a-e**) were prepared from their corresponding epoxy cyclopropanes via ring opening of the epoxide by sodium azide and subsequent triphenylphosphine induced cyclization. BF_3-induced reaction of compounds **3a-e** resulted in a rearrangement via a cyclopropyl carbinyl cation intermediate. In the case of tosylaziridine **3c** bicyclic product **5**, (tropane skeleton), was formed as the major product. With carbamate derivative **3a** exclusive rearrangement to fluorocyloheptene **7** took place. Copyright © 1996 Elsevier Science Ltd

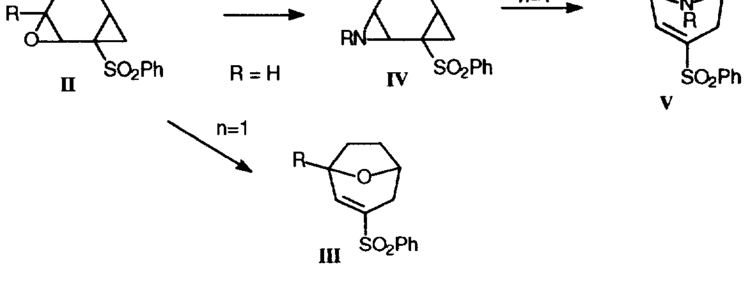
2-Phenylsulfonyl 1,3-dienes **I**, are now firmly established as useful building blocks in synthetic organic chemistry. While most applications to date have been in the area of cycloaddition chemistry,[1,2] it is also possible to carry out a number of regioselective addition reactions to either of the two double bonds.[1a, 3] These have very different reactivities due to a large difference in electron density.



I

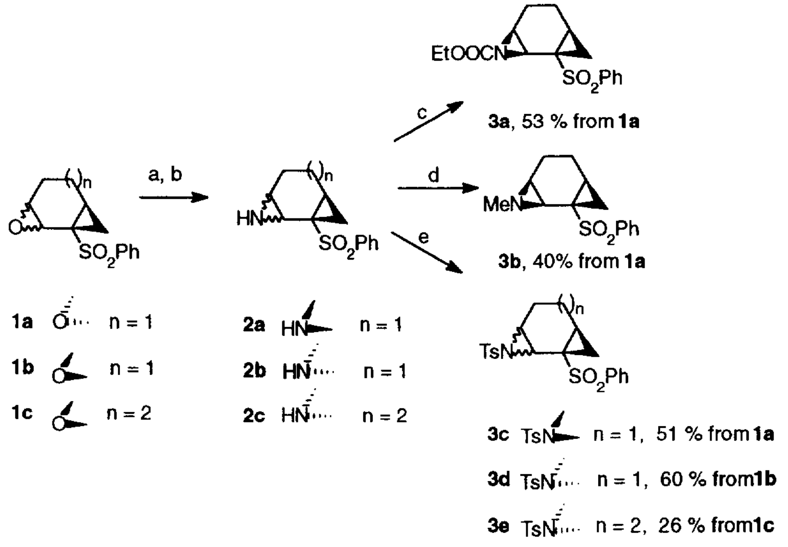
Among such addition reactions previously developed in our group are cyclopropanations[4] and epoxidations.[5] Recently we reported on the BF_3-induced rearrangement of some 3,4-epoxy-1,2-methylene-2-phenylsulfonyl cycloalkanes **II**, to bicyclic compounds of general structure **III** (Scheme 1).[6] An obvious extension of this work was to attempt the same type of rearrangement with the analogous aziridines **IV**, since this would give access to compounds **V**, containing the tropane alkaloid skeleton. In this paper we report on the synthesis of some compounds with structure **IV** and their subsequent rearrangement to **V**.

Scheme 1



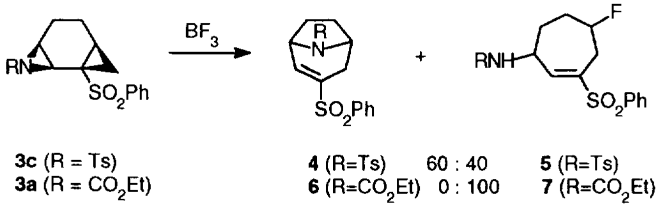
Aziridine synthesis. Epoxide **1a** was converted to aziridine **2a** via ring opening with sodium azide[7,8] and subsequent cyclization with triphenylphosphine.[8] Aziridine **2a** was then easily derivatized into either tosylamide **3c**[9], *N*-methyl aziridine **3b**[10] or carbamate **3a**.[10] Similarly aziridines **2b** and **2c** were synthesized from epoxides **1b** and **1c** and converted into their respective tosylamides **3d** and **3e** (Scheme 2).

Scheme 2[a]



[a]Reagents: (a) NaN_3, NH_4Cl; (b) PPh_3; (c) $ClCO_2Et$, $NaHCO_3$;(d) MeI, NEt_3; (e) TsCl, NEt

Rearrangement reactions. In analogy with our method for rearrangement of 3,4-epoxy-1,2-methylene-2-(phenylsulfonyl)alkanes, aziridines **3a-e** were treated with BF_3-etherate. In the case of substrate **3c** the main product formed (45 % isolated yield) was indeed the bicyclic pyrrolidine **4**, corresponding to the products of our previously reported rearrangements of epoxycyclopropanes (eq 1).[6] However an additional product identified as the fluoroamidosulfone **5** was also formed, the ratio of **4** to **5** being 3 : 2. When substrate **3a** was subjected to the identical reaction conditions as those used for **3c**, there was no formation of the corresponding bicylic compound **6**, the only product formed being fluoroamidoslulfone **7**. In the reactions with substrates **3d** and **3e** only complex mixtures of products were obtained.

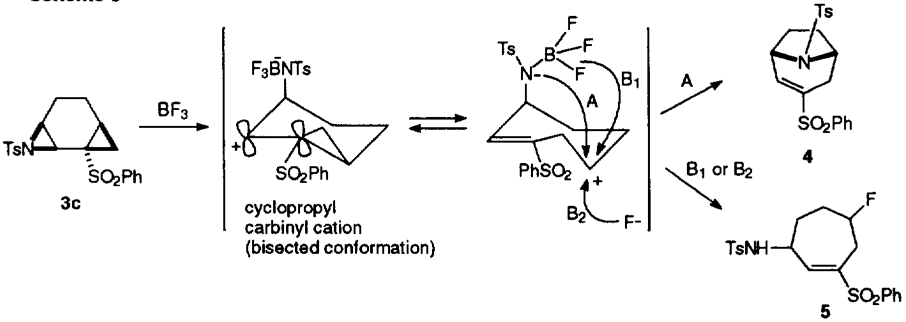


(1)

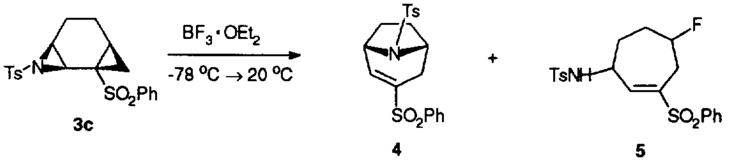
3c (R = Ts) **4** (R=Ts) 60 : 40 **5** (R=Ts)
3a (R = CO_2Et) **6** (R=CO_2Et) 0 : 100 **7** (R=CO_2Et)

The rearrangement of **3c** to **4** proceeds via a cyclopropyl carbinyl cation **8**,[11,12] which in the case of **3c** will lead to the favored bisected conformation. Nitrogen attack (path A) will lead to the observed tropane skeleton, whereas fluoride attack (path B) yields **5**. A similar mechanism was previously proposed in the rearrangement of the epoxy analogue **1b** (cf. **II** → **III** in Scheme 1).[6] For carbamate derivative **3a** only fluoride attack is observed due to the lower nucleophilicity of the carbamate nitrogen. At present we can not distinguish between pathways B1 and B2 for the fluoride attack although the ^{1}H NMR spectrum of **5** suggests that path B2 operates leading to the trans isomer.[13] Since the fluoride attack according to path B2 is bimolecular, while the formation of the desired product **4** must be monomolecular a rearrangement of **3c** with 10-fold dilution of the reaction mixture was carried out. This reaction did not, however, result in any significant decrease in the yield of fluoride adduct **5**.

Scheme 3



Other attempts at increasing the ratio of **4** over **5** including changes of solvent, reaction temperature and amount of acid catalyst were made. The temperature and amount of acid catalyst did not have any significant effect on the ratio of **4** to **5**. However, the polarity of the solvent did have an effect on the product ratio and the less polar solvent toluene gave a ratio **4**:**5** of 40:60 (eq 2). This suggests that **4b** would be favored by an increased polarity. To effect this increase addition of 10 % v/v of nitromethane to methylene chloride was tried. In this case none of **5** was present in the crude reaction mixture, however another byproduct (as yet not identified) was formed in a ratio of ~ 35/65 to the desired product **4**. Variations in the amount of added nitromethane gave no substantial increase in the relative yield of **4** over its competitor. Although the isolated yield did not undergo any significant increase when nitromethane was added, the isolation of **4** by flash chromatography was much easier than in the experiment where **5** was the side product. With compound **3a** the addition of nitromethane as co-solvent did not result in any detectable formation of **6**.



(2)

	4		5
toluene	40	:	60
CH_2Cl_2	60	:	40
CH_2Cl_2-CH_3NO_2 (9:1)	100	:	0

This reaction is to the best of our knowledge the first of its kind reported for an aziridine and provides a new approach for the synthesis of substances containing the tropane alkaloid skeleton.

Acknowledgments. This work was financially supported by the Swedish Natural Science Research Council. Dr. Adolf Gogoll is gratefully acknowledged for assistance with the ^{19}F decoupling experiment.

References and Notes

(1) (a) Bäckvall, J. E.; Juntunen, S. K. *J. Am. Chem. Soc.* **1987**, *109*, 6396. (b) Bäckvall, J. E.; Plobeck, N. A.; Juntunen, S. K.; *Tetrahedron Lett.* **1989**, *30*, 2589. (c) Plobeck, N. A.; Bäckvall, J. E. *J. Org. Chem.* **1991**, *55*, 4528. (d) Bäckvall, J. E.; Rise, F. R. *Tetrahedron Lett.* **1989**, *30*, 5347. (e) Bäckvall, J. E.; Löfström, C.; Maffei, M.; Langer, V. *Ibid.* **1992**, *33*, 2417.

(2) (a) Inomata, K.; Kinoshita, H.; Takemoto; H., Murata, Y.; Kotake, H. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 3341. (b) Chou, T. S.; Hung, S. C. *J. Org. Chem.* **1988**, *53*, 3020. (c) Chou, S. S. P.; Wey, S. J. *J. Org. Chem.*, **1990**, *55*, 1270. (d) Padwa, A.; Gareau, Y.; Harrison, B; Norman, B. H. *J. Org. Chem.* **1991**, *56*, 2713. (e) Cuvigny, T.; Herve de Penhoat, C.; Julia, M. *Tetrahedron*, **1986**, *42*, 5329.

(3) (a) Bäckvall, J. E.; Ericsson, A. M.; Plobeck, N. A.; Juntunen, S. K. *Tetrahedron Lett.* **1992**, *33*, 131. (b) Ericsson, A. M.; Plobeck, N. A.; Bäckvall, J. E. *Acta Chem. Scand.* **1994**, *48*, 252. (c) Plobeck, N. A.; Bäckvall, J. E. *J. Org. Chem.* **1991**, *56*, 4508.

(4) Bäckvall, J. E.; Löfström, C.; Juntunen, S. K.; Mattson, M. *Tetrahedron Lett.* **1993**, *34*, 2007.

(5) (a) Bäckvall, J. E.; Juntunen, S. K. *J. Org. Chem.* **1988**, *53*, 2398. (b) Bäckvall, J. E.; Ericsson, A. M.; Juntunen, S. K.; Nájera, C.; Yus, M. *J. Org. Chem.* **1993**, *58*, 5221.

(6) Löfström, C. M. G.; Ericsson, A. M.; Bourrinet, L; Juntunen, S. K., Bäckvall, J. E. *J. Org . Chem.* **1995**, *60*, 3586.

(7) Saito, S; Bunya, N.; Inaba, M.; Morikawe, T; Torii, S *Tetrahedron Lett.* **1985**, *26*, 5309.

(8) Tanner, D; Birgersson, C; Gogoll, A; Luthman, K. *Tetrahedron* **1994**, *50*, 9797.

(9) Duréault, A.; Greck, C.; Depezay, J. C., *Tetrahedron Lett.* **1986**, *27*, 4157.

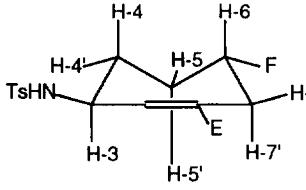
(10) Möller, O.; Steinberg, E. M.; Torssell, K, *Acta Chem. Scand.* **1978**, *B 32*, 98.

(11) (a) Richey, H. G. Jr. in *Carbonium Ions* Vol. III, Eds. Olah, G. A.; Schleyer, P. v. R., Wiley, New York, 1972, pp 1201 - 1294. (b) Buss, V.; Gleiter, R.; Schleyer, P. v. R. *J. Am. Chem Soc.* **1971**, *93*, 3927. (c) Poulter, C. D.; Spillner, C. J. *J. Am. Chem Soc.* **1974**, *96*, 7591

(12) (a) Pittman C. U.; Olah, G. A. *J. Am. Chem. Soc.* **1965**, *87*, 5123. (b) Kabakoff D. S.; Namanworth, E. *J. Am. Chem. Soc.* **1970**, *92*, 3234.

(13) ^{19}F decoupled ^{1}H NMR of **5** indicates the conformation shown with the trans configuration

$J_{6,7'}$ = 10 Hz
$J_{5',6}$ = 10 Hz
$J_{5,6}$ = 3 Hz
$J_{6,7}$ = 3 Hz
$J_{3,4}$ = 10 Hz



E = $PhSO_2$

(*Received in UK* 8 *February* 1996; *accepted* 22 *March* 1996)