Remote Intramolecular Functionalization of Arylnitrenium Ions. Seven-membered Ring Formation

Rudolph A. Abramovitch,* Ramasubbu Jeyaraman, and Konstantina Yannakopoulou

Department of Chemistry, Clemson University, Clemson, SC 29634, U.S.A.

Acid-catalysed decomposition of 3'-azido-1,3-diaryl-propane and -propanones leads to 3-amino-6,7-dihydro-5*H*-dibenzo[*a,c*]-cycloheptatriene (**3**) and -cycloheptatrienone derivatives (**5**) and (**9**).

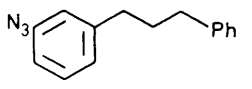
Nitrenium ions continue to receive a great deal of attention[1] because of fundamental interest in their chemistry and possible synthetic applications and owing to their importance as putative intermediates in the mechanism of action of several carcinogenic aromatic amides.[2] We have recently shown[3] that six-membered rings can be prepared readily by intramolecular cyclizations at aromatic carbon by the acid-catalysed decomposition of aryl azides. We now report seven-membered ring formation using this procedure.

The intramolecular cyclization of arylnitrenium ions at carbon bears a superficial resemblance to the well-known Pschorr cyclization of aryldiazonium salts.[4] The reactions are quite different mechanistically, however. The Pschorr reaction involves an intramolecular attack by a σ-radical or -cation (depending on the reaction conditions) upon an adjacent aromatic nucleus, whereas with arylnitrenium ions it is a π-carbocation that is involved, so that the geometries of the two transition states will be very different. With the arylnitrenium ions one would visualize an almost parallel approach of the aromatic nuclei to each other, resulting in five-membered ring formation being difficult compared with *inter*molecular processes. On the other hand, five-membered rings are formed with relative ease in the Pschorr cyclization. As far as we know, however, seven-membered rings have not been prepared by this method. We now show this is possible, starting from arylnitrenium ions.

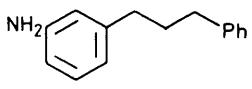
3'-Azido-1,3-diphenylpropane (**1**), b.p. 110—115 °C/0.2 mm,† was readily obtained (72%) from the corresponding primary amine (**2**), b.p. 130—135 °C/0.01 mm, itself prepared (91%) by catalytic reduction of *m*-nitrobenzylidene-acetophenone.[5] Decomposition of (**1**) in CF_3CO_2H (TFA) under N_2 at 0—5 °C with CF_3SO_3H (TFSA) was complete in less than 10 min. Work-up gave 3-amino-6,7-dihydro-5*H*-dibenzo[*a,c*]cycloheptatriene (**3**) (80%), b.p. 115—120 °C/0.2 mm, phthalimide m.p. 179—180 °C,† together with (**2**) (5%) and one unidentified product (*ca.* 2%).

For a synthesis of the dibenzotropone ring system, the required 1-(3-azidophenyl)-3-phenylpropan-1-one (**4**) was obtained from benzylidene-*m*-nitroacetophenone[6] *via* protection of the carbonyl group as the 1,3-dioxolane (78%), and catalytic reduction to 2-(3-aminophenyl)-2-phenethyl-1,3-dioxolane (100%). Diazotisation and treatment with sodium azide gave (**4**) (69%). If the carbonyl group was not protected the work-ups were more difficult and the final yield lower. Decomposition of the azide at −5 °C followed by g.c.–mass spectrometric analysis indicated that the desired cyclization product had been formed in reasonable yield (estimated 30%). Isolation was difficult. Only when the decomposition was effected with TFSA and trifluoroacetic anhydride (instead of TFSA) as solvent could three of the eight products detected be isolated: 3-amino-6,7-dihydro-5*H*-dibenzo[*a,c*]cycloheptatrienone (6.7%) (**5**), the 1-amino derivative (**6**) (3.2%), and an open-chain amino trifluoromethanesulphonate (**7**) (4.3%).

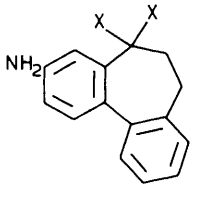
With a view to synthesising a possible precursor to colchicine the decomposition of azide (**8**) with TFSA in TFA was examined. Again, g.c.–mass spectrometric analysis indicated the formation of the desired cyclized ketone. Chromatographic separation on neutral alumina failed to give *any* cyclized amino ketone, however. The major product† (24.7%) proved to be the enol trifluoromethanesulphonate (**9**) of the expected 9-amino-1,2,3-trimethoxy-5,6-dihydro-5*H*-benzo[*a,c*]cycloheptatrienone (yellow oil). A second

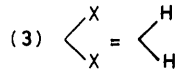


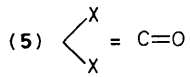
(**1**)

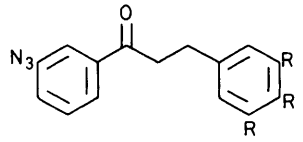


(**2**)

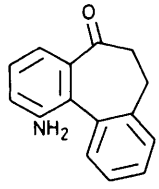


(**3**) 

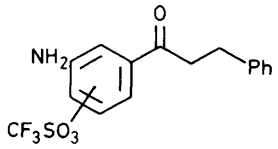
(**5**) 



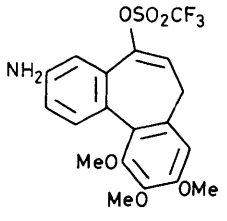
(**4**) R = H
(**8**) R = OMe



(**6**)



(**7**)



(**9**)

† All new compounds gave the expected microanalytical and spectral data.

product was isolated in much lower yield, whose i.r. and mass spectra suggest that the product is a 1:1-adduct of the expected cycloheptanone and TFSA. If the latter were indeed the main product formed in the reaction this might explain the above observations: elimination of CF_3SO_3H in the g.s.–mass spectrometer inlet would lead to the observed ketone, whereas dehydration on the alumina column would lead to (**9**). In any event, a possible colchicine precursor can be obtained in this manner.

Support from the National Science Foundation for this work is gratefully acknowledged.

Received, 25th April 1985; Com. 547

References

1 R. A. Abramovitch and R. Jeyaraman, in 'Azides and Nitrenes: Reactivity and Utility,' ed. E. F. V. Scriven, Academic Press, Orlando, Florida, 1984, pp. 297—357.
2 E. C. Miller and J. A. Miller, *Cancer,* 1981, **47**, 2327; M. Novak and A. K. Roy, *J. Org. Chem.*, 1985, **50**, 571, and references cited therein.
3 R. A. Abramovitch, M. Cooper, S. Iyer, R. Jeyaraman, and J. A. R. Rodriguez, *J. Org. Chem.*, 1982, **47**, 4819.
4 R. A. Abramovitch, in 'Advances in Free-Radical Chemistry,' ed. G. H. Williams, Logos Press, London, 1967, p. 87.
5 B. R. Baker, B. T. Ho, and G. J. Lourens, *J. Pharm. Sci.*, 1967, **56**, 737.
6 R. E. Lyle and L. P. Paradis, *J. Am. Chem. Soc.*, 1955, **77**, 6667.