

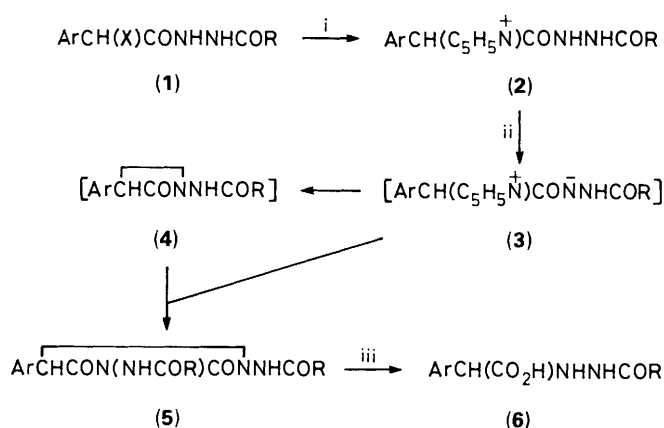
Hydrazidopyridinium Salts as Precursors of *N,N'*-Diaminohydantoins and α -Hydrazino Acids

Claudie Florac, Philippe Le Grel, Michèle Baudy-Floc'h, and Albert Robert*

Groupe de Recherches de Chimie structurale, Unité de Recherches associée au C.N.R.S., U.R.A. D0704, Université de Rennes, F-35042 Rennes Cédex

N,N'-Diaminohydantoins are obtained in good yield through the reaction of hydrazidopyridinium salts in a basic medium. The hydrolysis of these hydantoins leads to α -hydrazino acids.

α -Halogenohydrazides (1), easily prepared from gem dicyano epoxides,¹ react rapidly in a basic medium with nucleophiles to give α -functionalized hydrazides.² When the nucleophile is pyridine or a substituted pyridine, very good yields of hydrazidopyridinium salts (2) are obtained (see Scheme).



Scheme. Reagents and conditions: i, C_5H_5N (3 equiv.), MeCN, reflux, 4 h; ii, NEt_3 (2 equiv.), MeCN, reflux, 4 h; iii, $Ar = p\text{-MeC}_6H_4$, $R = Ph$, $Ba(OH)_2$ (5 equiv.), H_2O , reflux, 5 days.

Although many pyridinium salts are available by treatment of pyridine with halogenated derivatives,^{3,4} few hydrazidopyridinium salts have been described⁵⁻⁸ and their reactivity has only been poorly investigated. Taking into account previous literature results,^{2,3} it seemed to us of interest to study the reactivity of hydrazidopyridinium salts in a basic medium.

The reaction of the pyridinium salts (2) with triethylamine (2 equiv.) gives, in a very simple way, the *N,N'* diaminohydantoins (5). It seems likely that such a reaction proceeds through the intermediates (3) and (4) (see Scheme). In fact (3) is a tautomeric form of a pyridinium ylide which is expected when (2) is treated with a base,³ while the formation of (4) from (3) is similar to the formation of (4) from α -halogenohydrazides.² The reaction of (3) acting as a nucleophile, with (4) to give the *N,N'*-diaminohydantoin (5) is also an expected reaction.

This simple route to *N,N'*-aminohydantoins is of interest since to the best of our knowledge only one *N,N'*-diamino substituted hydantoin has previously been prepared, and this by the reaction of a *N,N'*-unsubstituted hydantoin with chloramine/NaH.^{10,11} The compounds described are precursors of α -hydrazino acids (6), themselves of interest, and work is now in progress in our laboratory both to establish unequivocally the mechanism of the reaction and to extend its scope.

Experimental

Hydrazidopyridinium Salts (2). α -Bromohydrazide (1; $X = Br$) (10 mmol) and pyridine (30 mmol) were allowed to react in

boiling MeCN (50 ml) during 20 h. After the mixture had been cooled at room temperature, the precipitated salt (2) was recovered and recrystallised from methanol.

N,N'-Diaminohydantoins (5). Hydrazidopyridinium bromide (2) (10 mmol) and NEt_3 (2 ml) were heated under reflux in acetonitrile (50 ml) for 4 h. After evaporation of acetonitrile (30 ml), the residue was diluted with water (100 ml) and extracted with dichloromethane. Evaporation of the extract then gave the *N,N'*-diaminohydantoin (5) as a solid which was recrystallised from benzene.

(5; $Ar = p\text{-ClC}_6H_4$, $R = OMe$) (60%), m.p. 190 °C; $\delta_H(CDCl_3 + CF_3CO_2H)$ 3.75 (s, 3 H), 3.82 (s, 3 H), 5.30 (s, 1 H), and 7.37 (m, 4 H); $\delta_C(CDCl_3 + CF_3CO_2H)$ 51.4 (q, CH_3), 54.7 (q, CH_3), 64.1 (d, $CHAr$), 154.8 (s, CO), 156.0 (s, CO), 167.6 (s, CO), 128.4 (Ar), 129.7 (Ar), 129.8 (Ar), and 136.7 (Ar); ν_{max} 3 340br, 3 260br, 1 809s, 1 755s, 1 743s, and 1 722s.

(5; $Ar = Ph$, $R = OMe$) (55%), m.p. 148 °C; $\delta_H(CDCl_3)$ 3.62 (s, 3 H), 3.70 (s, 3 H), 5.25 (s, 1 H), and 7.37 (m, 5 H); $\nu_{max}(Nujol)$ 3 320br, 3 270br, 1 810m, 1 755s, 1 730s, and 1 710s cm^{-1} .

(5; $Ar = p\text{-MeC}_6H_4$, $R = OMe$) (75%), m.p. 171 °C; $\delta_H(CDCl_3 + CF_3CO_2H)$ 2.34 (s, 3 H), 3.72 (s, 3 H), 3.79 (s, 3 H), 5.26 (s, 1 H), and 7.40 (m, 4 H); $\nu_{max}(Nujol)$ 3 320br, 3 290br, 1 810m, 1 757s, 1 734s, and 1 725s cm^{-1} .

(5; $Ar = p\text{-MeC}_6H_4$, $R = Ph$) (60%), m.p. 256 °C; $\delta_H(CDCl_3 + CF_3CO_2H)$ 2.15 (s, 3 H), 5.31 (s, 1 H), and 7.40 (m, 14 H); $\nu_{max}(Nujol)$ 3 240br, 1 812m, 1 752s, and 1 655s cm^{-1} .

Satisfactory elemental analyses and mass spectra were obtained for all the hydantoins (5).

Hydrazino Acid (6; $Ar = p\text{-MeC}_6H_4$, $R = Ph$).—*N,N'*-Diaminohydantoin (5) ($Ar = p\text{-MeC}_6H_4$, $R = Ph$) (1 g) and $Ba(OH)_2 \cdot 8H_2O$ (3.7 g) in water (50 ml) were heated under reflux for 5 days, and then diluted with boiling water (200 ml). CO_2 was bubbled into the solution until it was pH 6–7. The precipitate of $BaCO_3$ was removed and water (200 ml) was evaporated under reduced pressure. The precipitate of (6; $Ar = p\text{-MeC}_6H_4$, $R = Ph$) was isolated and recrystallised from acetone. Yield 25% (not optimized), m.p. > 260 °C; $\delta_H(DMSO)$ 2.22 (s, 3 H), 5.77 (s, 1 H), and 7.47 (m, 9 H); $\nu_{max}(Nujol)$ 3 330s, 3 200s, 3 100br, 1 686s, and 1 665m cm^{-1} .

References

- P. Legrel, M. Baudy Floc'h, and A. Robert, *Synthesis*, 1987, 306.
- P. Legrel, M. Baudy Floc'h, and A. Robert, *Tetrahedron*, 1988, **44**, 4805.
- I. Zugravescu and M. Petrovanu, 'N-Ylid Chemistry,' McGraw Hill, 1976, New York.
- G. H. Harris, R. S. Shelton, M. G. Van Campen, E. R. Andrews, and E. L. Shumann, *J. Am. Chem. Soc.*, 1951, **73**, 3959.
- S. M. Sicardi, U.S.P. 4, 382, 941, 10 Mai 1983 Appl. 210,585, 26 Nov. 1980 (*Chem. Abstr.*, 1983, **99**, 53617).
- S. M. Sicardi, C. M. Vega, and E. B. Cimijotti, *J. Med. Chem.*, 1980, **23**, 1139.
- V. A. Shrubovich, A. E. Feinerman, V. V. Shevchenko, and Y. S.

- Lipatov, USSR, SU 1, 141, 725, 07 Sept. 1985 Appl. 3 480,766, 04 Aug. 1982 (*Chem. Abstr.*, 1985, **105**, 61 481).
- 8 A. Robert, M. T. Thomas, and A. Foucaud, *J. Chem. Soc., Chem. Commun.*, 1979, 2048.
- 9 A. R. Katritzky, N. E. Grzeskowiak, J. Alvarez-Builla, and A. Tarragatomas, *J. Prakt. Chem.*, 1983, **325**, 177.
- 10 S. Karady, S. H. Pines, M. G. Ly, M. Sletzing, J. E. Allegretti, and A. Wildman, Merck and Co Inc., Ger. Offen 206 2285, 01 July 1971 (*Chem. Abstr.*, 1971, **75**, 118122); S. Karady, S. H. Pines, M. G. Ly, M. Sletzing, J. E. Allegretti, and A. Wildman, Merck and Co Inc., Ger. Offen., DE 206 2332, 15 July 1971 (*Chem. Abstr.*, 1971, **75**, 118120).
- 11 S. Karady, S. H. Pines, M. G. Ly, M. Sletzing, Merck and Co. Inc., Can. Patent, C.A. 951 661, 23 July 1974 (*Chem. Abstr.*, 1975, **82**, 139722).

Received 7th March 1989

(Accepted 11th June 1989); Paper 9/02940K