

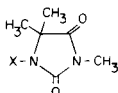
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1-Bromo (**1a**) and 1-chloro-3,5,5-trimethylhydantoin (**1b**) which are both useful halogenating and oxidizing agents, underwent halogen transposition from nitrogen to the 3-*N*-alkyl group when their boiling carbon tetrachloride solutions were irradiated.

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The 1-halo-3,5,5-trimethylhydantoins **1** have been synthesized by Orazi, *et al.* (3) and were reported as halogenating agents by the same authors (4) and also by Walling, *et al.* (5).

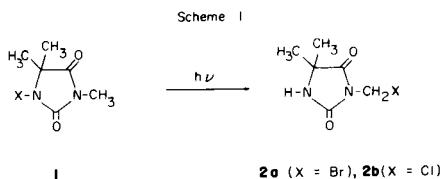


1a (X = Br), **1b** (X = Cl)

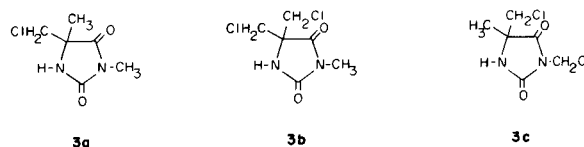
We have used these reagents in our laboratory for allylic (6) and benzylic (7) halogenation and for alcohol oxidation (8) because they are completely soluble in boiling carbon tetrachloride. As a result, we were interested in determining their stability under these same conditions.

Solutions of **1** (0.33 M) in carbon tetrachloride were heated at 80° in Pyrex equipment (cut off 320 nm) and irradiated with a sunlamp. The reactions were monitored by ¹H nmr and the absence of **1** was confirmed by a negative iodine test.

The main products of the reactions were the 3-haloalkyl derivatives **2** (Scheme 1). Results concerning **1a** are summarized in Table 1 and those concerning **1b** in Table 2.



This rearrangement did not occur when the reactions were carried out in the dark. When samples of **1a** were irradiated with wavelengths above 350 nm the yields of **2a** decreased strongly, but **1b** was insensitive to this change. Furthermore, monitoring the ¹H nmr spectra during the rearrangement of **1b** showed evidence for the formation of a secondary product or products. This was seen as a broad signal situated at 3.60-3.80 ppm. These results indicate that the secondary product may be a mixture of the 5-halomethyl derivatives **3**. This conclusion is consistent with the observed spectra of the product of photochemical halogenation of 5,5-dimethylhydantoin which showed a 3.60-3.80 ppm signal due to the 5-chloromethyl group.



The failure of the dark reactions suggested a radical mechanism. Besides, the higher selectivity of the rearrangement of **1a** is attributable to an attack on the 3-methyl group by the bromine atoms which are more selective than chlorine atoms. These findings can be explained if the Goldfinger mechanism (9) plays an important role under these conditions since the Bloomfield mechanism (10) should involve the same nitrogen centered radical as the hydrogen abstracting species in both cases.

On the other hand, the lack of rearrangement when the reactions of **1a** were performed in the dark with AIBN or with benzoyl peroxide, rules out a chain radical mechanism. In addition, the wavelength dependence of the **1a** halogen transposition can not be explained in terms of the Goldfinger mechanism.

It is therefore obvious that the decomposition of **1a** and **1b** proceeded by different routes because this later substrate underwent halogen rearrangement even at wavelengths >350 nm and in the dark initiated by AIBN (Table 2).

Consequently, studies directed towards further understanding of the mechanism or mechanisms involved are in progress. We are also interested in expanding the scope of this reaction to other hydantoin derivatives.

It is interesting to note that only when the substrates were unreactive could we detect the formation of the 3-haloalkyl derivatives. For example, the oxidation of some tertiary alcohols using **1a** took place so slowly that important amounts of **2a** were observed.

EXPERIMENTAL

Melting points were determined in closed capillary tubes and are uncorrected. The ir spectra (potassium bromide) were obtained on a Beckman IR-8 spectrophotometer. The ¹H nmr spectra were recorded on a Varian T-60 spectrometer in deuteriochloroform or carbon tetrachloride solutions containing TMS as the internal standard. The mass spectrum of **2a** was performed in the department of Chemistry of the University of California at Irvine, USA, and the mass spectrum of **2b**

Table 1

| Rearrangement of 1a in Carbon Tetrachloride at 80° (a) | | |
|---|-----------|---------|
| Conditions | Products | Yield % |
| h ν > 320 nm | 2a | 80 |
| h ν > 350 nm | 2a | 20 |
| dark | NR (c) | — |
| dark AIBN | NR | — |
| dark BPO (b) | NR | — |

(a) Reaction time, 1.5 hours. (b) BPO = benzoyl peroxide. (c) NR = no reaction.

Table 2

| Rearrangement of 1b in Carbon Tetrachloride at 80° (a) | | |
|---|-----------|---------|
| Conditions | Products | Yield % |
| h ν > 320 nm | 2b | 63 |
| | 3 | 28 |
| h ν > 350 nm | 2b | 61 |
| dark | NR (c) | — |
| dark AIBN | 2b | 26 |
| | 3 | 14 |
| dark BPO (b) | NR | — |

(a) Reaction time, 1.5 hours. (b) BPO = benzoyl peroxide. (c) NR = no reaction.

in LEA, University of San Luis, Argentina. Elemental analyses were carried out by UMIMFOR, Buenos Aires.

Silica gel Macherey Nagel (0.05-0.2 mm) was used for chromatography. 5,5-dimethylhydantoin was from Aldrich Chemical Company Inc. All solvents used were reagent grade. The compound 3,5,5-trimethylhydantoin was synthesized as described by Orio (11). Its 1-halo derivatives **1a** and **1b** were prepared as indicated by Orazi *et al.*, (3). Samples with more than 99% of theoretical halogen were used.

General Procedure for Transposition Reactions.

Solutions of **1** (1 mmole, 3 ml) in dry carbon tetrachloride were refluxed in a Pyrex vessel at 80° and irradiated with a sunlamp. Dark reactions were performed covering the glass vessel with aluminum foil. To prove the action of AIBN or benzoyl peroxide, 3% or these reagents was added. The end of the reactions was verified by an iodometric test and then a sample of the homogeneous solution obtained was analysed by H¹ nmr to determine the yields of products. When the mixture was insoluble in carbon tetrachloride at room temperature, the solvent was evaporated to dryness *in vacuo* and the sample was dissolved in deuteriochloroform in order to perform their H¹ nmr spectra.

3-Bromomethyl-5,5-dimethylhydantoin (**2a**).

This compound was isolated by solvent elimination at reduced pressure. Recrystallization from benzene yielded pure **2a** as a white solid mp 132-134°; H¹ nmr (deuteriochloroform): δ 1.50 (s, 6H), 5.24 (s, 2H), 7.66 (broad s, 1H); ir (potassium bromide): 3225 cm⁻¹ (N-H), 1720 and 1780 cm⁻¹ (C=O) indicated that the hydantoin ring had remained intact; ms: (m/e) 221/223 (M+1), 205/207, 141, 113 and 42 (100%).

Anal. Calcd. for C₆H₉BrN₂O₂: C, 32.60; H, 4.10; N, 12.67; Br, 36.15. Found: C, 32.50; H, 4.40; N, 12.50; Br, 36.05.

3-Chloromethyl-5,5-dimethylhydantoin (**2b**).

After removal of the solvent under vacuum, the residue was chromatographed on silica gel (ratio silica gel/substrate, 50/1 g). By elution with distilled chloroform/acetone, 80/20 (10 ml fractions) all of the chlorinated products were isolated in the 1-5 eluates (63%). Fraction 4 contained **2b** as the major component. Several recrystallizations from dry carbon tetrachloride afforded **2b** as a white solid mp 126-127°; H¹ nmr (deuteriochloroform): δ 1.46 (s, 6H), 5.23 (s, 2H), 7.86 (broad s, 1H); ir (potassium bromide): cm⁻¹ 3221 (N-H), 1720 and 1780 (hydantoin ring); ms: (m/e) 176/178 (M⁺), 161/163, 141, 113 and 42 (100%).

Anal. Calcd. for C₆H₉ClN₂O₂: C, 40.80; H, 5.13; N, 15.86; Cl, 20.07. Found: C, 40.41; H, 4.98; N, 15.80; Cl, 19.57.

There are no references to **2a** in the literature however **2b** has been referred to in two patents (12), but their physical constants have not been reported. Nevertheless, the spectral and analytical data in this paper are in good agreement with the proposed structures. They are based on known works reported ir (13), H¹ nmr (14) and mass spectra (15) of hydantoin.

Photochlorination of 5,5-Dimethylhydantoin.

Chlorine was bubbled through a suspension of 5,5-dimethylhydantoin (1 mmole) in boiling carbon tetrachloride (3 ml) while stirred and irradiated with a sunlamp. After refluxing 4 hours the solvent was evaporated *in vacuo*. The H¹ nmr of mixture performed in distilled chloroform, showed signals in the region 3.60-3.80 ppm in addition to the 5-methyl signal at 1.40-1.47 ppm. Removal of the solvent and several extractions with boiling water gave a white solid mp 138-141°. Reported for 5-chloromethyl-5-methylhydantoin 141-142° (16).

REFERENCES AND NOTES

- (1) To whom all correspondence should be addressed.
- (2) Grateful recipient of a Fellowship from the Consejo Nacional de Investigaciones Científicas y Técnicas, Argentina.
- (3a) O. Orazi and R. Corral, *An. Asoc. Quím. Argent.*, **45**, 139 (1957); (b) O. Orazi and R. Corral, *J. Org. Chem.*, **28**, 1100 (1963).
- (4a) O. Orazi and R. Corral, *An. Asoc. Quím. Argent.*, **43**, 98 (1955); (b) O. Orazi and R. Corral, *ibid.*, **45**, 151 (1957); (c) O. Orazi and R. Corral, *ibid.*, **42**, 139 (1954).
- (5) C. Walling and A. Rieger, *J. Am. Chem. Soc.*, **85**, 3139 (1963).
- (6a) O. Orio and A. Suárez, *An. Asoc. Quím. Argent.*, **65**, 163 (1977); (b) O. Orio and S. A. de Juliani, *ibid.*, **65**, 157 (1977); (c) O. Orio, A. Suárez and V. Balzaretta, *ibid.*, **68**, 163 (1980).
- (7a) See 6b; (b) O. Orio and A. Suárez, *ibid.*, **69**, 209 (1981).
- (8) O. Orio, A. Suárez and M. R. Mazzieri, *ibid.*, **66**, 219 (1978).
- (9a) P. Goldfinger, J. Adam and P. Gosselain, *Nature*, **171**, 704 (1959); (b) P. Goldfinger, J. Adam and P. Gosselain, *Bull. Soc. Chim. Belg.*, **65**, 533 (1956).
- (10) G. Bloomfield, *J. Chem. Soc.*, 114, 1944.
- (11) O. Orio, *Rev. Fac. Quím. Farm. La Plata*, **30**, 21 (1957).
- (12a) J. Habermeier, H. Batzer, L. Buxbaum, D. Porret and B. Schreiber, German Offen 2,436,149; *Chem. Abstr.*, **83**, 441704y (1975); (b) Y. Yokota, T. Aono and T. Hirose, German Offen 2,703,145 *ibid.*, **88**, 144302q (1978).
- (13) I. Elliot and P. Natarajan, *J. Pharm. Pharmacol.*, **19**, 215 (1967).
- (14) O. Orazi and R. Corral, *Spectrochim. Acta*, **21**, 2119 (1965).
- (15) K. Djerassi, O. Orazi, R. Corral and A. M. Duffield, *ibid.*, **5**, 551 (1971).
- (16) S. Tahara and Y. Obata, *Agr. Biol. Chem.*, **35**, 53 (1971).