## 2-Chloro-4,5-dihydroimidazole; I. Reactions with some Heteroaromatic *N*-Oxides, Cyclic Nitrones, and Aldoximes

Franciszek SĄCZEWSKI*

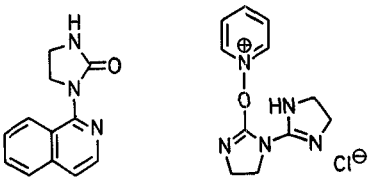
Department of Organic Chemistry, Medical Academy, K. Marksa 107, 80-416 Gdańsk, Poland

In a previous communication[1] we described the synthesis of some heterocyclic-fused imidazoline derivatives starting from 2-chloro-4,5-dihydroimidazole (**1**). We report here the results obtained from the reactions of compound **1** with some 1,3-dipolar compounds such as heteroaromatic *N*-oxides and cyclic nitrones.

It is known that a variety heteroaromatic *N*-oxides react with imidoyl chlorides or benzonitrilium salts to form acylamination products[2,3,4]. Compound **1** which is a carbamidine chloride reacts with heteroaromatic *N*-oxides to give 1-heteroaryl-2-oxoimidazolidines or 1,3-bis[heteroaryl]-2-oxoimidazolidines. These reactions proceed spontaneously and exothermically in polar aprotic solvents such as chloroform, dichloromethane, or dimethylformamide. The nature of the reactions products depend on the kind of *N*-oxide used. Thus, the reaction of **1** with quinoline *N*-oxide (**2**, R = H) affords two products: 2-oxo-1-(2-quinolinyl)-imidazolidine **(5a)** and 2-oxo-1,3-bis[2-quinolinyl]-imidazolidine **(8a)**.

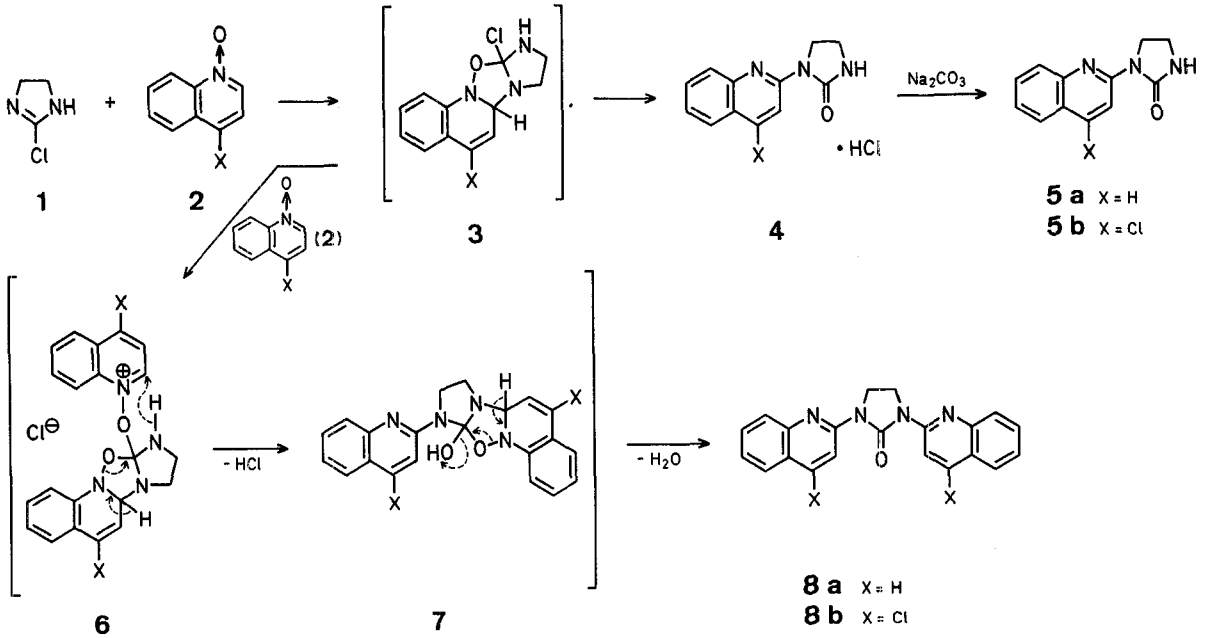
The first step of the reaction is the addition of compound **1** to the *N*-oxide **2** with formation of intermediate **3**. Elimination of hydrogen chloride from **3** with simultaneous rearomatization gives rise to compound **4**. On the other hand, attack of a second molecule of quinoline *N*-oxide **(2)** on the intermediate **3** leads to formation of intermediate **6**, which undergoes the rearrangement with elimination of hydrogen chloride (→**7**) and water to give compound **8**.

The reaction of compound **1** with isoquinoline *N*-oxide under analogous conditions affords only one product, 1-(1-isoquinolinyl)-2-oxoimidazolidine **(9)**. The method fails with pyridine *N*-oxide and its substitution products; thus, the reaction of **1** with pyridine *N*-oxide produces the unstable salt **10**. The method also fails with heteroaromatic *N*-oxides containing strongly electron-withdrawing groups such as 4-nitroquinoline *N*-oxide.



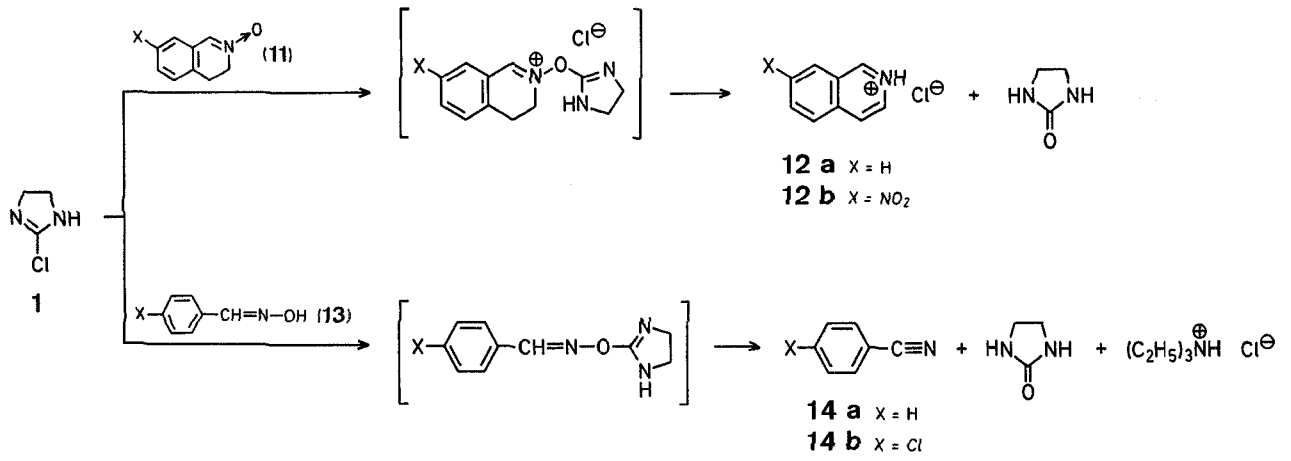
**9** **10**

The structures of the 2-oxoimidazolidine derivatives **5, 8,** and **9** were confirmed by microanalyses, M.S.-, I.R.-, and $^1$H-N.M.R.-spectrometric data.




**1** **2** **3** **4** **5a** X = H **5b** X = Cl

**6** **7** **8a** X = H **8b** X = Cl




The reaction of compound **1** with 3,4-dihydroisoquinoline *N*-oxide (**11**, X = H) or its 7-nitro derivative led only to the isoquinoline hydrochlorides **12a, b**, i.e., to the dehydration products of the cyclic nitrones **11**. The benzaldoximes **13** were also only dehydrated by compound **1** to give the nitriles **14**.

The yields obtained in these reactions ranged from 55 to 67% and thus were considerably lower as compared to methods using other dehydrating agents.

Melting points are not corrected. The mass spectra were recorded on a LKB 9000 spectrometer, the I.R. spectra on a Specord 75 IR spectrophotometer, and the $^1$H-N.M.R. spectra on a BS-487 Tesla Brno spectrometer at 80 MHz.

All reactions are carried out under dry nitrogen. The presence of air or moisture in the reaction apparatus decreases the yields considerably.

**Reaction of 2-Chloro-4,5-dihydroimidazole (1) with Quinoline *N*-Oxide:**

Freshly distilled quinoline *N*-oxide (3.6 g, 25 mmol) is added in one portion to a stirred solution of compound **1** (2.5 g, 25 mmol) in dichloromethane[5] (30 ml). Stirring is continued at room temperature until the exothermic reaction has subsided (~30 min), and the mixture then refluxed for 1 h. From the cooled mixture, the precipitated product **8a** is isolated by suction. The filtrate is concentrated to dryness and the residue stirred with water (20 ml). An additional quantity of compound **8a** (0.1 g) is precipitated, filtered off, and washed with water; total yield of *2-oxo-1,3-bis[2-quinolinyl]-imidazolidine* **(8a)**: 0.55 g (17%); m.p. 328–330 °C (from dimethylformamide).

| | | | | |
|---|---|---|---|---|
| $C_{21}H_{16}N_4O$ | calc. | C 74.10 | H 4.90 | N 16.46 |
| (340.4) | found | 74.36 | 4.74 | 16.17 |

M.S. (70 eV): $m/e$ = 340 ($M^+$, 74.6%); 169 (100); 171 (65); 170 (63); 129 (48); 128 (96.5); 101 (34.6).

I.R. (KBr): $\nu_{C=O}$ = 1700 cm$^{-1}$.

$^1$H-N.M.R. (TFA/$TMS_{ext}$): $\delta$ = 4.5 (s, 4H); 7.5–8.1 (m, 8H); 7.4 (d, 2H); 8.8 ppm (d, 2H, $J$ = 8 Hz).

The aqueous solution is made alkaline with aqueous 20% sodium carbonate. The free base **5a** thus obtained is isolated by suction, washed with water, and recrystallized from ethanol; yield of 2-oxo-1-(2-quinolinyl)-imidazolidine **(5a)**: 1.9 g (36%); m.p. 244–246 °C.

| | | | | |
|---|---|---|---|---|
| $C_{12}H_{11}N_3O$ | calc. | C 67.59 | H 5.20 | N 19.71 |
| (213.2) | found | 67.78 | 5.49 | 19.98 |

M.S. (70 eV): $m/e$ = 213 ($M^+$, 81%); 169 (100); 129 (62); 128 (56); 101 (23.7).

I.R. (KBr): $\nu_{C=O}$ = 1695 cm$^{-1}$.

$^1$H-N.M.R. (DMSO-$d_6$/$TMS_{int}$): $\delta$ = 3.3–3.7 (m, 2H); 4.0–4.3 (m, 2H); 8.25–8.0 (m, 4H); 8.25 (d, 1H); 8.55 ppm (d, 1H, $J$ = 10 Hz).

**Reaction of 2-Chloro-4,5-dihydroimidazole (1) with 4-Chloroquinoline *N*-Oxide:**

The reaction is performed with 4-chloroquinoline *N*-oxide (4.5 g, 25 mmol) as described above. From the cooled suspension obtained, product **8b** is isolated by suction. The filtrate is evaporated in vacuo and the residue stirred with water (30 ml) to precipitate an additional quantity of product **8b**; total yield of *1,3-bis[4-chloro-2-quinolinyl]-2-oxoimidazolidine* **(8b)**: 0.5 g (10%); m.p. 310–311 °C (from dimethylformamide).

| | | | | |
|---|---|---|---|---|
| $C_{21}H_{14}Cl_2N_4O$ | calc. | C 61.62 | H 3.45 | N 13.69 |
| (409.2) | found | 61.01 | 3.48 | 13.78 |

I.R. (KBr): $\nu_{C=O}$ = 1710 cm$^{-1}$.

$^1$H-N.M.R. (TFA/$TMS_{ext}$): $\delta$ = 4.65 (s, 4H); 7.7 (s, 2H); 7.8–8.6 ppm (m, 8H).

The filtrate is made alkaline with aqueous 20% sodium carbonate and extracted with chloroform (2 × 15 ml). The organic extract is dried with sodium sulfate, concentrated to dryness in vacuo, and the residue recrystallized from ethanol; yield of *1-(4-chloro-2-quinolinyl)-2-oxoimidazolidine* **(5b)**: 1.8 g (31%); m.p. 238–240 °C.

| | | | | |
|---|---|---|---|---|
| $C_{12}H_{10}ClN_3O$ | calc. | C 58.19 | H 4.07 | N 16.97 |
| (247.7) | found | 58.44 | 4.31 | 17.20 |

I.R. (KBr): $\nu_{C=O}$ = 1710 cm$^{-1}$.

$^1$H-N.M.R. (DMSO-$d_6$/$TMS_{int}$): $\delta$ = 3.35–3.75 (m, 2H); 4.1–4.4 (m, 2H); 7.5–8.25 (m, 4H); 8.75 ppm (s, 1H).

**Reaction of 2-Chloro-4,5-dihydroimidazole (1) with Isoquinoline *N*-Oxide:**

Anhydrous isoquinoline *N*-oxide (3.6 g, 25 mmol) is added to a stirred solution of compound **1** (2.5 g, 25 mmol) in chloroform (30 ml). After the exothermic reaction has subsided the mixture is refluxed for 1 h and then cooled. The solvent is evaporated and the oily residue made alkaline with aqueous 20% potassium carbonate. The precipitated product is isolated by suction, washed with water, and recrystallized from ethanol; yield of 1-(1-isoquinolinyl)-2-oxoimidazolidine **(9)**: 2.2 g (43%); m.p. 250–252 °C.

| | | | | |
|---|---|---|---|---|
| $C_{12}H_{11}N_3O$ | calc. | C 67.59 | H 5.20 | N 19.71 |
| (213.2) | found | 67.29 | 5.47 | 19.48 |

M.S. (70 eV): $m/e$ = 213 ($M^+$, 100%); 169 (42); 157 (31.6); 129 (64); 128 (41); 101 (14).

I.R. (KBr): $\nu_{C=O}$ = 1705 cm$^{-1}$.

$^1$H-N.M.R. (DMSO-$d_6$/$TMS_{int}$): $\delta$ = 3.3–3.7 (m, 2H); 4.1–4.4 (m, 2H); 7.1–8.25 ppm (m, 6H).

**Reaction of 2-Chloro-4,5-dihydroimidazole (1) with 3,4-Dihydroisoquinoline *N*-Oxide:**

A solution of compound **1** (5 g, 50 mmol) in dichloromethane (80 ml) is added dropwise to a stirred solution of 3,4-dihydroisoquinoline *N*-oxide[6] (**11**, X = H; 6.6 g, 45 mmol) in dichloromethane (20 ml). The resultant solution is allowed to stand at room temperature for 1 h, and

then evaporated to dryness in vacuo. The oily residue is made alkaline with aqueous 20% sodium carbonate, and extracted with chloroform (2 × 20 ml). The extract is dried with magnesium sulfate, the solvent evaporated, and the residual crude isoquinoline distilled under reduced pressure; yield: 4.6 g (81%); picrate, m.p. 222–223 °C (Ref.[6], m.p. 223 °C).

The reaction of compound **1** with 7-nitro-3,4-dihydroisoquinoline *N*-oxide (**11**, X = $NO_2$) under analogous conditions affords 7-nitroisoquinoline **(12b)**; yield: 54%; m.p. 173–175 °C (Ref.[7], m.p. 176 °C).

**Reaction of 2-Chloro-4,5-dihydroimidazole (1) with Benzaldoxime:**
A solution of benzaldoxime (**13**, X = H; 6 g, 50 mmol) and triethylamine (5 g, 50 mmol) in dichloromethane (20 ml) is added dropwise to a stirred solution of compound **1** (5 g, 50 mmol) in dichloromethane (80 ml). The resultant mixture is refluxed for 3 h, then allowed to cool, and extracted successively with water (20 ml), aqueous 5% sodium hydroxide (20 ml), and water (30 ml). The organic phase is evaporated to dryness and the residual product distilled at reduced pressure to give benzonitrile **(14a)**; yield: 3.4 g (67%); b.p. 85–86 °C/20 torr (Ref.[7], b.p. 82 °C/22 torr).

The reaction of compound **1** with 4-chlorobenzaldoxime (**13**, X = Cl) under analogous conditions affords 4-chlorobenzonitrile **(14b)**; yield: 55%; m.p. 93–94 °C (Ref.[7], m.p. 94 °C).

Received: November 26, 1982
(Revised form: February 9, 1983)

---

* Temporary address: University of Florida, Department of Chemistry, Gainesville, Florida 32611, U.S.A.

[1] F. Sączewski, H. Foks, *Synthesis* **1981**, 154.
[2] R. A. Abramovitch, G. M. Singer, *J. Am. Chem. Soc.* **91**, 5672 (1969).
[3] R. A. Abramovitch, R. B. Rogers, *Tetrahedron Lett.* **1971**, 1951.
[4] R. A. Abramovitch, R. B. Rogers, *J. Org. Chem.* **40**, 41 (1975).
[5] A. Trani, E. Belasio, *J. Heterocycl. Chem.* **11**, 257 (1974).
[6] E. Schmitz, *Chem. Ber.* **91**, 1488 (1958).
[7] *Beilsteins Handbuch der Organischen Chemie.*