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Puzzling Formation of Bisimidazole Derivatives from Hexachloroacetone and Diamines

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Abstract: The reaction of hexachloroacetone with different diamines leads to formation of the bisimidazole derivatives **2**, **3**, and **4**, a process which is facilitated by sonication of the reacting mixtures.

Trichloroketones are useful, selective, acylating agents.[1-5] The incorporation of two -CCl_3 groups in hexachloroacetone, **1**, makes this ketone a versatile reagent for the preparation of amides and /or cyclic ureas, and a useful alternative to toxic gaseous phosgene. The reaction of **1** with nucleophiles is well documented. It reacts with water in the presence of catalytic amounts of base to form chloroform , a reaction which has been utilized for the preparation of $CDCl_3$.[6] It is converted into alkyl trichloroacetates by treatment with alcohols[7,8] and into the corresponding amides by reaction with RNH_2.[9-11] With di- and trialkylphosphites trichloroketones form halogenovinylphosphites,[12-14] which are useful as insecticides and fungicides.

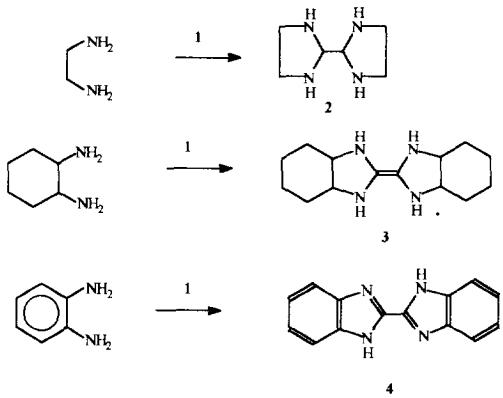
We were concerned with the preparation of cyclic ureas from **1** and diamines, in analogy with the formation of 2-imidazolidinone by reaction of excess ethylenediamine with methyl trichloroacetate, reported by Durden and Heywood.[15] This reaction attracted our attention because conflicting reports on its outcome were found in the literature: a different cyclization product, N-trichloroacetyl-2-trichloromethylimidazoline, had been obtained previously by Madeleine and Day,[16] a result which could not be confirmed by the former authors.[15] In addition, depending on the reaction conditions, an open-chain diamide was sometimes obtained, rather than cyclic urea.

We anticipated for **1** a behaviour analogous to that of methyl trichloroacetate, and we decided to carry out the reaction under different conditions to see if one, or both products could be obtained. To our surprise, when we employed a 10:1 excess of the diamine we isolated a crystalline product which possessed no carbonyl groups. The reaction was rather slow at room temperature and the yield was not high (*ca* 20 %). Carrying out the reaction in an atmosphere of oxygen seemed to shorten the reaction time at room temperature from three months to about one week, though the yield remained the same. The use of low

power sonication for 12 h raised the temperature of the reaction mixture to about 50°C and improved the yield of the crystalline product to 60 %. The product was identified by its spectra and elementary analysis as 2,2'-bisimidazolidine **2**.

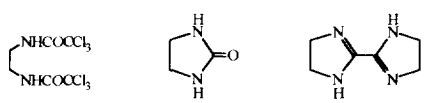
In order to check the generality of this conversion, we reacted **1** with excess 1,2-diaminocyclohexane (cis-trans mixture). After 16 h of ultrasonic irradiation, a crystalline product precipitated and was identified as the 2,2'-bis(4,5-cyclohexane)-2-imidazolidinene **3**, in 49 % yield.

Finally, when we reacted a 10:1 excess 1,2-phenylenediamine with **1** in ethyleneglycol under the same conditions, we isolated, after 1 h reaction, 82 % of compound **4**.



The mechanism of these conversions is not clear. The diamide **5** is probably a precursor because its reaction with excess diamine gave the same product with yield, under similar conditions that gave the bisimidazolidine **2** . The reaction is not restricted to the ketone **1**. Ethyl trichloroacetate reacts similarly with excess ethylenediamine under ultrasonic irradiation to give **2** in 60 % yield. Even carbon dioxide, after being converted into solid $^{+}NH_3CH_2CH_2\ NHCO_2^{-}$ by reaction with excess ethylenediamine at 0°C, gave, after 2 months at room temperature, 54 % of **2**.

Neither 2-imidazolidinone **6** nor 2,2'-bis(2-imidazoline) **7** are precursors of **2**. Both compounds were sonicated for 48 h in the presence of excess ethylenediamine without reaction.



In conclusion, reaction of hexachloroacetone with a large excess of a 1,2-diamine gives bisimidazolidines or their derivatives. These conversions are not restricted to ketone **1** but also work with

trichloroacetate esters and even carbon dioxide. Reaction times may be considerably shortened and yields increased by sonication of the reaction mixture.

We are presently interested in extending this puzzling conversion to the preparation of other heterocyclic systems. The mechanism of these reactions is also being investigated in our laboratories.

Experimental:

Melting points were recorded on a Koffler hot-stage apparatus and were not corrected. UV spectra were obtained with a Hewlett-Packard diode array 8452A spectrometer. RMN spectra were recorded on a Brucker AC 200 Mhz instrument, employing tetramethylsilane as internal reference. Mass spectra were obtained with a CG/MS Shimadzu 2000A equipment.

Cis,trans-diaminocyclohexane was purchased from Aldrich. Hexachloroacetone **1** was prepared by a reported procedure.[17]

2,2'-Bismidazolidine (**2**) - To a cooled (0°C) solution of 1,2-ethylenediamine (22.8 g, 0.38 mol) in a 50 mL round-bottomed flask was added dropwise hexachloroacetone (10.1 g, 0.038 mol). The flask was then stoppered and the resulting mixture was sonicated for 12 h, with the bath temperature attaining 50-60°C. The product, which crystallized in the form of needles out of the reaction mixture, was filtered, washed with ethanol and dried to give 3.2 g (60 % yield) of the 2,2'-bisimidazolidine , mp 182-184 °C. Anal. calcd. for $C_6H_{14}N_4$: C, 50.70 ; H, 9.86; N, 39.44. Found: C, 50.63; H, 9.90; N, 39.47. ^{1}H NMR (D_2O): δ 2.63 (4 H, d, J = 9 Hz), 2.77 (4 H, d, J = 9 Hz), 2.90 (2 H, s). ^{13}C NMR (D_2O): δ 45.9 and 74.2 . MS: m/e 44 (38), 58 (59), 71 (31), 83 (29), 99 (100) and 142 (14). UV (EtOH) 215 nm (ε 1050)

2,2'- Bis(4,5-Cyclohexane)-2-imidazolidinene (**3**) - Following the same procedure described for **2**, excess 1,2-diaminocyclohexane (11.4 g, 0.1 mol) and hexachloroacetone **1** (2.65 g,. 0.01 mol) gave, after 16 h sonication, 1.25 g (52 % yield) of compound **3**, mp 330 °C. Anal. calcd. for $C_{14}H_{24}N_4$: C, 67.74; H, 9.68; N, 22.58. Found : C, 67.70; H, 9.30; N, 22.42. ^{1}H NMR ($CDCl_3$): δ 1.35 (8 H, m), 1.80 (4 H, m), 1.95 (4 H, m), 3.05 (4 H, m), 3.15 (4 H, broad singlet). ^{13}C NMR ($CDCl_3$): δ 24.6, 32.2, 58.6 and 148.6. UV (EtOH) 258 nm (ε 2760).

2,2'-Bisbenzimidazole (**4**) - In a similar way, a solution of 1,2-phenylenediamine (10.8 g, 0.1 mol) and **1** (2.65 g, 0.01 mol) in ethyleneglycol (25 mL) was sonicated for 1 h. Product **4** which separated out of the reaction mixture weighed after filtration 1.80 g (82 % yield), mp > 300 °C. Anal. calcd. for $C_{14}H_{10}N_4$: C, 71.79 ; H, 4.27; N, 23.93. Found: C, 71.40; H, 4.40; N, 23.57. ^{1}H NMR (DMSO-d_6): δ 7.3 (4 H, d, J = 6 Hz), 7.6 (2 H, d, J = 6 Hz), 7.8 (2 H, d, J = 6 Hz), 13.7 (2 H, s). ^{13}C NMR (DMSO-d_6) : δ 112.2, 119.3, 122.3, 123.7 , 134.9 , 143.6 and 143.9. UV (EtOH) 323 nm (ε 40000).

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