[1,3,5]Triazino[1,2-*a*]azepines: A New Ring System

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The reaction of 2-pyrrolidino-1-aza-1-cycloheptene with aryl isocyanates leads, *via* 1,4-dipolar cycloaddition, to 1,3-diaryl-10a-pyrrolidinoperhydro[1,3,5]triazino[1,2-*a*]azepine-2,4-diones. The reaction provides a facile route to the novel [1,3,5]triazino[1,2-*a*]azepine ring system.

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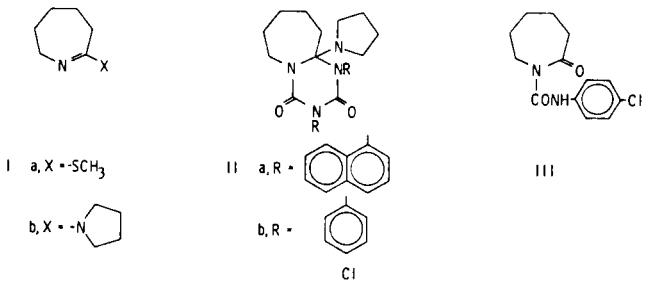
The reaction of open-chain and cyclic *N,N,N'*-trisubstituted amidines with isocyanates is known to lead to 1,3,5-triazine-2,4-diones (1-7). Work on cyclic amidines has, however, been restricted to five- and six-membered rings.

We wish to report that the reaction of 2-pyrrolidino-1-aza-1-cycloheptene (Ib) with aryl isocyanates gives the novel 1,3,5-triazino[1,2-*a*]azepine ring system (II). Thus, the amidine Ib, prepared from the imino thioether Ia, on reaction with 1-naphthyl isocyanate, gave 1,3-bis(1-naphthyl)-10a-pyrrolidinoperhydro[1,3,5]triazino[1,2-*a*]azepine-2,4-dione (IIa) in high yield at room temperature. 4-Chlorophenyl isocyanate reacted similarly, but the isolated yield of product was much lower.



The products gave satisfactory microanalyses and pmr spectra, and showed two strong peaks in the infrared region (1690 and 1650 cm^{-1}) characteristic of carbonyl absorptions in 1,3,5-triazines (4). The assigned structure was confirmed by acetic acid-catalysed hydrolysis of IIb to give 4-chloroacetanilide and 2,3,4,5,6,7-hexahydro-2-oxo-1*H*-azepine-1-(4-chlorocarboxanilide) (III), whose spectroscopic properties were identical to those of a reference sample prepared according to the general procedure of Wiley (8).

This dipolar cycloaddition involving the azepine ring is analogous to the reported conversion of 2-dimethylamino-Δ^1-pyrroline to pyrrolo[1,2-*a*][1,3,5]triazines (4).

EXPERIMENTAL

Melting points were determined using a Buchi capillary melting point apparatus, and are uncorrected. Infrared spectra were run on a Perkin Elmer Model 157 spectrometer using sodium chloride plates. Pmr spectra were recorded at 60 MHz using a Varian A-60 or Perkin Elmer R-12 spectrometer. Mass spectra were determined on an AEI-MS902 instrument, and microanalyses were carried out on a Carlo Erba Elemental Analyser Model 1104.

2-Methylthio-1-aza-1-cycloheptene (Ia).

Iodomethane (114 g., 0.8 mole) was added to a solution of ω-thiocaprolactam (85 g., 0.66 mole) in acetone (800 ml.) and the mixture stirred at room temperature overnight. The precipitate was collected, washed with acetone, and dried to give 132 g. (74%) of Ia as the hydriodide, m.p. 182-184°, lit. 175-177° (9); pmr (DMSO-d_6): δ, 1.6-2.1 (m, 6, CH_2-CH_2-CH_2), 2.9-3.3 (m, 2, CH_2-C=N), 3.1 (s, 3, CH_3S-), 4.0-4.4 (m, 2, CH_2-N=C).

Anal. Calcd. for $C_7H_{14}INS$: C, 31.0; H, 5.17; N, 5.17. Found: C, 31.4; H, 5.2; N, 5.1.

2-Pyrrolidino-1-aza-1-cycloheptene (Ib).

A solution containing Ia (30.4 g., 0.21 mole) (prepared from the hydriodide by treatment with 0.5*N* sodium hydroxide) and pyrrolidine (17.8 g., 0.25 mole) in ethanol (50 ml.) was refluxed for 24 hours, and the evolved methanethiol absorbed in aqueous sodium hydroxide. The solvent and excess pyrrolidine were removed from the reaction mixture under reduced pressure and the residue distilled to give 27.0 g. (79%) of Ib as a colourless liquid b.p. 107-109°/2.5 mm; ir (film): 1610 cm^{-1} (C=N); pmr (deuteriochloroform): δ, 1.3-2.1 (m, 10, $CH_2CH_2CH_2$), 2.4-2.7 (m, 2, CH_2C=N), 3.0-3.7 (m, 6, CH_2N-).

Anal. Calcd. for $C_{10}H_{18}N_2$: C, 72.3; H, 10.8; N, 16.9. Found: C, 72.0; H, 10.8; N, 17.1.

1,3-Bis(1-naphthyl)-10a-pyrrolidinoperhydro[1,3,5]triazino[1,2-*a*]-azepine-2,4-dione (IIa).

1-Naphthyl isocyanate (4.2 g., 0.025 mole) in acetone (10 ml.) was added dropwise, with stirring, to a solution of 2-pyrrolidino-1-aza-1-cycloheptene (Ib) (2.1 g., 0.0125 mole) in acetone (10 ml.). An immediate exotherm was observed, followed by the rapid formation of a white precipitate. Collection of the precipitate after 18 hours gave 5.0 g. (79%) of IIa as a white crystalline solid m.p. 167-169°; ir (nujol): 1690 and 1650 cm^{-1} (C=O); pmr (DMSO-d_6): δ, 1.2-2.1 (m, 12, -CCH_2C-), 2.9-3.5 (m, 6, CH_2N-), 6.5-8.2 (m, 14, ArH); mass spectrum: m/e 504 (M^+).

Anal. Calcd. for $C_{32}H_{32}N_4O_2$: C, 76.2; H, 6.39; N, 11.1. Found: C, 76.1; H, 6.6; N, 10.7.

1,3-Bis(4-chlorophenyl)-10a-pyrrolidinoperhydro[1,3,5]triazino-[1,2-*a*]azepine-2,4-dione (IIb).

A solution of 4-chlorophenyl isocyanate (3.84 g., 0.025 mole) in acetone (10 ml.) was added dropwise, with stirring, to a solution of Ib (2.1 g., 0.0125 mole) in acetone (10 ml.). An immediate exotherm was observed, but the reaction mixture remained homogeneous. After 18 hours at room temperature the reaction mixture was cooled to *ca.* 0°, and the precipitate which formed was separated and dried to give 0.9 g. (15%) of IIb as a white crystalline solid m.p. 158-160°; ir (nujol): 1690 and 1650 cm^{-1} (C=O); pmr (deuteriochloroform): δ, 1.2-2.15 (m, 12, -CCH_2C-), 2.8-3.7 (m, 6, CH_2N-), 7.1-7.6 (m, 8, ArH); mass spectrum: m/e 401 (m-pyrrolidine), 319 (M-[4-chlorophenyl isocyanate], 153 (4-chlorophenyl isocyanate), 166 (Ib).

Anal. Calcd. for $C_{24}H_{26}Cl_2N_4O_2$: C, 60.9; H, 5.54; N, 11.8. Found: C, 60.7; H, 5.7; N, 11.6.

Hydrolysis of 1,3-bis(4-chlorophenyl)-10a-pyrrolidinoperhydro-[1,3,5]triazino[1,2-*a*]azepine-2,4-dione (IIb).

A suspension of IIb (2.0 g., 4.2 mmoles) in a mixture of water (3 ml.) and acetic acid (20 ml.) was heated on a steam bath for 48 hours. The reaction mixture was cooled, diluted with water, and the precipitate obtained washed well with water and dried, to give 0.2 g. (18%) of 2,3,4,5,6,7-hexahydro-2-oxo-1*H*-azepine-1-(4-chlorocarboxanilide) (III) m.p. 107-109°, whose ir and pmr spectra were identical to those of a reference sample.

Extraction of the filtrate with chloroform gave, after drying (magnesium sulfate) and evaporation, 0.37 g. (52%) of 4-chloroacetanilide m.p. 173-175°, lit. 172-173° (10); pmr (deuteriochloroform): δ, 2.1 (s, 3, $CH_3C(O)$-), 7.1-7.8 (m, 4, ArH), 9.7-10.0 (br., 1, NH); mass spectrum: m/e 169 (M^+), 126 (M-$COCH_3$).

2,3,4,5,6,7-Hexahydro-2-oxo-1*H*-azepine-1-(4-chlorocarboxanilide) (III).

A solution of caprolactam (2.26 g., 0.02 mole) and 4-chlorophenyl isocyanate (3.07 g., 0.02 mole) in toluene (50 ml.) was heated at reflux for 24 hours. Evaporation of the solvent under reduced pressure left a white solid, which, on recrystallisation from ethanol, gave 4.8 g. (91%) of III, m.p. 114-116°; ir (nujol): 3100 cm^{-1} (NH), 1700 and 1650 cm^{-1} (C=O); pmr (deuteriochloroform): δ, 1.6-2.1 (m, 6, $CH_2CH_2CH_2$), 2.6-3.0 (m, 2, $CH_2C(O)$-), 3.9-4.3 (m, 2, $CH_2NC(O)$-), 7.2-7.7 (m, 4, ArH), 11.3-11.7 (br., 1, NH).

Anal. Calcd. for $C_{13}H_{15}ClN_2O_2$: C, 58.5; H, 5.63; N, 10.5. Found: C, 58.5; H, 5.6; N, 10.2.

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