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NOVEL SYNTHESIS OF N,N'-BIS(α-ISOCYANATO ALKYL)DIAZENES

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Abstract - The conversion of aliphatic ketazines 1 with cyanic acid into the "criss cross" cycloadducts, the triazolo-triazole-diones 2, followed by oxidative ring opening provides an efficient synthetic route to the title compounds 4.

Dialkyldiazenes (azo alkanes) are known to serve as sources for thermally or photochemically generated carbon radicals and nitrogen. In particular, α,α'-di-substituted dialkyldiazenes have found industrial use as radical chain initiators and cross linking agents in polymerization processes and as foaming agents for resins. Beside the conventional azo-bis(isobutyronitrile) (AIBN) aliphatic diazenes with various α-substituents have aroused some interest: The variation of the α-substituent offers the potential of modifying both the chemical reactivity of the diazenes (e.g. thermostability and thereby the decomposition temperature) and the properties of the decomposition products (e.g. toxicity).

The synthesis of α,α'-diisocyanato azoalkanes 4 has been first reported in a patent[1], and two papers have been concerned with the structure[2] and with some reactions[2,3] of compound 4a. The preparation of the diazenes 4 as described in the literature[1-3] involves the 1,4-addition of chlorine[4,5] to aliphatic ketazines 1 and subsequent displacement of the chlorine substituents by cyanate ion. - In the course of our work related to cycloadditions of protic heterocumulenes (e.g. cyanic acid) to ketohydrazones affording triazolidinones[6] and their conversion into azo-alkylisocyanates[7] a novel and efficient synthesis of N,N'-bis(α-isocyanatoalkyl)-diazenes 4 has been developed (Scheme).

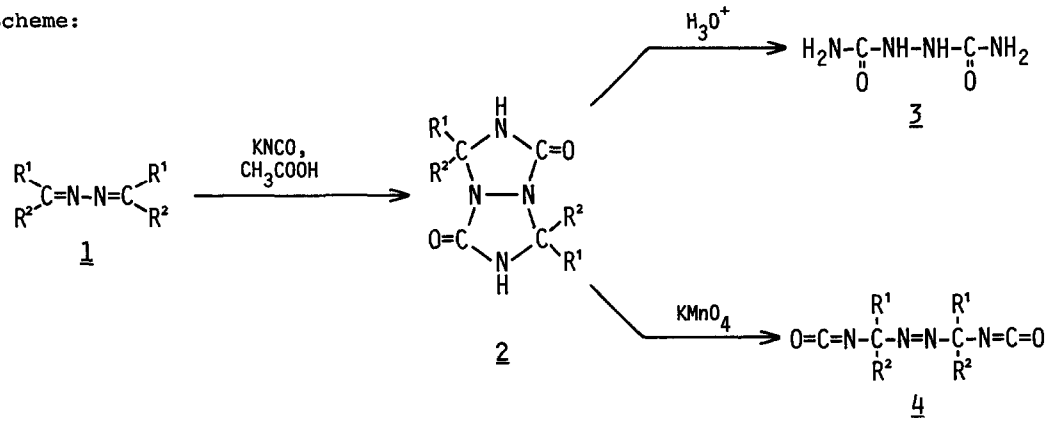
The reaction of azines with thiocyanic acid has been reported to proceed in the manner of a "criss cross" cycloaddition affording triazolo-triazole-dithione derivatives[8,9]. The analogous reaction with cyanic acid has been accomplished with benzaldazine 1 and provides the bicyclic adduct 2 ($R^1 = H$, $R^2 = C_6H_5$)[10]. Similarly, cyanic acid derivatives like phenylisocyanate[8], acylisocyanates[11] and sulfonyl-isocyanates[12,13] react only with aromatic aldazines furnishing the corresponding N,N'-disubstituted triazolo-triazole-diones 2. However, according to the literature[8,11,12] the conversion of ketazines into cycloadducts 2 failed.

Under appropriate reaction conditions the "criss cross" cycloaddition of cyanic acid to azines turned out to be applicable to derivatives of aliphatic ketones as well. Due to their keto aminal functions the cycloadducts 2 are sensitive

toward acid catalyzed hydrolysis causing the formation of 1,2-hydrazinedicarboxamide 3[14]. Thus, by avoiding any excess of acetic acid in the course of the reaction (required for the in situ generation of cyanic acid from potassium cyanate) the hydrolysis of 2 can be retarded.

Like similar triazolidinone derivatives[7] the triazolo-triazol-diones 2 undergo oxidation under concomitant ring opening. Using an aqueous potassium permanganate solution the bicyclic compounds 2 were converted into N,N'-bis(α-isocyanato alkyl)-diazenes 4 in good yields.

Scheme:



1 2 4	a	b	c	d	e
R^1	CH_3	CH_3	CH_2CH_3	CH_3	$(CH_2)_5$
R^2	CH_3	CH_2CH_3	CH_2CH_3	$CH_2CH(CH_3)_2$	

The ketazines 1 were employed as obtained by known procedures[15-18], compounds 1b,d were mixtures of configurational isomers[19]. The "criss cross" cycloaddition of cyanic acid to the ketazines 1 is anticipated to proceed stereospecifically (like related 1,4-additions[20]). Therefore, the adducts 2b,d as well as their oxidation products 4b,d are expected to reflect the stereoisomerism of the starting material 1b,d. In fact, as indicated by ^{1}H-NMR, mixtures of diastereomers 2b,d and 4b,d respectively, were formed, but were not analyzed further.

Remarkably, the isocyanate functions of the diazenes 4 (like that of other geminal azoalkylisocyanates[7]) are not affected by water, thus permitting their preparation to be carried out in aqueous solution; moreover, the oxidation of 2c-e requires the presence of alkali, the products 4c-e being stable under these conditions. The unusual chemical reactivity of N,N'-bis(1-isocyanato-1-methylethyl)-diazene (4a) has been noted[2], in particular the failure to prepare any derivatives of 4a. The result of the investigation about the reaction products of 4a with nucleophiles will be communicated separately.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage microscope (Reichert). Mass spectra were obtained with a Varian MAT 44S mass spectrometer using isobutane for CI-MS. Infrared spectra were recorded on a Beckman AccuLab 4 spectrophotometer. Ultraviolet and Visible spectra were measured on a Gilford 250 instrument. ^{1}H-NMR spectra were run at 60 MHz on a JEOL-PMX-60 spectrometer, the chemical shifts (δ) are reported with respect to the signal of TMS.

4,4,8,8-Tetramethyl-1,3,5,7-tetraazabicyclo[3.3.0]octan-2,6-dione (2a): A solution of acetone azine 1a (22.4 g, 0.2 mol) in acetic acid (28.8 g, 0.48 mol) was added dropwise over a period of 15 min. to a stirred solution of potassium cyanate (38.9 g, 0.48 mol) in water (70 mL) at 0°C. Immediately afterwards the colorless crystals formed were filtered off, washed with water and subsequently with ether. Drying at 30°C/1 Pa afforded the product 2a (32.2 g, 81%) sufficiently pure for further use, m.p. (dec.) 179-181°C (ethanol). Anal. Calcd. for $C_8H_{14}N_4O_2$ (198.22): C 48.47; H 7.12; N 28.26. Found: C 49.44; H 6.71; N 27.94. CI-MS: m/z (%) 199 (100) M+1; 156 (7); 113 (39). IR (KBr): 3170, 3080 (NH); 1715, 1735 sh (C=O). ^{1}H-NMR (DMSO-d_6): δ 7.8 (NH); 1.47 (CH_3). From the filtrate 1,2-hydrazinedicarboxamide 3[14] crystallized after some time.

Compounds 2b-e were prepared accordingly:

2b (76% mixture of diastereomers): CI-MS: m/z (%) 227 (100) M+1; 141 (50). IR (KBr): 3200 3090 (NH), 1710 (C=O). ^{1}H-NMR (DMSO-d_6): δ 7.83 (NH); 1.48 and 1.42 (s,s, CH_3); 2.1-1.4 (m, CH_2); 0.90 (t, CH_3).

2c (66%), m.p. (dec.) 255-260°C. CI-MS: m/z (%) 255 (97) M+1; 169 (100). IR (KBr): 3200, 3090 (NH); 1705 (C=O). ^{1}H-NMR (DMSO-d_6): δ 7.56 (NH); 2.1-1.4 (m, CH_2 diastereotopic); 0.85 (t, CH_3).

2d (49% mixture of diastereomers): CI-MS: m/z (%) 283 (100) M+1; 197 (21). IR (KBr): 3350, 3200, 3095 (NH); 1705 (C=O). ^{1}H-NMR (DMSO-d_6): δ 7.33 (NH); 1.50 and 1.42 (s,s, CH_3); 2.0-1.3 (m, CH_2, CH); 0.93 (d, CH_3).

2e (70%), m.p. (dec.) 206-208°C (methanol). CI-MS: m/z (%) 279 (10) M+1; 193 (100). IR (KBr): 3190, 3080 (NH); 1700, 1715 sh (C=O). ^{1}H-NMR (DMSO-d_6): δ 8.10 (NH); 2.3-1.1 (m, CH_2).

1,2-Bis(1-isocyanato-1-methylethyl)diazene (4a): To a vigorously stirred suspension of finely powdered 2a (9.91 g, 50 mmol) in ether (300 mL) a solution of potassium permanganate (10 g, 63 mmol) in water (300 mL) was added within 5 min. After the addition was complete stirring was continued for 15 min. The reaction mixture was then filtered from manganese dioxide and the two liquid phases were separated. The organic phase was washed until neutral and dried over magnesium sulfate. Evaporation of the solvent afforded the pure crystalline product 4a (8.73 g, 89%; overall yield from 1a: 72%, lit.: 23%[1], 12%[2]), m.p. (sealed tube) 71.5-72.5°C (sublimed at 20°C/1 Pa) (lit.[3] 68.5-70°C). UV (n-hexane): λ_{max} 337 nm (log ε 1.56). Other spectral data correspond to those reported[3].

The same procedure was used to prepare compound 4b (94% mixture of diastereomers): Anal. Calcd. for $C_{10}H_{16}N_4O_2$ (224.26): C 53.55; H 7.19; N 24.98. Found: C 53.25; H 7.28; N 25.09. IR ($CHCl_3$): 2220 (N=C=O). UV (n-hexane): λ_{max} 339 nm (log ε 1.56). ^{1}H-NMR ($CDCl_3$): δ 2.2-1.7 (m, CH_2); 1.53 and 1.50 (s,s, CH_3); 1.1-0.7 (m, CH_3).

Compounds 4c-e were prepared under slightly changed conditions: Ether was replaced by dichloromethane, 2N sodium hydroxide (100 mL) was added before oxidation with potassium permanganate, and the reaction time was extended to 30 min.

4c (77%), oil, purified by column chromatography [silica gel (deactivated with water 10% w/w) and ether/petroleum ether (boiling range 40-60°C)], n_D^{20} 1.4578. Anal. Calcd. for $C_{12}H_{20}N_4O_2$ (252.32): C 57.12; H 7.99; N 22.21. Found: C 57.04; H 8.06; N 22.49. IR ($CHCl_3$): 2220 (N=C=O). UV (n-hexane): λ_{max} 340 nm (log ε 1.58). ^{1}H-NMR ($CDCl_3$): δ 2.2-1.7 (m, CH_2 diastereotopic); 0.85 (t, CH_3).

4d (76% mixture of diastereomers): Anal. Calcd. for $C_{14}H_{24}N_4O_2$ (280.37): C 59.98; H 8.63; N 19.98. Found: C 60.12; H 8.57; N 19.90. IR ($CHCl_3$): 2220 (N=C=O). UV (n-hexane): λ_{max} 334 nm (log ε 1.58). ^{1}H-NMR ($CDCl_3$): δ 2.0-1.4 (m, CH, CH_2);

1.52 and 1.48 (s,s, CH_3); 1.1-0.8 (m, CH_3).

4e (82%), m.p. 127-128°C (n-hexane) (lit.[1] m.p. 38-40°C). Anal. Calcd. for C 60.85; H 7.30; N 20.28. Found: C 60.97; H 7.31; N 20.52. IR ($CHCl_3$): 2230 (N=C=O). UV (n-hexane): λ_{max} 341 nm (log ε 1.54). ^{1}H-NMR ($CDCl_3$): δ 2.2-1.3 (m, CH_2).

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