N-Isocyanoimines. Preparation and Characterisation

PALLE JAKOBSEN

Medicinsk-Kemisk Institut, University of Copenhagen, Rådmandsgade 71, DK-2200 Copenhagen, Denmark

Aromatic N-isocyanoimines have been reported as intermediates in the synthesis of formhydrazonoesters. 1-3 In a few cases the N-isocyanoimines have been isolated, but comments on yield and reactivity are sparse. Aliphatic Nisocyanoimines have not been described.

This paper reports the synthesis of aliphatic N-isocyanoimines. The hitherto unknown compounds were characterized by their α-addition products from reactions with piperidine and

with ethanethiol.

N-Isocyanoimines (1) were synthesized by two different methods: dehydration of N'alkylidene formohydrazides by means of POCl₃ and triethylamine in CH2Cl2-solution (method A), and reaction between hydrazones and CHCl₃ in NaOH-solution, with use of benzyltriethylammonium chloride as phase transfer catalyst (Method B).

$$RR'C = N - NHCHO + (A)$$

$$POCl_3 + Et_3N$$

$$RR'C = N - NH_2 + (B)$$

$$CHCl_3 + OH$$

Scheme 1. (Compound, R, R'): (a, Me, Me), (b, Et, Et), (c, Pri, Pri), (d, Me, Ph), (e, Ph,

Attempts to purify N-isocyanoimines by distillation in vacuo resulted in products contaminated with triethylamine. The distillate was collected in an acetone/dry ice trap. The compounds (1) decomposed rapidly at room temperature, whereas they were stable for some days in solution. All formed N-isocyanoimines showed strong, sharp IR absorptions around 2100 cm⁻¹, and had the characteristic isocyanide smell. The use of pyridine in the dehydrating step instead of triethylamine gave no N-isocyanoimine.

For further characterisation of 1a-e the CH₂Cl₂-phase from the reaction mixture was used. The reaction with piperidine, catalysed by CuCl, was found to be convenient for trapping the N-isocyanoimines, as it took about 2 h at room temperature, giving formamidra-zones in overall yields from 11 to 38 %. The analogous reaction for t-butyl isocyanide proceeds in 10 h at room temperature.

$$RR'C = N - N \equiv C + HN(CH_2)_5 \rightarrow 1a - d$$

$$RR'C = N - N = CH - N(CH_2)_5$$

 $2a - d$

Scheme 2.

N-Isocyano-3-pentanimine (1b) was used for investigations of the reactivity in other α -addition reactions. The reaction with aniline, which is known to give good yields of formamidine on boiling with normal isocyanide 4 gave no α-addition product. This is probably due to the elevated temperature which causes rapid decomposition of the N-isocyanoimine. Reaction with ethanethiol 5 catalysed by CuCl resulted in formation of the a-addition product (3b) in low yield. No isothiocyanate was de-

$$(\text{Et})_2\text{C} = \text{N} - \text{N} \Longrightarrow \text{C} + \text{EtSH} \Rightarrow \\ Ib \\ (\text{Et})_2\text{C} = \text{N} - \text{N} = \text{CH} - \text{SEt} \\ 3b$$

Scheme 3.

Experimental. Microanalyses were carried out in the Microanalysis Department of Chemical Laboratory II, The H. C. Ørsted Institute. ¹H NMR spectra were obtained on a JEOL JNM MH 60/II instrument. IR spectra were recorded on a Perkin-Elmer model 225 grating spectrograph or model 157 NaCl spectrophotometer. Mass spectra were taken on an AEI-902 instrument operating at 70 eV. Melting points are uncorrected.

are uncorrected.

N'-(3-Pentylidene) formohydrazide and N'(1-phenylethylidene) formohydrazide were prepared as described for N'-(2-propylidene) formohydrazide. N'-(3-Pentylidene) formohydrazide.
Yield 89 %, m.p. 73 – 74 °C. Anal. C₆H₁₂N₂O:
C, H, N. N'-(1-Phenylethylidene) formohydrazide. Yield 60 %, m.p. 157 – 158 °C. Anal.
C₉H₁₀N₂O: C, H, N. N'-[2,4-Dimethyl-(3-pentylidene)] formohydrazide was prepared by reflux
ing 2,4-dimethyl-3-pentanone hydrazone 8 (0.19
mol) in ethyl formate (60 ml) for 6 h. After mol) in ethyl formate (60 ml) for 6 h. After subsequent stirring at room temperature for 10 days, the mixture was evaporated to dryness and the resulting product was recrystallized from ethanol. M.p. 113 °C, yield 55 %. Anal. C₈H₁₆N₂: C, H, N. N-Isocyano-2-propanimine (1a). N'-(2-Pro-

pylidene) formohydrazide (0.1 mol) and triethylamine (60 ml) were dissolved in CH₂Cl₂ (50 ml). POCl₃ (9.3 g) was added dropwise under cooling with ice. The temperature was 42-45 °C. The resulting mixture was stirred at room temperature for 3 h. Saturated Na₂CO₃solution (70 ml) was added under cooling, the CH2Cl2-layer separated, dried over K2CO3,

and used for further reactions.

An attempt to isolate the N-isocyanoimine by distillation of a CH2Cl2-layer evaporated previously to ca. 30 ml gave 1.5 g of a liquid, b.p. 15-20 °C/1 mmHg. The distillate was cooled in dry ice/acetone. IR absorption (CH₂Cl₂): NC 2100 cm⁻¹. On heating to room temperature the liquid decomposed rapidly, with a colour change from light yellow to dark brown. In CH₂Cl₂ or CCl₄-solution, the decomposition proceeded slower; there was still an NC IR absorption in CCl₄-solution after 7 h at room temperature. ¹H NMR spectra showed that the distillate was a mixture of triethylamine and N-isocyanoimine.

N¹-Pentamethylene-N³-(2-propylidene) forma-mide hydrazone (2a). The CH₂Cl₂-phase described above was mixed with piperidine (0.1 mol) and CuCl (100 mg). After stirring for 2 h at room temperature the mixture was filtered and the filtrate distilled in vacuo. B.p. 63-64 °C/0.1 mmHg, yield 22 %. Anal. C₃H₁₇N₃: C, H, N. ¹H NMR (CDCl₃): 7.86 (1 H, s), 3.1 – 3.5 (4 H, m), 2.02 (3 H, s), 1.95 (3 H, s), 1.33 – 1.75 (6 H, m). MS m/e (% of base peak): $167(57)M^+$, 152(5), 111(11), 84(74), 83(100), 58(13), 56(24), 55(40), 42(35), 41(30).

N-Isocyano-3-pentanimine (1b) was prepared in CH₂Cl₂/Et₂N-solution as described for (1a). Evaporation in vacuo to a volume of ca. 30 ml followed by distillation in vacuo, gave 2.4 g of a mixture of N-isocyanoimine (1b) and triethylamine b.p. 14-18 °C/0.5 mmHg. IR absorption (CH₃Cl₂): NC 2100 cm⁻¹.

N-Pentamethylene-N³-(3-pentylidene) forma-

mide hydrazone (2b) was prepared analogous to 2a. B.p. 75 °C/0.05 mmHg, yield 38 %. Anal. C₁₁H₂₁N₃: C, H, N. ¹H NMR (CDCl₃): δ 7.82 (1 H, s), 3.2 – 3.5 (4 H, m), 2.51 (2 H, q), 2.25 (2 H, q), 1.5 – 1.7 (6 H, m) 1.11 (3 H, t), 1.07 (3 H, t). MS m/e (% of base peak): 196(14), 195(64)M+, 166(13), 111(53), 86(27), 84(100),

83(91), 69(11), 56(34), 55(34), 42(10), 41(27).

N³-(2,4-Dimethyl-3-pentylidene) N¹-pentamethyleneformamide hydrazone (2c) was prepared from N-isocyano-2,4-dimethyl-3-pentanimine (Method A) as described for 2a, yield 36%, b.p. 78-80 °C/0.02 mmHg. Anal. $C_{13}H_{36}N_{3}$: C, H, N. ¹H NMR (CDCl₃): δ 7.76 (1 H, s), 3.51 (1 H, sep.), 3.48 – 3.19 (4 H, m), 2.58 (1 H, sep.), 1.55-1.65 (6 H, m), 1.17 (6 H, s), 1.06 (6 H, s). MS m/e (% of base peak): 224(11), 223(50)M+, 180(16), 139(22), 114(11), 113(11), 112(15), 111(27), 85(9), 84(100), 83(42), 70(13), 69(16), 56(13), 55(31), 42(23), 42(27), 41(37).

N-Isocyano-2, 4-dimethyl-3-pentanimine (1c). (Method B). A mixture of diisopropyl ketone hydrazone ⁸ (0.1 mol), chloroform (0.1 mol), aqueous NaOH-solution (50 ml, 50 %), benzyltriethylammonium chloride (0.5 g) and CH₂Cl₂ (50 ml) was stirred at room temperature for 2.5 h (slightly exothermic reaction). The CH₂Cl₂-layer was separated and dried over K₂CO₃. IR (CH₂Cl₂): NC 2095 cm⁻¹. The Nisocyanoimine could be stored for a few days in solution, with slight decomposition. Subsequent treatment with piperidine and CuCl as described for 1a gave 11 % of 2c.

N-Isocyano-1-phenylethanimine (1d). Preparation by Method B gave mainly acetophenone azine. Method A gave the *N*-isocyanoimine in solution, IR (CH₂Cl₂): NC 2090 cm⁻¹.

N¹-Pentamethylene-N³-(1-phenylethylidene) N¹-Pentamethylene-N³-(1-phenylethyliaene) formamide hydrazone (2d). Prepared analogous to 2a. B.p. 138-140 °C/0.05 mmHg, m.p. 43 °C (EtOH), yield 30 %. Anal. $C_{14}H_{19}N_3$: C, H, N. ¹H NMR (CDCl₃): δ 8.05 (1 H, s), 7.2-7.8 (5 H, m), 3.2-3.6 (4 H, m), 2.42 (3 H, s), 1.5-1.7 (6 H, m). MS m/e (% of base peak): (azine contaminated) 230(15), 229(70)M⁺, 217(62), 145(15), 120(85), 119(15), 118(17), 111(23), 110(13), 104(32), 103(36), 99(21), 97(25), 85(10), 84(77), 83(100), 77(60), 72(51), 111(23), 71(32), 58(13), 57(13), 56(47), 55(38), 51(27), 50(12), 44(40), 43(15), 42(38), 41(34), 40(9).

N-Isocyanodiphenylmethanimine (1e). Benzophenonehydrazone (0.1 mol), CHCl₃ (0.1 mol), NaOH-solution (50 ml, 50 %) and benzyltriethylammonium chloride (0.5 g) were stirred in 50 ml CH₂Cl₂ for 5 days at room temperature. The CH₂Cl₂ layer was separated and dried over K₂CO₃. IR (CH₂Cl₂): NC 2060 cm⁻¹. After treatment with piperidine no formamide

hydrazone was isolated.

S-Ethyl-N-(3-pentylidene) thioformhydrazonate (3b). N-Isocyano-3-pentanimine in CH2Cl2/ Et, N-solution, ethanethiol (0.5 mol) and CuCl (0.5 mmol) were stirred at room temperature for 1 h. The solvent was evaporated and the residue distilled in vacuo, b.p. 46 °C/0.1 mmHg, yield 19 %. ¹H NMR (CDCl₂): δ 8.25 and 7.65 (1 H, singlets, intensity 1/3), 3.1-2.1 (6 H, 3 quartets), 1.5-0.8 (9 H, 3 triplets). MS m/e (% of base peak): $172(32)M^+$, 143(14), 139(13), 111(25), 88(42), 86(21), 84(10), 61(25), 60(13), 56(100), 55(10), 54(19), 45(11), 41(17).

- 1. Hagedorn, I. Angew. Chem. 74 (1962) 499.
- 2. Hagedorn, I. Angew. Chem. 75 (1963) 305.
- 3. Hagedorn, I. Belg. Pat. 630516 (1963); Chem.
- Abstr. 61 (1964) 611.
 4. Saegusa, T., Ito, Y., Kobayashi, S., Hirota, K. and Yoshioka, H. Tetrahedron Lett. 49 (1966) 6121.
- Saegusa, T., Kobayashi, S., Hirota, K., Okumura, Y. and Ito, Y. Bull. Chem. Soc. Jpn. 41 (1968) 1638.
- 6. Spialter, L., O'Brien, D. H., Unterheimer, G. L. and Rush, W. A. J. Org. Chem. 30 (1965) 3278.
- 7. Yandowskii, V. N. and Zamorina, I. A. Zh.
- Org. Khim. 12 (1976) 457.
 8. Anthoni, U. and Berg, C. Acta Chem. Scand. 23 (1969) 3602.

Received June 15, 1976.