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Note

Synthetic potentiality of α-chloronitrone in aldehyde synthesis: A new approach

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N-Phenyl-*N*-cyclohexyl-α-chloronitrones have been synthesized and a new method of synthesis of aldehyde has been discovered involving SN^i and SN^2 reactions with benzyl chloride.

Keywords: *N*-Phenyl-*N*-cyclohexyl-α-chloronitrone, SN^2 reaction, aldehyde synthesis

The synthesis of N-phenyl-*N*-cyclohexyl-α-chloronitrones[1] **1a,b** and their 1,3-dipolar cycloaddition reaction with different dipolarophiles have been already established. Existing reports[2-7] already describe the general method of the synthesis of the said nitrones and the cycloaddition reaction to form isoxazolidines. In the light of Eschenmoser's chloronitrone[8] and considering the synthetic potentiality of *N*-phenyl-*N*-cyclohexyl-α-chloronitrones[1], SN^2 reaction of the nitrones with benzyl chloride have been studied. SN^2 reaction of *N*-cyclohexyl-α-amino nitrone with benzyl chloride and isopropyl bromide has been already reported[9]. The present paper reports a new method of synthesis for aldehydes using *N*-phenyl-*N*-cyclohexyl-α-chloronitrones[1]. This is completely a new approach of aldehyde synthesis using nitrone as a reactive intermediate. Both the nitrones **1a,b** are synthesized from a mixture of chlorohydrin and its tautomer with *N*-phenyl-*N*-cyclohexyl hydroxylamines respectively with constant stirring for 24 hr with magnetic stirrer under N_2 atmosphere at RT where ethanol and dry ether are used as solvents. Chlorohydrin and its tautomer are obtained when 2,3-dihydro-4*H*-pyran is subjected to chlorohydrination with HOCl[10]. *N*-Phenyl-α-chloronitrone is a yellowish white crystalline solid, m.p. 44°C, while *N*-cyclohexyl-α-chloronitrone is a white crystalline solid, m.p. 58°C. Both the nitrones are highly unstable and hence they are used immediately after their formation for the SN^2 reaction with benzyl chloride (*in situ* reaction).

The most remarkable feature of both the nitrones **1a,b** is that they undergo SN^2 reaction with benzyl chloride leading to the formation of benzaldehyde, a significant reaction in nitrone chemistry which proceeds through SN^i reaction initially and forms transient nitrones **2a,b**. A new mechanistic pathway has been suggested for the synthesis of aldehyde (**Scheme I**).

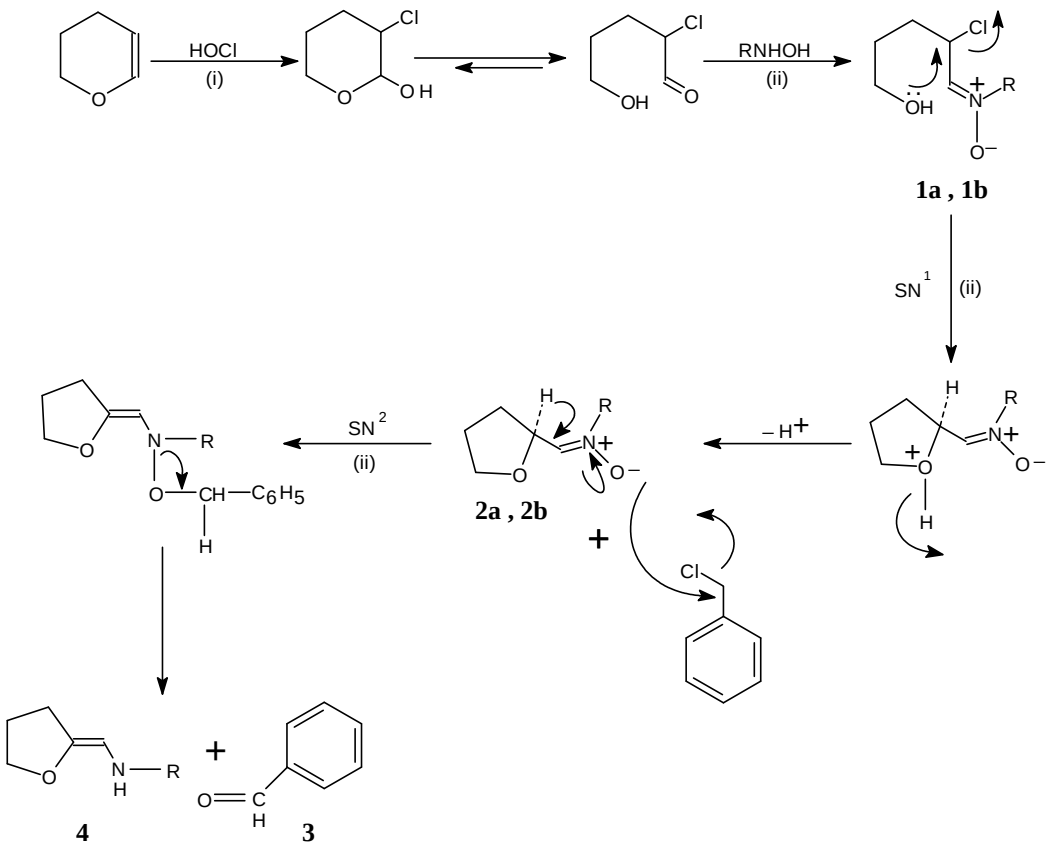
The lone pair of electrons of the OH group of the nitrones **1a,b** play the most significant role in SN^i mechanism for the formation of transient nitrones **2a,b** which reacts very quickly with benzyl chloride and results in the formation of benzaldehyde with a very good yield (72% and 63% respectively) along with furan derivative.

Experimental Section

Hand drawn silica gel (E. Merck) plates of 0.5-0.7 mm thickness are used for TLC. Silica gel (LOBA, 60-200 mesh) is used for column chromatography. Melting point is determined in open capillary tube. IR spectra are recorded as film or in solution by Perkin-Elmer 881 machine. ^1H and ^{13}C NMR spectra are recorded by Bruker WM (400 MHz, FT NMR) and 79.739 MHz spectrometers respectively. Mass spectra are recorded by Jeol D-300 (CI) spectrometers. Chemical analysis are carried out on Carlo-Erba EA 1108 elemental analyzer.

Preparation of nitrones 1a,b and benzaldehyde

N-Phenylhydroxylamine[1] (2.20 mmole) is added to a solution of chlorohydrine (1 equivalent) in dry distilled ethanol (100 mL) and is kept at RT for 24 hr with constant stirring with a magnetic stirrer under N_2 atmosphere. The formation of nitrone is monitored by TLC having R_f=0.36 (silica gel, ethyl acetate:benzene = 1:10). Benzyl chloride (1 equivalent) is added at this stage and the reaction mixture is kept for further 8 hr. Similarly *N*-cyclohexyl hydroxyl amine[11] (2.17 mmol) is added to a solution of chlorohydrine (1 equivalent) in dry ether (150 mL) and anhydrous $MgSO_4$ and is kept at RT for 24 hr with constant stirring with a magnetic stirrer under N_2 atmosphere. The formation of nitrone is monitored by TLC having R_f = 0.28 (silica gel, ethyl acetate:benzene = 1:10). Benzyl chloride (1 equivalent) is added at this stage



1a, **2a**: R=C_6H_5; (i) Dry ether; (ii) Dry distilled ethanol
1b, **2b**; R=C_6H_{11}; (ii) Dry ether

Scheme I

and the reaction mixture is kept for further 10 hr. During this process both the transient nitrones **2a,b** react very quickly with benzyl chloride and develop an intermediate compound which has a labile N-O bond and is easily cleaved[12] into benzaldehyde and furan derivatives. Two distinct spots are identified in TLC in both the reactions. For nitrone **1a** with benzyl chloride reaction, the R_f values are 0.40 and 0.56 respectively while for nitrone **1b** with benzyl chloride reaction, the R_f values are 0.44 and 0.60 respectively. The solvent is evaporated off in both the cases using vacuum pump and the products are distinguished by column chromatography (20 g silica gel column) using benzene-pet ether (60°-80°C) as eluent. Benzaldehyde is obtained as colourless liquid using pet ether:benzene = 60:40 ratio in case of nitrone **1a** and pet ether:benzene = 80:20 ratio for nitrone **1b** while furan derivatives are obtained as yellow gummy liquids using benzene as eluent in both the cases. The structure of the nitrones **1a,b**, benzaldehyde and furan derivatives are confirmed by ^1H and ^{13}C NMR, MS and IR spectra respectively.

Considering the spectral data of compound **3** in both the cases, the formation of benzaldehyde is confirmed. The sharp singlet signals at δ 9.76, 9.80 and δ 198.6, 198 in the NMR spectrum agrees well with the structure of benzaldehyde. The molecular ion peak at 106 and the base peak at 105 are also in support of benzaldehyde.

Spectral data

Nitrone **1a**: IR ($CHCl_3$): 3600-3530 (br), 1620 (s), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.55-7.44 (m, 5H, C_6H_5), 7.10-6.88 (d, 1H, $CH=N^+$), 5.40-5.30 (br, 1H, CH_2OH, exchanged in D_2O), 4.66-4.52 (q, 1H, CHCl), 3.05-2.00 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 143 ($CH=N^+$), 132, 130, 128, 126, 125, 122 (6 aromatic carbons), 96.5 (CHCl), 45, 41, 37 (3 CH_2 carbons). Anal. Found: C, 57.30; H, 9.55; N, 6.10. $C_{11}H_{14}ClO_2N$ requires C, 57.42; H, 9.62; N, 6.22%.

Nitrone **1b**: IR ($CHCl_3$): 3500-3450 (br), 1680 (s), 1610 (m), 1155 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.05-6.90 (d, 1H, $CH=N^+$), 5.15-5.05 (br, 1H, CH_2OH, exchanged in D_2O), 4.30-4.15 (q, 1H, CHCl), 3.70-3.50 (m, 1H, N-CH proton), 2.60-0.5 (m, 16H); ^{13}C NMR ($CDCl_3$): δ 142.6 ($CH=N^+$), 95 (CHCl), 63.2 (CH_2OH), 53 (N-CH), 50-10 (7 signals, cyclohexyl and other CH_2 carbons). Anal. Found: C, 56.50; H, 8.52; N, 5.92. $C_{11}H_{20}ClO_2N$ requires C, 56.53; H, 8.56; N, 5.99%.

Compound **3** (Obtained from the reaction between **1a** and benzyl chloride): IR ($CHCl_3$): 1695 (s), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.76 (s, 1H, CHO), 7.50-7.40 (m, 5H,C_6H_5); ^{13}C NMR ($CDCl_3$): δ 198.6 (CHO), 137, 135, 134, 130, 126, 123 (6 aromatic carbons); MS: *m/z* 106 (M^+), 105 (B.P), 77, 51, 28.

Compound **3** (Obtained from the reaction between nitrone **1b** and benzyl chloride): IR ($CHCl_3$): 1700 (s), 780(s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.8 (s, 1H, CHO), 7.60-7.44 (m, 5H, C_6H_5); ^{13}C NMR ($CDCl_3$): δ 198 (CHO), 136-120 (6 signals, 6 aromatic carbons); MS: *m/z* 106 (M^+), 105 (B.P), 77, 51, 28.

Compound **4** (Obtained from the reaction between nitrone **1a** and benzyl chloride): IR ($CHCl_3$): 3050 (m), 2960 (s), 1650 (s), 1470 (m), 770 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.60-7.48 (m, 5H, C_6H_5 protons), 4.80 (s, 1H, C=CH), 2.10-1.72 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 138, 136, 134, 130, 128, 126 (6 aromatic carbons), 112, 110 (double bonded carbons), 42, 37, 29 (3 CH_2 carbons); MS: *m/z* 175 (M^+), 98, 92, 83, 77.

Compound **4** (Obtained from the reaction between nitrone **1b** and benzyl chloride): IR ($CHCl_3$): 3060-3020 (br), 2980 (m), 1650(s), 1486 (m), 1245 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.88 (s, 1H, C=CH), 3.82-3.70 (m, 1H, N-CH proton), 2.86-1.10 (m, 16H); ^{13}C NMR ($CDCl_3$): δ 139, 112 (2 signals, double bonded carbons), 70-16 (8 signals, cyclohexyl and furan ring carbons); MS: *m/z* 181 (M^+), 97, 84, 83.

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