Synthesis of Some 2-Aminonitroethanes *via* Tin(II)chloride Mediated Addition Reaction of Bromonitromethane to Imines

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In the presence of tin(II)chloride, bromonitromethane reacts with imines derived from aromatic aldehydes and ammonia to yield 2-amino-2-aromatic substituted nitroethane derivatives *via* an addition reaction in good yields.

Key words: Bromonitromethane, Imines, Benzaldimines

Introduction

In chemical synthesis, bromonitromethane was reported to behave as a versatile electrophile, for example in the synthesis of nitrothiophenes and related compounds [1]. It is a C-1 building block with the advantage of bearing a nitro group [2]. A potential conversion of the nitro group into an amino group *via* reduction and the ease of replacement of the nitro group by a hydrogen atom (denitration) using tributyltin hydride makes bromonitromethane a useful synthon.

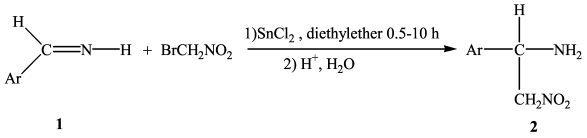
Imines (azomethines or Schiff bases) react with electrophiles, HCl for example, under anhydrous conditions to form iminium salts [3]. They were also reported to allow 1,2-addition across the carbon-nitrogen double bond; for example nitrosyl chloride (NOCl), at −30 °C adds to imines to give *N*-nitrosoamines with a chlorine atom bonded to the carbon atom of the former imine carbon atom [4]. Alkylation of *N*-alkyl-aldimines and -ketimines occurs at the *N*-atom to give the corresponding iminium salts [5]. In general, processes of this type are subject to steric hindrance and electronic activation so that imines having bulky groups or *N*-aryl substituents *N*-alkylate only with difficulty and require the use of more powerful reagents. Nucleophilic reagents attack the imine function at the carbon atom this was in fact found to be the case [6].

Imines lacking hydrogen atoms α- to the carbon-nitrogen double bond react with Grignard and organolithium reagents analogous to carbonyl compounds to give adducts which on hydrolytic work up afford secondary amines in good to excellent yield [7]. The addition of hydrogen cyanide to imines occurs readily and provides a viable route to α-aminonitriles, which in turn can be used as precursors for synthesis of α-amino acids [8].

Bromonitromethane was found to form β-nitroalcohols *via* a tin(II)chloride mediated addition reaction to aliphatic aldehydes [9]. Here the polarity of bromonitromethane is reversed from an electrophile to a nucleophile. Trichloronitromethane reacts with acyl chlorides in the presence of tin(II) chloride to produce dichloronitroketones *via* a substitution reaction [10]. In this work the results of the reaction of bromonitromethane with imines derived from aromatic aldehydes and ammonia, in the presence of tin(II)chloride using diethyl ether as solvent are reported.

Results and Discussion

Primary α-nitroamines **2** were obtained from benzaldimines **1** and bromonitromethane in the presence of a stoichiometric amount of $SnCl_2$ (Scheme 1, Table 1).



1 **2**

Scheme 1.

Tin(II)chloride changes the character of bromonitromethane from a powerful electrophile to a nucleophile leading to the formation of a carbon-carbon bond between the CH_2NO_2 unit and the imine function.

The ^{1}H NMR spectrum of compound **2d** shows a broad signal at $\delta = 3.18$ which could be quenched

Table 1. Yields of amines **2** from the reaction of imines **1** and bromonitromethane.

2	Ar	Yield [%]
a	C_6H_5	83
b	4-Nitro-C_6H_4	90
c	3-Nitro-C_6H_4	87
d	4-Methyl-C_6H_4	82
e	4-Ethyl-C_6H_4	80
f	2,4-Dimethyl-C_6H_4	82
g	2-Methyl-C_6H_4	77
h	4-Methoxy-C_6H_4	76

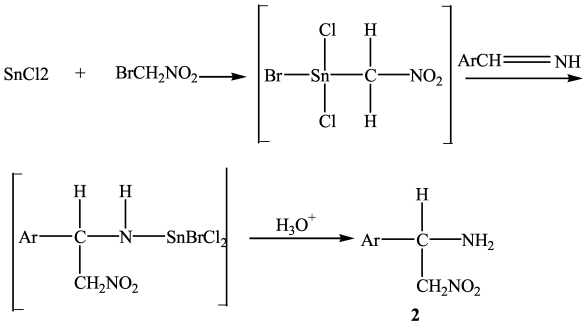
with deuterium oxide, for the NH_2 proton, a multiplet at $\delta = 4.55$ (CH_2NO_2) and a multiplet at $\delta = 5.35$ (benzylic CH). The ^{13}C NMR spectrum showed characteristic signals at $\delta = 70.1$ (benzylic carbon) and 81.5 ppm (CH_2NO_2). The compound showed a strong IR absorption at 1554 cm^{-1} for the NO_2 group. All other prepared products gave ^{1}H NMR, ^{13}C NMR and IR signals consistent with the assigned structures. The electron impact mass spectrum of compound **2d** at 70 eV showed the M^+ peak at $m/e = 180$ (4%), the [M^+-NO_2] peak at 134 (65%), and a very intense peak at 119 (98%) due to [M^+-CH_3NO_2]; the base peak at 91 is possibly due to the a tropylium ion $C_7H_7^+$.

When the reactions were performed in tetrahydrofuran, dimethyl sulfoxide, or acetonitrile, no dramatic increase in the yields was noticed. The yields were enhanced when the amount of tin(II) chloride was increased. As an example, the yield of **2d** was increased from 82% to 87% when the mole ratio was changed from 1:1:1 to 1:1.2:1 (imine : tin(II) chloride : $BrCH_2NO_2$).

Conclusion

As can be seen from the results, bromonitromethane can be considered a valuable C-1 unit in C-C bond formation reactions. Functionalities present in the products may be suitable for a wide range of other chemical manipulations. The CH_2NO_2 unit, for example, can be transformed into a carbonyl group by the Nef reaction [11], and then to carboxylic acid, making products **2** precursors to some α-amino acids. High yields, relatively short reaction time, low cost and easy handling are additional advantages of this reaction. Imines prepared from aromatic aldehydes and aniline derivatives and aliphatic amines gave similar reaction products and the results will be sent to publication later on.

The mechanism of this reaction remains uncertain, however, a proposed mechanism as shown in Scheme 2 is suggested.



Scheme 2.

Experimental Section

All reagents were of commercial grade, and reagent quality solvents were used without further purification. IR spectra were determined on a Mattson 5000 spectrometer. NMR spectra were determined on Bruker AC 200 MHz instrument. In all cases, samples were dissolved in $CDCl_3$ using TMS as internal standard. The elemental analysis were performed at the Middle East Technical University-Analyses Center.

Bromonitromethane was prepared according to the following improved procedure [12]: A mixture of water (500 ml), ice (200 g), NaOH (20 g, 0.5 mol) and nitromethane (36.6 g, 0.6 mol) was vigorously stirred using a mechanical stirrer for 30 min during which the temperature was kept around 0 °C. Bromine (60 g, 0.4 mol) was added to the solution at once with continuous stirring. After 4 h the solution was steam distilled. The product was isolated, dried over anhydrous $MgSO_4$ and fractionally distilled. Bromonitromethane was collected at 134 – 136 °C; yield: 30 g (56%). – ^{1}H NMR: $\delta = 5.45$ (s, CH_2). IR (neat): $\nu = 1565$, 1370, 1260 cm^{-1}.

Imines were prepared from aromatic aldehydes and ammonia according to the literature general procedure [13]:

*General procedure for the synthesis of products (***2a** – **h***)*

A mixture of $SnCl_2$ (1.0 g, 5.3 mmol), CH_3BrNO_2 (0.7 g, 5 mmol) and Na-dried diethyl ether (50 ml) was stirred in a 100 ml flask. To the flask another mixture of the imine (5 mmol) in dry ether (10 ml) was added. The mixture was left stirring for 5 h during which the reaction was monitored by TLC using an ethyl acetate/hexane mixture (1:5) as eluent. The mixture was then diluted with ether (50 ml), washed successively with (3×20 ml) portions of 0.1 M aqueous HCl solution, saturated aqueous $NaHCO_3$ (30 ml) solution and brine (30 ml), and dried over anhydrous $MgSO_4$. The crude product was purified by column chromatography (silica gel, ethyl acetate/hexane mixture (1:4) as eluent). Solid products were purified by recrystallization from saturated hot ethanol solution.

2-Amino-2-phenyl-1-nitroethane **(2a)**: Oil. IR (film): ν = 3429 (NH_2), 1554 (NO_2), 1397, 1066, 765, 700 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): δ = 3.1 (broad, 2H, NH_2), 4.6 (m, 2H, CH_2NO_2), 5.45 (m, 1H, C_6H_5CH), 7.4 (m, 5H, C_6H_5). – $^{13}C\{H\}$ NMR (200 MHz, $CDCl_3$): δ = 71.2 (C_6H_5CH), 81.5 (CH_2NO_2), 126.4, 128.2, 129.2, 138.0 (C_6H_5). – $C_8H_{10}N_2O_2$ (166.18): calcd. C 57.82, H 6.07, N 16.86; found C 57.79, H 6.68, N 16.92.

2-Amino-2-(4-nitrophenyl)-1-nitroethane **(2b)**: M. p. 54 – 56 °C. IR (KBr): ν = 3421 (NH_2), 1554, 1536 (NO_2), 1350, 1085, 856 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): δ = 3.2 (broad, 2H, NH_2), 4.55 (m, 2H, CH_2NO_2), 5.6 (m, 1H, C_6H_4CH), 7.2, 8.3 (2 d, 4H, C_6H_4). – $^{13}C\{H\}$ NMR (200 MHz, $CDCl_3$): δ = 70.0 (C_6H_4CH), 80.5 (CH_2NO_2), 124.1, 127.2, 145.0, 149.3 (C_6H_4). – $C_8H_9N_3O_4$ (211.18): calcd. C 45.50, H 4.30, N 19.90; found C 45.56, H 4.32, N 19.94. – MS (EI, 70 eV): *m/z* (%) = 211 (4) [M^+], 194 (5), 179 (2), 165 (78), 150 (45), 120 (12), 105 (24), 91 (67), 65 (27), 28 (89), 18 (100).

2-Amino-2-(3-nitrophenyl)-1-nitroethane **(2c):** M. p. 69 – 72 °C. IR (KBr): ν = 3420 (NH_2), 2926, 1556, 1540 (NO_2), 1354, 1072, 736 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): δ = 3.1 (broad, 2H, NH_2), 4.6 (m, 2H, CH_2NO_2), 5.6 (m, 1H, C_6H_4CH), 7.6 – 8.4 (m, 4H, C_6H_4). – $^{13}C\{H\}$ NMR (200 MHz, $CDCl_3$): δ = 70.2 (C_6H_4CH), 80.5 (CH_2NO_2), 121.2, 124.0, 130.2, 1324, 140.1, 148.7 (C_6H_4). – $C_8H_9N_3O_4$ (211.18): calcd. C 45.50, H 4.30, N 19.90; found C 45.43, H 4.43, N 19.95. – MS (EI, 70 eV): *m/z* (%) = 211 (3) [M^+] 179 (22), 165 (4), 151 (28), 133 (42), 105 (45), 55 (84), 29 (100), 18 (42).

2-Amino-2-(4-methylphenyl)-1-nitroethane (**2d**): M. p. 47 – 49 °C. IR (KBr): ν = 3477 (NH_2), 2924, 1554 (NO_2), 1379, 1080, 819 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): δ = 2.35 (s, 3H, Me), 3.18 (broad, 2H, NH_2), 4.55 (m, 2H, CH_2NO_2), 5.35 (m, 1H, C_6H_4CH), 7.15, 7.3 (dd, 4H, C_6H_4). – $^{13}C\{H\}$ NMR (200 MHz, $CDCl_3$): δ = 21.1 (Me), 70.2 (C_6H_4CH), 81.5 (CH_2NO_2), 126.1, 130.5, 135.0,138.5 (C_6H_4). – $C_9H_{12}N_2O_2$ (180.39): calcd. C 59.93, H 6.71, N 15.63; found C 59.84, H 6.66, N 15.70. – MS (EI, 70 eV): *m/z* (%) = 180 (4) [M^+], 134 (65), 119 (88), 91 (100).

2-Amino-2-(4-ethylphenyl)-1-nitroethane (**2e**): Oil, IR (film): ν = 3418 (NH_2), 2924, 1554 (NO_2), 1419, 1379, 1082, 833 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.25 (t, 3H, Me), 2.7 (q, 2H, CH_2Me), 2.85 (broad, 2H, NH_2), 4.55 (m, 2H, CH_2NO_2), 5.45 (m, 1H, C_6H_4CH), 7.15, 7.4 (dd, 4H, C_6H_4). – $^{13}C\{H\}$ NMR (200 MHz, $CDCl_3$): δ = 15.5 (Me), 28.5 (CH_2), 71.2 (C_6H_4CH), 81.5 (CH_2NO_2), 126.2, 128.5, 136.0, 145.5 (C_6H_4). – $C_{10}H_{14}N_2O_2$ (194.23): calcd. C 61.84, H 7.27, N 14.42; found C 61.92, H 7.30, N 14.66. – MS (EI, 70 eV): *m/z* (%) = 194 (2) [M^+] 177 (4), 148 (66), 133 (84), 91 (63), 79 (68), 28 (100), 18 (38).

2-Amino-2-(2,4-dimethylphenyl)-1-nitroethane (**2f**): M. p. 52 – 55 °C. IR (KBr): ν = 3469 (NH_2), 2924, 1554 (NO_2), 1465, 1379, 1072, 821 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): δ = 2.3 (s, 3H, Me), 2.35 (s, 3H, Me), 2.65 (broad, 2H, NH_2), 4.5 (m, 2H, CH_2NO_2), 5.65 (m, 1H, C_6H_4CH), 6.8 – 7.42 (m, 3H, C_6H_3). – $^{13}C\{H\}$ NMR (200 MHz, $CDCl_3$): δ = 19.2 (Me), 21.5 (Me), 68.2 (C_6H_4CH), 81.3 (CH_2NO_2), 126.0, 128.0, 132.0, 133.5, 134.8, 139 (C_6H_4). – $C_{10}H_{14}N_2O_2$ (194.23): calcd. C 61.84, H 7.27, N 14.42; found C 61.92, H 7.30, N 14.66.

2-Amino-2-(2-methylphenyl)-1-nitroethane (**2g**): Oil. IR (film): ν = 3416 (broad NH_2), 2930, 1550 (s, NO_2), 1462, 1379, 1070 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): δ = 2.35 (s, 3H, Me), 2.85 (broad, 2H, NH_2), 4.5 (m, 2H, CH_2NO_2), 5.68 (m, 1H, C_6H_4CH), 7.15, 7.60 (m, 4H, C_6H_4). – $^{13}C\{H\}$ NMR (200 MHz, $CDCl_3$): δ = 18.5 (Me), 68.5 (C_6H_4CH), 80.5 (CH_2NO_2), 126.1, 127.5, 129.0, 131.4, 134.5, 136.5 (C_6H_4). – $C_9H_{12}N_2O_2$ (180.39): calcd. C 59.93, H 6.71, N 15.63; found C 59.94, H 6.68, N 15.70.

2-Amino-2-(4-methoxyphenyl)-1-nitroethane (**2h**): Oil. IR (film): ν = 3416 (broad NH_2), 2926, 1612, 1554 (s, NO_2), 1379, 1249, 1178, 1030 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): δ = 3.08 (broad, 2H, NH_2), 3.80 (s, 3H, Me), 4.55 (m, 2H, CH_2NO_2), 5.38 (m, 1H, C_6H_4CH), 6.90, 7.20 (dd, 4H, C_6H_4). – $^{13}C\{H\}$ NMR (200 MHz, $CDCl_3$): δ = 55.2 (OMe), 71.0 (C_6H_4CH), 81.5 (CH_2NO_2), 114.5, 127.5, 130, 160.4 (C_6H_4). – $C_9H_{12}N_2O_3$ (196.38): calcd. C 55.04, H 6.16, N 14.36; found C 55.10, H 6.22, N 14.40.

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