Tin(II)chloride Mediated Addition Reaction of Bromonitromethane to Aldehydes

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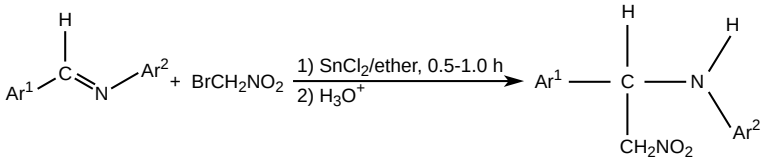
Bromonitromethane adds to aliphatic aldehydes in the presence of tin(II) chloride to yield β-nitro alcohols *via* a Reformatsky-type reaction in high yields, while aromatic aldehydes give low yields. The products were characterized by IR, NMR, and mass spectroscopy and by elemental analysis.

Key words: Bromonitromethane, Aliphatic Aldehydes, β-Nitro Alcohols, Reformatsky Reaction

Introduction

As an electrophile, bromonitromethane was used as a versatile reagent in the synthesis of aminothiophenes and their derivatives as well as in the reaction with nucleophiles such as thiolates, sulphides, thiourea, thiocyanate, iodide and phosphorus based species [1]. Bromonitromethane contains only one carbon atom, therefore it is relevant to C-1 chemistry [2]. In chemical synthesis, it has two advantages over other C-1 synthons: (a) the nitro group of the product can be reduced to an amino group; (b) α-hydrogen atoms adjacent to the nitro group in the product, being acidic, are consequently useful for further C-C bond formation via deprotonation-alkylation reactions [3]. It was found that bromonitromethane reacts with imines derived from aromatic aldehydes and ring substituted anilines in the presence of tin(II) chloride to give β-nitroamines *via* an addition reaction (Scheme 1) [4]. The polarity of bromonitromethane is thereby reversed from an electrophile to a nucleophile.



Scheme 1.

Similarly β-nitro alcohols can be prepared by a tin(II) chloride mediated addition of bromonitromethane and aliphatic aldehydes as reported here. Nitroalcohols were prepared in good yields by the addition of α,α-doubly metalated nitroalkanes to aldehydes at -90 °C [5] or from the reaction of nitroalkanes and aldehydes on an alumina surface [6] or alumina-supported potassium fluoride in the absence of a solvent [7], and from nitroalkanes and aldehydes using sodium hydroxide and a phase transfer catalyst [8]. All of these reactions are considered as examples of the general Henry reaction. In this work an alternative route for the synthesis of β-nitroalcohols is reported. Nitroalcohols are useful precursors for the preparation of amino alcohols, some of them are biologically important.

Results and Discussion

As shown in Scheme 2, bromonitromethane was reacted with cinnamaldehyde, for example, in the presence of tin(II)chloride in diethyl ether at room temperature for 1 h. After the workup of the reaction mixture and purification of the product, 1-nitro-4-phenyl-3-buten-2-ol (**2e**) was isolated in 65% yield.

The ^{1}H NMR spectrum of the compound **2e** showed a broad singlet at 2.7 ppm (OH group) which could be quenched with deuterium oxide, and a doublet at

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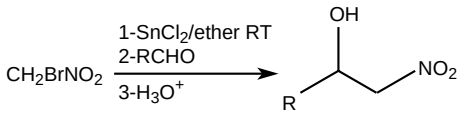


Scheme 2.

4.5 ppm for CH_2NO_2 methylene protons, while the ^{13}C NMR spectrum showed a signal at 70.0 ppm for a CHOH carbon atom and at 80.0 ppm for CH_2NO_2 carbon atom. The IR spectrum showed a broad absorption band at 3439 cm^{-1} corresponding to the hydroxyl group and another one at 1556 cm^{-1} corresponding to the nitro group. All other prepared nitroalcohols gave ^1H NMR, ^{13}C NMR and IR signals consistent with the assigned structures.

The electron impact mass spectrum of compound **2e** at 70 eV showed the M^+ peak at $m/e = 193$ with an intensity less than 1%, [M^+-H_2O] (1.5%) at 175, [M^+-NO_2–H] (13%) at 146, [M^+-CH_3NO_2] (22%) at 132, and [M^+-CH_3NO_2-H] (44%) at 131. Loss of CO from the 131 peak gives a peak at 103 (55%) which possibly produces the base peak at 77. The electron impact mass spectra of the other products did not show any M^+ peak, therefore, their composition was confirmed by elemental analysis together with spectroscopic methods.

When the reactions were performed in tetrahydrofuran, dimethyl sulfoxide, or acetonitrile, no dramatic increase in the yields of the products was noticed. But the yields were enhanced when the amount of $SnCl_2$ was increased. As an example, the yield of **2e** was increased from 65% to 72% when the mole ratio was changed from1:1:1 to 1:1.5:1 (aldehyde/ tin(II) chloride/ bromonitromethane). Different aliphatic aldehydes were reacted with bromonitromethane in the presence of tin(II) chloride to give yields summarized in Table 1. On the other hand the reaction of aromatic aldehydes with bromonitromethane in the presence of $SnCl_2$ gave low yields of the corresponding alcohols, which were unstable and decomposed readily at room temperature. It was also found that ketones were practically not reactive.

Conclusion

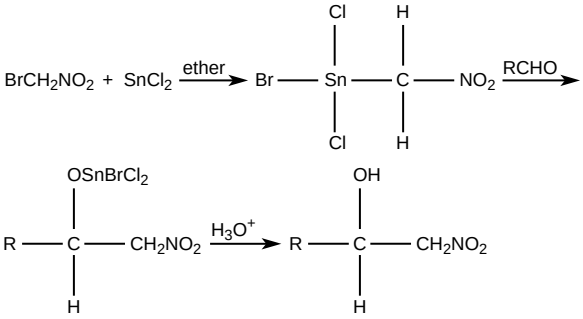
Bromonitromethane proved to be a valuable C-1 unit in C-C bond formation. Functionalities present in the products may be suitable for a wide range of other chemical manipulations. A potential conversion of the nitro group into amino group *via* reduction and the ease of replacement of the nitro group by a hydrogen atom

Table 1. Yields of the reactions of aliphatic aldehydes and bromonitromethane.

2	R	Yields [%]	[Ref.]
a	CH_3	75	[9]
b	C_2H_5	70	[10]
c	$CH_3CH{=}CH$	68	
d	$CH_3(CH_2)_4CH_2$	72	
e	$C_6H_5CH{=}CH$	72	
f	$C_6H_5CH_2CH_2$	70	

(denitration) using tributyltin hydride make bromonitromethane an interesting useful synthon. High yields, relatively short reaction time, low cost of starting materials and easy handling of the reactions are other remarkable advantages.

The mechanism of this reaction is not studied yet but a Reformatsky-type mechanism is proposed [11].



Experimental Section

All reagents were commercial grade and were used without further purification. IR spectra were determined on a Mattson 5000 spectrometer. NMR spectra were determined on a Bruker AC 200 MHz instrument. In all cases, samples were dissolved in $CDCl_3$ using TMS as internal standard. Mass spectra were recorded on a Finnigian Mat 731 spectrometer at 70 eV. Elemental analysis were performed at the Middle East Technical University-Analyses center.

Bromonitromethane was prepared according to the following improved procedure [7]:

A mixture of water (500 ml), ice (200 g), NaOH (20 g, 0.50 mol) and nitromethane (36.6 g, 0.60 mol) was vigorously stirred using a mechanical stirrer for 30 min during which the temperature was kept around 0 °C. Bromine (60 g, 0.40 mol) was added at once to the solution with continuous stirring. After 4 h the solution was steam distilled. The crude product was isolated, dried over anhydrous $MgSO_4$ and fractionally redistilled. Bromonitromethane was collected at 134 – 136 °C to produce 30 g (56% yield). ^1H NMR: $\delta = 5.45$ ppm (s, CH_2). IR (neat): $\tilde{\nu} = 1565$, 1373, 1260 and 747 cm^{-1}.

*General procedure for the synthesis of β-nitroalcohols (**2a** – **f**)*

To a mixture of $SnCl_2$ (1.42 g, 7.5 mmol) in Et_2O (40 ml), the aldehyde (5 mmol) was added at 0 °C. To this mixture while stirring bromonitromethane (5 mmol) dissolved in 2 ml of dry ether was added. The mixture was left stirring for 4 h during which the reaction was monitored by TLC. The reaction mixture was then diluted with ether (50 ml) and washed successively with 1M HCl, H_2O, saturated $NaHCO_3$ solution and brine. The organic layer was separated and dried over anhydrous Na_2SO_4. The crude product was purified by TLC to give the following nitroalcohols:

*1-Nitro-3-penten-2-ol (**2c**):* IR (film): $\tilde{\nu} = 3447$ (OH), 1556 (NO_2), 1453, 1385, 1202, 1132 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.75$ (d, $^3J = 5$ Hz, 3 H, CHMe), 2.60 (broad, 1 H, OH), 4.45 (d, $^3J = 5$ Hz, 2 H, $CHNO_2$), 4.80 (m, 1 H, CHOH), 5.50 and 5.90 (m, 2 H, CH=CH). – $^{13}C\{^1H\}$ NMR (200 MHz, $CDCl_3$): $\delta = 17.5$ (CHMe), 69.5 (CHOH), 80.3 ($CHNO_2$), 128.6, 131.0 (CH=CH). – $C_5H_9NO_3$ (131.132): calcd. C 45.70, H 6.92, N 10.68; found C 45.75, H 6.88, N 10.66.

*1-Nitro-2-octanol (**2d**):* IR (film): $\tilde{\nu} = 3440$ (OH), 3931, 3861, 1554 (NO_2), 1480, 1430, 911 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.85$ (t, $^3J = 5$ Hz, 3 H, CHMe), 1.3 – 1.5 (m, 10 H, 5×CH_2), 3.00 (broad, 1 H, OH), 4.30 (broad, 1 H, CHOH), 4.40 (d, 2 H, $^3J = 5$ Hz, $CHNO_2$). – $^{13}C\{^1H\}$ NMR (200 MHz, $CDCl_3$): $\delta = 14.2$ (CHMe), 22.5, 25.2, 28.8, 31.6, 33.8 (5×CH_2), 68.8 (CHOH), 80.7 ($CHNO_2$). – MS (EI, 70 eV): *m/e* (%) = M^+ (absent) 128 (< 1), 113 (5), 97 (15), 95 (26), 90 (15), 83 (14), 81 (20), 69 (74), 57 (68), 55 (79), 43 (100), 41 (82). – $C_8H_{17}NO_3$ (175.232): calcd. C 54.85, H 9.78, N 7.83; found C 54.56, H 9.81, N 7.83.

*1-Nitro-4-phenyl-3-buten-2-ol (**2e**):* IR (film): $\tilde{\nu} = 3439$ (OH), 1556 (NO_2), 914 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): $\delta = 2.70$ (broad, 1 H, OH), 4.50 (d, $^3J = 5$ Hz, 2 H, $CHNO_2$), 5.05 (q, $^3J = 5$ Hz, 1 H, CHOH), 6.10 (dd, $^3J = 5$, $^3J = 15$ Hz, 3-H), 6.80 (d, 1 H, $^3J = 15$ Hz, 4-H), 7.40 (m, 5 H, ArH). – $^{13}C\{^1H\}$ NMR (200 MHz, $CDCl_3$): $\delta = 70.0$ (CHOH), 80.0 ($CHNO_2$), 124.9, 126.7, 128.5, 128.8, 133.5, 135.5 (C_6H_5CH=CH). – MS (EI, 70 eV): *m/e* (%) = M^+ 193 (< 1), 175 (1.5), 146 (13), 132 (22), 103 (55), 77 (100), 51 (98). $C_{10}H_{11}NO_3$ (193.24): calcd. C 62.17, H 5.74, N 7.25; found C 62.12, H 5.76, N 7.20.

*1-Nitro-4-phenyl-2-butanol (**2f**):* M.p. 82 – 83 °C. – IR (KBr): $\tilde{\nu} = 3402$ (OH), 2949, 1549 (NO_2), 1493, 1454, 1423, 1384, 1205 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.80$ (m, 2 H, $PhCH_2$), 2.60 (d , $^3J = 5$ Hz, 1 H, OH), 2.80 (m, 2 H, $PhCH_2CH_2$), 4.30 (m, 1 H, CHOH), 4.40 (d, 2 H, $^3J = 5$ Hz, CH_2NO_2). 7.25 (m, 5H, Ph). – $^{13}C\{^1H\}$ NMR (200 MHz, $CDCl_3$): $\delta = 31.2$ ($PhCH_2$), 35.3 (C-3), 68.0 (CHOH), 80.5 (CH_2NO_2), 126.3, 128.3, 128.6, 140.8 (C_6H_5). – MS (EI, 70 eV): *m/e* (%) = M^+ (absent), 133 (32), 130 (46), 105 (86), 104 (70), 91 (100), 92 (70), 77 (48), 65 (37), 51 (26), 43 (48). $C_{10}H_{13}NO_3$ (195.24) calcd. C 61.15, H 6.69, N 7.17; found C 61.17, H 6.72, N 7.20.

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