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Henry and Mannich reactions of polynitroalkanes in ionic liquids

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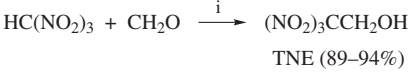
Based on Henry and Mannich reactions of polynitroalkanes for the first time implemented in ionic liquids, ecologically pure and safe methods for the synthesis of polynitro alcohols and *N*-2,2,2-trinitroethyl derivatives of low basic amino compounds (urea, acetamide, 4-amino-3-methylfuroxan) have been elaborated.

Ionic liquids (ILs) represent one point of 'green chemistry', since they are non-flammable, non-volatile, can be regenerated and reused repeatedly.[1–5] Moreover, being highly polar compounds, ILs accelerate diverse heterolytic processes, including reactions of CH-acids and 1,3-dipoles.[6–9] Examples of Henry and Mannich reactions in ILs deal mostly with addition of carbonyl compounds to CH-acids containing a nitrile or alkoxycarbonyl group as the activating substituent.[10–13] Data on reaction of nitro compounds in ILs are scarce: primary mononitroalkanes were involved in the Henry reaction[14–16] and in a three-component Mannich condensation.[17] ILs have not hitherto been used in reactions of polynitroalkanes.

In this work we report on the application of ILs as reaction media and catalysts in syntheses of polynitroalcohols [2,2,2-trinitroethanol (TNE) and 2,2-dinitropropane-1,3-diol] and trinitroethylamino compounds based on Henry and Mannich reactions. TNE is the starting compound in syntheses of energy-rich materials such as *N*,*N*′-bis(2,2,2-trinitroethyl)urea,[18] *N*,*N*′-bis-(2,2,2-trinitroethyl)ethylenedinitramine,[19] tetrakis(2,2,2-trinitroethyl)orthocarbonate (TNEOC) oxidant.[20] A known method for TNE synthesis involves heating of equimolar amounts of nitroform and paraformaldehyde in CCl_4 at 60–65 °C.[21]

In our experiments for the preparation of TNE, we studied the effect of the IL anion and cation {1-butyl-3-methylimidazolium tetrafluoroborate (hexafluorophosphate) [bmim][BF_4]([PF_6]) and 1-ethyl-3-methylimidazolium hydrogensulfate [emim][HSO_4]} on the reaction between trinitromethane and paraformaldehyde (with a small excess of trinitromethane) (Scheme 1).† The highest yield (89%) was achieved when the reaction was carried out in [emim][HSO_4] at 20 °C for 24 h (Table 1, entry 3). The yield of TNE under the same conditions was 50% in [bmim][PF_6] and 81% in [bmim][BF_4]. After extraction of TNE with *tert*-butyl methyl ether from [emim][HSO_4], the IL was reused providing to similar yields; the yield of TNE after water treatment followed by extraction with Bu^{t}OMe in the fourth experiment was 94% (Table 1, entry 3). Evidently, TNE was extracted incompletely in the previous experiments. It is important that, unlike in the known method,[21] extraction from the IL followed by solvent evaporation *in vacuo* gives crystalline TNE with mp 70–72 °C, as that of the analytically pure specimen.[21]



Scheme 1 *Reagents and conditions*: i, CH_2O (1.0 mmol), $CH(NO_2)_3$ (1.2 mmol), IL (1 g), 20 °C, 24 h.

Table 1 Synthesis of TNE in ILs.

Entry	IL	Yield of TNE (%) (cycle)
1	[bmim][BF_4]	80
2	[bmim][PF_6]	50
3	[emim][HSO_4]	89 (1), 86 (2), 83 (3), 94 (4)

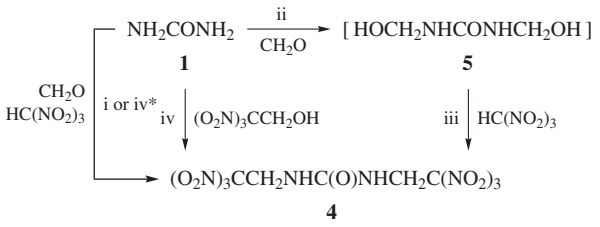
The similar technique was used for the synthesis of 2,2-dinitropropane-1,3-diol (DNPD)‡ from paraformaldehyde and dinitromethane generated from dinitromethane sodium salt by treatment with various acids (HCl, CF_3COOH, AcOH) [molar ratio CH_2O:$NaCH(NO_2)_2$:acid = 2.2:1.0:1.0]. In this case, the ILs, the reaction temperature and time were also varied. A rather satisfactory procedure comprised the reaction in [bmim][BF_4] at 1–3 °C using an equimolar amount of AcOH with respect to $NaCH(NO_2)_2$; however, the yield of DNPD even under these conditions was as low as 40%, which was lower than the 66% yield in water.[22]

Further we studied the reaction of TNE with poorly basic amino compounds such as urea **1** (pK_a 0.1[23]), acetamide **2** (pK_a –0.4[23]) and 4-amino-3-methylfuroxan **3** (pK_a –3.01[24]) in 'acidic' IL [emim][HSO_4]. The synthesis of 1,3-bis(2,2,2-trinitroethyl)urea **4** was carried out at 20 °C without a catalyst or in the presence of a catalytic amount of H_2SO_4. Three procedures were used for this purpose (Scheme 2, Table 2): (1) simultaneous

† IR spectra were measured on a Specord-M82 spectrometer. NMR spectra were recorded using a Bruker AM-300 spectrometer (300 for ^{1}H, 75.47 for ^{13}C and 21.69 MHz for ^{15}N). TMS was used as the internal standard in ^{1}H and ^{13}C spectra and $MeNO_2$ as the external standard in ^{14}N NMR spectra. TLC was performed on silica gel plates (Silufol UV-254). 4-Amino-3-methylfuroxan was synthesized according to a procedure reported elsewhere.[26]

2,2,2-Trinitroethanol (TNE). The mixture of trinitromethane (0.36 g, 2.4 mmol) and paraformaldehyde (0.06 g, 2 mmol) was stirred in 1 g of [emim][HSO_4] for 24 h at 20 °C. 2,2,2-Trinitroethanol was extracted with Bu^{t}OMe (3×3 ml). The extract was washed with water (5×3 ml) and dried with $MgSO_4$; the solvent was evaporated *in vacuo*. Yield 0.32 g (89%), mp 71–72 °C (Bu^{t}OMe) (lit.,[21] mp 72 °C). ^{1}H NMR (CD_3CN) δ: 4.0 (br.s, 1H, OH), 4.95 (s, 2H, CH_2). ^{13}C NMR (CD_3CN) δ: 63.5 (CH_2), 127.5 [$C(NO_2)_2$]. ^{14}N NMR (CD_3CN) δ: –30.35 (NO_2). The IL was evaporated *in vacuo* with heating and used for the three syntheses. Reaction mixture of the fourth synthesis after the reaction completion was treated with water (3 ml) followed by extraction with Bu^{t}OMe.

‡ *2,2-Dinitropropane-1,3-diol (DNPD)*. Yield 40%, mp 141–142 °C (Bu^{t}OMe) (lit.,[22] mp 142 °C). ^{1}H NMR (CD_3CN) δ: 3.9 (br.s, 2H, OH), 4.44 (s, 4H, CH_2). ^{13}C NMR (CD_3CN) δ: 61.15 (CH_2), 119.4 [$C(NO_2)_3$]. ^{14}N NMR (CD_3CN) δ: –12.04 (NO_2).



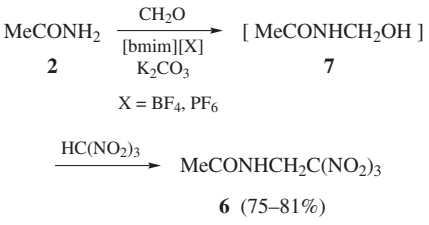
Scheme 2 *Reagents and conditions*: i, [emim][HSO_4], cat. H_2SO_4, 20 °C, 48 h; ii, [emim][HSO_4], 50 °C, 0.4 h; iii, [emim][HSO_4], cat. H_2SO_4, 20 °C, 24 h; iv*, [emim][HSO_4], CH_2O + $CH(NO_2)_3$, then **1**; iv, [emim][HSO_4], 20 °C, 48 h.

Table 2 Synthesis of 1,3-bis(2,2,2-trinitroethyl)urea **4** in [emim][HSO_4].

Entry	Method	IL/g	*T*/°C	Time/h	Yield (%) (cycle)
1	i	2.0 + H_2SO_4 (7 drops)	50	24	Decomp.
2	i	3.5 + H_2SO_4 (7 drops)	20	48	60
3	ii iii	3.5 + H_2SO_4 (7 drops)	50 20	0.4 24	60
4	iv*	3.5	20	24	52
5	iv	3.5	20	24	36
6	iv	3.5 + H_2SO_4 (7 drops)	20	24	77
7	iv	3.5	20	48	90 (1), 86 (2), 84 (3), 88 (4)

mixing of three components, *viz.* urea **1**, paraformaldehyde and trinitromethane (pathway i, entries 1, 2), (2) reaction of presynthesised *in situ* 1,3-bis(hydroxymethyl)urea **5** with trinitromethane (pathways ii, iii, entry 3) and (3) condensation of urea **1** with TNE (pathway iv, entries 4–7), including preliminary one-pot preparation of the latter in an IL without isolation in pure form followed by addition of urea (entry 4). The target product **4** was formed in all the reactions, but the highest yield (90%) was reached where the reaction of urea **1** with TNE was carried out for 48 h in the absence of H_2SO_4 (Table 2, entry 7); when the IL itself acted as a catalyst. In the optimum case, the IL was recycled three times after extraction of the final product without a considerable decrease in the product yield (Table 2, entry 7). The product obtained had a high quality and did not need additional purification.[§]

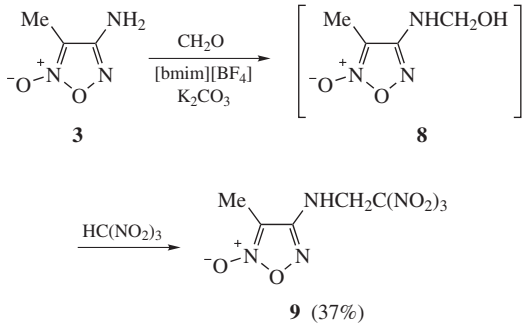
The reaction of acetamide **2**, paraformaldehyde and nitroform (Scheme 3) was also performed in three ways in two different ILs, *viz*. [bmim][BF_4] and [bmim][PF_6]; however, in this case the highest yield 75–81% of *N*-(2,2,2-trinitroethyl)acetamide **6**[¶] was achieved when acetamide **2** was treated with paraformaldehyde to furnish *in situ* formed *N*-hydroxymethylacetamide **7**, which was then treated with nitroform. In this manner, the first stage was carried out in the presence of a catalytic amount of



Scheme 3

K_2CO_3, while the entire process took 24 h at 20 °C. The yield and quality of the final product were not essentially dependent on the IL used; IL could be recycled at least three times without a considerable decrease in the yield.

Similarly, 3-methyl-4-(2,2,2-trinitroethyl)aminofuroxan **9**[††] was obtained in 37% yield in [bmim][BF_4] (Scheme 4) through the preliminary *in situ* obtaining *N*-hydroxymethyl derivative **8** from 4-amino-3-methylfuroxan **3** and paraformaldehyde. The attempted reactions of acetamide **2** and aminofuroxan **3** with TNE in ILs failed to produce the corresponding Mannich products **6** and **9**.



Scheme 4

It is evident that conditions for the formation of Mannich products are largely determined by the basicity of the starting amino compound. Apparently, more basic urea can be transformed into the product **4** by any of procedures (see Scheme 2), however, the reaction with TNE was found to be the optimum one. As for less basic amino compounds **2** and **3**, the target products **6** and **9** can be accessed only after the preliminary synthesis of the corresponding *N*-hydroxymethyl derivatives.

Previously,[18] compound **4** was prepared by heating of urea, paraformaldehyde and nitroform in molar ratio 1:2:2 in water at 80 °C followed by crystallization from aqueous EtOH in 62% yield. Compound **6** was synthesized by reaction of *N*-hydroxymethylacetamide with nitroform,[25] and although its yield (75%) was comparable with that in ILs (75–81%), the conversional means required heating (50–70 °C).[25] Mannich reaction of amino furoxans with polynitroalkanes was not before studied.

Thus, Henry and Mannich reactions of polynitroalkanes have been for the first time performed in ILs as reaction medium. As exemplified on TNE, 1,3-bis(2,2,2-trinitroethyl)urea and *N*-(2,2,2-trinitroethyl)acetamide, replacement of organic solvents by ILs allowed one not only to raise yields of these compounds and to provide their high quality, but also to improve appreciably ecological characteristics and safety of these processes. The data obtained can be extended on other polynitro compounds with practically useful properties.

[§] *1,3-Bis(2,2,2-trinitroethyl)urea* **4**. The mixture of urea (0.06 g, 1 mmol) and TNE (0.4 g, 2.2 mmol) in 3.5 g of [emim][HSO_4] was stirred for 48 h at 20 °C. 1,3-Bis(2,2,2-trinitroethyl)urea was extracted with Bu^{t}OMe (3×3ml). The extract was washed with water (5×3 ml) and dried with $MgSO_4$; the solvent was evaporated *in vacuo*. Yield 0.35 g (90%), mp 170–171 °C (Bu^{t}OMe) (lit.,[18] mp 170–171 °C). ^{1}H NMR (CD_3CN) δ: 4.95 (d, 4H, CH_2, ^3J 7 Hz), 6.16 (t, 2H, NH, ^3J 7 Hz). ^{13}C NMR (CD_3CN) δ: 44,60 (CH_2), 117.0 [$C(NO_2)_3$], 156.25 (C=O). ^{14}N NMR (CD_3CN) δ: –30.62 (NO_2). The IL was evaporated *in vacuo* with heating and used for the next synthesis.

[¶] N-*(2,2,2-Trinitroethyl)acetamide* **6**. Yield 81%, mp 89–90 °C (Bu^{t}OMe) (lit.,[25] 88–90 °C). ^{1}H NMR (DMSO-d_6) δ: 1.95 (s, 3H, Me), 5.07 (d, 2H, CH_2, ^3J 6.5 Hz), 8.75 (t, 1H, NH, ^3J 6.5 Hz). ^{13}C NMR (DMSO-d_6) δ: 22.80 (Me), 63.23 (CH_2), 126.00 [$C(NO_2)_3$], 173.60 (C=O). ^{14}N NMR (DMSO-d_6) δ: –31.98 (NO_2). IR (ν/cm^{-1}): 3272 (NH), 3060, 3012, 2960 (CH), 1676 (C=O), 1588, 1360 (NO_2), 1304, 1132, 1092, 808.

[††] *3-Methyl-4-(2,2,2-trinitroethyl)aminofuroxan* **9**. Yield 37%, mp 124–125 °C. ^{1}H NMR (acetone-d_6) δ: 2.15 (s, 3H, Me), 5.38 (d, 2H, CH_2, ^3J 7.0 Hz), 6.85 (t, 1H, NH, ^3J 7.0 Hz). ^{13}C NMR (acetone-d_6) δ: 5.94 (Me), 45.16 (CH_2), 106.6 (C^3 fur. ring), 125.40 [$C(NO_2)_3$], 156.40 (C^4 fur. ring). ^{14}N NMR (acetone-d_6) δ: –30.68 (NO_2). IR (ν/cm^{-1}): 3360, 3284 (NH), 3052, 3000, 2948 (CH), 1632 (fur. ring), 1528, 1336 (NO_2), 1296, 1212, 1028, 808.

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