An Improved, Fully Heterogeneous, Diastereoselective Synthesis of (Z)-α-Bromonitroalkenes

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Abstract: α-Bromonitroalkenes are both key starting materials for the preparation of complex structures and possess antimicrobial activity. In this context, we disclose a simple, fully heterogeneous synthetic approach for their preparation in good overall yields.

Key words: Henry reaction, dehydration, diastereoselectivity, α-bromonitroalkanes, heterogeneous catalysis

Unsaturated nitro compounds are an important class of valuable precursors to a wide variety of target molecules. They are generated by Henry reaction followed by elimination, troalkenes involve bromination–debromination of nitromethane in the presence of tri-n-butylarsine. Thus, a simpler method would be valuable. In this context, based on our previous experience in the nitroaldol (Henry) reaction, we have developed a new, simple, mild, and fully heterogeneous approach for the synthesis of α-bromonitroalkenes 5 starting from the Henry reaction between aldehydes 1 and bromonitromethane 6, followed by the dehydration of the obtained crude nitro alcohols (Scheme 2).

We chose, as a model system, the reaction 6 with hexanal (1a) under basic and solvent-free conditions (carbonate on silica), in which the crude nitroalkanol 7a can be directly dehydrated, by Amberlyst 15/Ac₂O into the target compound 5a avoiding any intermediate purification step.

As reported in Table 1, the optimal result was obtained by employing 0.3 equivalents of carbonate on silica, coupled with 500 mg/mmol of Amberlyst 15 and three equivalents of Ac₂O.

In order to assess the generality of our procedure we investigated a variety of substrates and, as reported in Table 2, satisfactory to good yields (55–85%) were achieved with aromatic and aliphatic aldehydes, including functionalized substrates. Only 5-bromo-2-furfural 1k (Table 2, entry 11) afforded a low yield (31%) of alkene 5k, probably due to the chemical frailty of the furan ring.

Furthermore, all the obtained α-bromonitroalkenes were isolated as a single Z-diastereomer. The configuration was established by comparison with the literature data.
In conclusion, our procedure offers important advantages with respect to the previous reported approaches since it gives access to the target compounds, without the need for excess bromonitromethane, under mild reaction conditions (room temperature) and short reaction times, with evident economical and environmental benefits. Moreover, a variety of other important functionalities can be tolerated giving access to polyfunctionalized α-bromonitroalkenes that could be of interest as targets with potential biological activities. Finally, it is important to point out that our method employs a fully heterogeneous procedure and that the final dehydration of nitroalkanol proceeds under acidic conditions, contrary to the standard procedures that usually employ basic conditions.

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References and Notes


(9) Usually, the dehydration of bromoalkanes is performed under basic conditions, see ref. 6.

(10) Typical Procedure for the Synthesis of Compounds 5

The catalyst (0.56 g, 0.3 mmol) was slowly added at r.t. to a mechanically stirred mixture of the bromonitromethane (6, 1 mmol, 0.155 g, pure 90%) and the requisite aldehyde 1 (1 mmol), and the reaction was stirred for the appropriate time (see Table). The mixture was then treated with EtOAc (5 mL), and the catalyst was filtered off and washed with additional EtOAc (10 mL). The solution was concentrated under reduced pressure to a volume of 3 mL and then treated with Ac₂O (306 mg, 3 mmol) and Amberlyst 15 (0.5 g) and stirred, at r.t., for an additional 1.5 h. Finally, the Amberlyst 15 was removed by filtration, washing with EtOAc (7 mL), and the solution was concentrated under vacuum giving the crude product 5 which was purified by flash chromatography (hexane–EtOAc = 9:1).

(Z)-1-Bromo-1-nitrohept-1-ene (5a)

Light yellow oil. IR (neat): ν = 3045, 1551, 1325, 1261, 942, 722 cm⁻¹. 1H NMR (400 MHz, CDCl₃): δ = 0.91 (t, 3 H, J = 6.8 Hz), 1.30–1.40 (m, 4 H), 1.51–1.61 (m, 1 H), 2.37 (q, 2 H, J = 7.3 Hz), 7.27 (t, 1 H, J = 7.3 Hz). 13C NMR (100 MHz, CDCl₃): δ = 14.1, 22.5, 27.3, 31.3, 31.6, 131.2, 141.6. MS (EI, 70 eV): m/z (%) = 165, 142, 119, 65, 59, 41 (100), 39, 30. Anal. Calcd for C₇H₁₂BrNO₂ (234.09): C, 41.05; H, 5.17; N, 5.98. Found: C, 41.04; H, 5.17; N, 5.98.

(Z)-1-Bromo-1-nitronon-1-ene (5b)

Light yellow oil. IR (neat): ν = 3040, 1542, 1321, 1254, 960, 768 cm⁻¹. 1H NMR (400 MHz, CDCl₃): δ = 0.89 (t, 3 H, J = 6.8 Hz), 1.23–1.41 (m, 8 H), 1.50–1.61 (m, 1 H), 2.37 (q, 2 H, J = 7.3 Hz), 7.26 (t, 1 H, J = 7.3 Hz). 13C NMR (100 MHz, CDCl₃): δ = 14.3, 22.8, 27.6, 29.1, 29.4, 31.3, 31.9, 131.2, 141.6. MS (EI, 70 eV): m/z (%) = 165, 142, 119, 65, 59, 41 (100), 39, 30. Anal. Calcd for C₉H₁₄BrNO₂ (258.08): C, 37.86; H, 5.45; N, 5.61. Found: C, 37.91; H, 5.49; N, 6.28.

(Z)-2-Bromo-2-nitrovinyl)cyclohexane (5e)

Light yellow oil. IR (neat): ν = 3030, 1539, 1320, 971, 760 cm⁻¹. 1H NMR (400 MHz, CDCl₃): δ = 1.18–1.44 (m, 6 H), 1.65–1.84 (m, 4 H), 2.59–2.53 (m, 1 H), 7.48 (d, 1 H, J = 9.8 Hz). 13C NMR (100 MHz, CDCl₃): δ = 25.3, 25.7, 30.8, 40.8, 129.1, 145.3. MS (EI, 70 eV): m/z (%) = 218, 216, 137, 119, 97, 81, 79, 71, 69, 55 (100), 41, 39. Anal. Calcd for C₁₁H₁₂BrNO₂ (250.13): C, 43.22; H, 6.45; N, 5.60. Found: C, 43.27; H, 6.49; N, 5.58.

(Z)-2-Bromo-2-nitrovinyl)cyclohexane (5e)

Light yellow oil. IR (neat): ν = 3030, 1539, 1320, 971, 760 cm⁻¹. 1H NMR (400 MHz, CDCl₃): δ = 2.71 (q, 2 H, J = 7.7 Hz), 2.88 (t, 2 H, J = 7.7 Hz), 7.17–7.36 (m, 5 H). 6.77 (t, 1 H, J = 7.7 Hz). 13C NMR (100 MHz, CDCl₃): δ = 33.0, 33.6, 127.0, 128.5, 129.0, 131.8, 139.7, 140.2. MS (EI, 70 eV): m/z (%) = 240, 238, 129, 91 (100). 65. Anal. Calcd for C₁₉H₁₉BrNO₂ (246.10): C, 46.90; H, 3.94; N, 5.47. Found: C, 46.88; H, 3.97; N, 5.44.

(Z)-2-Bromo-2-nitrovinyl)cyclohexane (5d)

Light yellow oil. IR (neat): ν = 3035, 1618, 1525, 1331, 937, 750, 724, 698 cm⁻¹. 1H NMR (400 MHz, CDCl₃): δ = 2.71 (q, 2 H, J = 7.7 Hz), 2.88 (t, 2 H, J = 7.7 Hz). 7.17–7.36 (m, 5 H). 6.77 (t, 1 H, J = 7.7 Hz). 13C NMR (100 MHz, CDCl₃): δ = 33.0, 33.6, 127.0, 128.5, 129.0, 131.8, 139.7, 140.2. MS (EI, 70 eV): m/z (%) = 240, 238, 129, 91 (100). 65. Anal. Calcd for C₁₉H₁₉BrNO₂ (246.10): C, 46.90; H, 3.94; N, 5.47. Found: C, 46.88; H, 3.97; N, 5.44.

(Z)-2-Bromo-5-(2-Bromo-2-nitrovinyl)furane (5k)

Light yellow oil. IR (neat): ν = 3134, 3036, 1618, 1537, 1505, 1348, 1292, 1025, 948, 818, 786, 645 cm⁻¹. 1H NMR (400 MHz, CDCl₃): δ = 3.01 (s, 3 H, J = 3.4 Hz), 7.37 (d, 1 H, J = 3.4 Hz), 8.50 (s, 1 H). 13C NMR (100 MHz, CDCl₃): δ = 115.8, 122.3, 124.0, 125.1, 129.6, 148.6. MS (EI, 70 eV): m/z (%) = 299, 297, 295, 225, 223, 221, 135, 133, 79, 63 (100). Anal. Calcd for C₁₉H₁₉BrNO₂ (296.90): C, 24.27; H, 1.02; N, 4.72. Found: C, 24.30; H, 1.03; N, 4.69.