SUPPORTING INFORMATION

Ammonium Ylides for the Diastereoselective Synthesis of Glycidic Amides

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1. General Information:

Melting points were measured on a Kofler melting point microscope (Reichert, Vienna). $^1$H- and $^{13}$C-NMR spectra were recorded on a Bruker Avance DRX 500 MHz spectrometer using a TXI cryoprobe with z -gradient coil and on a Bruker Avance DPX 200 MHz spectrometer. Typical resolutions and chemical shift precisions were +/- 1 Hz for $^1$H and +/- 0.8 Hz for $^{13}$C. All NMR spectra were referenced on the solvent peak. High resolution mass spectra were obtained using an Agilent 6520 Q-TOF mass spectrometer with an ESI source and an Agilent G1607A coaxial sprayer. All analyses were made in the positive ionization mode. Purine (exact mass for $[M+H]^+$ = 121.050873) and 1,2,3,4,5,6-hexakis(2,2,3,3-tetrafluoropropoxy)-1,3,5,2,4,6-triazatriphosphinane (exact mass for $[M+H]^+$ = 922.009798) were used for internal mass calibration. IR spectra were recorded on a Shimadzu IR Affinity-1 fourier transform infrared spectrometer. All chemicals were purchased from commercial suppliers and used without further purification unless otherwise stated. All reactions were performed under an Ar-atmosphere.

2. Syntheses of DABCO-Ammonium Salts 2, 4, 6, and 8:

General Procedure: One equivalent of DABCO was added to a solution of one equivalent of the $\alpha$-bromo amide in THF (15 mL / g amide) and stirred for 24 h at room temperature. The resulting suspension was centrifuged, the solid washed 3 times with EtOAc and dried in vacuo to give the product in sufficient purity for the epoxide formation reaction.
Ammonium Salt 2. Prepared from 2-bromo-N,N-diethylacetamide\(^1\) (4.06 g, 20.9 mmol) in 73% (4.65 g, 15.2 mmol). White solid. M.p.: 190-193 °C; \(^1\)H NMR (500 MHz, δ, CDCl\(_3\), 298 K): 1.13 (t, \(J = 7.5\) Hz, 3H), 1.22 (t, \(J = 7.5\) Hz, 3H), 3.22 (t, \(J = 7.3\) Hz, 6H), 3.34 (q, \(J = 7.5\) Hz, 2H), 3.48 (q, \(J = 7.5\) Hz, 2H), 4.07 (t, \(J = 7.3\) Hz, 6H), 4.73 (s, 2H) ppm; \(^13\)C NMR (125 MHz, δ, CDCl\(_3\), 298 K): 12.8 (-CH\(_3\)-), 14.4 (CH\(_3\)-), 41.0 (-CH\(_2\)-), 42.1 (-CH\(_2\)-), 45.4 (-NCH\(_2\)-), 53.0 (-NCH\(_2\)-) 61.2 (-C\(_6\)H\(_2\)CO-), 162.2 (-CO-) ppm; IR (film): \(\bar{\nu} = 3532, 3406, 2972, 2941, 2893, 1632, 1489, 1479, 1470, 1431, 1397, 1368, 1310, 1265, 1215, 1109, 1072, 1053, 961, 893, 839\) cm\(^{-1}\); HRMS (ESI): m/z calcd for C\(_{12}\)H\(_{24}\)N\(_3\)O\(^+\): 226.1919 [M\(^+\)]; found: 226.1922.

Ammonium Salt 4. Prepared from 2-bromo-N,N-dibenzylacetamide\(^2\) (1.56 g, 4.92 mmol) in 78% (1.65 g, 3.84 mmol). White solid. M.p.: decomp > 220 °C; \(^1\)H NMR (200 MHz, δ, CDCl\(_3\), 298 K): 2.91 (t, \(J = 7.0\) Hz, 6H), 3.90 (t, \(J = 7.0\) Hz, 6H), 4.33 (s, 2H), 4.54 (s, 2H), 5.03 (s, 2H), 7.13-7.20 (m, 10H) ppm; \(^13\)C NMR (50 MHz, δ, CDCl\(_3\), 298 K): 45.3 (-NCH\(_2\)-), 48.8 (-CH\(_2\)-Ar), 50.7 (-CH\(_2\)-Ar), 53.0 (-NCH\(_2\)-), 61.7 (-CH\(_2\)-CO), 127.9 (Ar-C), 128.0 (Ar-C), 128.1 (Ar-C), 128.3 (Ar-C), 129.0 (Ar-C), 129.3 (Ar-C), 135.2 (Ar-C\(_{\text{quat}}\)), 135.8 (Ar-C\(_{\text{quat}}\)), 164.1 (-CO-) ppm; IR (film): \(\bar{\nu} = 3399, 2974, 2943, 2887, 1655, 1493, 1481, 1449, 1418, 1397, 1364, 1234, 1117, 1057, 1026, 994, 841, 752, 739, 725, 694\) cm\(^{-1}\); HRMS (ESI): m/z calcd for C\(_{22}\)H\(_{28}\)N\(_3\)O\(^+\): 350.2232 [M\(^+\)]; found: 350.2234.

Ammonium Salt 6. Prepared from N-benzyl-2-bromoacetamide\(^3\) (4.50 g, 19.8 mmol) in 62% (4.15 g, 12.2 mmol). White solid. M.p.: 148-151 °C; \(^1\)H NMR (500 MHz, δ, CDCl\(_3\), 298 K): 3.16 (t, \(J = 7.0\) Hz, 6H), 3.74 (t, \(J = 7.0\) Hz, 6H), 4.44 (d, \(J = 6.1\) Hz, 2H), 4.67 (s, 2H), 7.26 (m, 1H), 7.32 (m, 2H), 7.38 (m, 2H), 9.42 (bs, 1H) ppm; \(^13\)C NMR (125 MHz, δ, CDCl\(_3\), 298 K): 34.6 (-CH\(_2\)-Ar), 45.4 (-NCH\(_2\)-), 53.5 (-NCH\(_2\)-), 63.2 (-CH\(_2\)-CO), 127.6 (Ar-C), 128.1 (Ar-C), 128.8 (Ar-C), 137.6 (Ar-C\(_{\text{quat}}\)), 162.8 (-CO-) ppm; IR (film): \(\bar{\nu} = 3173, 3035, 2962, 2951, 2912, 2884, 1663, 1553, 1495, 1452, 1431, 1367, 1331, 1315, 1294, 1223, 1103, 1055, 1026, 993, 841, 729, 708, 607\) cm\(^{-1}\); HRMS (ESI): m/z calcd for C\(_{15}\)H\(_{22}\)N\(_3\)O\(^+\): 260.1763 [M\(^+\)]; found: 260.1757.

**Ammonium Salt 8.** Prepared from 2-bromo-1-(piperidin-1-yl)ethanone\(^4\) (1.10 g, 5.36 mmol) in 70% (1.19 g, 3.75 mmol). Hygroscopic white solid. M.p.: 164-167 °C; \(^1\)H NMR (500 MHz, \(\delta\), CDCl\(_3\), 298 K): 1.27-1.37 (m, 6H), 2.93 (m, 6H), 3.15-3.34 (m, 4H), 3.83 (m, 6H), 4.65 (s, 2H) ppm; \(^13\)C NMR (125 MHz, \(\delta\), CDCl\(_3\), 298 K): 23.8 (-CH\(_2\)), 25.1 (-CH\(_2\)), 26.0 (-CH\(_2\)), 42.6 (-CON-CH\(_2\)), 45.2 (-NCH\(_2\)), 46.1 (-CON-CH\(_2\)), 52.4 (-NCH\(_2\)), 60.9 (-CH\(_2\)CO-), 161.1 (-CO-) ppm; IR (film): \(\tilde{\nu}\) = 2930, 2856, 1638, 1472, 1435, 1402, 1346, 1323, 1238, 1248, 1061, 1017, 990, 848, 787, 745 cm\(^{-1}\); HRMS (ESI): \(m/z\) calcd for C\(_{13}\)H\(_{24}\)N\(_3\)O\(^+\): 238.1919 [M\(^+\)]; found: 238.1925.

3. **Syntheses of Glycidic Amides:**

![Diagram of glycidic amide synthesis](image)

**General procedure for the preparation of epoxides using homogeneous or liquid/solid conditions (Table 1, entries 1-8):** 1.2 equiv. of t-BuOK (or other base) were added to a mixture of ammonium salt 2 in THF (or other solvent) at 0 °C and stirred for 5 min. After addition of the indicated amount of aldehyde 1 the mixture was stirred at 0 °C for 1 h followed by stirring at 25 °C for 23 h. After extraction with EtOAc and NH\(_4\)Cl the organic layer was washed with brine, dried over Na\(_2\)SO\(_4\) and evaporated to dryness. Column chromatography (silica gel, hexanes/EtOAc = 7:3) gave 3 in the reported yields.

**Optimized procedure for the preparation of epoxides under biphasic conditions (using 2 equiv. of aldehyde):** A vigorously stirred solution of ammonium salt (2 mmol) in CH\(_2\)Cl\(_2\) (30 mL) was cooled to 0 °C, followed by addition of 50% NaOH (15 mL). After 5 min the aldehyde (4 mmol) was added in one portion. The biphasic mixture was warmed to 25 °C over 1 h and vigorously stirred for 23 h. After extraction with EtOAc the organic layer was washed with brine, dried over Na\(_2\)SO\(_4\) and evaporated to dryness. Column chromatography (silica gel, hexanes/EtOAc = 7:3) gave the glycidic amides in the reported yields (For copies of NMR spectra of 2 representative trans-epoxide products see chapter 5).

trans-\(N,N\)-diethyl-3-phenyloxirane-2-carboxamide (3). Obtained in 67% using the biphasic procedure as a white to yellow solid. Analytical data are in full accordance with those reported in literature.\(^5\) \(^1\)H NMR (500 MHz, \(\delta\), CDCl\(_3\), 298 K): 1.16 (t, \(J = 7.3\) Hz, 3H), 1.20 (t, \(J = 7.3\) Hz, 3H), 3.40-3.51 (m, 4H), 3.58 (d, \(J = 1.4\) Hz, 1H), 4.09 (d, \(J = 1.4\) Hz, 1H), 7.32-7.39 (m, 5H) ppm; \(^{13}\)C NMR (125 MHz, \(\delta\), CDCl\(_3\), 298 K): 13.1, 15.0, 41.0, 41.6, 57.3, 57.7, 125.8, 128.6, 128.7, 135.9, 165.8 ppm; HRMS (ESI): \(m/z\) calcd for C\(_{13}\)H\(_{17}\)NO\(_2\): 220.1332 \([\text{M+H}]^+\); found: 220.1329.

trans-\(N,N\)-dibenzyl-3-phenyloxirane-2-carboxamide (5). Obtained in 72% using the biphasic procedure as a white to yellow solid. Analytical data are in full accordance with those reported in literature.\(^6\) \(^1\)H NMR (500 MHz, \(\delta\), CDCl\(_3\), 298 K): 3.70 (d, \(J = 1.2\) Hz, 1H), 4.14 (d, \(J = 1.2\) Hz, 1H), 4.55 (s, 2H), 4.69 (d, \(J = 4.8\) Hz, 2H), 7.15-7.41 (m, 15H) ppm; \(^{13}\)C NMR (125 MHz, \(\delta\), CDCl\(_3\), 298 K): 48.8, 49.4, 57.5, 58.2, 125.8, 126.7, 127.8, 128.0, 128.4, 128.6, 128.7, 128.8, 129.2, 135.4, 135.9, 136.5, 167.3 ppm; HRMS (ESI): \(m/z\) calcd for C\(_{23}\)H\(_{21}\)NO\(_2\): 344.1645 \([\text{M+H}]^+\); found: 344.1644.

trans-\(N\)-benzyl-3-phenyloxirane-2-carboxamide (7). Obtained in 24% using the biphasic procedure as a white solid. Analytical data are in full accordance with those reported in literature.\(^7\) \(^1\)H NMR (500 MHz, \(\delta\), CDCl\(_3\), 298 K): 3.58 (d, \(J = 1.2\) Hz, 1H), 3.90 (d, \(J = 1.2\) Hz, 1H), 4.49 (m, 2H), 6.57 (bs, 1H), 7.26-7.36 (m, 10H) ppm; \(^{13}\)C NMR (125 MHz, \(\delta\), CDCl\(_3\), 298 K): 43.0, 59.1, 59.2, 125.9, 127.8, 127.9, 128.8, 128.9, 129.2, 134.9, 137.6, 167.4 ppm; HRMS (ESI): \(m/z\) calcd for C\(_{16}\)H\(_{15}\)NO\(_2\): 276.0995 \([\text{M+Na}]^+\); found: 276.0997.


**trans-(3-phenyloxiran-2-yl)(piperidin-1-yl)methanone (9).** Obtained in 58% using the biphasic procedure as a yellowish oil. Analytical data are in full accordance with those reported in literature.\(^8\) \(^1\)H NMR (500 MHz, \(\delta\), CDCl\(_3\), 298 K): 1.57-1.67 (m, 6H), 3.46-3.65 (m, 4H), 3.61 (d, \(J = 1.9\) Hz, 1H), 4.05 (d, \(J = 1.9\) Hz, 1H), 7.26-7.38 (m, 5H) ppm; \(^13\)C NMR (125 MHz, \(\delta\), CDCl\(_3\), 298 K): 24.5, 25.5, 26.6, 43.4, 46.1, 57.6, 57.7, 125.7, 128.7, 128.8, 135.9, 164.9 ppm; HRMS (ESI): \(m/z\) calcld for C\(_{14}\)H\(_{17}\)NO\(_2\): 232.1332 \([M+H]^+\); found: 232.1330.

**trans-N,N-diethyl-3-(\(p\)-tolyl)oxirane-2-carboxamide (11).** Obtained in 68% using the biphasic procedure white to yellow solid. Analytical data are in full accordance with those reported in literature.\(^5\) \(^1\)H NMR (500 MHz, \(\delta\), CDCl\(_3\), 298 K): 1.15 (t, \(J = 7.1\) Hz, 3H), 1.19 (t, \(J = 7.1\) Hz, 3H), 2.34 (s, 3H), 3.38-3.49 (m, 4H), 3.57 (d, \(J = 1.7\) Hz, 1H), 4.03 (d, \(J = 1.7\) Hz, 1H), 7.16 (d, \(J = 8.2\) Hz, 2H), 7.20 (d, \(J = 8.2\) Hz, 2H) ppm; \(^13\)C NMR (125 MHz, \(\delta\), CDCl\(_3\), 298 K): 13.0, 15.0, 21.3, 40.9, 41.5, 57.2, 57.7, 125.7, 129.4, 132.8, 138.7, 165.9 ppm; HRMS (ESI): \(m/z\) calcld for C\(_{14}\)H\(_{19}\)NO\(_2\): 234.1489 \([M+H]^+\); found: 234.1494.

**trans-3-(4-chlorophenyl)-N,N-diethyloxirane-2-carboxamide (13).** Obtained in 72% using the biphasic procedure as a white solid. Analytical data are in full accordance with those reported in literature.\(^5\) \(^1\)H NMR (500 MHz, \(\delta\), CDCl\(_3\), 298 K): 1.16 (t, \(J = 7.2\) Hz, 3H), 1.20 (t, \(J = 7.2\) Hz, 3H), 3.38-3.48 (m, 4H), 3.53 (d, \(J = 1.3\) Hz, 1H), 4.07 (d, \(J = 1.3\) Hz, 1H), 7.25 (d, \(J = 8.4\) Hz, 2H), 7.33 (d, \(J = 8.4\) Hz, 2H) ppm; \(^13\)C NMR (125 MHz, \(\delta\), CDCl\(_3\), 298 K): 12.5, 14.5, 40.5, 41.1, 56.5, 56.7, 126.5, 128.4, 133.9, 134.1, 164.9 ppm; HRMS (ESI): \(m/z\) calcld for C\(_{13}\)H\(_{16}\)ClNO\(_2\): 276.0762 \([M+Na]^+\); found: 276.0762.

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trans-N,N-diethyl-3-(4-methoxyphenyl)oxirane-2-carboxamide (15). Obtained in 47% using the biphasic procedure at 25 °C as a bright yellow solid. Analytical data are in full accordance with those reported in literature.\(^9\) \(^1\)H NMR (200 MHz, δ, CDCl₃, 298 K): 1.11-1.23 (m, 6H), 3.37-3.52 (m, 4H), 3.58 (d, \(J = 1.8\) Hz, 1H), 3.80 (s, 3H), 4.02 (d, \(J = 1.8\) Hz, 1H), 6.88 (d, \(J = 8.8\) Hz, 2H), 7.23 (d, \(J = 8.8\) Hz, 2H) ppm; \(^{13}\)C NMR (50 MHz, δ, CDCl₃, 298 K): 12.6, 14.8, 40.8, 41.4, 55.2, 57.0, 57.5, 114.1, 127.0, 127.7, 160.0, 165.8 ppm; HRMS (ESI): m/z calc'd for C₁₄H₁₉NO₃: 272.1257 [M+Na]⁺; found: 272.1251.

trans-N,N-diethyl-3-(4-dimethylaminophenyl)oxirane-2-carboxamide (17). \(^1\)H NMR of the crude product showed less than 20% of 17 besides unreacted starting material 16. The product decomposed during column chromatography. \(^1\)H NMR and HRMS of the crude product were consistent with formation of the trans-epoxide: \(^1\)H NMR (200 MHz, δ, CDCl₃, 298 K): 1.18 (m, 6H), 2.89 (s, 6 H), 3.37 (m, 4H), 3.58 (d, \(J = 1.7\) Hz, 1H), 3.92 (d, \(J = 1.7\) Hz, 1H), 6.61 (d, \(J = 8.5\) Hz, 2H), 7.13 (d, \(J = 8.5\) Hz, 2H) ppm; HRMS (ESI): m/z calc'd for C₁₅H₂₂N₂O₂: 263.1754 [M+Na]⁺; found: 263.1756.

trans-N,N-diethyl-3-(4-nitrophenyl)oxirane-2-carboxamide (19). \(^1\)H NMR of the crude product showed less than 10% of 19 and the corresponding Cannizzaro disproportionation products. \(^1\)H NMR signals of the trans-oxirane ring are in accordance with literature.\(^5\) The formation of the product was also evidenced by HRMS. HRMS (ESI): m/z calc'd for C₁₃H₁₆N₂O₄: 287.1002 [M+Na]⁺; found: 287.1002.

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4. NMR Spectra of the Novel Ammonium Salts 2, 4, 6, and 8:
5. Representative NMR Spectra for *trans*-Epoxide Products: