Supporting Information

Construction of Highly Functional α-Amino Nitriles *via* a Novel Multicomponent Tandem Organocatalytic Reaction: a Facile Access to α-Methylene γ-Lactams

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I. General Information

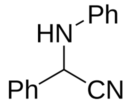
Flasks and reaction tubes were sealed with rubber plugs. Reactions were monitored by thin-layer chromatography (TLC) visualizing with ultraviolet light (UV), $KMnO_4$, iodine, *p*-anisaldehyde stain, and phosphomolybdic acid (PMA) stain. Organic solutions were concentrated under reduced pressure using a rotary evaporator with an ice-water bath. Column chromatography was performed using silica gel (200-300) mesh.

Materials. All reagents were obtained commercially and used without further purification with the following exceptions. Dichloromethane (DCM), toluene, acetonitrile (CH_3CN), and *tert*-butyl alcohol (*t*-BuOH) were dried by distillation from CaH_2; tetrahydrofuran (THF) and 1,4-Dioxane were dried by distillation from Na; benzaldehyde and furaldehyde were purified by distillation at reduced pressure; 1,4-diazabicyclo[2.2.2]octane (DABCO) was purified by recrystallization; triethylamine (TEA) was purified by distillation from CaH_2.

Instrumentation. Proton nuclear magnetic resonance (^1H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Varian Mercury (300 or 400 and 75 or 100 MHz, respectively). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane (TMS) and are referenced to residual protium in the NMR solvent ($CHCl_3$ = δ 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane (TMS) and are referenced to the carbon resonances of the solvent residual peak ($CDCl_3$ = δ 77.16 ppm). NMR data are presented as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant in Hertz (Hz), integration.

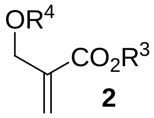
Mass spectra were in general recorded on the Bruker MicrOTOF Q II.

II. Preparation of Substrates



1a

α-Aminonitriles (**1a**) was prepared according to a published procedure[1]; the spectral data were in agreement with literature values.



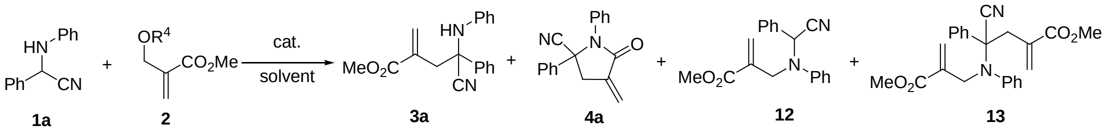
2

MBH carbonates **2** were prepared according to a published procedure [2, 3, 4], spectral data were in agreement with literature values.

III. General Procedure for Screening Reaction

To a dried reaction tube were added **1a** (0.3 mmol), DABCO (20%), CH_3CN (3 ml) and **2** (0.45 mmol). The mixture was stirred at 30 °C and the reaction was monitored by TLC. Upon completion, the stirring bar was removed and the mixture was evaporated under reduced pressure to give the crude products. The crude mixture was purified by column chromatography (silica gel, EtOAc/Petroleum) to provide following compounds.

Table 1 Optimization of Lewis base-Catalyzed Direct Allylic Alkylation of α-Amino Nitrile 1a with MBH Carbonate 2 [a]



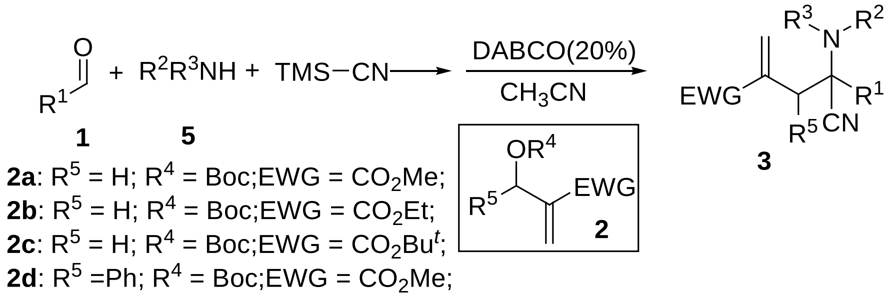
2a: R^4 = Boc; **2e**: R^4 = Ac;

entry	catalyst	solvent	*t* (h)	yield （%） [b]
1	DABCO	$PhCH_3$	4	52(**3a**); 14(**13**)
2	DABCO	DCM	9	50(**3a**); 18(**13**)
3	DABCO	THF	4	36(**3a**); 33(**13**)
4	DABCO	$CHCl_3$	22	40(**3a**); 43(**12**) [e]
5	DABCO	1,4-dioxane	15	62(**3a**)
6	DABCO	*t*-BuOH	9	56(**3a**)
7	DABCO	DMF	2	79(**3a**); 5(**4a**)
8	DABCO	CH_3CN	3.5	32(**3a**); 50(**4a**)
9[c]	DABCO	CH_3CN	14	93(**3a**)

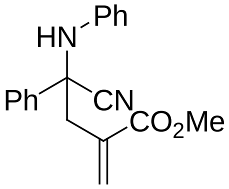
10[d]	DABCO	CH_3CN	22	35(**3a**)
11	DMAP	CH_3CN	2.5	44(**3a**); 50(**4a**)
12	Ph_3P	CH_3CN	2.5	50(**3a**)

[a] Unless otherwise noted, reactions were performed with 0.3 mmol of **1a**, 0.45 mmol of **2a**, and 20 mol % of catalyst in 3.0 mL of solvent at 30 °C. [b] Isolated yield. [c] 4Å molecular sieve was added and the reaction was performed at 0 °C. [d] MBH acetate **2e** (0.45 mmol) was employed. [e] Based on ^{1}H NMR of the mixture **1a** and **12** which can't be separated by column chromatography.

IV. General Procedure for Tandem Organocatalytic Strecker-Allylic-Alkylation Reaction



To a dried reaction tube were added aldehyde (0.3 mmol) and amine (0.315 mmol). After the mixture was stirred at rt for 10 min, TMSCN (0.33 mmol) was added, and the mixture was vigorously stirred.[1] After 50 min, CH_3CN (3 ml), DABCO (20%) and compound **2** (0.45 mmol) were added. The reaction was monitored by TLC. Upon completion, the stirring bar was removed and the mixture was evaporated under reduced pressure to give the crude products. The crude mixture was purified by column chromatography (silica gel, EtOAc/Petroleum) to provide **3.**



3aa

3aa: This compound was synthesized according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 87 mg of a white solid. (95%, yield). mp 118 -119 °C. ^{1}H NMR (300 MHz, $CDCl_3$) 7.61-7.58 (m, 2H), 7.42 - 7.34 (m, 3H), 7.11 - 7.06 (m, 2H), 6.76-6.71 (m, 1H), 6.52 – 6.47 (m, 2H), 6.46 - 6.44 (m, 1H), 5.86 (br,1H), 5.73 - 5.72 (m, 1H), 3.82 (s, 3H), 3.08 (d, J = 13.8 Hz, 1H), 3.01 (d, J = 13.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.60, 143.40, 138.07, 133.19, 132.82, 128.91, 128.77, 128.63, 125.66, 119.16, 119.04, 115.09, 61.98, 52.56, 46.14. IR (KBr): 3371, 3065, 3028, 2925, 2869, 2245, 1726, 1632, 1607, 1527, 1499, 1321, 1203, 756, 732, 696 cm^{-1}. HRMS (ESI): HRMS (ESI): calcd. for $C_{19}H_{18}N_2O_2Na$ ($[M+Na]^+$): 329.1260, found 329.1258.

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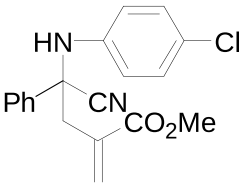
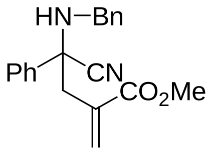
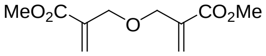


3ab

3ab: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 87 mg of a white amorphous solid (85%, yield). ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.57-7.54 (m, 2H), 7.43-7.35 (m, 3H), 7.03 (d, *J* = 8.7 Hz, 2H), 6.46 (s, 1H), 6.42 (d, *J* = 8.6 Hz, 2H), 6.07 (br, 1H), 5.74 (s, 1H), 3.83 (s, 3H), 3.06 (d, *J* = 13.9 Hz, 1H), 2.98 (d, *J* = 13.9 Hz, 1H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 168.79, 142.03, 137.61, 133.10, 133.00, 129.01, 128.79, 128.65, 125.55, 123.79, 118.88, 116.16, 62.05, 52.66, 46.10. IR (KBr): 3357, 3063, 2951, 2928, 2229, 1727, 1630, 1600, 1493, 1446, 1310, 1203, 818, 735, 698 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{18}ClN_2O_2$ ([M+H]$^+$): 341.1051, found 341.1052.

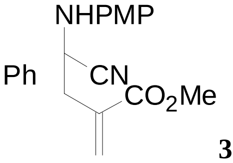


3ac



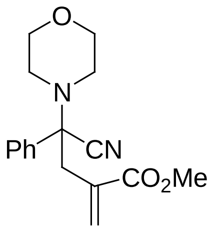
8

3ac: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded a oil (inseparate mixture of **3ac** (77%, yield) and ether **8** [8] (**3ac**/**8** = 7.2/1, based on ^{1}H NMR).^{1}H NMR (300 MHz, CDCl$_3$) δ 7.67 – 7.63 (m, 2H), 7.43 – 7.24 (m, 8H), 6.28 (s, 1H), 5.45 (s, 1H), 3.86 (d, *J* = 12.5 Hz, 1H), 3.67-2.52 (m, 1H), 3.62 (s, 3H), 3.14 (d, *J* = 13.5 Hz, 1H), 2.94 (d, *J* = 13.5 Hz, 1H), 2.16 (br, 1H). HRMS (ESI): calcd. for $C_{20}H_{20}N_2O_2Na$ ([M+H]$^+$): 343.1417, found 343.1410.



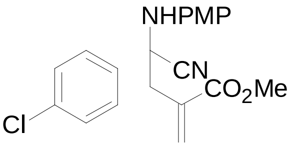
3ad

3ad: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:13), which afforded 97 mg of a white solid (96%, yield). mp 105 -107 °C. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.61-7.57 (m, 2H), 7.42-7.34(m, 3H), 6.68 – 6.65 (m, 2H), 6.47 – 6.44 (m, 2H), 6.43-6.41 (m, 1H), 5.67-5.66 (m, 1H), 5.42 (br, 1H), 3.80 (s, 3H), 3.68 (s, 3H), 3.04 (s, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 163.25, 148.08, 133.11, 132.22, 128.24, 127.29, 123.76, 123.53, 120.77, 114.39, 111.70, 109.25, 57.69, 50.48, 47.56, 40.85. IR (KBr): 3378, 3034, 2929, 2854, 2227, 1724, 1629, 1521, 1512, 1464, 1461, 1246, 1170, 813, 746, 693 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{21}N_2O_3$ ([M+H]$^+$): 337.1547, found 337.1541.



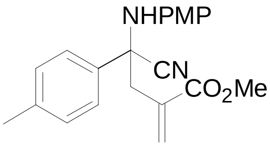
3ae

This compound was prepared according to the general procedure, except that **2** (3.0 eq) was added before the excess of TMSCN was evaporated under reduced pressure when the first step was finished. The product was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 60 mg of a white solid (67%, yield). mp 56 – 59 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 - 7.48 (m, 2H), 7.35 – 7.31 (m, 3H), 6.13 (s, 1H), 5.49 (s, 1H), 3.82 – 3.69 (m, 4H), 3.43 (s, 3H), 3.20 (d, *J* = 12.9 Hz, 1H), 2.97 (d, *J* = 12.9 Hz, 1H), 2.76-2.73 (m, 2H), 2.56-2.50 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.40, 130.55, 129.05, 124.86, 123.60, 123.19, 122.47, 111.36, 66.13, 61.66, 46.58, 43.55, 34.60. IR (KBr): 3002, 2959, 2891, 2852, 2217, 1721, 1631, 1487, 1246, 1202, 724, 703 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{21}N_2O_3$ ($[M+H]^+$): 301.1547, found 301.1544.



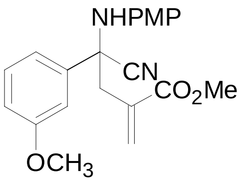
3b

3b: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:13), which afforded 78 mg of a white solid (70%, yield). mp 90 -91 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.6 Hz, 2H), 7.36 (d, *J* = 8.6 Hz, 2H), 6.67 (d, *J* = 8.9 Hz, 2H), 6.45 – 6.43 (m, 3H), 5.67 (s, 1H), 5.44 (s, 1H), 3.79 (s, 3H), 3.68 (s, 3H), 3.02 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.27, 153.22, 136.89, 136.79, 134.48, 133.01, 132.70, 128.99, 127.34, 119.05, 116.74, 114.33, 62.11, 55.36, 52.52, 45.77. IR (KBr): 3336, 3045, 2938, 2838, 1724, 1512, 1487, 1314, 1248, 1199, 815, 772 cm^{-1}. HRMS (ESI): calcd. For $C_{20}H_{19}ClN_2O_3Na$ ($[M+Na]^+$): 393.0976, found 393.0972.



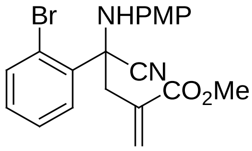
3c

3c: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 95 mg of a white solid (91%, yield). mp 70 - 72 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.2 Hz, 2H), 6.68 – 6.64 (m, 2H), 6.49 – 6.44 (m, 2H), 6.42 (s, 1H), 5.67 (s, 1H), 5.38 (br, 1H), 3.79 (s, 3H), 3.68 (s, 3H), 3.02 (s, 2H), 2.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.41, 153.16, 138.49, 137.46, 135.29， 133.44, 132.41, 129.53, 125.79, 119.60, 116.82, 114.35, 62.47, 55.43, 52.48, 46.06, 20.99. IR (KBr): 3371, 3033, 2951, 2857, 1732, 1511, 1248, 1203, 814, 774 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{22}N_2O_3Na$ ($[M+Na]^+$): 373.1523, found 373.1521.



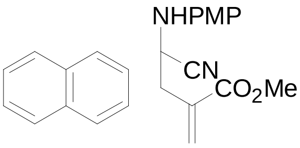
3d

3d: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 87 mg of a colourless oil (79%, yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.9 Hz, 1H), 7.20-7.18 (m, 1H), 7.14–7.12 (m, 1H), 6.87 (dd, *J* = 8.0, 2.4 Hz, 1H), 6.69 – 6.66 (m, 2H), 6.49 – 6.46 (m, 2H), 6.44(s, 1H), 5.71 (s, 1H), 5.43 (br, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.68 (s, 3H), 3.08 – 2.98 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.50, 160.03, 153.25, 140.08, 137.36, 133.41, 132.50, 129.96, 119.38, 118.06, 116.75, 114.35, 114.02, 111.55, 62.69, 55.44, 55.27, 52.52, 45.97. IR (film): 3365, 3057, 2838, 2229, 1706, 1511, 1488, 1243, 1199, 825, 739 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{22}N_2O_4Na$ ($[M+Na]^+$): 389.1472, found 389.1475.



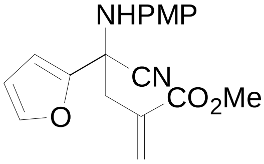
3f

3f: This compound was prepared according to the general procedure except that the excess of TMSCN was evaporated under reduced pressure after the 1ststep Strecker reaction was run for 4 h. The product was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded a inseparate mixture of **3f** (78%, yield) and α-amino nitrile **9** which was generated from 2-Bromobenzaldehyde, *p*-anisidine and TMSCN (**3f**/**9** = 8.4/1, based on ^{1}H NMR). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 – 7.63 (m, 2H), 7.34 – 7.28 (m, 1H), 7.24 – 7.18 (m, 1H), 6.72 – 6.66 (m, 2H), 6.51 – 6.46 (m, 3H), 5.89-5.87 (m, 2H), 3.84 (s, 3H), 3.69 (s, 3H), 3.40 (d, *J* = 13.5 Hz, 1H), 3.22 (d, *J* = 13.9 Hz, 1H). HRMS (ESI): calcd. for $C_{20}H_{20}BrN_2O_3$ ($[M+H]^+$): 415.0652, found 415.0647.



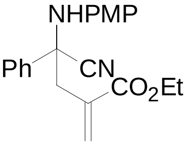
3g

3g: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 96 mg of a white solid (83%, yield). mp 103-104 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.87-7.82 (m, 3H), 7.69-7.66 (m, 1H), 7.52-7.49 (m, 2H), 6.63 (d, *J* = 8.9 Hz, 2H), 6.50 (d, *J* = 8.9 Hz, 2H), 6.42 (s, 1H), 5.69 (s, 1H), 5.51 (s, 1H), 3.73 (s, 3H), 3.64 (s, 3H), 3.15 (d, *J* = 13.8 Hz, 1H), 3.09 (d, *J* = 13.8 Hz, 1H). ^{13}C (75 MHz, $CDCl_3$) δ 168.39, 153.34, 137.45, 135.88, 133.50, 133.28, 133.05, 132.59, 129.03, 128.30, 127.65, 126.73，126.64, 125.51，123.09，119.56, 117.03, 114.45, 63.02, 55.42, 52.49, 45.91. IR (KBr): 3402, 3062, 2955, 2852, 1657, 1513, 1242, 1174, 818 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{22}N_2O_3Na$ ($[M+Na]^+$): 409.1523, found 409.1519.



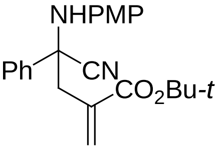
3h

3h: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:13), which afforded 74 mg of a yellow oil (76%, yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 1.7, 0.8 Hz, 1H), 6.74 – 6.70 (m, 2H), 6.66 – 6.63 (m, 2H), 6.45-6.43 (m, 1H), 6.39 (dd, *J* = 3.3, 0.8 Hz, 1H), 6.33 (dd, *J* = 3.3, 1.8 Hz, 1H), 5.73-5.71 (m, 1H), 4.90 (br, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 3.26 (d, *J* = 13.8 Hz, 2H), 3.15 (d, *J* = 13.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.86, 154.24, 149.21, 143.04, 136.94, 133.14, 131.93, 118.78, 117.77, 114.24, 110.54, 109.81, 58.76, 55.35, 52.44, 42.05. IR (film): 3062, 3035, 2954, 2192, 1718, 1650, 1509, 1150, 819 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{19}N_2O_4$ ([M+H]$^+$): 327.1339, found 327.1338.



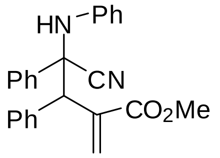
3af

3af: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 100 mg of a white solid (95%, yield). mp 80 -82 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61-7.58 (m, 2H), 7.42 – 7.33 (m, 3H), 6.68-6.64 (m, 2H), 6.47-6.43 (m, 3H), 5.66 (s, 1H), 5.50 (br, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.68 (s, 3H), 3.04 (s, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.04, 153.15, 138.45, 137.37, 133.63, 132.24, 128.87, 128.60, 125.85, 119.48, 116.71, 114.38, 62.68, 61.68, 55.54， 46.00, 14.05. IR (KBr): 3376, 2997, 2832, 2231, 1718, 1627, 1518, 1240, 1189, 829, 759, 698 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{22}N_2O_3Na$ ([M+Na]$^+$): 373.1523, found 373.1521.



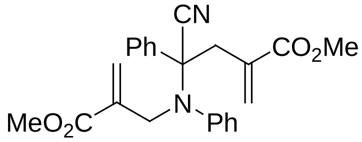
3ag

3ag: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 106 mg of a white solid (94%, yield). mp 93 - 95 °C. ^{1}H NMR (300 MHz, $CDCl_3$) 7.61-7.58 (m, 2H), 7.42 – 7.33 (m, 3H), 6.68 – 6.65 (m, 2H), 6.45 – 6.42 (m, 2H), 6.34 (s, 1H), 5.64 (s, 1H), 5.58 (br, 1H), 3.67 (s, 3H), 3.02 (d, *J* = 13.7 Hz, 1H), 2.96 (d, *J* = 13.8 Hz, 1H), 1.53 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.46, 153.13, 138.70, 137.58, 135.01, 131.54, 128.95, 128.61, 125.85, 119.55, 116.58, 114.47, 82.17, 62.84, 55.52, 45.94, 27.99. IR (KBr): 3381, 3065, 3031, 2949, 2234, 1709, 1626, 1525, 1507, 1246, 1161, 818, 754, 692 cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{26}N_2O_3$ Na ([M+Na]$^+$): 401.1836, found 401.1834.



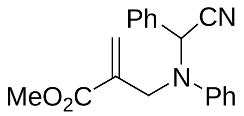
3ah

3ah: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:10), which afforded a crude product which was recrystallized to provide a white solid (9%, yield). mp 167-168 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 – 7.62 (m, 4H), 7.45 – 7.34 (m, 6H), 7.03 (t, *J* = 7.8 Hz, 2H), 6.75 (t, *J* = 7.3 Hz, 1H), 6.55 (s, 1H), 6.36 (d, *J* = 8.0 Hz, 2H), 6.33 (s, 1H), 4.76 (s, 1H), 4.48 (s, 1H), 3.42 (s, 3H). IR (KBr): 3373, 3113, 3060, 2872, 2241, 1726, 1631, 1602, 1500, 1450, 1248, 1146, 750, 698 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{23}N_2O_2$ ($[M+H]^+$): 383.1754, found 383.1747.



13

13: (see Table 1); mp 91-94 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 – 7.67 (m, 2H), 7.53 – 7.50 (m, 2H), 7.40 – 7.33 (m, 5H), 7.30-7.26 (m, 1H)， 6.09 (s, 1H), 6.06 (t, *J* = 1.3 Hz, 1H), 5.63-5.61 (m, 1H), 5.40-5.38 (m, 1H), 4.06 (d, *J* = 14.7 Hz, 1H), 3.70 (dt, *J* = 15.0, 3.0 Hz, 1H), 3.63 (s, 3H), 3.34 (s, 3H), 2.93 (d, *J* = 13.0 Hz, 1H), 2.47 (d, *J* = 13.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.56, 166.50, 145.22, 136.64, 136.54, 134.17, 130.29, 129.18, 128.96, 128.49, 128.23, 127.69, 127.43, 118.73, 71.03, 52.63, 51.69, 42.74. IR (KBr): 3348, 3061, 2929, 2854, 2224, 1725, 1633, 1494, 1200, 1155, 729, 703 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{25}N_2O_4$ ($[M+H]^+$): 405.1809, found 405.1815.

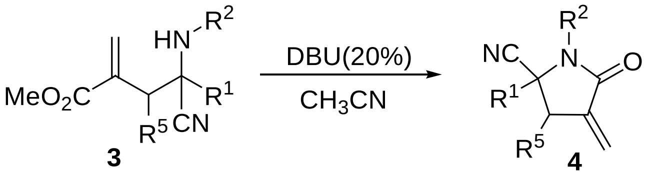


12

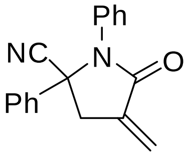
Inseparate mixture of **12**, **1a** and ether **8** (See Table 1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 – 7.38 (m, 5H), 7.30 – 7.25 (m, 2H), 6.99 – 6.89 (m, 3H), 6.25 – 6.24 (m, 1H), 5.85 (s, 1H), 5.74 – 5.73 (m, 1H), 4.20 (d, *J* = 18.0 Hz, 1H), 4.07 (d, *J* = 17.8 Hz, 1H). HRMS (ESI): calcd. for $C_{19}H_{19}N_2O_2$ ($[M+H]^+$): 307.1441, found 307.1435.

V. General Procedure for the Synthesis of α-Methylene-γ-Butyrolactones

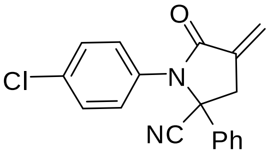


To a dried round-bottom flask were added **3** (0.25 mmol) and CH_3CN (2.5 mL). To this solution was added DBU (20%) at 0 ^{o}C and the mixture was warmed to rt. The reaction was monitored by TLC. Upon completion, the reaction mixture was washed with brine. The mixture was extracted with ethyl acetate. The combined organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo.* The crude mixture was purified by column chromatography (silica gel, EtOAc/Petroleum) to provide **4** .



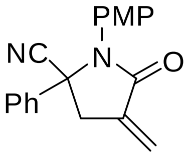
4a

4a: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 61 mg of a white solid (89%, yield). mp 80-82 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 – 7.45 (m, 2H), 7.41 – 7.37 (m, 3H), 7.31 – 7.20 (m, 5H), 6.38 (t, *J* = 2.6 Hz, 1H), 5.66 (t, *J* = 2.3 Hz, 1H), 3.75 (dt, *J* = 17.0, 2.4 Hz, 1H), 3.32 (dt, *J* = 17.0, 2.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.42, 136.76, 135.47, 134.78, 129.45, 129.22, 128.89, 127.45, 125.79, 125.35, 119.69, 118.81, 63.61, 43.16. IR (KBr): 3062, 3008, 2927, 2854, 1717, 1661, 1592, 1491, 1452, 1350, 759, 699 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{15}N_2O$ ([M+H]$^+$): 275.1179, found 275.1172.



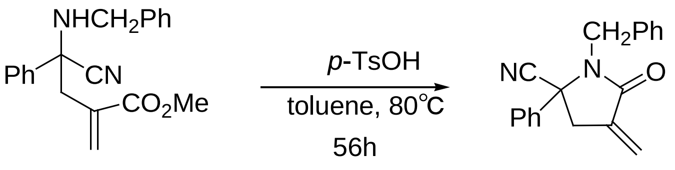
4b

4b: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 51 mg of a white solid (66%, yield). mp 75-77 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 – 7.39 (m, 5H), 7.25 (d, *J* = 8.8 Hz, 2H), 7.16 (d, *J* = 8.8 Hz, 2H), 6.38 (t, *J* = 2.5 Hz, 1H), 5.67 (t, *J* = 2.1 Hz, 1H), 3.75 (dt, *J* = 17.0, 2.2 Hz, 1H), 3.30 (dt, *J* = 17.0, 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.41, 136.51, 134.49, 134.07, 133.22, 129.71, 129.45, 129.19, 126.99, 125.34, 120.22, 118.68, 63.58, 43.17. IR (KBr): 3105, 3049, 2955, 2921, 1714, 1665, 1493, 1452, 1340, 828, 759, 696 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{14}ClN_2O$([M+H]$^+$): 309.0789, found 309.0798.



4c

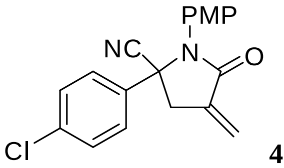
4c: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 70 mg of a white solid (92%, yield). mp 100-102°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48-7.44 (m, 2H), 7.40-7.37 (m, 3H), 7.05 (d, *J* = 9.0 Hz, 2H), 6.77 (d, *J* = 9.1 Hz, 2H), 6.34 (t, *J* = 2.7 Hz, 1H), 5.63 (t, *J* = 2.3 Hz, 1H), 3.76 – 3.69 (m, 1H), 3.71 (s, 3H), 3.33 (dt, *J* = 17.2, 2.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.63, 158.77, 136.82, 134.80, 129.46, 129.15, 127.95, 127.87, 125.50, 119.38, 118.82, 114.24, 63.95, 55.14, 42.58. IR (KBr): 3106, 3063, 2959, 2937, 2909, 1716, 1670, 1511, 1451, 1356, 1255, 828, 751, 699 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{17}N_2O_2$ ([M+H]$^+$): 305.1285, found 305.1281.



3ac **4d**

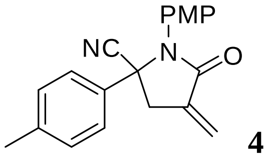
To a solution of **3ac** (98 mg, 0.3 mmol) in toluene (3 ml) was added *p*-TsOH (10 mg, 0.06 mmol) and stirred at 80℃ for 56 h.[7] The mixture was filtrated through a pad of Celite and the precipitate washed with dichloromethane (3×10 ml). The organic phase was evaporated in vapor and the residue was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6) to give **4d** (45 mg, 52%) as yellow oil.

4d: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 5H), 7.21 – 7.16 (m, 3H), 7.12– 7.09 (m, 2H), 6.30 (t, *J* = 2.7 Hz, 1H), 5.56 (t, *J* = 2.3 Hz, 1H), 4.73 (d, *J* = 14.9 Hz, 1H), 4.18 (d, *J* = 14.9 Hz, 1H), 3.58 (dt, *J* = 17.3, 2.4 Hz, 1H), 3.14 (dt, *J* = 17.3, 2.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.48, 136.02, 135.20, 134.60, 129.60, 129.25, 129.00, 128.28, 127.78, 125.62, 119.00, 118.15, 62.20, 45.67, 42.81. IR (KBr): 3065, 2956, 2852, 1709, 1665, 1497, 1452, 1355, 764, 701 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{17}N_2O$ ([M+H]$^+$): 289.1335, found 289.1338.



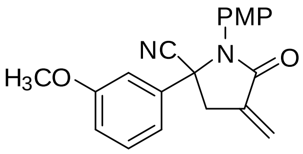
4e

4e: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 69 mg of a white solid (82%, yield). mp 136-137°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.35 (m, 4H), 7.05 (d, *J* = 9.0 Hz, 2H), 6.80 (d, *J* = 9.0 Hz, 2H), 6.37 (t, *J* = 2.7 Hz, 1H), 5.66 (t, *J* = 2.3 Hz, 1H), 3.78-3.71 (m, 1H), 3.75 (s, 3H), 3.28 (dt, *J* = 17.1, 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.52, 153.90, 130.51, 130.31, 129.36, 124.33, 122.84, 122.63, 122.02, 114.76, 113.51, 109.34, 58.42, 50.15, 37.44. IR (KBr): 3057, 3040, 2972, 2841, 1714, 1663, 1513, 1356, 1250, 823 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{16}ClN_2O_2$ ([M+H]$^+$): 339.0895, found 339.0903.



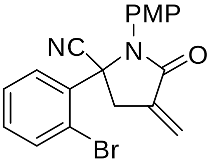
4f

4f: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 64 mg of a white amorphous solid (81%, yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.05 (d, *J* = 9.0 Hz, 2H), 6.78 (d, *J* = 9.0 Hz, 2H), 6.34 (t, *J* = 2.7 Hz, 1H), 5.63 (t, *J* = 2.3 Hz, 1H), 3.76 – 3.68 (m, 1H), 3.74 (s, 3H), 3.31 (dt, *J* = 17.1, 2.6 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.65, 153.75, 134.49, 129.89, 128.73, 124.74, 122.87, 120.40, 114.26, 113.93, 109.17, 58.78, 50.10, 37.61, 15.87. IR (KBr): 3031, 2957, 2933, 2839, 1713, 1663, 1513, 1358, 1249, 830, 815 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{19}N_2O_2$([M+H]$^+$): 319.1441, found 319.1446.



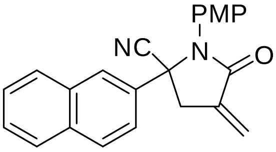
4g

4g: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 58 mg of a white solid (70%, yield). mp 107-109°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (t, *J* = 8.0 Hz, 1H), 7.12-7.08 (m, 2H), 7.06-7.03 (m, 1H), 6.98 – 6.96 (m, 1H), 6.91-6.88 (m, 1H), 6.82 – 6.79 (m, 2H), 6.35 (t, *J* = 2.7 Hz, 1H), 5.64 (t, *J* = 2.3 Hz, 1H), 3.78 (s, 3H), 3.76 – 3.68 (m, 1H), 3.75 (s, 3H), 3.31 (dt, *J* = 17.2, 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.72, 160.04, 158.81, 138.39, 134.76, 130.36, 127.99, 127.77, 119.49, 118.84, 117.58, 114.58, 114.27, 111.52, 63.88, 55.26, 55.19, 42.63. IR (KBr): 3069, 2967, 2840, 2239, 1714, 1662, 1601, 1513, 1494, 1465, 1355, 1248, 812, 793, 704 cm^{-1}. HRMS (ESI): calcd. For $C_{20}H_{19}N_2O_3$ ([M+H]$^+$): 335.1390, found 355.1384.



4h

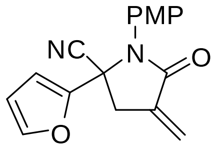
4h: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 55 mg of a colorless oil (58%, yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77-7.74 (m, 1H), 7.67-7.64 (m, 1H), 7.35-7.30 (m, 1H), 7.28 – 7.21 (m, 3H), 6.82-6.77 (m, 2H), 6.37 (t, *J* = 2.6 Hz, 1H), 5.64 (t, *J* = 2.3 Hz, 1H), 3.79 (dt, *J* = 17.6, 2.7 Hz, 1H), 3.73 (s, 3H), 3.67 (dt, *J* = 17.6, 2.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.11, 158.75, 136.18, 135.14, 132.69, 131.19, 130.80, 127.98, 127.86, 127.21, 120.52, 119.46, 118.91, 114.22, 65.35, 55.18, 39.52. IR (film): 3059, 2961, 2840, 1714, 1663, 1514, 1362, 1264, 736, 702 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{16}BrN_2O_2$([M+H]$^+$): 383.0390, found 383.0393.



4i

4i:This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 75 mg of a white solid (85%, yield). mp 135-136 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 – 7.99 (m, 1H), 7.90 (d, *J* = 8.7 Hz, 1H), 7.86 – 7.82 (m, 2H), 7.59 – 7.51 (m, 2H), 7.45 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.08 (d, *J* = 9.1

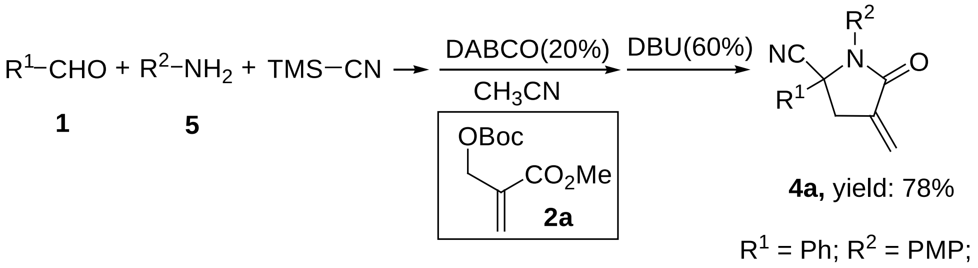
Hz, 2H), 6.74 (d, *J* = 9.1 Hz, 2H), 6.40 (t, *J* = 2.6 Hz, 1H), 5.67 (t, *J* = 2.2 Hz, 1H), 3.80 (dt, *J* = 17.3, 2.3 Hz, 1H), 3.70 (s, 3H), 3.42 (dt, *J* = 17.3, 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.83, 153.84, 129.80, 128.77, 128.14, 127.46, 124.71, 123.25, 122.96, 122.89, 122.55, 122.33, 122.10, 120.96, 116.54, 114.55, 113.90, 109.27, 59.22, 50.05, 37.33. IR (KBr): 3003, 2966, 2853, 1719, 1653, 1559, 1541, 1507, 1251, 828 cm^{-1}. HRMS (ESI): calcd. For $C_{23}H_{19}N_2O_2$ ([M+H]$^+$): 355.1441, found 355.1443.



4j

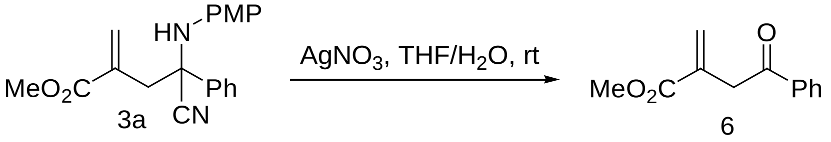
4j:This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 40 mg of a yellow oil (55%, yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 1.9, 0.9 Hz, 1H), 6.93-6.89 (m, 2H), 6.87-6.82 (m, 2H), 6.48 (dd, *J* = 3.4, 0.9 Hz, 1H), 6.34-6.32 (m, 2H), 5.66 (t, *J* = 2.3 Hz, 1H), 3.78(s, 3H), 3.64 (dt, *J* = 17.1, 2.7 Hz, 1H), 3.56 (dt, *J* = 16.8, 2.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.50, 159.64, 146.79, 144.29, 134.36, 128.97, 127.17, 119.43, 117.64, 114.53, 112.04, 110.97, 59.07, 55.28, 37.68. IR (film): 3061, 2963, 2935, 2840, 1711, 1668, 1512, 1362, 1265, 829 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{15}N_2O_3$([M+H]$^+$): 295.1077, found 295.1080.

Procedure for the One Pot Synthesis of *α*-Methylene-*γ*-Butyrolactam



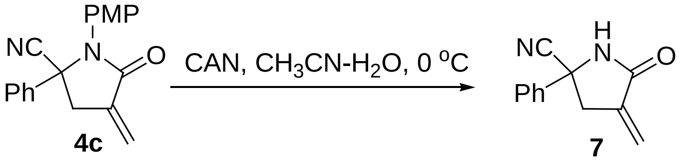
To a dried reaction tube were added aldehyde (0.3 mmol) and amine (0.315 mmol). After the mixture was stirred at rt for 10 min, TMSCN (0.33 mmol) was added. After the mixture was vigorously stirred for 50 min, CH_3CN (3 ml), DABCO (20%) and **2a** (0.45 mmol) were added. The reaction was monitored by TLC. After 2.5 h, DBU (60%) was added to the above mixture. Upon completion, the stirring bar was removed and the mixture was evaporated under reduced pressure to give the crude products. The crude mixture was purified by column chromatography (silica gel, EtOAc/Petroleum) to provide **4a.**

VI. Procedure for Chemical Transformations



3a (33.6 mg, 0.1 mmol) was dissolved in THF (0.68 mL) and treated with an aqueous solution (0.1 mL) of $AgNO_3$ (33.9 mg, 0.2 mmol) ^{5}. After stirring at room temperature for 18h, the solution was filtrated through a pad of Celite and the precipitate washed with ether (2×5 mL) and water (5 mL). The aqueous phase was extracted with ether (3×5 mL), the combined organic phase washed with brine (2×5 mL) and water (5 mL), dried over anhydrous Na_2SO_4, filtered and the solvent removed in vacuo. Purification by flash chromatography (silica gel, EtOAc/Petroleum 1/10) afforded the (16 mg, 78%) as red brown oil.[9]

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 – 7.90 (m, 2H), 7.66 – 7.31 (m, 3H), 6.51 – 6.30 (m, 1H), 5.79 – 5.60 (m, 1H), 4.10 – 3.95 (m, 2H), 3.74 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.84, 166.95, 136.59, 134.64, 133.33, 128.71, 128.66, 128.32, 52.15, 41.78.



To a solution of **4c** (213 mg, 0.7 mmol) in CH_3CN (5.0 ml) was added aqueous cerium ammonium nitrate (1.9 g, 3.43 mmol) solution (5.0 ml) at 0˚C. [6] After being stirred at 0 °C for 4 h, the reaction mixture was quenched by addition of sat. $NaHCO_3$ (aq.) solution (15 ml). The aqueous layer was extracted with diethyl ether (10 ml) and the combined organic layers were successively washed with 5% Na_2SO_3 solution, sat. $NaHCO_3$ (aq.) solution and brine, and dried over anhydrous Na_2SO_4. The solvent was evaporated in vacuo to leave crude material, which was purified by column chromatography (silica gel, EtOAc/Petroleum = 1:5) to afford 58 mg of a white solid in 42% yield. mp 88-90 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56-7.42 (m, 5H), 6.20 (t, J = 2.7 Hz, 1H), 5.55 – 5.54 (m, 1H), 3.65 (dt, J = 17.1, 2.1 Hz, 1H), 3.10 (dt, J = 17.1, 2.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.87, 138.23, 135.11, 129.48, 129.43, 124.62, 119.98, 119.57, 57.20, 43.76. IR (KBr): 3438, 3011, 2927, 2856, 1680, 1632, 1527, 1346, 740 cm^{-1}. HRMS (ESI): calcd. for $C_{12}H_{11}N_2O$ ($[M+H]^+$): 199.0866, found 199.0868.

VII. NMR Spectra and HPLC Spectra

VIII. References

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