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Asymmetric Synthesis of β-Nitro Ketones via Michael Addition of Lithiated α-Amino Nitriles to Nitroalkenes†

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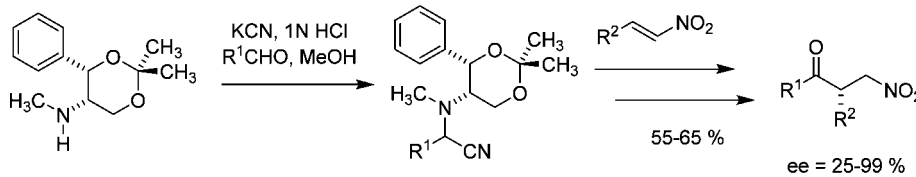

R^1 = Piperonyl, *p*-MeOPh, *p*-BrPh, *i*-Pr
R^2 = Et, *i*-Pr, *t*-Bu, *c*-Hex, *p*-Tol

α-Amino nitriles, easily prepared from aldehydes, KCN, and an enantiopure secondary amine auxiliary, are metalated and used as nucleophiles in asymmetric Michael additions to nitroalkenes to afford the Michael adducts in good yields and good to excellent diastereoselectivities. After chromatographic purification, the diastereomerically pure 1,4-adducts are cleaved under acidic conditions to give the β-nitro ketones in good yields and with two exceptions in good to excellent enantiomeric excesses (ee = 86−99%). The absolute configuration was determined by X-ray structure analysis.

Introduction

α-Amino nitriles have played an important role as bifunctional compounds in organic chemistry ever since the report on the Strecker reaction in 1850.[1] Among the various synthetic applications, the use of metalated α-amino nitriles as masked acyl anion equivalents is a powerful nucleophilic acylation method.[2] The most widely used method for the Umpolung of the carbonyl reactivity is the Corey−Seebach reaction employing lithiated 1,3-dithianes.[3] Other protocols include catalytic conditions, such as the Stetter reaction,[4] and even neutral conditions employing aldehyde *N*,*N*-dialkylhydrazones.[5]

In early attempts to develop asymmetric nucleophilic acylations via metalated α-amino nitriles, we mainly used proline-derived chiral auxiliaries, but the enantiomeric excesses remained relatively low.[6] Later, high levels of asymmetric inductions were reached with (*S*,*S*)-2,2-dimethyl-5-methylamino-4-phenyl-1,3-dioxane [(*S*,*S*)-**1**], a chiral secondary amine auxiliary easily prepared on a mole scale from a commercially available pharmaceutical intermediate (wrong enantiomer in the chloramphenicol synthesis),[7] and a variety of electrophiles including Michael acceptors could be used.[8] Moreover, we recently developed an asymmetric nucleophilic glyoxylation method via metalated α-amino nitriles.[9]

† Dedicated to the memory of Professor Albert I. Meyers, a pioneer of asymmetric synthesis.

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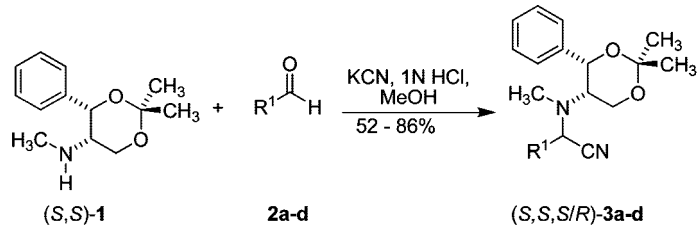
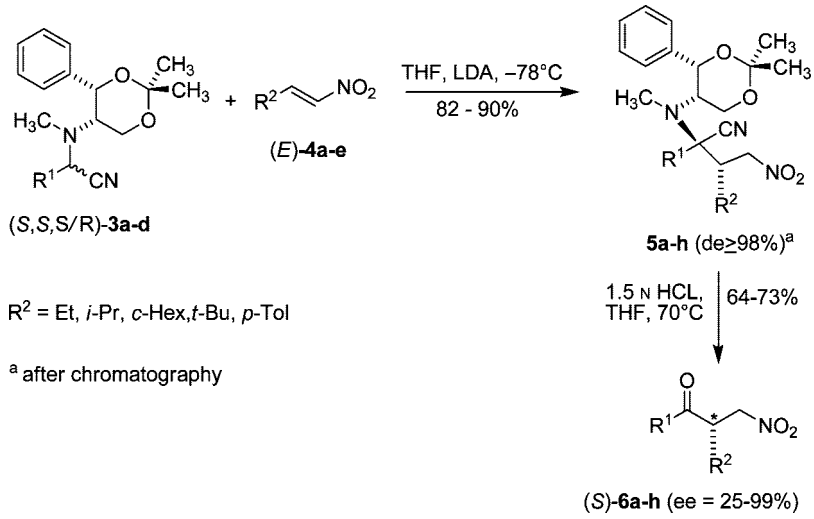
SCHEME 1. Preparation of the Chiral α-Amino Nitriles 3a−d



a: R^1 = Piperonyl (73%), **b**: R^1 = *p*-MeOPh (52%), **c**: R^1 = *p*-BrPh (78%), **d**: R^1 = *i*-Pr (86%)

SCHEME 2. Asymmetric Synthesis of β-Nitro Ketones 6



R^2 = Et, *i*-Pr, *c*-Hex,*t*-Bu, *p*-Tol

[a] after chromatography

Nitroalkenes are excellent Michael acceptors in asymmetric conjugate additions[10] and allow synthetic transformations of the nitro group to many other functionalities.[11] Based on our long experience with various nitroalkene 1,4-additions,[12] we envisaged the asymmetric synthesis of β-nitro ketones through a conjugate nucleophilic acylation protocol.[13]

Results and Discussion

β-Nitroketones constitute important bifunctional compounds, which may be transformed into other synthetic building blocks, such as β-aminoketones or 1,3-amino alcohols. Employing a well-established procedure,[8,14] we first synthesized four different α-amino nitriles **3a−d** derived from aromatic and an aliphatic aldehyde (**2a−d**) and the chiral auxiliary (*S*,*S*)-**1** in the presence of KCN under acidic conditions (Scheme 1). A chromatographic separation of the α-epimeric amino nitriles **3a−d** obtained in 52−86% yield is not necessary because in the subsequent metalation step the new stereogenic center is destroyed by formation of the corresponding *N*-lithio ketene imine intermediates.[8d,15]

As is depicted in Scheme 2, the conjugate addition of the α-amino nitriles **3** to aliphatic and aromatic *E*-configured nitroalkenes **4a−e**[16] was performed by lithiation of **3** for 1.5 h with 1.2 equiv of lithium diisopropylamide (LDA) in tetrahydrofuran at −78 °C, followed by the addition of the nitroalkenes **4** at −100 °C. In the case of the amino nitrile **3d** derived from the aliphatic aldehyde (R^1 = *i*-Pr), LDA had to be replaced by the stronger base potassium diisopropylamide (KDA) to reach good yields. The resulting Michael adducts **5a−h** were obtained in very good yields (82−90%) and moderate to excellent diastereoselectivities (ds = 62 − 97%) (Table 1). In all cases, a chromatographic purification gave the diastereomerically pure adducts **5** (de >98%). The best stereoselectivities were observed with sterically demanding groups R^2 (**5d**,**f**).

Finally, for the amino nitrile cleavage the standard protocols were tested using $CuSO_4$,[17] $AgNO_3$,[18] or HCl, respectively. The best results were obtained with 1.5 N HCl in refluxing THF for

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TABLE 1. Asymmetric Michael Addition of Lithiated Amino Nitriles 3a−d to Nitroalkenes 4a−e To Afford the 1,4-Adducts 5a−h

5	R^1	R^2	yield[a] (%)	ds[b] (de) (%)[c]	$[\alpha]_D^{26}$ ($CHCl_3$)
a	piperonyl	Et	90	63 (>98)	+73
b	piperonyl	*i*-Pr	89	88 (>98)	−19
c	piperonyl	*c*-Hex	90	74 (>98)	−39.5
d	piperonyl	*t*-Bu	82	95 (>98)	−37
e	piperonyl	tolyl	87	72 (>98)	+141
f	*p*-methoxyphenyl	*t*-Bu	82	97 (>98)	−7
g	*p*-bromphenyl	*t*-Bu	84	66 (>98)	−9.5
h	*i*-Pr	*i*-Pr	90	62 (>98)	−28.5

[a] Yield of the diastereomeric mixture. [b] Determined by HPLC. [c] Determined by NMR spectroscopy after chromatographic purification of the major diastereomer.

TABLE 2. Removal of the Chiral Auxiliary from the Michael Adducts 5a−h To Yield the β-Nitroketones 6a−h

6	R^1	R^2	yield (%)	ee[a] (%)	$[\alpha]_D^{26}$ ($CHCl_3$)
a	piperonyl	Et	73	86	−68
b	piperonyl	*i*-Pr	68	99	−83
c	piperonyl	*c*-Hex	70	95	−22
d	piperonyl	*t*-Bu	71	99	−81
e	piperonyl	tolyl	64	44	−8.5
f	*p*-methoxyphenyl	*t*-Bu	70	99	−138
g	*p*-bromphenyl	*t*-Bu	71	86	−100
h	*i*-Pr	*i*-Pr	72	25	−1.5

[a] Determined by HPLC on a chiral stationary phase (**6a**,**b**,**g**,**h**: Chiralpac OD, 250 mm × 4,6 mm, flow 0.5−1 mL/min, *n*-heptane/2-propanol 90:10−95:5; **6c**,**d**−**f**: Chiralpac AD, 250 mm × 4,6 mm, flow 0.5−1 mL/min, *n*-heptane/2-propanol 90:10−95:5).

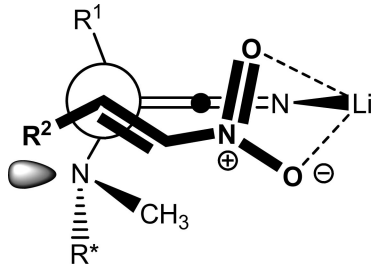

FIGURE 1. Proposed transition state.

15−30 min, and the β-nitro ketones **6a**−**h** could be isolated in good yields (64−73%) and high to excellent enantiomeric excesses (ee = 86−99%) (Table 2). However, in the case of an aromatic substituent R^2 (**6e**) and an aliphatic group R^1 (**6h**) a substantial racemization during the acidic nitrile cleavage could not be avoided.

The absolute configuration of the Michael adduct **5g** could be determined by X-ray structure analysis. In addition, suitable crystals of **6d** for X-ray analysis were obtained by slow crystallization from benzene.[19] Assuming a uniform reaction mechanism for all the Michael additions reported, the β-nitro ketone title compounds should all be *S*-configured.

It is interesting to note that the stereochemical outcome of the amino nitrile 1.4-additions to nitroalkenes is different from the relative topicity previously observed for other Michael acceptors.[8d] To explain the *S*-configuration, we propose the transition state given in Figure 1, which includes an *N*-lithio ketene imine to nitroalkene Si−Si attack and an attractive interaction via the lithium cation.

In conclusion, we have developed an efficient asymmetric synthesis of β-nitro ketones through the Michael addition of metalated α-amino nitriles to nitroalkenes and subsequent acidic hydrolysis. After chromatographic purification of the intermediate Michael adducts, high enantiomeric excesses (ee = 86−99%) of the title compounds could be obtained. In the case of an aromatic nitroolefin and an aliphatic aldehyde, however, a substantial racemization during the amino nitrile cleavage was observed. The absolute configuration of the β-nitro ketones could be determined as *S* by X-ray crystallography.

Experimental Section

(4*S*,5*S*,2*R*/*S*)-Benzo[1,3]dioxol-5-yl[*N*-(2,2-dimethyl-4-phenyl-1,3-dioxan-5yl)methylamino]acetonitrile (3a). Prepared from 33.40 g (150 mmol) of (*S*,*S*)-**1**, 22.50 g (150 mmol) of piperonal, and 9.80 g (150 mmol) of KCN. After crystallization from EtOH, **3a** was obtained as a diastereomeric mixture of colorless crystals (41.40 g, 73% yield): mp 118 °C; $[\alpha]^{26}_D = +108.8$ (c = 1.16, $CHCl_3$); IR (KBr) ν = 1483, 1237, 1204, 1087, 1039, 733 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.53, 1.57 (s, 3H), 1.55, 1.57 (s, 3H), 2.27, 2.40 (s, 3H), 2.85, 2,88 (td, J = 3.4, 1.4 Hz, 1H), 4.20, 4.32 (dd, J = 12.9, 3.3 Hz, 1H), 4,53,4.59 (dd, J = 12.9, 1.4 Hz, 1H), 5.24, 5.27 (d, J = 3.6 Hz, 1H), 5.40, 5.50 (s, 1H), 5.86 (d, J = 1.4 Hz, 1H), 5.87 (d, J = 1.4 Hz, 1H), 5.94−7.39 (m, 8H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 19.4, 30.1, 30.3, 33.8, 38.1, 57.6, 61.2, 58.0, 63.1, 59.7, 60.8, 74.1, 75.2, 99.6, 99.9, 101.8, 101.9, 108.0, 108.4, 108.2, 118.3, 118.6, 121.1, 121.2, 126.1, 126.3, 127.7, 128.6, 128.8, 129.5, 139.8, 140.9, 148.0, 148.3, 148.4, 148.6 ppm; MS (EI) m/z 380 (0.4 M^+), 216 (77), 215 (22), 176 (46), 175 (41), 161 (13), 160 (100), 91 (9), 77 (11), 41 (22). Anal. Calcd for $C_{22}H_{24}N_2O_4$ (380.44): C, 69.46; H, 6.36; N, 7.36. Found: C, 69.53, H, 6.45; N, 7.21.

(4*S*,5*S*,2*R*/*S*)-[*N*-(2,2-Dimethyl-4-phenyl-1,3-dioxan-5-yl)methylamino](4-methoxyphenyl)acetonitrile (3b). Prepared from 5.50 g (25 mmol) of (*S*,*S*)-**1**, 3.40 g (25 mmol) of *p*-methoxybenzaldehyde, and 1.63 g (25 mmol) of KCN. After crystallization from MeOH, **3b** was obtained as a diastereomeric mixture of colorless crystals (4.80 g, 52% yield): mp 128 °C; $[\alpha]^{26}D$ = + 104.07 (c = 1.43, $CHCl_3$); IR (KBr) ν 2947, 1610, 1509, 1382, 1253, 1200, 1175, 1121, 1079, 1045, 740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.53, 1.58 (s, 6H), 2.39 (s, 3H), 2.92 (m, 1H), 3.75 (s, 3H), 4.31, 4.35 (dd, J = 13.1, 3.4 Hz, 1H), 4.45 (s, 1H), 4.52, 4.57 (dd, J = 13.1, 1.5 Hz, 1H), 5.24 (d, J = 3.2 Hz, 1H), 6.60−7.40 (m, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 29.4, 33.1, 55.2, 60.2, 60.6, 62.3, 74.6, 99.1, 113.6, 117.8, 125.8, 126.0, 126.9, 128.1, 128.5, 140.1, 159.6 ppm; MS (EI) m/z 351 (3, M^+), 202 (52), 201 36), 162 (15), 161 (7), 147 (10), 146 (100), 91 (5). Anal. Calcd for $C_{22}H_{26}N_2O_3$ (366.45): C, 72.11; H, 7.15; N, 7, 64. Found: C, 72.42, H, 7.17; N, 7.73.

(4*S*,5*S*,2*R*/*S*)-2-(4-Bromophenyl)-2-[*N*-(2,2-dimethyl-4-phenyl-1.3-dioxan-5-yl)methylamino]acetonitrile (3c). Prepared from 11.06 g (50 mmol) of (*S*,*S*)-**1**, 9.25 g (50 mmol) of *p*-bromobenzaldehyde, and 2.70 g (5.4 mmol) of NaCN. After crystallization from MeOH, **3c** was obtained as a diastereomeric mixture of a colorless solid (16.10 g, 78% yield): mp 83 °C; $[\alpha]^{26}_D$ = + 94.17 (c = 1.00, $CHCl_3$); IR (KBr) ν 2986, 2939, 2869, 1479, 1383, 1197, 1074, 1046, 1002, 847, 741, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) major diastereomer δ 1.54, 1.59 (s, 6H), 2.39 (s, 3H), 2.90 (m, 1H), 4.21, 4.25 (dd, J = 13.1, 3.4 Hz, 1H), 4.45 (s, 1H), 4.52, 4.57 (dd, J = 13.1, 1.7 Hz, 1H), 5.29 (d, J = 3.3 Hz, 1H), 5.66 (s, 1H), 6.56−7.40 (m, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) major diastereomer δ 18.7, 29.7, 37.3, 57.6, 60.3, 74.5, 99.4, 117.1, 122.5, 125.6, 127.1, 128.2, 133.1, 134.2, 139.1, 140.1 ppm; MS (EI) m/z 401, 399 (4, $M^+ - CH_3$), 252 (99), 251 (80), 250 (100), 249 (67), 212 (18), 211 (25), 210 (19), 209 (25), 196

(19) CCDC 281281 (**5g**) and CCDC 696682 (**6d**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(30), 194 (28), 171 (28), 131 (60). Anal. Calcd for $C_{21}H_{23}N_2O_2Br$ (415.32): C, 60.73; H, 5.58; N, 6.74. Found: C, 61.02, H, 5.44; N, 6.06.

(4*S*,5S,2*R*/*S*)-2-[*N*-(2.2-Dimethyl-4-phenyl-1,3-dioxan-5-yl)methylamino]-3-methylbutanenitrile (3d). Prepared from 22.10 g (100 mmol) of (*S,S*)-**1**, 7.20 g (100 mmol) of 2-methylpropanal, and 6.5 g (100 mmol) of KCN. After crystallization from EtOH, **3d** was obtained as a diastereomeric mixture of a colorless solid (26.10 g, 86% yield): mp 58 °C; $[\alpha]^{26}_D = +110.84$ ($c = 1.00$, $CHCl_3$); IR (KBr) ν 2805, 1605, 1500, 1465, 1450, 1285 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.15, 0.30 (d, $J = 6.6$ Hz, 3H), 0.86, 0.94 (d, $J = 6.6$ Hz, 3H), 1.5−1.75 (m, 7H), 2.23, 2.53 (s, 3H), 2.66, 2.74 (m, 1H), 3.75, 4.55 (m, 3H), 5.15 (m, 1H), 7.28 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$ δ 17.6, 18.1, 18.5, 18.9, 19.7, 20.0, 29.2, 29.4, 29.6, 30.4, 32.8, 37.9, 58.2, 60.6, 59.7, 60.1, 61.8, 65.8, 73.6, 74.4, 99.0, 99.1, 119.2, 119.2, 119.5, 125.6, 125.7, 126.7, 126.9, 127.8, 127.9, 139.3, 139.9 ppm; MS (EI) *m*/*z* 302 (0.5, M^+), 287 (5), 244 (5), 227 (19), 138 (99), 123 (26), 105 (15), 98 (73), 96 (66), 95 (71), 91 (13), 77 (17), 57 (100), 43 (24), 42 (51), 41 (11), 28 (12), 27 (13). Anal. Calcd for $C_{18}H_{26}N_2O_2$ (302.42): C, 71.48; H, 8.66; N, 9.26. Found: C, 71.96, H, 8.67; N, 9.38.

General Procedure A. Diisopropylamine (1.2 equiv) was placed in a dry Schlenk flask, and absolute THF (10 mL per mmol diisopropylamine) was added. The reaction mixture was cooled to −78 °C, and *n*-BuLi (1.2 equiv) was added dropwise. The mixture was stirred at 0 °C for 30 min and cooled to −78 °C, and then the amino nitrile **3** (1.0 equiv) was added. After 1.5 h at −78 °C, the reaction mixture was cooled to −100 °C followed by addition of the Michael acceptor **4** (1.0 equiv) in THF (10 mL per mmol) via a syringe pump. The reaction mixture was stirred for 5 h and allowed to warm to −60 °C. After quenching by addition of satd NH_4Cl solution under vigorous stirring, H_2O was added and the organic phase was separated. The aqueous phase was extracted with Et_2O, and the combined organic layers were washed with brine, dried with $MgSO_4$, and evaporated in vacuo. The crude product **5** was purified by flash chromatography.

Amino Nitrile 5a. According to the general procedure A, the α-amino nitrile **3a** (1.14 g, 3.0 mmol), diisopropylamine (0.51 mL, 3.6 mmol) and *n*-BuLi (2.25 mL, 3.6 mmol) were dissolved in dry THF (30 mL). The nitroalkene **4a** (0.36 g, 3.6 mmol) was added immediately. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 2: 1 with 3% triethylamine) to afford the Michael adduct **5a** (1.29 g, 89% yield): mp 99 °C; $[\alpha]^{26}_D = +72.8$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 2988, 1555, 1488, 1441, 1380, 1243, 1035, 934, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.55 (m, 2H), 0.70 (t, $J = 7.4$ Hz, 3H), 1.46 (s, 3H), 1.52 (s, 3H), 2.71 (m, 1H), 3.04 (m, 1H), 3.14 (s, 3H), 3.55 (dd, $J = 13.7$, 4.1 Hz, 1H), 3.97 (dd,, $J = 13.4$, 4.1 Hz, 1H), 4.30 (d, br, $J = 13.7$ Hz, 1H), 4.66 (dd, $J = 13.4$, 1.3 Hz, 1H), 5.02 (d, $J = 3.8$ Hz, 1H), 5.96 (s, 2H), 6.64−7.44 (m, 8H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.3, 19.0, 25.6, 29.0, 35.0, 45.1, 54.0, 58.6, 72.3, 74.7, 75.4, 99.2, 101.7, 107.5, 108.4, 119.5, 125.7, 126.8, 127.6, 127.8, 127.9, 138.9, 148.0, 148.2 ppm; MS (EI) *m*/*z* 466 (6, $M^+ - CH_3^\bullet$), 317 (77), 301 (17), 300 (95), 271 (13), 261 (100), 257 (17), 231 (11), 215 (28), 214 (62), 185 (14), 184 (93), 177 (10), 156 (29), 128 (11), 105 (14), 91 (14), 83 (13), 72 (12). Anal.Calcd for $C_{26}H_{31}N_3O_6$ (481,55): C, 64.85; H, 6.49; N, 8.73. Found: C, 64.78; H, 6.26; N, 8.83.

Amino Nitrile 5b. According to the general procedure A, the α-amino nitrile **3a** (1.14 g, 3.0 mmol), diisopropylamine (0.51 mL, 3.6 mmol), and *n*-BuLi (2.25 mL, 3.6 mmol) were dissolved in dry THF (30 mL). The nitroalkene **4b** (0.41 g, 3.6 mmol) was added immediately. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 2:1 with 3% triethylamine) to afford the Michael adduct **5b** (1.33 g, 90% yield): mp 90 °C; $[\alpha]^{26}D = -19.1$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 3460, 2974, 1554, 1492, 1380, 1243, 1035, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.05 (d, $J = 7.1$ Hz, 3H), 0.86 (d, $J = 7.1$ Hz, 3H), 1.45, 1.53 (2s, 6H), 1.70 (m, 1H), 2.64 (s, 3H), 2.74 (m, 1H), 3.04 (m, 1H), 3.78 (dd, $J = 12.7$, 3.7 Hz, 1H), 3.96 (dd, $J = 13.5$, 4.1 Hz, 1H), 4.20 (d, br, $J = 12.7$ Hz, 1H), 4.66 (dd, $J = 13.5$, 1.9 Hz, 1H), 5.01 (d, $J = 4.4$ Hz, 1H), 5.98 (s, 2H), 6.84−7.44 (m, 8H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 19.1, 23.4, 27.2, 28.4, 31.1, 48.6, 53.8, 58.5, 71.0, 72.5, 75.4, 99.3, 101.6, 108.1, 108.4, 118.8, 125.7, 126.5, 127.2, 127.8, 128.0, 139.2, 148.0, 148.1 ppm; MS (EI) *m*/*z* 480 (2, $M^+ - CH_3$), 331 (46), 314 (48), 288 (14), 276 (16), 275 (100), 228 (33), 215 (12), 198 (21), 187 (20), 186 (26), 156 (26), 83 (14), 72 (11). Anal. Calcd for $C_{27}H_{33}N_3O_6$ (495.57): C, 65.44; H, 6.71; N, 8.48. Found: C, 65.31; H, 6.56; N, 8.61.

Amino Nitrile 5c. According to the general procedure A, the α-amino nitrile **3a** (1.14 g, 3.0 mmol), diisopropylamine (0.51 mL, 3.6 mmol), and *n*-BuLi (2.25 mL, 3.6 mmol) were dissolved in dry THF (30 mL). The nitroalkene **4c** (0.56 g, 3.6 mmol) was added immediately. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 2:1 with 3% triethylamine) to afford the Michael adduct **5c** (1.45 g, 90% yield): mp 102 °C; $[\alpha]^{26}_D = -39.5$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 2930, 2857, 1554, 1489, 1443, 1379, 1243, 1203, 1035 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.2−1.6 (m, 11H), 1.45 (s, 3H), 1.55 (s, 3H), 2.95 (m, 1H), 3.15 (s, 3H), 3.42 (m, 1H), 3.78 (dd, $J = 12.9$, 2.0 Hz, 1H), 3.96 (dd, $J = 13.1$, 4.2 Hz, 1H), 4.15 (d, br, $J = 12.9$ Hz, 1H), 4.67 (dd, $J = 13.1$, 2.0 Hz, 1H), 5.02 (d, $J = 4.2$ Hz, 1H), 5.98 (s, 2H), 6.84−7.44 (m, 8H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.2, 25.7, 26.1, 26.3, 26.9, 27.5, 28.9, 35.0, 38.7, 49.0, 53.9, 58.6, 71.2, 72.7, 75.6, 99.5, 101.8, 108.1, 108.5, 119.6, 125.8, 126.9, 127.4, 127.8, 128.1, 139.5, 148.1, 148.3 ppm; MS (EI) *m*/*z* 520 (3, $M^+ - CH_3^\bullet$), 371 (59), 354 (100), 315 (81), 311 (10), 288 (13), 268 (20), 215 (25), 187 (23), 186 (73), 156 (21), 83 (48), 72 (10), 55 (27). Anal. Calcd for $C_{30}H_{37}N_3O_6$ (535.64): C, 67.27; H, 6.96; N, 7.85. Found: C, 67.43; H, 6.87; N, 7.48.

Amino Nitrile 5d. According to the general procedure A, the α-amino nitrile **3a** (1.14 g, 3.0 mmol), diisopropylamine (0.51 mL, 3.6 mmol), and *n*-BuLi (2.25 mL, 3.6 mmol) were dissolved in dry THF (30 mL). The nitroalkene **4d** (0.46 g, 3.6 mmol) was added immediately. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 3:1 with 3% triethylamine) to afford the Michael adduct **5d** (1.25 g, 82% yield): mp 79 °C; $[\alpha]^{26}D = -36.9$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 2988, 1552, 1488, 1440, 1377, 1241, 1203, 1038, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.68 (s, 9H), 1.42 (s, 6H), 2.76 (s, 3H), 2.80 (dd, $J = 13.5$, 3.0 Hz, 1H), 3.22 (d, $J = 8.51$ Hz, 1H), 3.42 (m, 1H), 3.72 (dd, $J = 13.46$, 4.4 Hz, 1H), 3.8 (dd, $J = 15.4$, 4.4 Hz, 1H), 3.98 (dd, $J = 15.4$, 8.5 Hz, 1H), 5.24 (d, $J = 4.4$ Hz, 1H), 6.00 (s, 2H), 6.82−7.4 (m, 8H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 28.9, 29.7, 31.7, 35.1, 48.3, 55.0, 60.4, 69.2, 73.8, 74.3, 98.6, 101.6, 107.1, 107.7, 108.2, 119.2, 120.4, 125.6, 127.4, 127.8, 139.1, 147.3, 148.3 ppm; MS (EI) *m*/*z* 509 (0.4, M^+), 346 (10), 345 (61), 290 (18), 289 (100), 187 (14), 186 (87), 114 (51), 83 (48), 72 (30). Anal. Calcd for $C_{28}H_{35}N_3O_6$ (509.60): C, 65.99; H, 6.92; N, 8.25. Found: C, 65.68; H, 6.74; N, 8.58.

Amino Nitrile 5e. According to the general procedure A, the α-amino nitrile **3a** (1.14 g, 3.0 mmol), diisopropylamine (0.51 mL, 3.6 mmol), and *n*-BuLi (2.25 mL, 3.6 mmol) were dissolved in dry THF (30 mL). The nitroalkene **4e** (0.59 g, 3.6 mmol) was added immediately. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 3:1 with 3% triethylamine) to afford the Michael adduct **5e** (1.41 g, 87% yield): mp 122 °C; $[\alpha]^{26}D = +140.9$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 2987, 1555, 1487, 1442, 1379, 1242, 1202, 1121, 1037, 747 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.52 (s, 3H), 1.58 (s, 3H), 2.2 (s, 3H), 2.78 (s, 3H), 3.54 (m, 1H), 3.9 (dd, $J = 13.1$, 3.5 Hz, 1H), 4.1 (d, br, $J = 13.1$ Hz, 1H), 4.26 (dd, br, $J = 3.2$, Hz, 1H), 4.42 (dd, $J = 13.4$, 3.2 Hz, 1H), 5.00 (dd, $J = 13.4$, 3.5 Hz, 1H), 5.4 (d, $J = 3.5$ Hz, 1H), 5.9 (s, 2H), 6.8−7.5 (m, 12H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.0, 21.00, 29.3, 37.8, 48.5, 52.6, 58.9, 72.1, 73.5, 76.0, 99.5, 101.6, 107.0, 108.1, 118.9, 120.5, 125.9, 127.2, 128.1, 128.6, 129.2, 129.5, 130.2, 138.0, 139.0, 148.0, 148.2 ppm; MS (EI) *m*/*z* 528 (2, $M^+ - CH_3^\bullet$), 379 (94), 276 (11), 215 (100). Anal. Calcd

for $C_{31}H_{33}N_3O_6$ (543.62): C, 68.49; H, 6.12; N, 7.73. Found: C, 68.27; H, 6.40; N, 7.63.

Amino Nitrile 5f. According to the general procedure A, the α-amino nitrile **3b** (1.10 g, 3.0 mmol), diisopropylamine (0.51 mL, 3.6 mmol), and *n*-BuLi (2.25 mL, 3.6 mmol) were dissolved in dry THF (30 mL). The nitroalkene **4d** (0.46 g, 3.6 mmol) was added immediately. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 3:1 with 3% triethylamine) to afford the Michael adduct **5f** (1.22 g, 82% yield): mp 69 °C; $[\alpha]^{26}_D = -6.7$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 3679, 3451, 2962, 1609, 1552, 1511, 1377, 1260, 1187, 1028, 840, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.66 (s, 9H), 1.40 (s, 6H), 2.66 (dd, $J =$ 12.9, 1.7 Hz, 1H) 2.73 (s, 3H), 3.30 (dd, br, $J = 7.7$ Hz, 1H), 3.43 (m, 1H), 3.65 (dd, $J = 12.9$, 4.4 Hz, 1H), 3.82 (s, 3H), 3.84 (dd, $J = 15.7$, 7.7 Hz, 1H), 4.00 (dd, $J = 15.7$, 8.5 Hz, 1H), 5.24 (d, J = 4.4 Hz, 1H), 6.90−7.85 (m, 9H$_\cdot$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 28.9, 29.8, 31.5, 35.1, 48.3, 55.1, 55.2, 60.1, 69.0, 73.9, 74.4, 98.6, 113.5, 119.2, 125.7, 127.0, 127.8, 128.2, 131.8, 139.1, 159.8 ppm; MS (EI) *m*/*z* 495 (1, $M^{+\cdot}$), 331 (39), 275 (100), 172 (60), 114 (29), 83 (23), 72 (12), 57 (92). Anal. Calcd for $C_{28}H_{37}N_3O_5$ (495.62): C, 67.86; H, 7.52; N, 8.48. Found: C, 67.59; H, 7.87; N, 8.21.

Amino Nitrile 5g. According to the general procedure A, the α-amino nitrile **3c** (1.25 g, 3.0 mmol), diisopropylamine (0.51 mL, 3.6 mmol), and *n*-BuLi (2.25 mL, 3.6 mmol) were dissolved in dry THF (30 mL). The nitroalkene **4d** (0.46 g, 3.6 mmol) was added immediately. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 5:1 with 3% triethylamine) to afford the Michael adduct **5g** (1.37 g, 84% yield): mp 151 °C; $[\alpha]^{26}_D = -9.6$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 2931, 1731, 1544, 1483, 1376, 1285, 1124, 1078, 1015, 850, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.52 (s, 9H), 1.42 (s, 3H), 1.52 (s, 3H), 2.56 (m, 1H), 3.10 (s, 3H), 3.20 (d, $J = 8.5$ Hz, 1H) 3.84 (dd, $J = 8.5$, 1.9 Hz, 1H), 4.55 (dd, $J = 8.5$, 2.2 Hz, 1H), 4.95 (d, $J = 4.4$ Hz, 1H), 5.67 (dd, $J = 8.5$, 2.2 Hz, 1H), 7.20−7.65 (m, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3, 28.6, 29.9, 34.9, 35.3, 51.9, 53.7, 58.4, 69.4, 71.7, 75.1, 99.5, 120.2, 123.9, 126.9, 127.9, 128.3, 130.5, 132.5, 133.2, 139.2 ppm; MS (EI) *m*/*z* 529 (2, $M^+ - CH_3$), 381 (64), 379 (73), 323 (23), 276 (8), 249 (28), 149 (15), 57 (100). Anal. Calcd for $C_{27}H_{34}N_3O_4Br$ (544.48): C, 59.56; H, 6.29; N, 7.72. Found: C, 59.87; H, 6.54; N, 7.39.

Amino Nitrile 5h. According to the general procedure A, the α-amino nitrile **3d** (0.91 g, 3.0 mmol), diisopropylamine (0.51 mL, 3.6 mmol), and *n*-BuLi (2.25 mL, 3.6 mmol) were dissolved in dry THF (30 mL). The nitroalkene **4b** (0.41 g, 3.6 mmol) was added immediately. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 3:1 with 3% triethylamine) to afford the Michael adduct **5h** (1.12 g, 90% yield): colorless oil; $[\alpha]^{26}_D = -28.4$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 2987, 1456, 1379, 1201, 1080, 754 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (d, J = 6.9 Hz, 6H), 1.12 (d, $J = 6.7$ Hz, 6H), 1.17/1.20 (2s, 6H), 1.68/1.8 (2m, 1H), 2.27 (s, 3H), 2.59 (m, 1H), 2.92 (m, 1H), 3.55 (dd, $J = 11.3$, 1.7 Hz, 1H), 3.84 (dd, $J = 11.3$, 3.3 Hz, 1H), 4.13 (dd, $J = 13.2$, 9.1 Hz, 1H), 4.77 (dd, $J = 13.2$, 1.4 Hz, 1H), 5.19 (d, J = 9.4 Hz 1H), 7.30−7.47 (m, 5H$_\cdot$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.7, 18.8, 19.8, 23.1, 26.7, 31.7, 35.6, 48.5, 56.9, 69.1, 72.2, 74.1, 79.5, 100.7, 119.1, 126.7, 127.9, 128.5, 139.3 ppm; MS (EI) *m*/*z* 417 (1, M^+), 253 (22), 210 (31), 207 (13), 137 (30), 136 (88), 135 (51), 122 (16), 121 (100). Anal. Calcd for $C_{23}H_{35}N_3O_4$ (417.55): C, 66.16; H, 8.45; N, 10.06. Found: C, 66.42; H, 8.57; N, 9.89.

General Procedure B. The Michael adduct 5 was dissolved in THF (20 mL per mmol), 1.5 M hydrochloric acid (20 mL per mmol amino nitrile) was added, and the reaction mixture was refluxed for 30 min. The phases were separated, and the water phase was extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product **6** was purified by flash chromatography.

1-(Benzo[*d*][1,3]dioxol-6-yl)-2-(nitromethyl)butan-1-one (6a). Following general procedure B, the Michael adduct **5a** (500 mg, 1.04 mmol) was dissolved in THF (20 mL), 1.5 M hydrochloric acid (20 mL) was added, and the reaction mixture was refluxed for 30 min. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 3: 1) to afford **6a** as a colorless solid (190 mg, 73% yield): mp 69 °C; ee ≥ 86%; $[\alpha]^{26}D = -67.7$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 3442, 1659, 1607, 1554, 1448, 1255, 1031, 927, 885 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, $J =$ 7.4, 3H), 1.62 (m, 1H), 1.78 (m, 1H), 4.13 (m, 1H), 4.49 (dd, $J =$ 14.3, 4.4 Hz, 1H), 5.00 (dd, $J = 14.3$, 9.3 Hz, 1H), 6.06 (s, 2H), 6.90 (d, $J = 8.2$ Hz, 1H), 7.45 (d, $J = 1.7$ Hz, 1H), 7.60 (dd, $J =$ 8.2, 1.9, Hz, 1H$_\cdot$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.0, 23.5, 44.6, 74.8, 102.0, 108.0, 108.1, 124.7, 130.3, 148.3, 152.2, 197.2 ppm; MS (EI) *m*/*z* 251 (23, M^+), 149 (100), 121 (12), 65 (6). Anal. Calcd for $C_{12}H_{13}NO_5$ (251.24): C, 57.37; H, 5.22; N, 5.58. Found: C, 57.05; H, 5.59; N, 5.50.

1-(Benzo[*d*][1,3]dioxol-6-yl)-3-methyl-2-(nitromethyl)butan-1-one (6b). Following general procedure B, the Michael adduct **5b** (500 mg, 1.01 mmol) was dissolved in THF (20 mL), 1.5 M hydrochloric acid (20 mL) was added, and the reaction mixture was refluxed for 30 min. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 3:1) to afford **6b** as a colorless solid (182 mg, 68% yield): mp 126 °C; ee ≥ 99%; $[\alpha]^{26}_D = -83.0$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 1655, 1555, 1446, 1372, 1255, 1034 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (d, J = 6.9 Hz, 3H), 1.03 (d, $J = 6.9$ Hz, 3H), 2.13 (m, 1H$_\cdot$), 4.06 (m, 1H), 4.49 (dd, $J = 14.6$, 3.3 Hz, 1H), 5.05 (dd, $J = 14.6$, 10.2 Hz, 1H), 6.06 (s, 2H), 6.90 (d, $J = 8.2$ Hz, 1H), 7.46 (d, $J = 1.7$, Hz, 1H), 7.60 (dd, $J = 8.2$, 1.7, Hz, 1H$_\cdot$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.8, 20.9, 29.5, 49.1, 73.2, 101.9, 107.9, 108.1, 124.7, 131.0, 148.2, 152.1, 197.2 ppm; MS (EI); *m*/*z* 265 (17, M^+), 149 (100), 121 (8). Anal. Calcd for $C_{13}H_{15}NO_5$ (265.27): C, 58.86; H, 5.70; N, 5.28. Found: C, 58.53; H, 5.67; N, 5.17.

1-(Benzo[*d*][1,3]dioxol-6-yl)-2-cyclohexyl-3-nitropropan-1-one (6c). Following general procedure B, the Michael adduct **5c** (1 g, 1.86 mmol) was dissolved in THF (37 mL), 1.5 M hydrochloric acid (37 mL) was added, and the reaction mixture was refluxed for 30 min. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 3:1) to afford **6c** as a colorless oil (396 mg, 70% yield): ee ≥ 95%; $[\alpha]^{26}_D = -22.2$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 2929, 2855, 1670, 1554, 1490, 1444, 1374, 1255, 1096, 1039, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.03−1.77 (m, 11H), 4.08 (m, 1H), 4.54 (dd, $J = 14.6$, 3.6 Hz, 1H), 5.06 (dd, $J = 14.6$, 10.4 Hz, 1H), 6.04 (s, 2H), 6.87 (d, $J =$ 8.2 Hz, 1H), 7.45 (d, $J = 1.7$ Hz, 1H), 7.60 (dd, $J = 8.2$, 1.9 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 26.2, 26.4, 29.6, 31.4, 39.4, 48.7, 73.8, 102.0, 107.9, 108.0, 124.8, 131.2, 148.2, 152.1, 197.4 ppm; MS (EI) *m*/*z* 305 (2, M^+), 216 (9), 176 (31), 148 (100), 120 (13), 90 (68), 72 (22). Anal. Calcd for $C_{16}H_{19}NO_5$ (305.33): C, 62.94; H, 6.27; N, 4.59. Found: C, 63.11; H, 6.51; N, 4.68.

1-(Benzo[*d*][1,3]dioxol-6-yl)-3,3-dimethyl-2-(nitromethyl)-butan-1-one (6d). Following general procedure B, the Michael adduct **5d** (470 mg, 0.92 mmol) was dissolved in THF (20 mL), 1.5 M hydrochloric acid (20 mL) was added, and the reaction mixture was refluxed for 30 min. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 3:1) to afford **6d** as a colorless solid (183 mg, 71% yield): mp 130 °C; ee ≥ 99%; $[\alpha]^{26}_D = -81.0$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 2363, 1653, 1555, 1495, 1369, 1252, 1034, 927, 881 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (s, 9H), 4.06 (dd, $J = 11.0$, 2.7 Hz, 1H), 4.57 (dd, $J = 14.6$, 2.8 Hz, 1H), 5.10 (dd, $J = 14.6$, 11.0 Hz, 1H), 6.04 (s, 2H), 6.87 (d, $J = 8.2$ Hz, 1H), 7.46 (d, $J = 1.6$, Hz, 1H$_\cdot$), 7.62 (dd, $J = 8.2$, 1.7, Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.5, 33.9, 51.4, 74.9, 102.1, 108.0, 108.1, 125.0, 133.3, 148.3, 152.0, 198.3 ppm; MS (EI) *m*/*z* 279 (20, $M^{\bullet+}$), 177 (15), 149 (100), 121 (7). Anal. Calcd for $C_{14}H_{17}NO_5$ (279.29): C, 60.20; H, 6.14; N, 5.02. Found: C, 60.37; H, 6.23; N, 5.22.

1-(Benzo[*d*][1,3]dioxol-6yl)-3-nitro-2-*p*-tolylpropan-1-one (6e). Following general procedure B, the Michael adduct **5e** (500 mg, 0.92 mmol) was dissolved in THF (20 mL), 1.5 M hydrochloric acid (20 mL) was added, and the reaction mixture was refluxed for 30 min. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 4:1) to afford **6e** as a colorless oil (184 mg, 64% yield): ee ≥ 44%; $[\alpha]^{26}_D = -8.4$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 1673, 1554, 1506, 1489, 1443, 1374, 1258, 1218, 1039, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 4.54 (dd, $J = 13.2$, 3.9 Hz, 1H), 5.22 (dd, $J = 13.2$, 9.3 Hz, 1H), 5.27 (dd, br, $J = 3.8$ Hz, 1H), 5.97 (s, 2H), 6.77−7.57 (m, 7H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 50.4, 76.2, 101.8, 107.9, 108.4, 125.4, 127.8, 128.7, 129.7, 130.6, 138.2, 148.0, 152.0, 193.6 ppm; MS (EI) *m*/*z* 313 (5, M^+), 195 (6), 149 (100), 121 (8), 118 (6). Anal. Calcd for $C_{17}H_{15}NO_5$ (313.31): C, 65.17; H, 4.83; N, 4.47. Found: C, 65.29; H, 4.59; N, 4.77.

1-(4-Methoxyphenyl)-3,3-dimethyl-2-(nitromethyl)butan-1-one (6f). Following general procedure B, the Michael adduct **5f** (300 mg, 0.6 mmol) was dissolved in THF (12 mL), 1.5 M hydrochloric acid (12 mL) was added, and the reaction mixture was refluxed for 30 min. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 3:1) to afford **6f** as a colorless solid (111 mg, 70% yield): mp 74 °C; ee ≥ 99%; $[\alpha]^{26}_D = -138.2$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 3426, 2963, 1667, 1604, 1550, 1422, 1376, 1258, 1220, 1172, 1025, 957, 847, 799, 525 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.97 (s, 9H), 3.87 (s, 3H), 4.13 (dd, $J = 11.1$, 2.8 Hz, 1H), 4.58 (dd, $J = 14.3$, 2.8 Hz, 1H), 5.13 (dd, $J = 14.3$, 11.0 Hz, 1H), 6.96 (dm, $J = 8.8$ Hz, 2H), 8.00 (dm, $J = 8.8$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 33.7, 51.0, 55.5, 74.9, 113.9, 130.8, 131.5, 163.7, 198.9 ppm; MS (EI) *m*/*z* 265 (14, M^+), 219 (5), 163 (19), 134 (100), 77 (5). Anal. Calcd for $C_{14}H_{19}NO_4$ (265.31): C, 63.38; H, 7.22; N, 5.28. Found: C, 63.24; H, 7.39; N, 5.03.

1-(4-Bromophenyl)-3,3-dimethyl-2-(nitromethyl)butan-1-one (6g). Following general procedure B, the Michael adduct **5g** (327 mg, 0.6 mmol) was dissolved in THF (12 mL), 1.5 M hydrochloric acid (12 mL) was added, and the reaction mixture was refluxed for 30 min. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 5:1) to afford **6g** as a colorless solid (134 mg, 71% yield): mp 52 °C; ee = 86%; $[\alpha]^{26}_D = -100.1$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 1677, 1560, 1371, 1214 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (s, 9H), 4.10 (dd, $J = 11.1$, 2.9 Hz, 1H), 4.59 (dd, $J = 14.8$, 2.7 Hz, 1H), 5.11 (dd, $J = 14.8$, 3.7 Hz, 1H), 5.13 (dd, $J = 14.3$, 11.0 Hz, 1H), 7.60 (dm, $J = 8.8$ Hz, 2H), 7.85 (dm, $J = 8.8$, Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 33.9, 51.5, 74.7, 128.6, 129.9, 132.1, 137.3, 199.8 ppm; MS (EI) *m*/*z* 314 (1, M^+), 211 (21), 183 (100), 155 (13), 132 (11), 57 (13). Anal. Calcd for $C_{13}H_{16}NO_3Br$ (314.17): C, 49.69; H, 5.13; N, 4.46. Found: C, 49.91; H, 5.30; N, 4.56.

2,5-Dimethyl-4-(nitromethyl)hexan-3-one (6h). Following general procedure B, the Michael adduct **5h** (200 mg, 0.48 mmol) was dissolved in THF (10 mL), 1.5 M hydrochloric acid (10 mL) was added, and the reaction mixture was refluxed for 30 min. The crude product was purified by flash chromatography (silica gel, pentane/diethyl ether 3:1) to afford **6h** as a colorless oil (64 mg, 72% yield): ee ≥ 25%; $[\alpha]^{26}_D = -1.8$ ($c = 1.0$, $CHCl_3$); IR (KBr) ν 2970, 1710, 1557, 1378 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (d, $J = 7.14$ Hz, 3H), 1.07 (d, $J = 6.9$ Hz, 3H), 1.10 (d, $J = 6.6$ Hz, 3H), 1.17 (d, $J = 7.15$ Hz, 3H), 2.15 (m, 1H), 2.83 (m, 1H), 3.46 (m, 1H), 4.31 (dd, $J = 14.28$, 3.3 Hz, 1H), 4.89 (dd, $J = 14.28$, 10.43 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.5, 18.2, 19.0, 21.0, 28.1, 39.9, 52.9, 71.9, 212.7 ppm; MS (EI) *m*/*z* 187 (0.4, M^+), 141 (5), 97 (31), 73 (5), 71 (100), 69 (25), 55 (23). Anal. Calcd for $C_9H_{17}NO_3$ (187.24): C, 57.73; H, 9.15; N, 7.48. Found: C, 57.45; H, 8.89; N, 7.32.

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Supporting Information Available: Proton and carbon NMR spectra of new compounds. Crystallographic information files (CIF) for **5g** and **6d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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