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Borane-Mediated Aldol Cycloreduction of Monoenone Monoketones: Diastereoselective Formation of Quaternary Centers

Ryan R. Huddleston, David F. Cauble, and Michael J. Krische*

Department of Chemistry and Biochemistry, University of Texas at Austin, Austin, Texas 78712

mkrische@mail.utexas.edu

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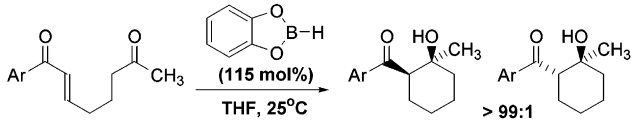
Exposure of monoenone monoketones to catecholborane in THF at ambient temperature results in tandem 1,4-reduction−aldol cyclization. For aromatic and heteroaromatic enones, six-membered cyclic aldol products are formed in excellent yield with high levels of syn diastereoselectivity. Five-membered ring formation proceeds less readily, but the yield of cyclized product is improved through introduction of Rh(I) salts.

Introduction

The aldol reaction represents a fundamental method of stereogenic C−C bond formation. Due to its broad significance, considerable effort has been invested in the development of catalytic processes that yield stereochemically defined aldol products.[1] Despite these efforts, a paucity of methods exists for catalytic aldol cyclization. Classically, aldol cyclization has been achieved through the use of organic catalysts.[2] Inspired by the recent introduction of methods for the catalytic reductive condensation of enones and aldehydes,[3,4] the first examples of metal-catalyzed aldol cyclization were recently reported from our lab, i.e., the diastereoselective Co-catalyzed aldol cycloreduction of monoenone monoaldehydes.[5]

Barring a single exception,[3e] all reported *catalytic* reductive aldol processes, including mechanistically related catalytic enone hydroallylation and hydrocarbamoylation,[6] utilize silane as a terminal reductant. Stimulated by the utility of boron enolates in the context of aldol chemistry[7] and accounts of sequential 1,4-enone hydroboration−intermolecular aldol condensation,[8] we herewith report studies on the catecholborane-mediated aldol cycloreduction of monoenone monoketones. Upon exposure to catecholborane, aromatic and heteroaromatic monoenone monoketones afford six-membered cyclic aldol products in excellent yield with high levels of syn diastereoselectivity (Scheme 1).

SCHEME 1. Catecholborane-Mediated Aldol Cycloreduction



Prior studies pertaining to sequential 1,4-enone hydroboration−intermolecular aldol condensation emphasize the sensitivity of the reaction with respect to the borane reagent.[8] Competitive carbonyl reduction for both enone and aldehyde partners is problematic, necessitating use of borane reagents that are highly selective for conjugate reduction. Moreover, in prior studies, the boron

(1) For selected reviews on catalytic enantioselective aldol reactions, see: (a) Machajewski, T. D.; Wong, C.-H., Lerner, R. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 1352. (b) Denmark, S. E.; Stavenger, R. A. *Acc. Chem. Res.* **2000**, *33*, 432. (c) Nelson, S. G. *Tetrahedron: Asymmetry* **1998**, *9*, 357. (d) Carreira, E. M. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. III, p 1. (e) Braun, M. In *Stereoselective Synthesis, Methods of Organic Chemistry (Houben-Weyl)*, ed. E21; Helmchen, G., Hoffman, R., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, 1996; Vol. 3, p 1730.

(2) Aldol cyclizations have been catalyzed by antibodies and chiral amines: (a) List, B.; Lerner, R. A.; Barbas, C. F., III. *Org. Lett.* **1999**, *1*, 59. (b) Eder, U.; Sauer, G.; Wiechert, R. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 496. (c) Hajos, Z. G.; Parrish, D. R. *J. Org. Chem.* **1974**, *39*, 1615. (d) Agami, C.; Platzer, N.; Sevestre, H. *Bull. Soc. Chim. Fr.* **1987**, *2*, 358. (e) Eder, U.; Weichert, R.; Sauer, G. German Patent DE 2014757, Oct. 7, 1971.

(3) For catalytic reductive aldol processes, see: (a) Revis, A.; Hilty, T. K. *Tetrahedron Lett.* **1987**, *28*, 4809. (b) Matsuda, I.; Takahashi, K.; Sato, S. *Tetrahedron Lett.* **1990**, *31*, 5331. (c) Isayama, S.; Mukaiyama, T. *Chem. Lett.* **1989**, 2005. (d) Kiyooka, S.; Shimizu, A.; Torii, S. *Tetrahedron Lett.* **1998**, *39*, 5237. (e) Ooi, T.; Doda, K.; Sakai, D.; Maruoka, K. *Tetrahedron Lett.* **1999**, *40*, 2133. (f) Taylor, S. J.; Morken, J. P. *J. Am. Chem. Soc.* **1999**, *121*, 12202. (g) Taylor, S. J.; Duffey, M. O.; Morken, J. P. *J. Am. Chem. Soc.* **2000**, *122*, 4528. (h) Zhao, C.-X.; Duffey, M. O.; Taylor, S. J.; Morken, J. P. *Org. Lett.* **2001**, *3*, 1829.

(4) For a review, see: Huddleston, R. R.; Krische, M. J. *Synlett* **2002**, in press.

(5) Baik, T.-G.; Luiz, A. L.; Wang, L.-C.; Krische, M. J. *J. Am. Chem. Soc.* **2001**, *123*, 5112. A nonstereoselective catalytic aldol cycloreduction was subsequently reported: Emiabata-Smith, D.; McKillop, A.; Mills, C.; Motherwell, W. B.; Whitehead, A. J. *Synlett* **2001**, 1302.

(6) (a) Muraoka, T.; Matsuda, I.; Itoh, K. *J. Am. Chem. Soc.* **2000**, *122*, 9552. (b) Muraoka, T.; Matsuda, I.; Itoh, K. *Organometallics* **2001**, *20*, 4676.

(7) For selected reviews on boron enolates, see: (a) Paterson, I.; Doughty, V. A.; Florence, G.; Gerlach, K.; McLeod, M. D.; Scott, J. P.; Trieselmann, T. ACS Symposium Series 783; American Chemical Society: Washington, DC, 2001; p 195. (b) Cowden, C. J.; Paterson, I. *Org. React.* 1997, *51*, 1. (c) Gennari, C. *Pure Appl. Chem.* **1997**, *69*, 507. (d) Paterson, I. *Chem. Ind.* **1988**, *12*, 390. (e) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1.

(8) (a) Boldrini, G. P.; Mancini, F.; Tagliavini, E.; Tromboli, C.; Umani-Ronchi, A. *Chem. Commun.* **1990**, 1680. (b) Evans, D. A.; Fu, G. C. *J. Org. Chem.* **1990**, *55*, 5678. (c) Matsumoto, Y.; Hayashi, T. *Synlett* **1991**, 349. (d) Boldrini, G. P.; Bortolotti, M.; Mancini, F.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1991**, *56*, 5820.

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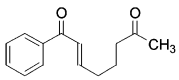
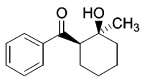
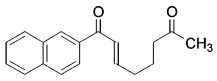
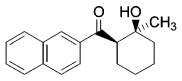
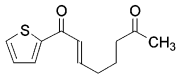
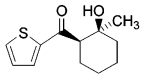
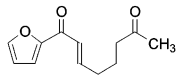
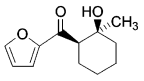
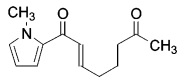
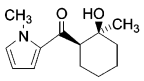
enolate was preformed in the absence of the aldehyde partner. Given this precedent, the outcome of a related intramolecular process was uncertain, as boron enolate formation must take place in the *presence* of the appendant electrophilic partner. Indeed, initial experiments directed toward the aldol cycloreduction of monoenone monoaldehyde substrates proved to be unsuccessful across a range of boranes due to competitive aldehyde reduction.

Results and Discussion

To attenuate and perhaps circumvent competitive reduction of the appendant electrophile, monoenone monoketone substrates **1a**−**6a** were examined.[9,10] Initial studies focused on the aldol cycloreduction of compound **1a**. Monoenone monoketone **1a** was screened against an assortment of borane reagents (9-BBN, BH_3-DMS, pinacolborane, diisopinocampheylborane, and catecholborane). Eventually, it was found that exposure of **1a** to a slight excess of catecholborane in dry tetrahydrofuran at ambient temperature provides the desired cycloreduction product **1b** in 89% isolated yield with a syn:anti ratio of >99:1, as determined by HPLC analysis (Table 1). As 1,4-enone hydroboration is known to result in the formation (*Z*)-boron enolates,[8c] the observed syn diastereoselectivity may be accounted for on the basis of a stereochemical model involving the intermediacy of a Zimmerman−Traxler-type transition state (Scheme 2).[11] The structural assignment of **1b** was corroborated by single-crystal X-ray diffraction analysis.[12] These conditions proved to be general for the cycloreduction of both aromatic and heteroaromatic monoenone monoketones **1a**−**5a** (Table 1). Aliphatic enones and enoates produce complex mixtures of reduction products under these conditions.

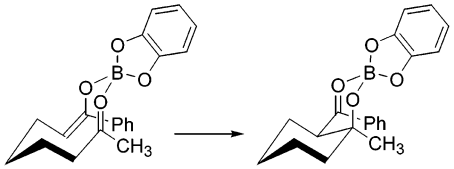
Five-membered ring formation was next explored. Exposure of phenyl-substituted monoenone monoketone **6a** to the conditions specified in Table 1 produced only a 5% yield of the desired cycloreduction product **6b**, along with the product of simple conjugate reduction and recovered starting material. In the course of previous studies on the sequential 1,4-enone hydroboration−aldol condensation, catalytic Rh(I) salts have been shown to

TABLE 1. Catecholborane-Mediated Aldol Cycloreduction of Monoenone Monoketones 1a−5a[a]

Entry	Substrate	Product	Isolated Yield (%)
1	 1a	 1b	89
2	 2a	 2b	91
3	 3a	 3b	83
4	 4a	 4b	86
5	 5a	 5b	80

[a] Standard Conditions: To a solution of monoenone monoketone (1.0 mmol, 100 mol %) in anhydrous THF (2 mL, 0.5 M) was added catecholborane (128 μL, 1.2 mmol, 120 mol %) dropwise over 2 min. The solution was stirred under an argon atmosphere for 3 h and then quenched by dropwise addition of methanol (1 mL). The reaction mixture was directly absorbed onto silica gel and purified by column chromatography to afford the cyclized product.

SCHEME 2. Stereochemical Model Accounting for the Observed Syn Diastereoselectivity of the Catecholborane-Mediated Aldol Cycloreduction



enable the condensation of α,β-unsaturated carbonyl compounds that otherwise do not participate in this transformation.[8b] Hence, catecholborane-mediated cycloreduction was attempted in the presence of Wilkinson's catalyst [$ClRh(PPh_3)_3$] (10 mol %). Ultimately, this system proved to be problematic due to background reactions involving nonproductive substrate reduction and decomposition. Hence, attention was turned to less reactive boranes. As established in our initial screening, substrates **1a**−**6a** are unreactive toward pinacolborane at ambient temperature over prolonged periods of exposure. Therefore, Rh-catalysis of the pinacolborane-mediated cycloreduction of **6a** was explored.

Whereas catecholborane-mediated cycloreduction of **6a** provides only a 5% yield of cycloreduction product **6b**, exposure of **6a** to pinacolborane and 10 mol % Wilkinson's catalyst affords a 22% yield of **6b**. Exposure of **6a** to pinacolborane and 10 mol % $[Rh(COD)Cl]_2$/BINAP im-

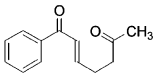
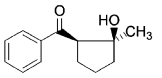
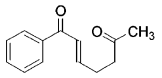
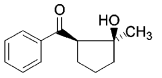
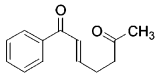
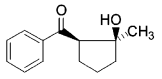
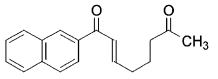
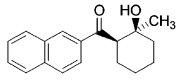
(9) Representative procedure for the preparation of substrates **1a**−**5a** is as follows. 1-Methylcyclopentene (30.4 mmol, 100 mol %) dissolved in $CHCl_3$ (200 mL, 0.15 M) was treated with ozone at −60 °C for 1.5 h. The solution was purged with N_2, and triphenylphosphine (30.4 mmol, 100 mol %) was added; the reaction mixture was allowed to stir for 2 h at 25 °C. At this point, the appropriate Wittig reagent (30.4 mmol, 100 mol %) was added in portions over 10 min and the solution stirred for 18 h. The residue was evaporated onto silica and subjected to column chromatography to afford monoenone monoketones **1a**−**5a**.

(10) Procedure for the preparation of substrate **6a** is as follows. To a stirred suspension of PCC (15.65 g, 72.6 mmol, 200 mol %) at ambient temperature in CH_2Cl_2 (100 mL, 0.36 M) was added dropwise 3-acetyl-1-propanol (3.61 g, 36.3 mmol, 100 mol %). The dark solution was stirred for 2 h at 25 °C and then filtered through a pad of silica. The product was purified by Kugelrohr distillation to afford 4-oxo-pentanal (2.71 g, 77% yield) as a clear colorless oil. A portion of the purified monoketone monoaldehyde (1.82 g, 18.2 mmol, 100 mol %) was dissolved in CH_2Cl_2 (200 mL, 0.091 M), and the acetophenone-derived Wittig reagent (18.2 mmol, 100 mol %) was added in portions over 10 min; the solution was allowed to stir for 18 h. The residue was evaporated onto silica and subjected to column chromatography to afford the monoenone monoketone **6a** (4.75 g, 86% yield) as a clear colorless oil.

(11) Zimmerman, H. E.; Traxler, M. D. *J. Am. Chem. Soc.* **1957**, *79*, 1920.

(12) See Supporting Information for crystallographic data.

TABLE 2. Rh-Catalyzed Aldol Cycloreduction of 6a and 2a[a]

Entry	Substrate	Product	Reducing System	Isolated Yield (%)
1	 6a	 6b	Catecholborane	5
2	 6a	 6b	Pinacolborane [RhCl(PPh$_3$)$_3$]	22
3	 6a	 6b	Pinacolborane [Rh(COD)Cl]$_2$ (R)-BINAP	32
4	 2a	 2b	Pinacolborane [Rh(COD)Cl]$_2$ (R)-BINAP	82

[a] Standard Conditions: Entry 1 was performed in accordance with the procedure outlined in ref 9 of the text. Entries 2 and 3 were performed in accordance with the following procedure. To a solution of Rh(I) catalyst (0.08 mmol, 8 mol %) and ligand (0.088 mmol, 8.8 mol %) in anhydrous THF (2 mL, 0.5 M) was added **6a** (202 mg, 1.0 mmol, 100 mol %). Pinacolborane (128 μL, 1.2 mmol, 120 mol %) was added dropwise over 2 min. The solution was stirred under an argon atmosphere for 18 h and then quenched by dropwise addition of methanol (1 mL). The reaction mixture was directly absorbed onto silica gel and purified by column chromatography to give **6b**. Entry 4 was performed in accordance with the procedure for entries 2 and 3 with the following adjustments: Rh(I) catalyst (0.01 mmol, 2 mol %), ligand (0.025 mmol, 5.0 mol %), anhydrous DCE (5 mL, 0.1 M), **2a** (132 mg, 0.5 mmol, 100 mol %), and pinacolborane (145 μL, 1.0 mmol, 200 mol %).

proved the isolated yield of **6b** to 32%. Additional screening of Rh(I) source and phosphine ligand did not result in any further improvement in yield for the cycloreduction of **6a**. Indeed, this study suggests that aldol cyclizations proceeding through the intermediacy of (*Z*)-boron enolates are intrinsically more difficult for five-membered ring formation than for six-membered ring formation. In support of this contention, exposure of **2a** to pinacolborane and 10 mol % [Rh(COD)Cl]$_2$/BINAP proceeds smoothly to give the six-membered ring aldol cycloreduction product **2b** in 82% yield as a single diastereomer. The acquisition of both **2b** and **6b** as nearly racemic materials (3 and 6% enantiomeric excess, respectively) supports the assertion that the aldol cycloreductions catalyzed by Rh(I) proceed through the intermediacy of the boron enolate, rather than the rhodium enolate (Table 2).

Conclusion

Exposure of monoenone monoketones to catecholborane in THF at ambient temperature results in tandem 1,4-reduction−aldol cyclization. For aromatic and heteroaromatic enones, six-membered cyclic aldol products are formed in excellent yield with exceptionally high levels of syn diastereoselectivity. Five-membered ring formation precedes less readily, but the yield of cyclized product is improved through introduction of Rh(I) salts. Future studies are aimed at developing catalyst systems of enhanced substrate scope, enantioselective catalytic systems, and the discovery of related catalytic functional group interconversions.

Experimental Section

All reactions were run under an atmosphere of argon, unless otherwise indicated. Anhydrous solvents were transferred by an oven-dried syringe. Flasks were flame-dried and cooled under a stream of nitrogen. Preparative column chromatography employing silica gel was performed according to the method of Still.[13] Solvents for chromatography are listed as volume/volume ratios. Melting points were determined in open capillaries and are uncorrected. High-resolution mass spectra (HRMS) are reported as *m/e* (relative intensity). Accurate masses are reported for the molecular ion (M + 1) or a suitable fragment ion. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 300 or 400 MHz in $CDCl_3$. Chemical Shifts are reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane. Coupling constants are reported in hertz (Hz). Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 75 or 100 MHz in $CDCl_3$. Chemical shifts are reported in delta (δ) units, parts per million (ppm) relative to the center of the triplet at 77.00 ppm for deuteriochloroform. ^{13}C NMR spectra were routinely run with broadband decoupling.

Representative procedures for the preparation of substrates **1a**−**5a** and substrate **6a** are provided in the text. Additionally, representative procedures for the cycloreduction of substrates **1a**−**5a** and substrate **6a** are provided in Tables 1 and 2, respectively.

1-Phenyl-oct-2-ene-1,7-dione (1a). In accordance with the procedure outlined in ref 9 of the text, the title compound was obtained in 81% yield as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.82 (qt, J = 7.2 Hz, 2H), 2.15 (s, 3H), 2.33 (m, 2H), 2.50 (t, J = 7.2 Hz, 2H), 6.89 (m, 1H), 7.01 (m, 1H), 7.46 (m, 2H), 7.55 (m, 1H), 7.92 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.4, 30.5, 32.3, 43.0, 126.6, 128.7, 128.7, 132.9, 138.0, 148.7, 190.7, 208.2. FTIR (NaCl): 2935, 2253, 1713, 1670, 1620, 1598, 1578, 1448, 1357, 1288, 1227, 1159, 907, 740, 650 cm^{-1}. HRMS: calcd [M + 1] for $C_{14}H_{16}O_2$ 217.1229, found 217.1229. Mp: 61−62 °C.

1-Naphthalen-2-yl-oct-2-ene-1,7-dione (2a). In accordance with the procedure outlined in ref 9 of the text, the title compound was obtained in 83% yield as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.85 (qt, J = 7.2 Hz, 2H), 2.16 (s, 3H), 2.38 (m, 2H), 2.52 (t, J = 7.2 Hz, 2H), 7.07 (m, 2H), 7.56 (m, 2H), 7.95 (m, 4H), 8.43 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.5, 30.5, 32.4, 43.1, 124.7, 126.5, 127.0, 128.0, 128.5, 128.7, 129.7, 130.2, 132.7, 135.3, 135.6, 148.6, 190.4, 208.2. FTIR (NaCl): 2942, 2253, 1713, 1666, 1630, 1617, 1468, 1356, 1294, 1220, 1188, 1126, 1095, 912, 741, 651 cm^{-1}. HRMS: calcd [M + 1] for $C_{18}H_{18}O_2$ 267.1385, found 267.1392. Mp: 69−70 °C.

1-Thiophen-2-yl-oct-2-ene-1,7-dione (3a). In accordance with the procedure outlined in ref 9 of the text, the title compound was obtained in 78% yield as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.79 (qt, J = 9.6 Hz, 2H), 2.11 (s, 3H), 2.31 (m, 2H), 2.45 (t, J = 9.6 Hz, 2H), 6.77 (m, 1H), 7.06 (m, 2H), 7.67 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.2, 30.3, 32.0, 42.8, 126.1, 128.5, 132.2, 134.1, 145.3, 148.0, 182.3, 208.4. FTIR (NaCl): 3054, 2987, 2358, 1714, 1657, 1610, 1515, 1415, 1354, 1265, 1083, 913, 744 cm^{-1}. HRMS: calcd for [M + 1] for $C_{12}H_{14}O_2S$ 223.0793, found 223.0795. Mp: 48−50 °C.

1-Furan-2-yl-oct-2-ene-1,7-dione (4a). In accordance with the procedure outlined in ref 9 of the text, the title compound was obtained in 79% yield as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.82 (qt, J = 7.2 Hz, 2H), 2.15 (s, 3H),

(13) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

2.32 (m, 2H), 2.50 (t, J = 7.2 Hz, 2H), 6.55 (m, 1H), 6.81 (m, 1H), 7.10 (m, 1H), 7.24 (m, 1H), 7.61 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.3, 30.5, 32.2, 43.0, 112.6, 117.9, 125.6, 146.7, 147.9, 153.4, 178.0, 208.2. FTIR (NaCl): 2900, 253, 1794, 1713, 1666, 1620, 1568, 1467, 1395, 1298, 1165, 1090, 1014, 912, 742, 650 cm^{-1}. HRMS: calcd for [M + 1] for $C_{12}H_{14}O_3$ 207.1021, found 207.1015. Mp: 58−60 °C.

1-(1-Methyl-1*H*-pyrrol-2-yl)-oct-2-ene-1,7-dione (5a). In accordance with the procedure outlined in ref 9 of the text, the title compound was obtained in 78% yield as a clear colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.79 (qt, J = 9.6 Hz, 2H), 2.13 (s, 3H), 2.29 (m, 2H), 2.48 (t, J = 9.6 Hz, 2H), 3.98 (s, 3H), 6.15 (m, 1H), 6.74−6.99 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.7, 30.4, 32.0, 38.2, 43.1, 108.4, 119.5, 127.6, 131.6, 131.7, 144.7, 180.0, 208.4. FTIR (NaCl): 2949, 2253, 1712, 1656, 1605, 1527, 1460, 1407, 1308, 1237, 1095, 1068, 984, 912, 742, 650 cm^{-1}. HRMS: calcd for [M + 1] for $C_{13}H_{17}NO_2$ 220.1338, found 220.1338.

1-Phenyl-hept-2-ene-1,6-dione (6a). In accordance with the procedure outlined in ref 10 of the text, the title compound was obtained in 66% yield as a clear colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.15 (s, 3H), 2.63 (m, 4H), 6.93 (m, 2H), 7.48 (m, 3H), 7.88 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.5, 30.0, 41.5, 126.5, 128.4, 132.6, 137.6, 147.4, 190.5, 206.7. FTIR (NaCl): 3055, 2987, 2685, 2411, 2306, 1716, 1671, 1651, 1622, 1599, 1579, 1447, 1422, 1366, 1265, 1180, 979, 896, 737, 704 cm^{-1}. HRMS: calcd for [M + 1] for $C_{13}H_{14}O_2$ 203.1072, found 203.1064.

(2-Hydroxy-2-methyl-cyclohexyl)-phenyl-methanone (1b). In accordance with the procedure outlined in Table 1 of the text, the title compound was obtained in 89% yield as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20 (s, 3H), 1.33 (m, 2H), 1.56 (m, 1H), 1.79 (m, 5H), 3.31 (dd, J = 3.6, 12.0 Hz, 1H), 4.45 (br, 1H), 7.49 (m, 2H), 7.60 (m, 1H), 7.95 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 25.8, 27.3, 29.9, 39.2, 51.7, 70.4, 128.5, 129.1, 133.9, 138.2, 207.4. FTIR (NaCl): 3481, 3081, 2991, 2954, 2912, 2815,1671, 1598, 1575, 1485, 1425, 1416, 1363, 1251, 1203, 987 cm^{-1}. HRMS: calcd for [M + 1] for $C_{14}H_{18}O_2$ 219.1385, found 219.1390. Mp: 59−60 °C.

(2-Hydroxy-2-methyl-cyclohexyl)-naphthalen-2-yl-methanone (2b). In accordance with the procedure outlined in Table 1 of the text, the title compound was obtained in 91% yield as a white crystalline solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (s, 3H), 1.38 (m, 2H), 1.60 (m, 1H), 1.90 (m, 5H), 3.31 (dd, J = 3.0, 12.2 Hz, 1H), 4.60 (br, 1H), 7.61 (m, 2H), 7.94 (m, 4H), 8.48 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.6, 25.8, 27.5, 30.1, 39.3, 51.7, 70.5, 124.0, 127.2, 128.0, 129.0, 129.1, 130.0, 130.4, 132.7, 134.2, 136.1, 207.3. FTIR (NaCl): 3961, 3699, 3613, 3421, 3023, 2996, 2925, 2888, 2802, 2654, 2301, 1651, 1642, 1461, 1256, 906 cm^{-1}. HRMS: calculated for [M + 1] for $C_{18}H_{20}O_2$ 269.1541, found 269.1539. Mp: 66−68 °C.

(2-Hydroxy-2-methyl-cyclohexyl)-thiophen-2-yl-methanone (3b). In accordance with the procedure outlined in Table 1 of the text, the title compound was obtained in 83% yield as a clear colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (s, 3H), 1.31 (m, 2H), 1.54 (m, 1H), 1.82 (m, 5H), 3.11 (dd, J = 3.6, 12.4 Hz, 1H), 4.27 (br, 1H), 7.16 (m, 1H), 7.69 (m, 1H), 7.76 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 25.9, 27.7, 30.2, 39.2, 53.9, 70.4, 128.6, 132.8, 135.2, 144.2, 199.5. FTIR (NaCl): 2936, 2862, 2253, 1793, 1636, 1563, 1518, 1460, 1443, 1414, 1386, 1288, 1263, 1235, 1212, 908, 726, 650 cm^{-1}. HRMS: calcd for [M + 1] for $C_{12}H_{16}O_2S$ 225.0949, found 225.0955.

Furan-2-yl-(2-hydroxy-2-methyl-cyclohexyl)-methanone (4b). In accordance with the procedure outlined in Table 1 of the text, the title compound was obtained in 86% yield as a clear colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20 (s, 3H), 1.31 (m, 2H), 1.53 (m, 1H), 1.82 (m, 5H), 3.12 (dd, J = 3.6, 12.2 Hz, 1H), 4.16 (br, 1H), 6.58 (m, 1H), 7.27 (m, 1H), 7.64 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 25.8, 27.0, 30.0, 39.2, 52.5, 70.4, 112.8, 118.7, 147.4, 152.4, 195.1. FTIR (NaCl): 3054, 2986, 2938, 2859, 2685, 2305, 1652, 1567, 1464, 1443, 1422, 1396, 1265, 1166, 956, 909, 741, 705 cm^{-1}. HRMS: calcd for [M + 1] for $C_{12}H_{16}O_3$ 209.1178, found 209.1175.

(2-Hydroxy-2-methyl-cyclohexyl)-(1-methyl-1*H*-pyrrol-2-yl)-methanone (5b). In accordance with the procedure outlined in Table 1 of the text, the title compound was obtained in 80% yield as a clear colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.18 (s, 3H), 1.28 (m, 2H), 1.51 (m, 1H), 1.78 (m, 5H), 2.98 (dd, J = 3.6, 12.2 Hz, 1H), 3.93 (s, 3H), 4.73 (br, 1H), 6.14 (m, 1H), 6.86 (m, 1H), 6.99 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7, 26.0, 28.0, 30.3, 38.4, 39.3, 52.7, 70.6, 108.6, 120.6, 130.7, 132.6, 197.1. FTIR (NaCl): 3442, 3054, 2986, 2937, 2305, 1623, 1422, 1408, 1392, 1265, 1096, 1068, 945, 901, 896, 738, 705 cm^{-1}. HRMS: calcd for [M + 1] for $C_{13}H_{19}NO_2$ 222.1494, found 222.1486.

(2-Hydroxy-2-methyl-cyclopentyl)-phenyl-methanone (6b). In accordance with the procedures cited in Table 2 of the text, the title compound was obtained in 22 and 32% yields as a clear colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38 (s, 3H), 1.93 (m, 6H), 3.47 (dd, J = 9.0, 10.6 Hz, 1H), 4.51 (br, 1H), 7.48 (m, 2H), 7.58 (m, 1H), 7.94 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.5, 27.0, 30.7, 41.1, 54.3, 81.2, 128.5, 128.9, 133.8, 137.4, 205.6. FTIR (NaCl): 3470, 3156, 2972, 2876, 2253, 1662, 1598, 1461, 1449, 1377, 1229, 912, 734, 650 cm^{-1}. HRMS: calcd for [M + 1] for $C_{13}H_{16}O_2$ 205.1229, found 205.1225.

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Supporting Information Available: Spectral data for all new compounds (^{1}H NMR, ^{13}C NMR, IR, HRMS), and crystallographic data for compound **1b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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