Communication

Synthesis of Substituted 4-Aroyl-1-indanone and 5-Aroyl-1-tetralone

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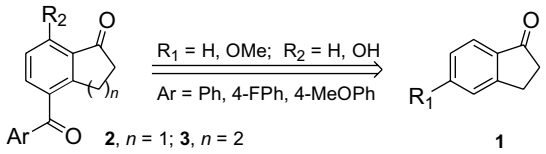
Several substituted 4-aroyl-1-indanones **2** and 5-aroyl-1-tetralones **3** were prepared in good yields from 1-indanones **1** via a series of reasonable transformations.

Keywords: Benzocycloalkanones; 4-Aroyl-1-indanone; 5-Aroyl-1-tetralone; Friedel-Crafts acylation.

INTRODUCTION

The bicyclic benzofused ring system, along with related structures such as indanone or tetralone, represents the structural motifs of benzocycloalkanones.[1] These cyclic systems incorporate two rings connected by a fused ring containing a benzene ring adjacent to the ring junction. This structural motif has been observed in a number of natural alkaloid products.[2] The structural frameworks of 1-indanones and 1-tetralones present a particular challenge and their formation is the main focus of the research presented in this area.[3] A number of unique approaches in regard to 1-indanones and 1-tetralones have been explored because it is an important intermediate for preparing natural products. Our interest is piqued by the synthesis of substituted 1-indanones and 1-tetralones with some different potential biological properties;[4] a facile method for the regioselective synthesis of substituted 4-aroyl-1-indanones **2** and 5-aroyl-1-tetralones **3** from indanones **1** is described in Scheme I.

Scheme I Synthetic approach toward substituted indanone



RESULTS AND DISCUSSION

Skeleton **1** was chosen as the starting materials for synthesizing substituted 4-aroyl-1-indanones **2** and 5-aroyl-1-tetralones **3**, as shown in Scheme II. Initially, skeleton **2** was provided by the Grignard addition of ketones **1a** (R_1 = H) and **1b** (R_1 = OMe) with arylmagnesium bromide (1.0 M in tetrahydrofuran, Ar = Ph, 4-FPh, 4-MeOPh) at rt for 4~5 h, followed by boron trifluoride etherate-mediated de-

Scheme II Synthesis of 4-aroyl-1-indanones **2** and 5-aroyl-1-tetralones **3**

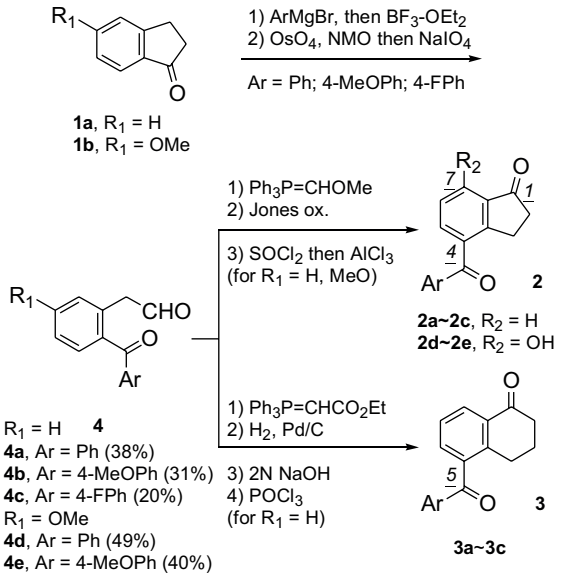


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Table 1. Synthesis of substituted 4-aroyl-1-indanones **2** and 5-aroyl-1-tetralones **3**[a]

Entry	**2**/**3**	R_2 group	Ar group	Yield (%)
1	**2a**	H	C_6H_5	81
2	**2b**	H	4-$CH_3OC_6H_5$	55
3	**2c**	H	4-FC_6H_5	62
4	**2d**	OH	C_6H_5	70
5	**2e**	OH	4-$CH_3OC_6H_5$	61
6	**3a**	H	C_6H_5	73
7	**3b**	H	4-$CH_3OC_6H_5$	59
8	**3c**	H	4-FC_6H_5	68

[a] The isolated products are > 95% pure as judged by ^{1}H-NMR analysis.

hydration of the resulting tertiary alcohol in dichloromethane at rt for 15~20 min. Without further purification, osmium tetroxide-mediated dihydroxylation reaction of the corresponding 1-arylindenes with N-methylmorpholine N-oxide in the co-solvent of t-butanol, tetrahydrofuran and water (v/v/v = 1/3/6) afforded vicinal diols at reflux temperature for 10~12 h, followed by sodium periodate-mediated bond cleavage for 1~2 h to give skeleton **4**. Compounds **4a**~**4e** were isolated in 20~49% total yields of four steps.

Furthermore, Wittig olefination of the skeleton **4**, subsequently followed by Jones oxidation, yielded keto-acids. Finally, five compounds **2a**~**2e** were isolated from the ring-closure process via acylation of acids with thionyl chloride and Friedel-Crafts reaction with aluminum chloride in 55~81% yields of four-steps.[5-6] With the results in hand, we envisioned that the demethylation should be induced via the chelated aluminum intermediate between the 1-carbonyl and 7-methoxy group during the Friedel-Crafts cyclization. To avoid demethylation, phorsphoryl trichloride was examined. When phorsphoryl trichloride-mediated the intramolecular ring-closure step of the model keto-acid (R_1 = OMe, Ar = 4-FPh) substrate, compound **2f** was achieved with 79% yield (three-steps) without the formation of demethylated product. The structural frameworks of compounds **2e** and **2f** were determined using single-crystal X-ray analysis.[7]

According to the similar synthetic strategy of skeleton **2**, skeleton **3** was also prepared from skeleton **4** via Wittig olefination, hydrogenation, base-induced hydrolysis and followed sequentially by Friedel-Crafts acylation with modest overall yields. The exhibited methodology could provide a new and efficient route for the preparation of various substituted 4-aroyl-1-indanones **2** and 5-aroyl-1-tetralones **3** by photolytic induced methodology, in search of useful compounds with potential biological activities.

In summary, we have successfully presented a convenient synthetic methodology for producing a series of 4-aroyl-1-indanones and 5-aroyl-1-tetralones. Further studies on the biological evaluation of the available compounds are actively underway in laboratories.

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6. For compound **2a**: HRMS (ESI, M^++1) calcd for $C_{16}H_{13}O_2$ 237.0916, found 237.0921; ^{1}H NMR (400 MHz): δ 7.95 (dd, *J* = 0.4, 7.6 Hz, 1H), 7.81-7.77 (m, 3H), 7.63 (tt, *J* = 1.2, 6.8 Hz, 1H), 7.53-7.46 (m, 3H), 3.36-3.33 (m, 2H), 2.74-2.71 (m, 2H); ^{13}C NMR (100 MHz): δ 206.47, 196.16, 155.52, 138.28, 137.42, 135.78, 135.71 (2x), 133.13, 129.91 (2x), 128.58, 127.07, 126.82, 36.18, 25.83; Anal. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.59; H, 5.23. For compound **2b**: HRMS (ESI, M^++1) calcd for $C_{17}H_{15}O_3$ 267.1021, found 267.1024; ^{1}H NMR (400 MHz): δ 7.92 (dd, *J* = 0.8, 7.6 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 2H), 7.74 (dd, *J* = 1.2, 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 3.89 (s, 3H), 3.30-3.27 (m, 2H), 2.72-2.69 (m, 2H); ^{13}C NMR (100 MHz): δ 206.56, 194.73, 163.78, 154.93, 138.10, 136.48, 134.99, 132.42 (2x), 129.93, 127.01, 126.23, 113.86 (2x), 55.54, 36.16, 25.49. For compound **2c**: HRMS (ESI, M^++1) calcd for $C_{16}H_{12}FO_2$ 255.0821, found 255.0822; ^{1}H NMR (400 MHz): δ 7.90 (dd, *J* = 0.8, 7.6 Hz, 1H), 7.83-7.78 (m, 2H), 7.72 (dd, *J* = 1.2, 7.6 Hz, 1H), 7.46 (dt, *J* = 0.8, 7.6 Hz, 1H), 7.18-7.12 (m, 2H), 3.31-3.28 (m, 2H), 2.70-2.67 (m, 2H); ^{13}C NMR (100 MHz): δ 206.22, 194.44, 166.92, 164.38, 155.29, 138.24, 135.34, 133.56, 132.54, 132.45, 127.04, 126.76, 115.83, 115.61, 36.04, 25.64; Anal. Calcd for $C_{16}H_{11}FO_2$: C, 75.58; H, 4.36. Found: C, 75.72; H, 4.63. For compound **2d**: HRMS (ESI, M^++1) calcd for $C_{16}H_{13}O_3$ 253.0865, found 253.0866; ^{1}H NMR (400 MHz): δ 9.73 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.74-7.71 (m, 2H), 7.62-7.57 (m, 1H), 7.52-7.47 (m, 2H), 6.82 (d, *J* = 8.4 Hz, 1H), 3.46-3.43 (m, 2H), 2.79-2.76 (m, 2H); ^{13}C NMR (100 MHz): δ 210.50, 195.24, 160.60, 158.47, 140.36, 138.29, 132.40, 129.52 (2x), 128.46 (2x), 126.81, 123.26, 113.27, 35.97, 26.95; Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.51; H, 4.98. For compound **2e**: HRMS (ESI, M^++1) calcd for $C_{17}H_{15}O_4$ 283.0970, found 283.0972; ^{1}H NMR (400 MHz): δ 9.65 (br s, 1H), 7.77-7.73 (m, 3H), 6.99-6.95 (m, 2H), 6.82 (d, *J* = 8.8 Hz, 1H), 3.89 (s, 3H), 3.39 (dt, *J* = 3.2, 5.6 Hz, 2H), 2.76 (dt, *J* = 3.2, 5.6 Hz, 2H); ^{13}C NMR (100 MHz): δ 210.47, 193.91, 163.28, 160.16, 157.76, 139.63, 132.06 (2x), 130.68, 127.45, 123.16, 113.75 (2x), 113.14, 55.51, 35.96, 26.58; Anal. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.65; H, 4.78. Single-crystal X-Ray diagram: crystal of compound **2e** was grown by slow diffusion of ethyl acetate into a solution of compound **2e** in dichloromethane to yield colorless prism. The compound crystallizes in the monoclinic crystal system, space group P 1 21/c 1, *a* = 10.8910(19) Å, *b* = 11.973(2) Å, *c* = 10.0539(17) Å, *V* = 1310.0(4) Å^3, *Z* = 4, *d*calcd = 1.431 g/cm^3, *F*(000) = 592, 2θ range 1.87~26.45°, R indices (all data) R1 = 0.0581, wR2 = 0.1540. For compound **3a**: HRMS (ESI, M^++1) calcd for $C_{17}H_{15}O_2$ 251.1072, found 251.1077; ^{1}H NMR (400 MHz): δ 8.21 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.82-7.78 (m, 2H), 7.61 (tt, *J* = 1.6, 8.0 Hz, 1H), 7.52-7.45 (m, 3H), 7.40 (t, *J* = 8.0 Hz, 1H), 2.92 (t, *J* = 6.0 Hz, 2H), 2.68 (dd, *J* = 6.0, 7.2 Hz, 2H), 2.11-2.05 (m, 2H); ^{13}C NMR (100 MHz): δ 197.68, 197.49, 142.71, 138.65, 137.10, 133.64, 133.31, 132.84, 130.04 (2x), 129.31, 128.65 (2x), 126.01, 38.82, 27.37, 22.83; Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.90; H, 5.87. For compound **3b**: HRMS (ESI, M^++1) calcd for $C_{18}H_{17}O_3$ 281.1178, found 281.1180; ^{1}H NMR (400 MHz): δ 8.17 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.79-7.76 (m, 2H), 7.47 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 6.95-6.92 (m, 2H), 3.87 (s, 3H), 2.88 (t, *J* = 6.4 Hz, 2H), 2.66 (t, *J* = 6.4 Hz, 2H), 2.09-2.03 (m, 2H); ^{13}C NMR (100 MHz): δ 197.74, 196.10, 164.05, 142.26, 139.19, 133.20, 132.44 (2x), 132.34, 129.94, 128.83, 125.98, 113.89 (2x), 55.52, 38.84, 27.24, 22.82. For compound **3c**: HRMS (ESI, M^++1) calcd for $C_{17}H_{14}FO_2$ 269.0978, found 269.0981; ^{1}H NMR (400 MHz): δ 8.19 (dd, *J* = 1.2, 7.6 Hz, 1H), 7.85-7.80 (m, 2H), 7.48 (dd, *J* = 1.2, 7.6 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.17-7.11 (m, 2H), 2.90 (t, *J* = 6.0 Hz, 2H), 2.67 (t, *J* = 6.0 Hz, 2H), 2.10-2.04 (m, 2H); ^{13}C NMR (100 MHz): δ 197.51, 195.84, 167.29, 164.74, 142.58, 138.33, 133.36, 132.76, 132.66, 132.59, 129.37, 126.05, 115.97, 115.75, 38.77, 27.30, 22.77; Anal. Calcd for $C_{17}H_{13}FO_2$: C, 76.11; H, 4.88. Found: C, 76.29; H, 5.02.
7. CCDC 802675 (**2e**) and CCDC 805713 (**2f**) contain the supplementary crystallographic data for this paper. This data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: 44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk)