Friedel–Crafts Acylation of Arenes Catalyzed by Bromopentacarbonylrhenium(I)

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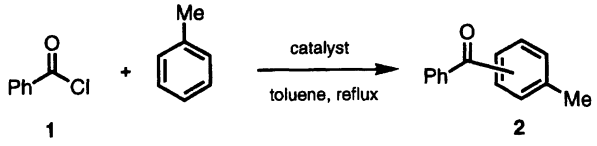
The intermolecular Friedel–Crafts acylation of aromatic compounds (such as toluene, *m*-xylene, and anisole) with various acid chlorides proceeds by using a catalytic amount of bromopentacarbonylrhenium(I) to afford aryl ketones. Intramolecular acylation is also catalyzed by the above-mentioned catalyst to give indanone and tetralone derivatives.

The Friedel–Crafts acylation of arenes is one of the most fundamental and useful transformations in organic synthesis.[1] This reaction generally requires at least an equimolar amount of Lewis acid because of the complexation of Lewis acid with the products. Although there have been reported some practical methods for the catalytic Friedel–Crafts acylation of anisole and mesitylene,[2,3] most of them are not utilized for acylation of less reactive arenes, such as xylene, toluene, and benzene. Very recently, it was reported that toluene and xylene could be acylated with acid anhydrides by a treatment with a catalytic amount of $Hf(OTf)_4$ in CH_3NO_2 containing $LiClO_4$.[4] Although trifluoromethanesulfonic acid also catalyzes the Friedel–Crafts acylation reaction, an acylating reagent is limited to benzoyl chloride.[5] During the course of our study for developing rhenium compound-catalyzed reactions, we found that bromopentacarbonylrhenium(I) ([$ReBr(CO)_5$]) promoted the Friedel–Crafts acylation of arenes with acid chlorides. This report summarizes the catalytic Friedel–Crafts acylation using [$ReBr(CO)_5$] as a catalyst.

Results and Discussion

Intermolecular Reaction. The Friedel–Crafts acylation of toluene with benzoyl chloride (**1**) was investigated, and the treatment of **1** with a 0.1 molar amount of [$ReX(CO)_5$] (X=Br or Cl) in refluxing toluene under an argon atmosphere gave an acylated product, 4-methylbenzophenone (**2**), in high yield (Table 1, Entries 1 and 2). This reaction also proceeded smoothly, even upon using a 0.05 or a 0.01 molar amount of the catalyst (Entries 3 and 4). However, when an analogous complex of the other element in a group 7, [$MnBr(CO)_5$], was employed as a catalyst, the reaction was hardly promoted (Entry 5).

Since [$ReX(CO)_5$] was found to be an effective catalyst for Friedel–Crafts acylation, reactions of toluene and *m*-xylene with several acid chlorides were examined by the catalytic use of [$ReBr(CO)_5$]. As shown in Tables 2 and 3, benzoyl, alkanoyl, and cycloalkanecarbonyl chlorides could be used as acylating reagents in these reactions, and the corresponding aryl ketones were obtained in good yield with high *para*-selectivity, although



1 **2**

Table 1. Effect of the Catalyst

Entry	Catalyst	Molar amount	Time/h	Yield/%
1	[$ReBr(CO)_5$]	0.1	2	91[a]
2	[$ReCl(CO)_5$]	0.1	2	90
3	[$ReBr(CO)_5$]	0.05	4	88
4	[$ReBr(CO)_5$]	0.01	5	72
5	[$MnBr(CO)_5$]	0.1	4	7

a) The ratio of *o* : *m* : *p* was 11 : 4 : 85.

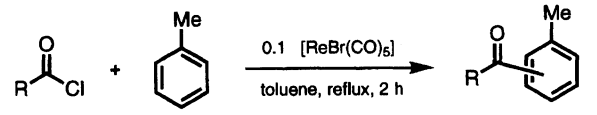


Table 2. Catalytic Friedel–Crafts Acylation of Toluene

Entry	R	Yield/%[a]	Ratio of *o* : *m* : *p*[b]
1	Ph	91	11 : 4 : 85
2	$PhCH_2$	84	5 : 3 : 92
3	*n*-C_5H_{11}	73	3 : 2 : 95
4	*c*-C_6H_{11}	72	6 : 2 : 92
5[c]	Me	40	6 : 3 : 91

a) The yield was based on acid chloride. b) The ratio of *o* : *m* : *p* was determined by GC analysis. c) The reaction was carried out at 120 °C in a sealed tube.

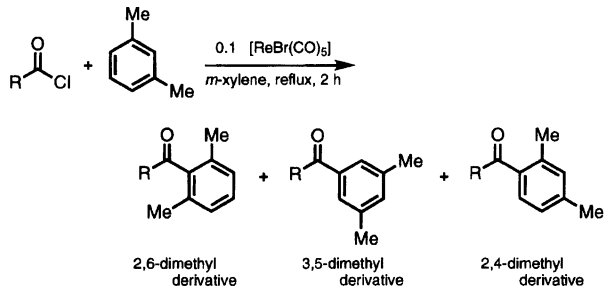


Table 3. Catalytic Friedel–Crafts Acylation of *m*-Xylene

Entry	R	Yield/%[a]	Isomer ratio[b] 2,6- : 3,5- : 2,4-
1	Ph	96	8 : 1 : 91
2	$PhCH_2$	88	4 : 1 : 95
3	*n*-C_5H_{11}	80	4 : 2 : 94
4	*c*-C_6H_{11}	70	6 : 2 : 92

a) The yield was based on acid chloride. b) The ratio of 2,6- : 3,5- : 2,4- was determined by GC analysis.

the acetylation of toluene with acetyl chloride gave *p*-methylacetophenone in low yield (Table 2, Entry 5). The regioselectivity in these reactions was almost at the same level as that in the reactions with $AlCl_3$ or $FeCl_3$.[6]

The acylation of anisole was catalyzed smoothly by the rhenium complex; the treatment of acid chlorides and 2 molar amounts of anisole with a 0.02 molar amount of [$ReBr(CO)_5$] in refluxing 1,2-dichloroethane gave the corresponding *p*-methoxyphenyl ketones in high yield (Table 4). Acetic anhydride could also be utilized as an acylating reagent for the acetylation of anisole (Eq. 1).

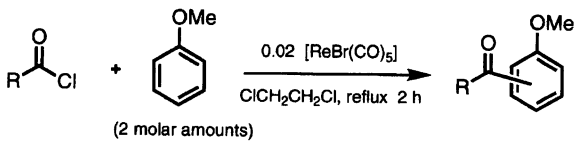
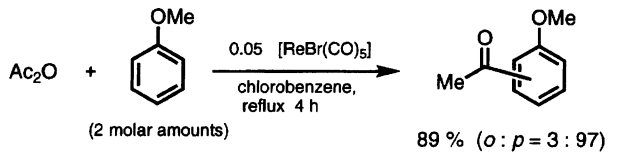


Table 4. Catalytic Friedel–Crafts Acylation of Anisole

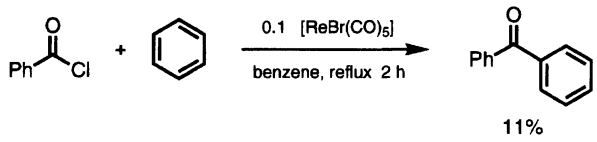
Entry	R	Yield/%[a]	Ratio of *o* : *m* : *p*[b]
1	Ph	92	5 : 0 : 95
2	*n*-C_5H_{11}	90	1 : 0 : 99
3	*c*-C_6H_{11}	95	1 : 0 : 99
4	PhCH=CH	60 (77)[c]	7 : 3 : 90

a) The yield was based on acid chloride. b) The ratio of *o* : *m* : *p* was determined by GC analysis. c) A 0.05 molar amount of [$ReBr(CO)_5$] was used.



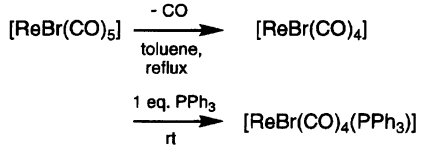
(1)

Although the acylation of toluene, *m*-xylene, and anisole proceeded smoothly by the catalytic use of [$ReBr(CO)_5$], the acylation of benzene was hardly promoted. The reaction of benzene with benzoyl chloride gave benzophenone in low yield (Eq. 2); the yield was not improved when the reaction was performed even at 120 °C in a sealed tube. The reaction with an aliphatic acid chloride, such as hexanoyl chloride, did not proceed at all.



(2)

Studies on the Active Catalytic Species. The present catalyst, [$ReBr(CO)_5$], is a coordinatively saturated 18-electron complex, and no additional coordination site remains on the rhenium. Therefore, the generation of a coordinatively unsaturated complex should be necessary to promote Friedel–Crafts acylation. It has been reported that a coordinatively unsaturated 16-electron complex, [$ReBr(CO)_4$], is generated from [$ReBr(CO)_5$] along with the liberation of CO in refluxing toluene. This compound is trapped by triphenylphosphine to form bromotetracarbonyl(triphenylphosphine)rhenium(I), [$ReBr(CO)_4(PPh_3)$] (Eq. 3),[7] or is converted to a dimeric rhenium carbonyl complex, [$ReBr(CO)_4]_2$, in the absence of ligands (Eq. 4).[8] Furthermore, this dimeric complex reacts very easily at room temperature with some ligands (L), such as triphenylphosphine or pyridine, to give a monomeric complex, [$ReBr(CO)_4(L)$], in 60—80% yield (Eq. 5).[9]



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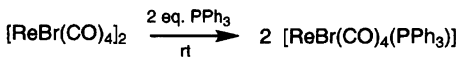
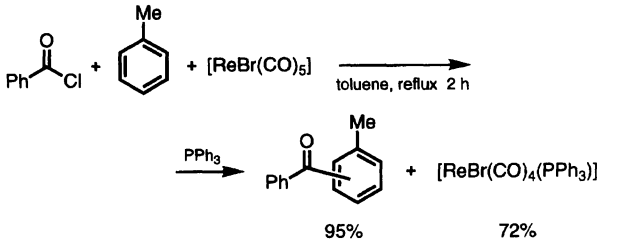


(5)

These facts have demonstrated that a possible catalytic species in the present Friedel–Crafts acylation is the coordinatively unsaturated [$ReBr(CO)_4$], which was generated by the liberation of carbon monooxide from [$ReBr(CO)_5$] and/or by the dissociation of the dimeric complex [$ReBr(CO)_4]_2$ to the monomeric complex. To confirm this consideration, the acylation reaction of toluene with benzoyl chloride was carried out using an equimolar amount of the catalyst to isolate rhenium residues after completion of the reaction. That is, when the acylation reaction of toluene with benzoyl chloride was performed using an equimolar amount of

$[ReBr(CO)_5]$ at reflux temperature for 2 h, the reaction mixture was then treated with an equimolar amount of triphenylphosphine after cooling to 40—50 °C; $[ReBr(CO)_4(PPh_3)]$ was obtained in 72% yield along with the acylated product in 95% yield (Eq. 6). The reaction was also examined by using a 0.05 molar amount of the dimeric rhenium complex, $[ReBr(CO)_4]_2$; the product was isolated in 93% yield, which was almost the same yield as that in the reaction catalyzed by $[ReBr(CO)_5]$ (Eq. 7). These two results strongly indicate that rhenium complexes exist as $[ReBr(CO)_4(L)]$ (L=product) and/or $[ReBr(CO)_4]_2$ after completion of the reaction. Presumably, the coordinatively unsaturated $[ReBr(CO)_4]$ works as a Lewis acid.



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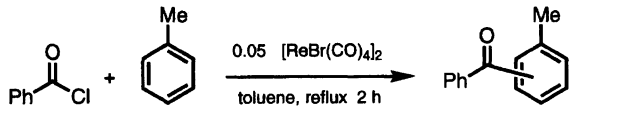
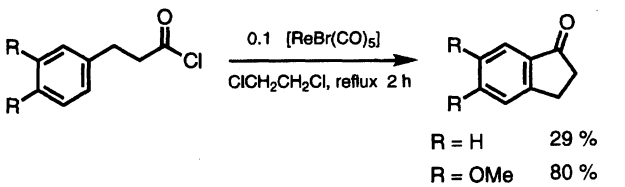


(7)

Intramolecular Reaction. The preparation of indanone and tetralone derivatives was investigated by $[ReBr(CO)_5]$-catalyzed intramolecular Friedel–Crafts acylation. Though the reaction of 3-phenylpropionyl chloride with a catalytic amount of $[ReBr(CO)_5]$ in refluxing 1,2-dichloroethane did not give a satisfactory result to yield 1-indanone in 29% yield, the 3′,4′-dimethoxy derivative cyclized smoothly to afford 5,6-dimethoxy-1-indanone in 80% yield (Eq. 8). In contrast to the above indanone formation, tetralone was formed very smoothly without introducing any other electron-donating groups; the treatment of 4-phenylbutyryl chloride with a 0.1 molar amount of $[ReBr(CO)_5]$ afforded 1-tetralone in 86% yield (Eq. 9).



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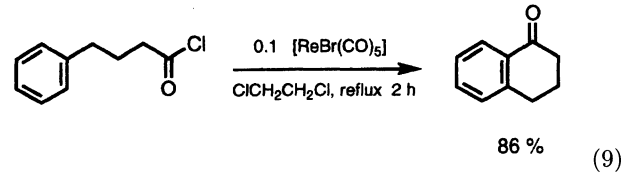

(9)

Experimental

General. The ^1H NMR (500 MHz) spectra in $CDCl_3$ were recorded on Bruker AM500 and JEOL α-500 spectrometers using chloroform as an internal standard (δ = 7.24). The ^{13}C NMR (125 MHz) spectra were measured with a Bruker AM500 spectrometer using $CDCl_3$ as an internal standard (δ = 77.0). IR spectra were recorded on a Horiba FT-300S spectrometer. Gas chromatography was performed with a Shimadzu GC-14BPFSC system. FAB-MS spectra were measured with a JEOL JMS-SX102A using 2-nitrophenyl octyl ether as a matrix. Preparative thin-layer chromatography (TLC) was carried out on a silica gel (Wakogel B-5F). Benzene, toluene, *m*-xylene, and anisole were distilled and dried over MS 4A. 1,2-Dichloroethane and chlorobenzene were distilled from P_2O_5, then from CaH_2, and dried over MS 4A. Acid chlorides were purchased from Tokyo Kasei Kogyo Co., Ltd. or Aldrich Chemical Co., Inc. and distilled from CaH_2. Triphenylphosphine was recrystallized from ethanol and dried under a vacuum. Bromopentacarbonylrhenium(I) was prepared from decacarbonyldirhenium and bromine according to a literature procedure[10] or purchased from Strem Chemicals Inc. Chloropentacarbonylrhenium(I) and bromopentacarbonylmanganese(I) were purchased from Strem Chemicals Inc. Bromotetracarbonylrhenium dimer was prepared from bromopentacarbonylrhenium(I) by the literature method.[8] All reactions were carried out under an argon atmosphere.

Typical Procedure for Acylation of Toluene or *m*-Xylene. To a *m*-xylene (3 ml) suspension of bromopentacarbonylrhenium(I) (38.2 mg, 0.094 mmol) was added a *m*-xylene solution (3 ml) of benzoyl chloride (128 mg, 0.91 mmol). After the mixture was heated to reflux for 2 h, the solvent was removed in vacuo. The crude materials were purified by thin-layer chromatography (silica gel, hexane : ethyl acetate=4 : 1) to give 4-methylbenzophenone (185 mg, 96% yield).

Typical Procedure for Acylation of Anisole. After 1,2-dichloroethane solutions (2 ml) of benzoyl chloride (173 mg, 1.23 mmol) and anisole (265 mg, 2.45 mmol) were added to a 1,2-dichloroethane (3 ml) suspension of bromopentacarbonylrhenium(I) (10.3 mg, 0.025 mmol), the mixture was heated to reflux for 2 h. The solvent was removed in vacuo and the crude materials were purified by thin-layer chromatography (silica gel, hexane : ethyl acetate=4 : 1) to give 4-methoxybenzophenone (240 mg, 92% yield).

Acetylation of Anisole with Acetic Anhydride. Chlorobenzene solutions (2 ml) of acetic anhydride (74.0 mg, 0.72 mmol) and anisole (167 mg, 1.50 mmol) were added to a chlorobenzene (2 ml) suspension of bromopentacarbonylrhenium(I) (15.4 mg, 0.037 mmol). After the mixture was heated to reflux for 2 h, the reaction was quenched with saturated aqueous sodium hydrogencarbonate. The mixture was extracted three times with dichloromethane, and the combined extracts were washed with brine and dried over anhydrous sodium sulfate. After the solvent was removed in vacuo, the crude materials were purified by thin-layer chromatography (silica gel, hexane : ethyl acetate=4 : 1) to give 4-methoxyacetophenone (96.2 mg, 89% yield).

Trapping Experiment of Rhenium Residues with Triphenylphosphine. A toluene solution (3 ml) of benzoyl chloride (37.0 mg, 0.26 mmol) was added to a toluene

(3 ml) suspension of bromopentacarbonylrhenium(I) (93.7 mg, 0.23 mmol); the mixture was then heated to reflux for 2 h. After cooling the mixture to 40—50 °C, a toluene solution (2 ml) of triphenylphosphine (66.1 mg, 0.25 mmol) was added and the mixture was stirred for 1 h. The solvent was removed in vacuo and the crude materials were purified by thin-layer chromatography (silica gel, hexane : ethyl acetate=10 : 1) to give 4-methylbenzophenone (50 mg, 95% yield) and bromotetracarbonyl(triphenylphosphine)rhenium(I) (106 mg, 72% yield).

Typical Procedure for Intramolecular Acylation. To a 1,2-dichloroethane (4 ml) suspension of bromopentacarbonylrhenium(I) (22.5 mg, 0.055 mmol) was added a 1, 2-dichloroethane solution (2 ml) of 4-phenylbutyryl chloride (91.4 mg, 0.50 mmol). After the mixture was heated to reflux for 2 h, the solvent was removed in vacuo. The crude materials were purified by thin-layer chromatography (silica gel, hexane : ethyl acetate=4 : 1) to give 1-tetralone (63 mg, 86% yield).

Spectral Data. All of the products are the known compounds, and their spectral data are in good agreement with those of the literature or authentic samples.

4-Methylbenzophenone:[11] ^{1}H NMR δ=2.42 (3H, s), 7.26 (2H, d, J=8.0 Hz), 7.43—7.48 (2H, m), 7.54—7.57 (1H, m), 7.71 (2H, d, J=8.0 Hz), 7.75—7.78 (2H, m).

Benzyl 4-Methylphenyl Ketone:[12] ^{1}H NMR δ=2.39 (3H, s), 4.24 (2H, s), 7.21—7.32 (7H, m), 7.90 (2H, d, J=8.2 Hz).

Pentyl 4-Methylphenyl Ketone:[11] ^{1}H NMR δ=0.88 (3H, t, J=7.0 Hz), 1.30—1.36 (4H, m), 1.67—1.72 (2H, m), 2.38 (3H, s), 2.90 (2H, t, J=7.4 Hz), 7.22 (2H, d, J=8.1 Hz), 7.83 (2H, d, J=8.1 Hz).

Cyclohexyl 4-Methylphenyl Ketone:[13] ^{1}H NMR δ=1.22—1.30 (1H, m), 1.32—1.42 (2H, m), 1.44—1.52 (2H, m), 1.69—1.75 (1H, m), 1.80—1.89 (4H, m), 2.39 (3H, s), 3.22 (1H, tt, J=3.2, 11.3 Hz), 7.23 (2H, d, J=8.4 Hz), 7.83 (2H, d, J=8.4 Hz).

4-Methylphenyl Methyl Ketone:[11] ^{1}H NMR δ=2.39 (3H, s), 2.56 (3H, s), 7.24 (2H, d, J=8.0 Hz), 7.84 (2H, d, J=8.0 Hz).

2,4-Dimethylbenzophenone:[11] ^{1}H NMR δ=2.32 (3H, s), 2.37 (3H, s), 7.03 (1H, d, J=7.8 Hz), 7.10 (1H, s), 7.22 (1H, d, J=7.8 Hz), 7.43 (2H, t, J=7.5 Hz), 7.55 (1H, t, J=7.5 Hz), 7.77 (2H, d, J=7.5 Hz).

Benzyl 2,4-Dimethylphenyl Ketone:[14] ^{1}H NMR δ=2.35 (3H, s), 2.48 (3H, s), 4.21 (2H, s), 7.05—7.08 (2H, m), 7.23—7.29 (3H, m), 7.31—7.34 (2H, m), 7.70 (1H, d, J=7.8 Hz).

Pentyl 2,4-Dimethylphenyl Ketone:[14] ^{1}H NMR δ=0.88 (3H, t, J=6.9 Hz), 1.29—1.35 (4H, m), 1.64—1.70 (2H, m), 2.33 (3H, s), 2.46 (3H, s), 2.84 (2H, t, J=7.4 Hz), 7.02—7.04 (2H, m), 7.54 (1H, d, J=8.3 Hz).

Cyclohexyl 2,4-Dimethylphenyl Ketone:[11] ^{1}H NMR δ=1.20—1.35 (3H, m), 1.37—1.46 (2H, m), 1.65—1.70 (1H, m), 1.75—1.86 (4H, m), 2.32 (3H, s), 2.39 (3H, s), 3.03 (1H, tt, J=3.4, 11.3 Hz), 7.01—7.04 (2H, m), 7.43 (1H, d, J=7.8 Hz).

4-Methoxybenzophenone:[11] ^{1}H NMR δ=3.86 (3H, s), 6.94 (2H, d, J=8.8 Hz), 7.45 (2H, dd, J=7.5, 7.8 Hz), 7.54 (1H, t, J=7.5 Hz), 7.74 (2H, d, J=7.8 Hz), 7.81 (2H, d, J=8.8 Hz); ^{13}C NMR δ=55.4, 113.5, 128.1, 129.7, 130.1, 131.8, 132.5, 138.3, 163.2, 195.5.

Pentyl 4-Methoxyphenyl Ketone:[15] ^{1}H NMR δ=0.86 (3H, t, J=7.4 Hz), 1.27—1.32 (4H, m), 1.65—1.69 (2H, m), 2.84 (2H, t, J=7.4 Hz), 3.79 (3H, s), 6.87 (2H, d, J=8.8 Hz), 7.88 (2H, d, J=8.8 Hz); ^{13}C NMR δ=13.8, 22.4, 24.2, 31.5, 38.1, 55.2, 113.5, 130.1, 130.2, 163.2, 199.0.

Cyclohexyl 4-Methoxyphenyl Ketone:[11] ^{1}H NMR δ=1.23—1.28 (1H, m), 1.31—1.40 (2H, m), 1.43—1.51 (2H, m), 1.67—1.73 (1H, m), 1.78—1.87 (4H, m), 3.19 (1H, tt, J=3.2, 11.4 Hz), 3.83 (3H, s), 6.90 (2H, d, J=8.9 Hz), 7.91 (2H, d, J=8.9 Hz); ^{13}C NMR δ=25.9, 26.0, 29.5, 45.3, 55.4, 113.7, 129.2, 130.5, 163.2, 202.4.

2- Phenylethenyl 4- Methoxyphenyl Ketone:[11] ^{1}H NMR δ=3.86 (3H, s), 6.96 (2H, d, J=8.9 Hz), 7.36—7.41 (3H, m), 7.55 (1H, d, J=15.7 Hz), 7.61—7.64 (2H, m), 7.79 (1H, d, J=15.7 Hz), 8.03 (2H, d, J=8.9 Hz); ^{13}C NMR δ=55.3, 113.7, 121.8, 128.2, 128.8, 130.2, 130.7, 131.0, 135.0, 143.8, 163.3, 188.6.

4-Methoxyphenyl Methyl Ketone:[11] ^{1}H NMR δ=2.53 (3H, s), 3.84 (3H, s), 6.91 (2H, d, J=8.9 Hz), 7.91 (2H, d, J=8.9 Hz).

Bromotetracarbonyl(triphenylphosphine)rhenium (I):[9] IR (KBr) 2106, 2021, 2004, 1946 cm^{-1}; FAB-MS Calcd for $C_{22}H_{15}{}^{79}BrO_4P{}^{187}Re$: M, 639.9432. Found: m/z 639.9393.

1-Indanone:[11] ^{1}H NMR δ=2.67 (2H, t, J=5.9 Hz), 3.12 (2H, t, J=5.9 Hz), 7.34 (1H, t, J=7.5 Hz), 7.46 (1H, d, J=7.5 Hz), 7.56 (1H, t, J=7.5 Hz), 7.74 (1H, d, J=7.5 Hz).

5,6-Dimethoxy-1-indanone:[11] ^{1}H NMR δ=2.64 (2H, t, J=5.6 Hz), 3.02 (2H, t, J=5.6 Hz), 3.88 (3H, s), 3.94 (3H, s), 6.86 (1H, s), 7.15 (1H, s); ^{13}C NMR δ=25.5, 36.5, 56.0, 56.2, 104.0, 107.4, 129.9, 149.3, 150.4, 155.3, 205.8.

1-Tetralone:[11] ^{1}H NMR δ=2.08—2.14 (2H, m), 2.61—2.65 (2H, m), 2.92—2.96 (2H, m), 7.23 (1H, d, J=7.6 Hz), 7.28 (1H, t, J=7.6 Hz), 7.44 (1H, dt, J_d=1.3 Hz, J_t=7.6 Hz), 8.01 (1H, dd, J=1.3, 7.6 Hz); ^{13}C NMR δ=23.2, 29.6, 39.1, 126.5, 127.0, 128.7, 132.5, 133.3, 144.4, 198.2.

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