Conversion of Ketone Trimethylsilylcyanohydrins to Several Types of Compounds

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Cyclic ketone *O*-trimethylsilylcyanohydrins (2) were prepared and converted to various compounds: α-hydroxyketones (3), dehydroxylated ketones (4), α,β-unsaturated ketones (9), tricyclic ketones (10), 1-ethoxycarbonyl-4-phenyl-1,2,4a,5,6,7,8,8a-octahydro-2-naphthalenone (13), 1-phenylperhydroisocoumarin (18) and 1,2,3,4,4a,10,11,11a-octahydro-5*H*-benzo[*a*,*d*]cyclohepten-10-one (20).

Key words *O*-trimethylsilylcyanohydrin; MOPAC; Nazarov cyclization; α,β-unsaturated ketone; lactone; tricyclic ketone

Aldehydes and ketones can be readily converted to the corresponding *O*-trimethylsilylcyanohydrins (**2**; TMSCH) by treatment with trimethylsilyl cyanide in the presence of lithium cyanide or zinc iodide, and the products (**2**) can be easily reconverted to the original carbonyl compounds by treatment with acid and subsequent dehydrocyanation with base.[1] In the field of organic synthesis, the TMSCH (**2**) have been conveniently used as a source of α-cyanohydrin,[2] a protected form of carbonyl group[1b-e] and a carbonyl anion-equivalent ($R^1R^2C=O$).[3,4] In the literature, there are a few other synthetic uses of TMSCH in conversion to α,β-unsaturated nitriles by dehydration with acid,[5] conversion to β-aminoalcohols by reduction with hydride reagent,[6] and some others.[5] We have explored new synthetic applications of compound **2**, which are readily available from carbonyl compounds, and this paper deals with conversions of cyclic ketone TMSCH to several types of compounds. According to the reported procedure,[1] various TMSCH (**2**) were prepared by treatment of carbonyl compounds with trimethylsilyl cyanide (TMSCN) in the presence of a catalytic amount of *n*-butyllithium, and the prepared TMSCH (**2**) are listed in Table 1 (Chart 1).

First, we tried reaction of TMSCH (**2**) with phenylmagnesium bromide followed by acidic treatment to give the corresponding α-hydroxyketones (**3**) in good to fair yields with recovery of a considerable amount of the starting TMSCH (**2**), but the formation of α-hydroxyketones (**3**) by reaction of **2** with alkylmetal reagents such as methylmagnesium bromide, allylmagnesium bromide, methyllithium and *n*-butyllithium hardly proceeded, and most of the starting material (**2**) was recovered probably because of the steric hindrance around the nitrile function of **2**. When a catalytic amount of triethylaluminum was added in order to activate the nitrile function of **2**, reaction of **2a**[1] with 2-phenylethylmagnesium bromide proceeded to give **3g** in moderate yield after a prolonged reaction time. However, it is noteworthy that increase in the amount of triethylaluminum rather decreased the yield of **3g** with an increase in the yield of **3h** (Chart 2, Table 2).

Reductive dehydroxylation of the α-*tert*-hydroxyketone (**3**) was tried. The hydroxyketone (**3a**)[6] was treated with zinc dust in acetic acid–10% hydrochloric acid at 90 °C (entry 7 in Table 3) to give the dehydroxylated ketone (**4a**[7]; 73.0%) and the over-reduced and dehydrated product (**5**,[8] 20.3%). Table 3 shows results from zinc-reduction under various conditions: the best yield of **4a** (83.3%) was obtained in run 8 (60 °C/4 h in acetic acid) accompanied with the alkene **5** in 5.3% yield. The result of this reductive dehydroxylation of **3** to **4** can be regarded as a formal one-carbon shift from the position of the carbonyl group of the original cyclic ketone (**1**). Table 4 shows results of the zinc metal reduction for the various hydroxyketones (**3b—f**) to **4b—f**, **5** and the over-reduced products (**6b**,[9] **6c**,[10] **7**,[11] and **8**[12]) under the same reaction conditions (except for run 9) as used for runs 7 and 8 in Table 3. As shown in Table 4, production of the by-products in the zinc-reduction varied depending on the substrate (**3**).

After several attempts, it was found that dehydration

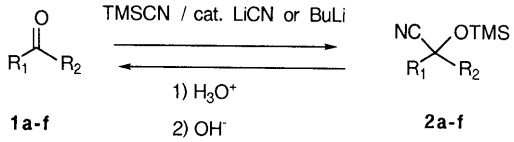

Chart 1

Table 1. Preparation of TMSCH (**2**)

Entry	1		Yield of 2 (%)	IR (C≡N in $CHCl_3$)	bp (°C) (mmHg)
1	**1a**: R_1, R_2=		**2a**: 94.9	2215	104 (23)
2	**1b**: R_1, R_2=		**2b**: 97.4	2210	90 (6)
3	**1c**: R_1, R_2=		**2c**: 96.7	2210	111 (7)
4	**1d**: R_1, R_2=		**2d**: 90.6	2210	mp 37.3—39.0
5	**1e**: R_1, R_2=		**2e**: 98.2	2210	148 (3)
6	**1f**: R_1=H, R_2=		**2f**: 98.3	2210	84 (4)

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Table 2. Reaction of TMSCH (**2**) with Grignard Reagent

Entry	**2**	RMgX (Solv.)	Equiv. of Et_3Al	Temp./time	Isolated yield of **3** (%)
1	**2a**: $R_1, R_2=$  ($n=1$)	C_6H_5MgBr (Et_2O)	—	r.t./3 h	**3a**: 86.5
2	**2b**: $R_1, R_2=$  ($n=2$)	C_6H_5MgBr (Et_2O)	—	r.t./3 h	**3b**: 82.8
3	**2c**: $R_1, R_2=$  ($n=3$)	C_6H_5MgBr (Et_2O)	—	r.t./3 h	**3c**: 83.7
4	**2d**: $R_1, R_2=$  ($n=7$)	C_6H_5MgBr (Et_2O)	—	r.t./3 h	**3d**: 72.7
5	**2e**: $R_1, R_2=$ 	C_6H_5MgBr (Et_2O)	—	r.t./3 h	**3e**: 51.9
6	**2f**: $R_1=H, R_2=$ 	C_6H_5MgBr (Et_2O)	—	r.t./3 h	**3f**: 54.1
7	**2a**: $R_1, R_2=$ 	$C_6H_5CH_2CH_2MgBr$ (Et_2O)	—	r.t./7 d	**3g**: 15.2
8	**2a**: R_1, R_2 	$C_6H_5CH_2CH_2MgBr$ (Et_2O)	0.025	r.t./7 d	**3g**: 47.5
9	**2a**: R_1, R_2 	$C_6H_5CH_2CH_2MgBr$ (Et_2O)	0.1	r.t./3 d	**38**: 18.0
10	**2a**: R_1, R_2 	$C_6H_5CH_2CH_2MgBr$ (THF)	0.1	r.t./24 h	**3g**: 11.3
11	**2a**: R_1, R_2 	$C_6H_5CH_2CH_2MgBr$ (Et_2O)	0.1	r.t./7 d	**3h**: 76.6
12	**2a**: R_1, R_2 	$CH_2=CH_2MgBr$ (Et_2O)	—	r.t./3 d	**3i**: 5.0

Table 3. Acidic Reduction of the Hydroxyketone (**3**) with Zn

Entry	Solvent (acid)	Zn (eq)	Temp. (°C)	Reaction time (h)	Isolated yield (%)		
					3a	**4a**	**5**
1	AcOH	1	r.t.	24	76.3	4.7	—
2	AcOH	1	Reflux	4	29.2	55.1	—
3	AcOH/10%HCl (1/1)	1	r.t.	24	72.7	10.3	—
4	AcOH/10%HCl (1/1)	1	Reflux	4	35.2	48.5	—
5	AcOH	3	90 °C	2	22.0	64.9	1.1
6	AcOH	5	90 °C	2	—	72.1	5.4
7	AcOH	7	90 °C	2	—	73.0	20.3
8	AcOH	7	60 °C	4	—	83.3	5.3
9	AcOH	7	r.t.	24	31.9	49.7	—

4a: $R_1, R_2=-(CH_2)_5-$; R = Ph.

of the hydroxyketone (**3a**) to the corresponding α,β-unsaturated ketone (**9a**)[13] was best achieved by stirring a two-layer mixture consisting of a solution of **3a** in chloroform and concentrated sulfuric acid at room temperature to give **9a** in 71.0% yield accompanied with a small amount of the Nazarov-type cyclization product (**10a**,[14] 3.8% yield). The tricyclic ketone (**10a**) seems to be produced *via* the unsaturated ketone **9a** because similar treatment of **9a** with sulfuric acid in chloroform gave **10a** in 53.6% yield. The stereochemistry of the ring juncture of **10a** was considered to be *cis* on the basis of the proton nuclear magnetic resonance spectrum (^{1}H-NMR) [J values between 9b-H and 4a-H = 7.0 Hz]. Several other α-hydroxyketones (**3b—d, g**) were similarly treated with sulfuric acid, and it was found that the yields of the dehydrated products (**9**) decreased with increase in

Table 4. Reduction of the Hydroxyketones (**3**) under the Conditions of Entry 8 in Table 3

Entry	**3**	Temp. (°C)	Time (h)	Isolated yield (%)			
				3	**4**	**6**	**7** or **8**
1	**3b**	60	8	**3b**: 4.3	**4b**: 81.3	**6b**: 7.2	—
2	**3b**	90	2	**3b**: 0	**4b**: 71.6	**6b**: 12.6	—
3	**3c**	60	12	**3c**: 2.5	**4c**: 83.1	**6c**: 3.2	—
4	**3c**	90	4	**3c**: 0	**4c**: 77.7	**6c**: 10.9	—
5	**3d**	60	24	**3d**: 14.5	**4d**: 56.3	—	—
6	**3d**	90	9	**3d**: 0.5	**4d**: 84.9	—	—
7	**3e**	60	24	**3e**: 19.5	**4e**: 53.5	—	**7**: 3.8
8	**3e**	90	24	**3e**: 11.4	**4e**: 60.1	—	**7**: 3.8
9	**3e**	Refl.	3	**3e**: 0	**4e**: 67.2	—	**7**: 8.2
10	**3f**	60	24	**3f**: 22.6	**4f**: 0	—	**8**: 60.8
11	**3f**	90	24	**3f**: 12.9	**4f**: 0	—	**8**: 70.5

R^1, R^2, and R of **4**, **6**, **7** and **8** are the same as those of the corresponding **3a—f** shown in Table 2.

the value of n-number ($n=1$, 2, 3) while the yields of the Nazarov-type cyclization products (**10**) decreased correspondingly, as shown in Table 5. In the cases of the large ring ketone **3d** ($n=7$) and aliphatic acyclic ketone **3g**, the corresponding Nazarov-type products were not obtained at all probably because of elevation of the activation energy for the such Nazarov-type cyclization owing to steric factors. We calculated the activation enthalpies of bond formation between the possible carbonium ions (**11a—d**) and the *ortho*-position of the phenyl group by use of a personal computer program, "Pasocon MOPAC/

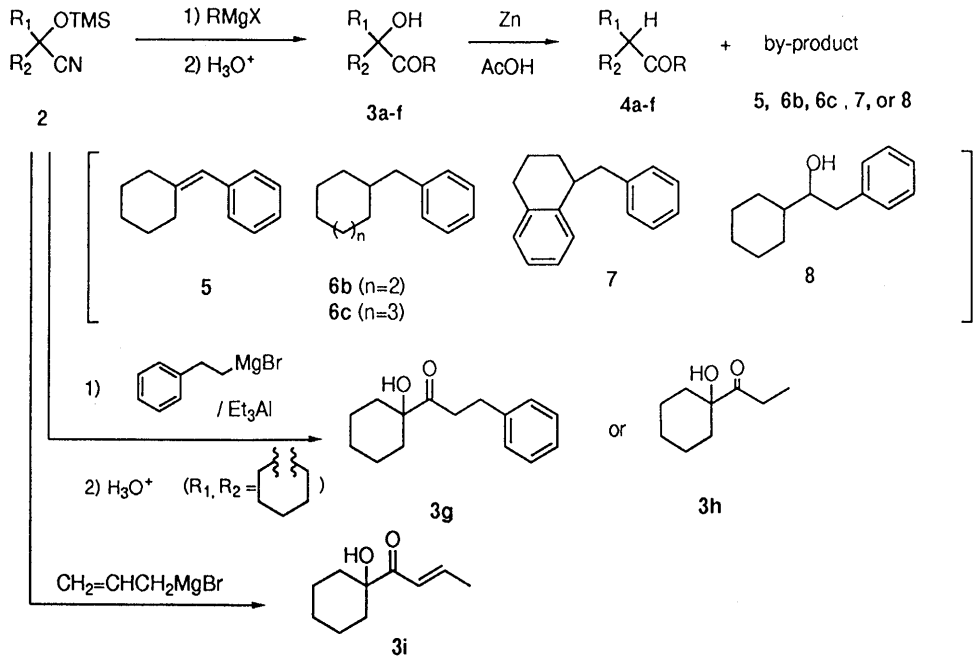


Chart 2

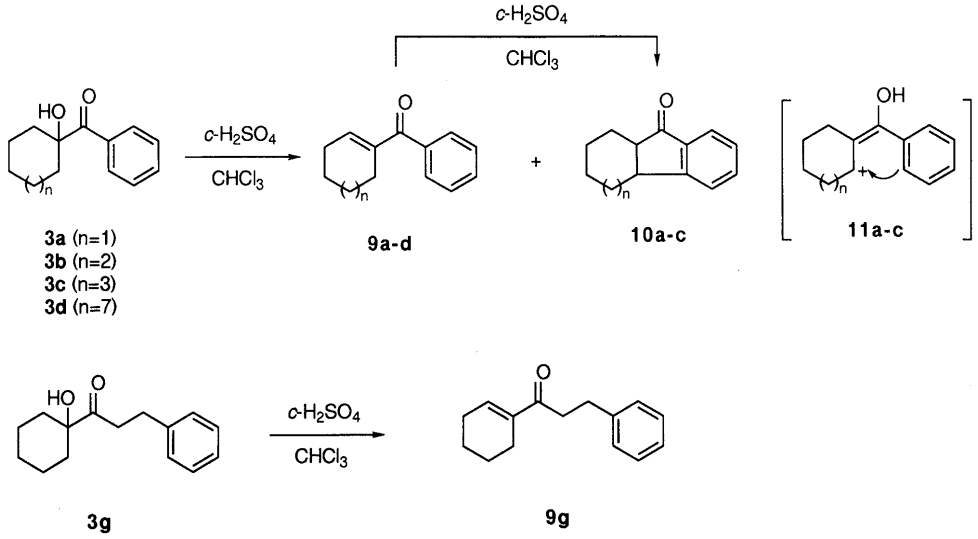


Chart 3

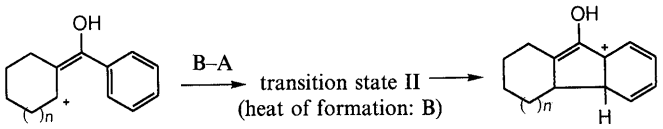
Table 5. Dehydration and Cyclization of the Hydroxyketones (3)

Entry	3	n	Isolated yield (%) of products	
			9	10
1	3a	1	9a: 71.0	10a: 3.8
2	3b	2	9b: 10.1	10b: 79.4
3	3c	3	9c: 12.2	10c: 64.4
4	3d	7	9d: 60.3	—
5	3g	—	9g: 80.2	—

386,"[12] which is based on MOPAC (V3.1 QCPE No. 455),[15] and the results are summarized in Table 6. As shown in Table 6, the order of the differences of B–A is $n=1>n=2>n=3$. This is consistent with the cyclization yields in the conversions of **3a**, **3b** and **3c** to **10a**, **10b** and **10c**, respectively.

Next, Michael reactions of the α,β-unsaturated ketone

Table 6. MOPAC Calculation for Transition Energies in the Cyclization of **3a—c** to **10a—c**



intermediate I ($n=1, 2, 3$) (heat of formation: A)

intermediate III ($n=1, 2, 3$) (heat of formation: C)

n	A Heat of formation of the intermediate I (kcal/mol)	B Heat of formation of the transition state I (kcal/mol)	Difference B–A (kcal/mol)	C Heat of formation of the intermediate III (kcal/mol)
1	154.16	182.28	28.12	166.45
2	153.35	179.50	26.15	163.55
3	151.38	176.82	25.44	162.52

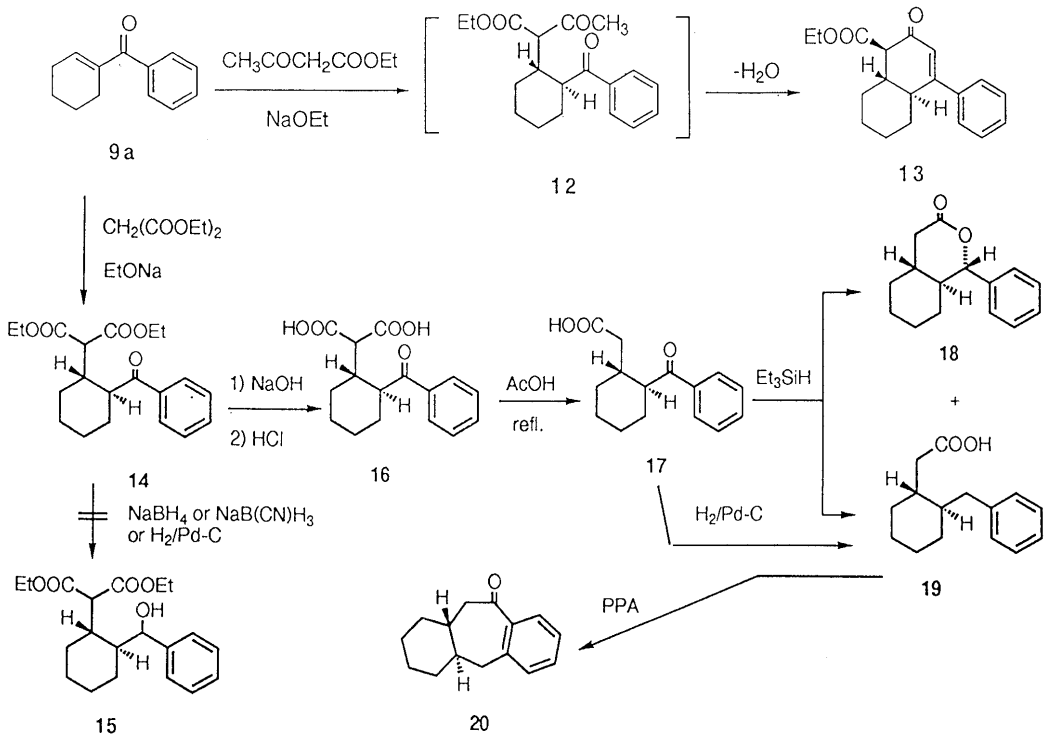
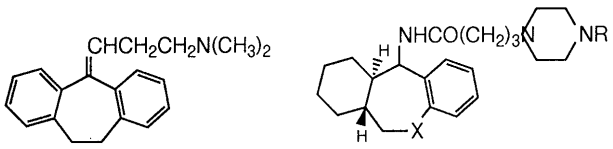


Chart 4

(**9a**) with active methylene compounds were examined. The unsaturated ketone (**9a**) was treated with ethyl acetoacetate in the presence of a catalytic amount of sodium ethoxide to give a highly functionalized bicyclic compound having a pendant phenyl group (**13**) in 63.8% yield *via* the Michael adduct (**12**). Reaction of **9a** with ethyl malonate in the presence of sodium ethoxide gave the Michael adduct (**14**) in 72.9% yield. The stereochemistry of the product **14** was considered to be *trans* on the basis of the ^{1}H-NMR data (J value between C_1-H and C_2-H = 7.6 Hz), so the stereochemistry of **13** was similarly concluded to be *trans*.

In order to obtain a six-membered lactonic compound such as **18**, we attempted to convert the ketone carbonyl group of the ketodiester (**14**) to a hydroxy group by treatment with reducing agents such as sodium borohydride, sodium cyanoborohydride and hydrogen in the presence of palladium catalyst on carbon. However, surprisingly, the carbonyl group of **14** was not reduced at all under these reaction conditions, probably because of steric hindrance of the di(ethoxycarbonyl)methyl group and/or inhibition of the approach of the reducing agent [BH_4^- or $B(CN)H_3^-$] to the carbonyl group by an initially formed anion moiety $^-C(COOEt)_2$. So, the ketodiester (**14**) was hydrolyzed with an excess of sodium hydroxide, and the intermediate crystalline dicarboxylic acid (**16**) was heated in acetic acid to give the monocarboxylic acid (**17**) in 92.2% overall yield. Considering the reaction conditions, we presumed that the *trans* stereochemistry of **14** was retained in **17**, and indeed, esterification of the dicarboxylic acid (**16**) by treatment with ethanol in the presence of sulfuric acid gave **14** in 70.5% yield. The monocarboxylic acid (**17**) could be smoothly reduced with triethylsilane in trifluoroacetic acid to give a mixture of the perhydrocoumarin derivative (**18**) and the over-



21 (amitriptylin: tranquilizer)[16] 22 (X=S, O; strong calcium antagonistic activity)[17]

Fig. 1

reduced compound (**19**), and the mixture could be separated by silica gel column chromatography to give **18** and **19** in 73.3% and 18.4% yields, respectively. The structure of **18** was estimated to be as illustrated in Chart 4 on the basis of its ^{1}H-NMR [J value of a signal assigned as the C_1-H = 10.3 Hz (d, 4.87 ppm)] and infrared absorption (IR) [$\nu_{C=O}$: 1724 cm^{-1} (δ-lactone)] spectra, so it was considered that the reduction proceeded stereoselectively.

The over-reduced product (**19**) could also be directly obtained from the ketoacid (**17**) in 81.4% yield by catalytic hydrogenation in the presence of palladium on carbon. The acid (**19**) was treated with polyphosphoric acid (PPA) to give readily the tricyclic dibenzocycloheptenone derivative (**20**) in 73.2% yield, but similar treatment of **17** gave only a resinous complex mixture. The dibenzocycloheptane skeleton and its isosters can be seen in pharmacologically interesting compounds such as amitriptyline (**21**)[16] and **22**[17] (Fig. 1), and the partially hydrogenated tricyclic ketone (**20**) seems to be a pharmaceutically interesting compound because of the possibility of further derivatizations at the carbonyl function.

Experimental

Melting points were measured with a Yanaco micromelting point apparatus without correction. IR spectra were taken with a Shimadzu

IR-435 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were obtained on a JEOL EX-270 spectrometer or on a Varian XL-300 spectrometer, and the chemical shifts are expressed in δ (ppm) values with tetramethylsilane as an internal standard. Abbreviations of ^{1}H-NMR signal patterns are as follows: s (singlet); d (doublet); dd (double doublet); t (triplet); dt (double triplet); tt (triple triplet); q (quartet); m (multiplet); br (broad). High-resolution mass spectra (HRMS) were obtained on a Hitachi M-80 spectrometer. A Kugel-Rohr apparatus was used for vacuum distillation of oily crude products. Silica gel 60 (Merck Art. 7734) and Silica gel 60 PF 254 (Nacalai Tesque Co., Ltd.) were used in column chromatography and preparative thin-layer chromatography (PTLC), respectively.

General Procedure for Synthesis of TMSCH from Ketones; 1-Trimethylsilyloxy-1-cyclohexanecarbonitrile (2a)[6d] as an Example TMSCN (1.68 ml, 12 mmol) was added to a solution of cyclohexanone (**1a**, 1.04 ml, 10 mmol) in dry tetrahydrofuran (THF) (20 ml) under an N_2 atmosphere, and then 1.6 M *n*-BuLi in hexane (0.1 ml) was added to the mixture under ice-cooling followed by stirring at room temperature for 2 h. The reaction was quenched by addition of water (10 ml), and the THF was evaporated. The residue was extracted with Et_2O (20 ml × 3) and the combined ethereal extract was dried over anhydrous Na_2SO_4. The solvent was evaporated and the oily residue was purified by distillation under vacuum. Colorless oil (bp_{23} 104 °C). Yield, 1.87 g (94.9%). IR ($CHCl_3$): 2215 (–CN) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.22—2.08 (m, 10H, –CH_2– × 5), 0.24 (s, 9H, –Si(CH_3)$_3$). LRMS *m/z*: 197 (M^+).

1-Trimethylsilyloxy-1-cycloheptanecarbonitrile (**2b**): Obtained in a similar manner from cycloheptanone (1.18 ml, 10 mmol). Colorless oil. Yield, 2.06 g (97.4%). bp_6 90 °C. IR ($CHCl_3$): 2210 (–CN) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.58—2.17 (m, 12H, –CH_2– × 6), 0.23 (s, 9H, –Si(CH_3)$_3$). LRMS *m/z*: 211 (M^+).

1-Trimethylsilyloxy-1-cyclooctanecarbonitrile (**2c**)[6d]: Obtained in a similar manner from cyclooctanone (1.32 ml, 10 mmol). Colorless oil (bp_7 111 °C). Yield, 2.18 g (96.7%). IR ($CHCl_3$): 2210 (–CN) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.57—2.17 (m, 14H, –CH_2– × 7), 0.22 (s, 9H, –Si(CH_3)$_3$). LRMS *m/z*: 225 (M^+).

1-Trimethylsilyloxy-1-cyclododecanecarbonitrile (**2d**)[6d]: Obtained in a similar manner from cyclododecanone (1.82 g, 10 mmol). Colorless crystals (bp_3 150 °C; mp 37.3—39.0 °C). Yield, 2.55 g (90.6%). IR ($CHCl_3$): 2210 (–CN) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.34—1.95 (m, 22H, –CH_2– × 11), 0.23 (s, 9H, –Si(CH_3)$_3$). *Anal.* Calcd for $C_{16}H_{31}NOSi$: C, 68.27; H, 11.10; N, 4.98. Found: C, 68.03; H, 11.47; N, 4.98.

1-Trimethylsilyloxy-1-(α-tetraline)carbonitrile (**2e**)[6d]: Obtained in a similar manner from α-tetralone (1.33 ml, 10 mmol). Pale yellow oil (bp_3 148 °C). IR ($CHCl_3$): 2210 (–CN) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.63—7.66 (m, 1H, Ar-H), 7.22—7.29 (m, 2H, Ar-H), 7.08—7.11 (m, 1H, Ar-H), 2.82 (t, 2H, –CH_2–, J=6.3 Hz), 1.95—2.38 (m, 4H, –CH_2– × 2), 0.21 (s, 9H, –Si(CH_3)$_3$). LRMS *m/z*: 245 (M^+).

1-Trimethylsilyloxy-1-cyclohexaneacetonitrile (**2f**): Obtained in a similar manner from cyclohexanecarboxyaldehyde (1.21 ml, 10 mmol). Pale yellow oil (bp_4 84 °C). Yield, 2.08 g (98.3%). IR ($CHCl_3$): 2210 (–CN) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.14 (d, 1H, NC-CH-OTMS, J=6.3 Hz), 1.02—1.85 (m, 11H, other protons on cyclohexyl group), 0.20 (s, 9H, –Si(CH_3)$_3$). LRMS *m/z*: 211 (M^+).

General Procedure for the Grignard Reaction of TMSCH (2); Synthesis of 1-Benzoylcyclohexanol (3a)[6] as an Example A solution of bromobenzene (21.6 ml, 200 mmol) in dry Et_2O (70 ml) was added dropwise at room temperature (in order to maintain this temperature an ice-water bath was occasionally used) to a stirred mixture of magnesium turnings (6.08 g, 250 mmol), I_2 (1 mg) and dry Et_2O (20 ml). After completion of the addition, stirring was continued for 1 h. A solution of **2a** (14.8 g, 75 mmol) in dry Et_2O (20 ml) was added to the solution of phenylmagnesium bromide, and the reaction mixture was stirred for **3h**. The reaction was quenched by addition of water (50 ml) and 10% HCl (100 ml) under ice-cooling, and the resultant was extracted with AcOEt (150 ml × 2). It was dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. A solution of the residue in THF (50 ml) and 10% HCl (10 ml) was stirred for 2 h at room temperature. THF was evaporated under reduced pressure, and the residue was extracted with AcOEt (150 ml × 3). After drying of the organic solution over anhydrous Na_2SO_4 and evaporation of the solvent, the residual viscous oil was purified by silica gel column chromatography (solvent: AcOEt/hexane = 1/5), and the major product obtained was recrystallized from *n*-hexane to give white fine crystals. Yield, 13.3 g (86.5%). mp 44.0—45.5 °C. IR ($CHCl_3$): 3420 (OH), 1661 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.99—8.02 (m, 2H, Ar-H), 7.41—7.56 (m, 3H, Ar-H), 3.43 (s, 1H, –OH), 1.63—2.05 (m, 10H, –CH_2– × 5). *Anal.* Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.29; H, 8.04. HRMS *m/z*: Calcd for $C_{13}H_{16}O_2$, 204.1150. Found, 204.1148 (M^+).

1-Benzoylcycloheptanol (**3b**): Obtained in a similar manner from **2b** (2.1 g, 10 mmol). The crude product was purified by column chromatography (solvent: AcOEt/hexane = 1/10) and recrystallization from pentane to give colorless needles. Yield, 1.81 g (82.8%). mp 50.5—50.8 °C. IR ($CHCl_3$): 3410 (OH), 1664 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.97—8.00 (m, 2H, Ar-H), 7.42—7.57 (m, 3H, Ar-H), 3.67 (s, 1H, –OH), 1.59—2.27 (m, 12H, –CH_2– × 6). *Anal.* Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.30; H, 8.38.

1-Benzoylcyclooctanol (**3c**): Obtained in a similar manner from **2c** (2.3 g, 10 mmol). The crude product was purified by column chromatography (solvent: AcOEt/hexane = 1/20) and recrystallization from pentane to give colorless needles. Yield, 1.94 g (83.7%). mp 70.5—71.1 °C. IR ($CHCl_3$): 3410 (OH), 1666 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 8.01—8.04 (m, 2H, Ar-H), 7.42—7.57 (m, 3H, Ar-H), 3.36 (s, 1H, –OH), 1.63—2.24 (m, 14H, –CH_2– × 7). *Anal.* Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.27; H, 8.94.

1-Benzoylcyclododecanol (**3d**): Obtained in a similar manner from **2d** (2.8 g, 10 mmol). The crude product was purified by column chromatography (solvent: AcOEt/hexane = 1/20) and recrystallization from pentane to give colorless needles. Yield, 2.10 g (72.7%). mp 134.2—135.1 °C. IR ($CHCl_3$): 3400 (OH), 1672 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 8.10—8.17 (m, 2H, Ar-H), 7.35—7.55 (m, 3H, Ar-H), 2.28 (br, 1H, –OH), 1.81—2.04 (m, 4H, –CH_2– × 2), 1.36 (s, 18H, –CH_2– × 9). *Anal.* Calcd for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79. Found: C, 78.79; H, 9.90.

1-Benzoyl-1-hydroxytetraline (**3e**): Obtained in a similar manner from **2e** (2.5 g, 10 mmol). The crude product was purified by column chromatography (solvent: AcOEt/hexane = 1/20) and recrystallization from pentane to give colorless fine crystals. Yield, 1.31 g (51.9%). mp 77.4—78.0 °C. IR ($CHCl_3$): 3416 (OH), 1667 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 6.90—7.57 (m, 9H, Ar-H), 5.15 (s, 1H, –OH), 2.97 (t, 2H, –CH_2–, J=6.1 Hz), 2.66 (t, 2H, –CH_2–, J=6.5 Hz), 2.10—2.23 (m, 2H, –CH_2–). *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 81.14; H, 6.59.

2-Cyclohexyl-2-hydroxy-1-phenylethanone (**3f**): Obtained in a similar manner from **2f** (2.1 g, 10 mmol). The crude product was purified by column chromatography (solvent: AcOEt/hexane = 1/20) and recrystallization from pentane to give colorless needles. Yield, 1.18 g (54.1%). mp 88.0—88.8 °C. IR ($CHCl_3$): 3440 (OH), 1674 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.88—7.92 (m, 2H, Ar-H), 7.48—7.66 (m, 3H, Ar-H), 4.94 (dd, 1H, >C<u>H</u>–OH, J=2.3, 6.6 Hz), 3.61 (d, 1H, >CH–O<u>H</u>, J=6.6 Hz), 1.01—1.82 (m, 11H, other protons on cyclohexyl group). *Anal.* Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.16; H, 8.19.

1-(1-Oxo-3-phenylpropyl)cyclohexanol (**3g**): Obtained in a similar manner from phenethyl Grignard reagent in the presence of 0.91 M triethylaluminum solution in hexane (0.3 ml, 0.25 mmol). The crude product was purified by column chromatography (solvent: AcOEt/hexane = 1/20) and recrystallization from pentane to give a colorless oil. Yield, 1.10 g (47.5%). bp_3 168 °C. IR ($CHCl_3$): 3452 (OH), 1696 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.17—7.31 (m, 5H, Ar-H), 3.49 (s, 1H, –OH), 2.85—2.96 (m, 4H, –CH_2– × 2), 1.61—1.75 (m, 8H, –CH_2– × 4), 1.20—1.44 (m, 2H, –CH_2–). ^{13}C-NMR ($CDCl_3$) δ: 213.80, 140.85, 128.50, 128.29, 126.21, 77.96, 37.67, 33.71, 29.77, 25.25, 21.00. HRMS *m/z*: Calcd for $C_{15}H_{20}O_2$, 232.1460. Found, 232.1450 (M^+).

1-Propanoylcyclohexanol (**3h**): This was obtained in a similar manner from phenethyl Grignard reagent in the presence of 0.91 M triethylaluminum solution in hexane (11 ml, 10 mmol). The crude product was purified by column chromatography (solvent: AcOEt/hexane = 1/20) and recrystallization from pentane to give a colorless oil. Yield, 1.20 g (76.6%). bp_9 138 °C. IR ($CHCl_3$): 3446 (OH), 1696 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.60 (s, 1H, –OH), 2.60 (q, 2H, –CH_2CH_3, J=7.3 Hz), 1.46—1.74 (m, 10H, –CH_2– × 5), 1.10 (s, 3H, –CH_2CH_3, J=7.2 Hz). ^{13}C-NMR ($CDCl_3$) δ: 215.38, 77.89, 34.00, 28.92, 25.31, 21.09, 7.86.

1-(2-Butenoyl)cyclohexanol (**3i**)[18]: Obtained in a similar manner from allyl Grignard reagent by stirring for 3 d. The crude product was purified by column chromatography (solvent: AcOEt/hexane = 1/20) to give a colorless oil. Yield, 24.3 mg (5.0%). IR ($CHCl_3$): 3435 (OH), 1679 (C=O), 1626 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.14 (dq, 1H, –C<u>H</u>=CH–CH_3, J=15.1, 7.0 Hz), 6.54 (dq, 1H, –CH=C<u>H</u>–CH_3, J=15.2, 1.6 Hz), 3.80 (s, 1H, –OH), 1.95 (dd, 3H, –CH=CH–C<u>H</u>$_3$, J=1.7, 7.0 Hz), 1.24—1.78 (m, 10H, –CH_2– × 5). ^{13}C-NMR ($CDCl_3$) δ:

202.43, 145.85, 124.15, 78.17, 40.60, 33.79, 25.25, 21.00, 18.56.

Benzoylcyclohexane (4a)[7] and Benzylidenecyclohexane (5)[8] A mixture of 1-benzoylcyclohexanol (**3a**, 0.61 g, 3 mmol), AcOH (10 ml) and zinc powder (0.20 g, 21 mmol) was stirred at 60 °C for 4 h. The zinc powder was removed by filtration, and the residue after evaporation of the filtrate was extracted with AcOEt (10 ml × 3) and water (5 ml). The organic layer was washed with water (20 ml × 2), dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude products were purified by column chromatography (solvent: AcOEt/hexane = 1/20). **4a**: Yield, 470.5 mg (83.3%). Colorless needles from pentane, mp 49.9—51.9 °C [lit. mp 55—57 °C].[7] IR ($CHCl_3$): 1675 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.93—7.97 (m, 2H, Ar-H), 7.43—7.58 (m, 3H, Ar-H), 3.27 (tt, 1H, >CH–benzoyl, J=3.2, 11.1 Hz), 1.25—1.92 (m, 10H, $-CH_2-\times 5$). *Anal.* Calcd for $C_{13}H_{16}O$: C, 82.94: H, 8.57. Found: C, 83.20: H, 8.72. LRMS *m/z*: 188 (M^+). **5**: Yield, 27.4 mg (5.3%). Colorless oil, bp_3 160 °C. IR ($CHCl_3$): 2913 (CH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.12—7.33 (m, 5H, Ar-H), 6.23 (s, 1H, >C=CH–), 2.37 (t, 2H, $-CH_2-C=$, J=5.6 Hz), 2.26 (t, 2H, $-CH_2-C=$, J=5.5 Hz), 1.52—1.68 (m, 6H, $-CH_2-$). LRMS *m/z*: 172 (M^+).

Benzoylcycloheptane (**4b**)[19] and Benzylcycloheptane (**6b**)[9]: Obtained in a similar manner from **3b** (0.65 g, 3 mmol) by stirring for 8 h at 60 °C. The crude products were purified by column chromatography (solvent: AcOEt/hexane = 1/20). **4b**: Yield, 493.6 mg (81.3%). Colorless oil, bp_6 190 °C. IR ($CHCl_3$): 1675 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.94 (dt, 2H, Ar-H, J=7.0, 1.6 Hz), 7.42—7.55 (m, 3H, Ar-H), 3.44 (tt, 1H, >CH–benzoyl, J=4.0, 8.7 Hz), 1.56—1.96 (m, 12H, $-CH_2-\times 6$). LRMS (*m/z*): 202 (M^+). **6b**: Yield, 40.5 mg (7.2%). Colorless oil. IR ($CHCl_3$): 2983 (CH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 6.98—7.33 (m, 5H, Ar-H), 2.25—2.30 (m, 2H, Ph–CH_2–CH<), 1.13—1.79 (m, 13H, other protons on cycloheptyl group).

Benzoylcyclooctane (**4c**)[19] and Benzylcyclooctane (**6c**)[10]: Obtained in a similar manner from **3c** (0.70 g, 3 mmol) by stirring for 12 h at 60 °C. The crude products were purified by column chromatography (solvent: AcOEt/hexane = 1/20). **4c**: Yield, 539.0 mg (83.1%). Colorless oil, bp_3 160 °C. IR ($CHCl_3$): 1672 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.92—7.95 (m, 2H, Ar-H), 7.43—7.57 (m, 3H, Ar-H), 3.49 (tt, 1H, >CH–benzoyl, J=4.1, 8.6 Hz), 1.58—1.89 (m, 14H, $-CH_2-\times 7$). LRMS (*m/z*): 216 (M^+). **6c**: Yield, 19.3 mg (3.2%). Colorless oil. IR ($CHCl_3$): 2978 (CH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.01—7.31 (m, 5H, Ar-H), 2.01—2.15 (m, 2H, Ph–$C\underline{H}_2$–CH<), 1.00—1.82 (m, 15H, other protons on cyclooctyl group).

Benzoylcyclododecane (**4d**): Obtained in a similar manner from **3d** (0.87 g, 3 mmol) by stirring for 9 h at 90 °C. The crude product was purified by column chromatography (solvent: AcOEt/hexane = 1/20). **4d**: Yield, 693.9 mg (84.9%). Colorless crystals from pentane, mp 73.0—73.8 °C. IR ($CHCl_3$): 1674 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.93—7.96 (m, 2H, Ar-H), 7.44—7.59 (m, 3H, Ar-H), 3.51—3.60 (m, 1H, >CH–benzoyl), 1.31—1.79 (m, 22H, $-CH_2-\times 11$). *Anal.* Calcd for $C_{19}H_{28}O$: C, 83.77; H, 10.36. Found: C, 83.44; H, 10.54.

1-Benzoyltetralone (**4e**) and 1-(1,2,3,4-Tetrahydronaphthyl)phenylmethane (**7**)[11]: Obtained in a similar manner from **3e** (0.76 g, 3 mmol) by stirring for 3 h at 60 °C. The crude products were purified by column chromatography (solvent: AcOEt/hexane = 1/20). **4e**: Yield, 476.0 mg (67.2%). Colorless needles from pentane, mp 92.4—93.3 °C. IR ($CHCl_3$): 1676 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 8.01 (dd, 2H, Ar-H, J=1.6, 7.0 Hz), 7.58 (tt, 1H, Ar-H, J=1.7, 7.3 Hz), 7.46—7.52 (m, 2H, Ar-H), 7.16 (dd, 2H, Ar-H, J=1.2, 5.0 Hz), 7.07—7.11 (m, 1H, Ar-H), 6.91 (d, 1H, Ar-H, J=7.3 Hz), 4.83 (t, 1H, >CH–benzoyl, J=6.6 Hz), 2.82—2.91 (m, 2H, $-CH_2-$), 2.07—2.16 (m, 4H, $-CH_2-\times 2$). *Anal.* Calcd for $C_{17}H_{16}O$: C, 86.41; H, 6.82. Found: C, 86.50; H, 6.83. HRMS *m/z*: Calcd for $C_{17}H_{16}O$, 236.1200. Found, 236.1228 (M^+). **7**: Yield, 54.2 mg (8.2%). Colorless oil. IR ($CHCl_3$): 2919 (CH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 6.98—7.31 (m, 9H, Ar-H), 3.05—3.18 (m, 1H, CH_2–C$\underline{H}$<), 2.64—2.81 (m, 2H, Ph–$C\underline{H}_2$–CH<), 1.54—2.06 (m, 6H, $-CH_2-\times 3$).

1-Cyclohexyl-2-phenylethanol (**8**)[12]: Obtained in a similar manner from **3f** (0.66 g, 3 mmol) by stirring for 24 h at 60 °C. The crude product was purified by column chromatography (solvent: AcOEt/hexane = 1/20). **8**: Yield, 399.5 mg (65.2%). Colorless crystals from pentane, mp 172.5—174.3 °C. IR ($CHCl_3$): 3510 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.13—7.22 (m, 5H, Ar-H), 2.23 (s, 1H, –OH), 2.19 (dd, 2H, >CH–OH, J=4.0, 14.7 Hz), 1.67—1.75 (m, 2H, >CH–CH_2–), 0.73—1.75 (m, 11H, cyclohexyl-H). ^{13}C-NMR ($CDCl_3$) δ: 141.99, 127.50, 127.03, 126.50, 82.36, 42.46, 34.94, 33.63, 30.89, 26.31, 26.18. *Anal.* Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.28; H, 9.58. LRMS *m/z*: 204 (M^+).

1-Benzoylcyclohexene (9a)[13] and 2,3,4,4a-Tetrahydro-1*H*-fluorene-9(9aH)-one (10a)[14] A mixture of **3a** (2.04 g, 10 mmol), $CHCl_3$ (40 ml), hydroquinone (trace) and concentrated H_2SO_4 (2 ml) was stirred at room temperature for 6 h. Ice-water (200 ml) was added slowly to the reaction mixture under stirring, and the $CHCl_3$ layer was separated. The aqueous layer was extracted with $CHCl_3$ (100 ml × 3), and combined $CHCl_3$ layer was washed with water (50 ml × 3), then dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oily residue, which was distilled under vacuum (bp_3 155 °C). The distillate was further purified by column chromatography (solvent: AcOEt/hexane = 1/20) to give two fractions, each as an oil. **9a**: Yield, 1.32 g (71.0%). Colorless oil. IR ($CHCl_3$): 1630 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.36—7.64 (m, 5H, Ar-H), 6.55—6.59 (m, 1H, –CH=C<), 2.18—2.44 (m, 4H, $-CH_2-\times 2$), 1.62—1.77 (m, 4H, $-CH_2-\times 2$). ^{13}C-NMR ($CDCl_3$) δ: 198.22, 144.00, 138.73, 131.22, 129.11, 127.98, 26.10, 23.93, 22.00, 21.65. LRMS *m/z*: 186 (M^+). **10a**: Yield, 0.07 g (3.8%). Colorless oil. IR ($CHCl_3$): 1700 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.76 (dd, 1H, Ar-H, J=0.5, 7.6 Hz), 7.57 (td, 1H, Ar-H, J=7.4, 1.2 Hz), 7.45 (d, 1H, Ar-H, J=7.7 Hz), 7.36 (td, 1H, Ar-H, J=7.6, 0.7 Hz), 3.39 (dt, 1H, >CH–C=O, J=9.2, 6.9 Hz), 2.76 (dt, 1H, >CH–Ar, J=4.9, 6.8 Hz), 2.07—2.14 (m, 2H, $-CH_2-$), 1.19—1.77 (m, 6H, $-CH_2-\times 3$). ^{13}C-NMR ($CDCl_3$) δ: 207.82, 158.38, 135.66, 134.24, 127.27, 124.90, 123.97, 48.52, 38.81, 31.34, 23.12, 22.63, 22.37. HRMS *m/z*: Calcd for $C_{13}H_{14}O$, 186.1050. Found, 186.1016 (M^+).

1-Benzoylcycloheptene (**9b**) and 4b,5,6,7,8,9,9a,10-Octahydrobenzazulen-10-one (**10b**): Obtained in a similar manner from **3b** (2.18 g, 10 mmol). The crude products were purified by column chromatography (solvent: AcOEt/hexane = 1/20). **9b**: Yield, 0.20 g (10.1%). Colorless oil. IR ($CHCl_3$): 1673 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.92—7.95 (m, 2H, Ar-H), 7.44—7.56 (m, 3H, Ar-H), 5.78—5.98 (m, 1H, –CH=C<), 1.40—2.38 (m, 10H, $-CH_2-\times 5$). LRMS *m/z*: 200 (M^+). **10b**: Yield, 1.59 g (79.4%). Colorless oil, bp_3 162 °C. IR ($CHCl_3$): 1698 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.74 (d, 1H, Ar-H, J=8.0 Hz), 7.61 (td, 1H, Ar-H, J=7.4, 1.1 Hz), 7.50 (dd, 1H, Ar-H, J=0.8, 7.8 Hz), 7.36 (t, 1H, Ar-H, J=7.4 Hz), 3.54—3.61 (m, 1H, >CH–C=O), 2.86 (dq, 1H, >CH–Ar, J=10.7, 4.0 Hz), 2.13—2.21 (m, 2H, $-CH_2-$), 1.34—1.81 (m, 8H, $-CH_2-\times 4$). ^{13}C-NMR ($CDCl_3$) δ: 209.22, 158.60, 136.26, 134.75, 127.36, 125.53, 123.51, 52.97, 44.37, 32.50, 31.21, 28.51, 28.34, 28.02. HRMS *m/z*: Calcd for $C_{14}H_{16}O$, 200.1200. Found, 200.1188 (M^+).

1-Benzoylcyclooctene (**9c**) and 4b,5,6,7,8,9,10,10a-Octahydrocycloocta[*a*,*c*]inden-11-one (**10c**): Obtained in a similar manner from **3c** (2.32 g, 10 mmol). The crude products were purified by column chromatography (solvent: AcOEt/hexane = 1/20). **9c**: Yield, 0.26 g (12.3%). Colorless oil, bp_2 175 °C. IR ($CHCl_3$): 1675 (C=O) cm^{-1}. ^{1}H-NMR δ: 7.89—7.95 (m, 2H, Ar-H), 7.43—7.55 (m, 3H, Ar-H), 5.70—5.78 (m, 1H, –CH=C<), 1.48—2.33 (m, 12H, $-CH_2-\times 6$). ^{13}C-NMR ($CDCl_3$) δ: 203.45, 132.72, 132.00, 128.62, 128.30, 128.27, 127.71, 46.67, 29.25, 28.49, 27.36, 25.77, 24.35. LRMS *m/z*: 214 (M^+). **10c**: Yield, 1.38 g (64.4%). Colorless crystals from MeOH, mp 54.4—55.7 °C. IR ($CHCl_3$): 1700 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.73 (d, 1H, Ar-H, J=7.6 Hz), 7.61 (td, 1H, Ar-H, J=7.4, 1.2 Hz), 7.50 (dd, 1H, Ar-H, J=0.8, 7.7 Hz), 7.36 (t, 1H, Ar-H, J=7.4 Hz), 3.21 (dt, 1H, >CH–C=O, J=12.2, 4.1 Hz), 2.50 (dt, 1H, >CH–Ar, J=11.9, 4.4 Hz), 2.33—2.40 (m, 2H, $-CH_2-$), 1.32—1.91 (m, 8H, $-CH_2-\times 4$). ^{13}C-NMR ($CDCl_3$) δ: 208.75, 158.41, 135.69, 134.77, 127.35, 125.01, 123.54, 53.47, 44.07, 35.24, 30.35, 27.40, 26.93, 25.07, 24.73. *Anal.* Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 83.72; H, 8.55. HRMS *m/z*: Calcd for $C_{15}H_{18}O$, 214.1360. Found, 214.1357 (M^+).

1-Benzoylcyclododecene (**9d**): Obtained in a similar manner from **3d** (1.44 g, 5 mmol). The crude product was purified by column chromatography (solvent: AcOEt/hexane = 1/20). Yield, 815.4 mg (60.3%). Colorless crystals from hexane, mp 71.7—72.9 °C. IR ($CHCl_3$): 1640 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.65—7.69 (m, 2H, Ar-H), 7.39—7.54 (m, 3H, Ar-H), 6.19 (t, 1H, –CH=C<, J=7.9 Hz), 2.58 (t, 2H, $-CH_2-C=$, J=6.7 Hz), 2.32 (q, 2H, $-CH_2-CH=$, J=7.3 Hz), 1.27—1.58 (m, 16H, $-CH_2-\times 8$). ^{13}C-NMR ($CDCl_3$) δ: 199.16, 145.72, 141.26, 139.21, 131.45, 129.35, 128.05, 26.39, 26.03, 25.62, 25.02, 24.88, 24.02, 23.40, 22.58, 22.19. *Anal.* Calcd for $C_{19}H_{26}O$: C, 84.39; H, 9.69. Found: C, 84.12; H, 9.99.

1-(3-Phenylpropanoyl)cyclohexene (**9g**): Obtained in a similar manner from **3g** (115 mg, 0.5 mmol). The crude product was purified by preparative thin-layer chromatography (TLC; solvent: AcOEt/hexane = 1/5). Yield, 89 mg (80.2%). Colorless oil. IR ($CHCl_3$): 1658 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.19—7.31 (m, 5H, Ar-H), 6.86—6.90 (m,

1H, –CH=C<), 2.92—2.97 (m, 4H, $-CH_2-\times 2$), 2.19—2.26 (m, 4H, $-CH_2-\times 2$), 1.56—1.67 (m, 4H, $-CH_2-\times 2$). ^{13}C-NMR ($CDCl_3$) δ: 201.49, 141.64, 139.87, 139.13, 128.40, 125.94, 38.87, 30.57, 26.04, 23.13, 21.93, 21.53. HRMS *m/z*: Calcd for $C_{15}H_{18}O$, 214.1360. Found, 214.1336 (M^+).

4a,10a-*trans*-1,2,4a,5,6,7,8,8a-Octahydro-1-ethoxycarbonyl-4-phenylnaphthalen-2-one (13) Sodium hydride (24 mg, 1 mmol) was added slowly with ice-cooling under an N_2 atmosphere to a solution of ethyl acetoacetate (1.53 ml, 12 mmol) and **9a** (1.86 g, 10 mmol) in EtOH (15 ml). The reaction mixture was stirred for 15 min, then refluxed at 80 °C for 24 h. The reaction quenched by addition of water (5 ml). Ethanol was evaporated under reduced pressure, and the residue was extracted with Et_2O (30 ml × 3). The ethereal layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to give an oily residue. The crude product was purified by column chromatography (solvent: AcOEt/hexane = 20/1) and by distillation *in vacuo*. Yield, 1.90 g (63.8%). Pale yellow oil, bp_3 215 °C. IR ($CHCl_3$): 1728 (C=O), 1660 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$) δ: 7.37—7.39 (m, 3H, Ar-H), 7.22—7.27 (m, 2H, Ar-H), 6.09 (d, 1H, >C=CH–, J = 2.4 Hz), 4.28 (q, 2H, $-OCH_2CH_3$, J = 7.2 Hz), 3.30 (d, 1H, >CH–CH<, J = 13.3 Hz), 2.59—2.69 (m, 1H, >CH–CH<), 2.22—2.36 (m, 1H, >CH–CH<), 1.71—1.84 (m, 4H, $-CH_2-\times 2$), 1.25—1.46 (m, 4H, $-CH_2-\times 2$), 1.32 (t, 3H, $-OCH_2CH_3$, J = 7.2 Hz). HRMS *m/z*: Calcd for $C_{19}H_{22}O_3$, 298.1570. Found, 298.1555 (M^+).

Diethyl *trans*-2-(2-Benzoyl)cyclohexylmalonate (14) This was obtained in a similar manner to that used for the synthesis of **13** except for the use of **9a** (559 mg, 3 mmol), diethyl malonate (0.61 ml, 4 mmol) instead of ethyl acetoacetate. The crude product was purified by column chromatography (solvent: AcOEt/hexane = 1/10) and vacuum distillation. Yield, 757.6 mg (72.9%). Colorless oil, $bp_{0.3}$ 247 °C. IR ($CHCl_3$): 1741 (C=O), 1719 (C=O), 1674 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.95—8.00 (m, 2H, Ar-H), 7.44—7.59 (m, 3H, Ar-H), 4.00—4.21 (m, 4H, $-O-CH_2CH_3\times 2$), 3.57 (td, 1H, >CH–benzoyl, J = 7.6, 3.3 Hz), 3.50 (d, 1H, EtO_2C–CH–CO_2Et, J = 3.6 Hz), 2.62—2.70 (m, 1H, >CH–CH<), 1.96—2.07 (m, 2H, $-CH_2-$), 1.72—1.84 (m, 2H, $-CH_2-$), 1.28—1.55 (m, 4H, $-CH_2-\times 2$), 1.23 (t, 3H, $-O-CH_2CH_3$, J = 7.1 Hz), 1.06 (t, 3H, $-O-CH_2CH_3$, J = 7.3 Hz). HRMS *m/z*: Calcd for $C_{20}H_{26}O_5$, 346.1780. Found, 346.1799 (M^+).

2-*trans*-(2-Benzoyl)cyclohexylmalonic Acid (16) A mixture of **14** (346 mg, 1 mmol), THF (15 ml) and 20% NaOH (5 ml) was refluxed at 80 °C for 6 h. THF was evaporated under reduced pressure, and the residue was extracted with Et_2O (20 ml), then with 10% NaOH (20 ml × 3). The NaOH layer was acidified with concentrated HCl, and the separated product was extracted with Et_2O (50 ml × 3). The ethereal layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to give a crystalline residue, which was recrystallized from Et_2O–hexane. Yield, 275.8 mg (95.0%). Colorless crystals, mp 158.5—159.6 °C. IR (KBr): 1724 (C=O), 1699 (C=O), 1669 (C=O) cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 7.95 (d, 2H, Ar-H, J = 7.8 Hz), 7.65—7.50 (m, 3H, Ar-H), 3.58 (td, 1H, >CH–benzoyl, J = 7.1, 2.7 Hz), 3.18 (d, 1H, HO_2C–CH–CO_2H, J = 3.9 Hz), 2.35—2.45 (m, 1H, >CH–CH<), 1.84—1.95 (m, 2H, $-CH_2-$), 1.68—1.77 (m, 2H, $-CH_2-$), 1.19—1.45 (m, 4H, $-CH_2-\times 2$). ^{13}C-NMR (DMSO-d_6) δ: 202.78, 170.28, 169.84, 136.06, 133.25, 128.82, 128.04, 53.08, 46.94, 37.50, 31.24, 26.84, 25.26, 25.22. *Anal.* Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.17; H, 7.47. LRMS *m/z*: 246 (M^+). This product (**16**) was converted to the diethyl ester (**14**) by treatment with concentrated H_2SO_4 in EtOH at room temperature for 7 d (yield, 53.6%).

2-[*trans*-2-(Benzoyl)cyclohexyl]acetic Acid (17) A solution of **16** (1.45 g, 5 mmol) in AcOH (20 ml) was refluxed for 6 h at 120 °C. The solvent was evaporated under reduced pressure, and water (10 ml) was added to the residue. The aqueous phase was extracted with Et_2O (20 ml × 3), and the ethereal layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography (solvent: AcOEt/hexane = 1/1) and the obtained crystalline product was recrystallized from hexane. Yield, 1.20 g (97.1%). Colorless crystals, mp 96.8—97.5 °C. IR ($CHCl_3$): 1706 (C=O), 1675 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.95 (dd, 2H, Ar-H, J = 1.4, 7.2 Hz), 7.44—7.59 (m, 3H, Ar-H), 3.24—3.34 (m, 1H, >CH–benzoyl), 2.34—2.43 (m, 2H, >CH–CH_2–C=O), 2.09—2.17 (m, 1H, >CH–CH_2–C=O), 1.92—2.03 (m, 2H, $-CH_2-$), 1.75—1.88 (m, 2H, $-CH_2-$), 1.19—1.46 (m, 4H, $-CH_2-\times 2$). ^{13}C-NMR ($CDCl_3$) δ: 203.39, 178.12, 136.71, 133.12, 128.69, 128.25, 49.55, 39.00, 35.23, 31.27, 25.87, 25.58. *Anal.* Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 72.75; H, 7.43. HRMS *m/z*: Calcd for $C_{15}H_{18}O_3$, 246.1260. Found, 246.1269.

***trans*-(2-Benzyl)cyclohexylacetic Acid (19)** A mixture of **17** (246 mg, 1 mmol), AcOH (4 ml) and 5% Pd–C (20 mg) was stirred under an H_2 atmosphere (1 atm) for 3 h. The catalyst was removed by filtration and the filtrate was evaporated to give a viscous residue, to which water (10 ml) was added. The separated product was extracted with Et_2O (20 ml × 3), and the organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by PTLC (solvent: AcOEt/hexane = 2/1) to give an oily material. Yield, 189 mg (81.4%). IR ($CHCl_3$): 1701 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.12—7.30 (m, 5H, Ar-H), 3.00 (dd, 1H, $-CH_2-$COOH, J = 3.8, 13.3 Hz), 2.76 (dd, 1H, $-CH_2-$COOH, J = 4.3, 15.6 Hz), 2.18—2.28 (m, 2H, $-CH_2-$benzene), 1.83—1.87 (m, 1H, >CH–CH<), 0.94—1.70 (m, 9H, other protons on cyclohexyl group). ^{13}C-NMR ($CDCl_3$) δ: 179.50, 140.85, 129.20, 128.14, 125.73, 43.39, 40.20, 39.32, 39.19, 32.51, 31.22, 25.84, 25.76. HRMS *m/z*: Calcd for $C_{15}H_{20}O_2$, 232.1460. Found, 232.1483 (M^+).

4a,8a-*trans*-4a,5,6,7,8,8a-Hexahydro-1-phenyl-1*H*-benzo[*c*]pyran-3(4H)-one (18) and 19 Triethylsilylane (0.8 ml, 5 mmol) was added to a solution of **17** (492 mg, 2 mmol) in trifluoroacetic acid (5 ml) under an N_2 atmosphere, and the mixture was stirred at room temperature for 24 h. Trifluoroacetic acid was removed by evaporation under reduced pressure, and a solution of the residue in Et_2O (20 ml) was washed with water (5 ml × 3) and dried over anhydrous Na_2SO_4. Evaporation of the ethereal solution gave a viscous residue, which was separated by PTLC (solvent: AcOEt/hexane = 10/1). **18**: Colorless crystals, mp 86.7—87.4 °C. Yield, 338 mg (73.3%). IR ($CHCl_3$): 1724 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.25—7.39 (m, 5H, Ar-H), 4.87 (d, 1H, >CH–O–CO, J = 10.3 Hz), 2.79 (dd, 1H, J = 5.3, 18.1 Hz), 2.28 (dd, 1H, $-COCH_2-$, J = 12.3, 18.2 Hz), 1.70—1.85 (m, 4H, $-CH_2-\times 2$), 0.96—1.52 (m, 6H, $-CH_2-\times 3$). ^{13}C-NMR ($CDCl_3$) δ: 170.42, 138.17, 128.63, 128.44, 127.22, 88.24, 44.38, 37.49, 36.54, 32.68, 27.65, 25.27. *Anal.* Calcd for $C_{15}H_{18}O_2$: C, 78.23: H, 7.87. Found: C, 77.90: H, 8.00. HRMS *m/z*: Calcd for $C_{15}H_{18}O_2$, 230.1310. Found, 230.1321 (M^+). **19**: Oily material. Yield, 83 mg (18.4%). IR and ^{1}H-NMR spectra were superimposable on those of the above-mentioned **19**.

2,3,4,4a,5,11a-Hexahydro-1*H*-dibenzo[*a*,*d*]cycloheptan-10(11H)-one (20) A mixture of **19** (116 mg, 0.5 mmol) and polyphosphoric acid (**1g**) was heated at 90 °C for 3 h, and the cooled mixture was poured into ice-water (20 ml). The product was extracted with Et_2O (20 ml × 3), and the organic phase was washed with water (10 ml × 3) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave an oily residue, which was purified by PTLC (solvent: AcOEt/hexane = 5/1). Yield, 41.5 mg (73.2%). Colorless oil. IR ($CHCl_3$): 1671 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.59 (dd, 1H, Ar-H, J = 1.5, 7.5 Hz), 7.38 (td, 1H, Ar-H, J = 1.5, 7.4 Hz), 7.28 (td, 1H, Ar-H, J = 1.2, 7.4 Hz), 7.14 (d, 1H, Ar-H, J = 7.3 Hz), 3.01 (dd, 1H, >CH–CH_2–C=O, J = 4.5, 15.0 Hz), 2.65—2.74 (m, 2H, $-CH_2-$benzene), 2.57 (dd, 1H, >CH–CH_2–C=O, J = 8.5, 16.0 Hz), 1.18—1.75 (m, 10H, other protons on cyclohexyl group). ^{13}C-NMR ($CDCl_3$) δ: 206.30, 139.81, 139.58, 131.47, 130.00, 127.79, 126.49, 49.11, 43.58, 40.51, 40.28, 33.55, 26.41, 26.30. HRMS *m/z*: Calcd for $C_{15}H_{18}O$, 214.1360. Found, 214.1339 (M^+).

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