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Novel Enhancement of Diastereoselectivity of [2 + 2] Photocycloaddition of Chiral Cyclohexenones to Ethylene by Adding Naphthalenes

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The additive effect on the diastereoselective [2 + 2] photocycloaddition of chiral cyclohexenones **1** to ethylene is examined. A novel and fairly efficient method of increasing the diastereoselectivity in the reaction of **1a** was elucidated. The de value increased from 56% to 83% by the addition of 1-phenylnaphthalene. The major product **2a** was isolated by the recrystallization of the diastereomeric mixture (major/minor = 11/1), of which X-ray analysis confirmed the absolute configuration of the bicyclic system of **2a**. Hydrolysis for removing the chiral auxiliary and subsequent esterification afforded the optically pure bicyclo[4.2.0]octanone derivative **5**. From the fluorescence spectral analyses and other experimental results, the additive effect is attributed to the complex formation of chiral cyclohexenone **1a** and added naphthalenes.

Introduction

Photochemical [2 + 2] cycloadditions have emerged as valuable reactions in the construction of complex molecules.[1] In addition, these reactions readily prepare a framework for strained cyclobutane, which undergoes transportation to additional structures by ring expansion reactions.[2] We previously reported on the acid-catalyzed rearrangement of bicyclo[4.2.0]octanones, which were readily prepared by the [2 + 2] photocycloaddition of cyclohexenones to ethylene or allene, to give polyquinane-type compounds and related applications to the synthesis of various terpenoids.[3] Despite these useful applications, far less information about asymmetric photoreactions is known than that for thermal ones.[4,2e] The most promising method for asymmetric synthetic strategies may be diastereodifferentiating photoreactions using chiral auxiliaries. From this viewpoint, we have studied the diastereoselective [2 + 2] photocycloaddition of cyclohexenones having chiral auxiliaries with the smallest olefin, ethylene, to give bicyclo[4.2.0]octanones.[5] In this photoreaction, menthyl derivatives are effective auxiliaries in achieving a higher degree of chiral induction. Lange, Scharf, and other pioneering groups in this field reported asymmetric inductions in [2 + 2] photocycloadditions, which were limited to bulky olefins and relative low chemical yields with moderate selectivities.[6]

We describe herein a new entry of naphthylmenthyl to diastereoselective photoaddition as a chiral auxiliary and the novel enhancement in selectivity by the addition of naphthalenes. We also discuss the mechanistic study related to the origin of the selectivity as well as the insight of the additive effect.

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[3] The novel acid-catalyzed rearrangement of bicyclo[4.2.0]octanones gave various terpenoids having polyquinane skeletons, such as (±)-5-oxosilphiperfol-6-ene, (±)-silphiperfol-6-ene, (±)-3-oxosilphinene, and (±)-tetramethylmediterraneol B; see: (a) Kakiuchi, K.; Ue, M.; Tsukahara, H.; Shimizu, T.; Miyao, T.; Tobe, Y.; Odaira, Y.; Yasuda, M.; Shima, K. *J. Am. Chem. Soc.* **1989**, *111*, 3707. (b) Ue, M.; Ohnishi, Y.; Kobiro, K.; Kakiuchi, K.; Tobe, Y.; Odaira, Y. *Chem. Lett.* **1990**, 149. (c) Kakiuchi, K.; Nakamura, I.; Matsuo, F.; Nakata, M.; Ogura, M.; Tobe, Y.; Kurosawa, H. *J. Org. Chem.* **1995**, *60*, 3318 and references therein. (d) Kakiuchi, K.; Horiguchi, T.; Minato, K.; Tobe, Y.; Kurosawa, H. *J. Org. Chem.* **1995**, *60*, 6557.

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10.1021/jo0354746 CCC: $27.50

SCHEME 1

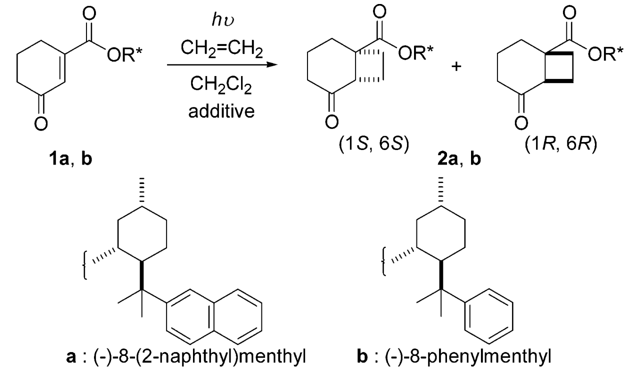

TABLE 1. Diastereoselective [2 + 2] Photocycloaddition of 1a,b to Ethylene[a]

entry	R*	additive (equiv[b])	T (°C)	time (h)	yield[c] (%)	% de[d]
1	**1a**		0	2	96	47
2	**1a**		−40	2	96	55
3	**1a**		−78	1.5	89	56
4	**1b**		−78	1.5	84	40
5	**1a**	naphthalene (10)	−78	1.5	91	71
6	**1a**	naphthalene (5)	−78	1.5	95	70
7	**1a**	naphthalene (1)	−78	1.5	99	58
8	**1a**	1-cyanonaphthalene (5)	−78	2	94	76
9	**1a**	1-cyanonaphthalene (10)	−78	1.5	85	81
10	**1a**	1-cyanonaphthalene (20)	−78	3	94	81
11	**1a**	1-cyanonaphthalene (10)	−40	4	99	72
12	**1a**	1-cyanonaphthalene (10)	0	5	17[e]	57
13	**1b**	1-cyanonaphthalene (10)	−78	1.5	99	40
14	**1a**	2-cyanonaphthalene (10)	−78	1.5	99	79
15	**1a**	1-methoxynaphthalene (10)	−78	1.5	95	77
16	**1a**	1-phenylnaphthalene (10)	−78	3	95	83

[a] Pyrex filter, 500-W high-pressure Hg lamp. [b] Based on **1**. [c] Isolated yield by column chromatography on SiO$_2$. [d] Determined by ^{1}H NMR. [e] 20% conversion for 5 h.

Results and Discussion

Diastereoselective [2 + 2] Photocycloadditions. We prepared the new chiral cyclohexenone **1a** containing the (−)-8-(1-naphthyl)menthyl group,[7] which is expected to shield an diastereoface of cyclohexenyl ring more effectively than the (−)-8-(phenyl)menthyl one. The photoreactions were carried out by irradiation with light through Pyrex ($\lambda > 280$ nm) from a 500-W high-pressure mercury lamp in a solution of cyclohexenone carboxylate derivative **1** saturated with ethylene (Scheme 1). Initially, photocycloaddition of **1a** with ethylene at 0 °C gave a diastereomeric mixture of adduct **2a** in excellent yield, which was purified by flash chromatography. The ^{1}H NMR spectrum of the mixture of **2a** shows two separate sets of resonance of the methyne protons at δ 2.70 and δ 2.54. The diastereomeric excess (de) of adduct **2a** was determined to be 47% by comparing the areas of their two signals, as shown in Table 1, entry 1. Subsequently, a gradual increase in the de's was observed at lower temperatures without any decrease in yield (Table 1, entries 1−3). The (−)-8-(1-naphthyl)menthyl group was a more effective chiral auxiliary than was (−)-8-(phenyl)menthyl (Table 1, entries 3 and 4).

The 56% de (Table 1, entry 3) was a good result for asymmetric photochemistry, but not high enough to be applicable to asymmetric synthesis. It is usually difficult to control the regio- and/or stereochemistry in photochemical reactions via a highly energetic and short-lived photoexcited state. Interestingly, we discovered a significant increase in de (from 56% to 71%) by the addition of naphthalene (10 equiv based on **1a**) (Table 1, entry 5). This additive effect was observed when adding 5 equiv of naphthalene but barely observable when adding 1 equiv (Table 1, entries 6 and 7). In the presence of 1-cyanonaphthalene, the de value increased to 76−81%. At the higher reaction temperatures, the de values increased by adding 1-cyanonaphthalene, but the reaction proceeded very slowly at 0 °C (Table 2, entries 1, 11, and 12). In comparison with **1a**, there was no additive effect on **1b** using 1-cyanonaphthalene as an additive (Table 2, entry 13). The irradiation of **1a** in the presence of other naphthalene derivatives afforded good yields (95−99%) of the diastereomeric mixture of **2a** with high diastereoselectivity (de = 77−83%; Table 1, entries 14−16). The diastereoselectivity increased with the use of the substituted naphthalenes, but any correlation between the de and the nature of the naphthalenes was not clear. The addition of naphthalenes in the reaction solution is an easy and effective method for increasing diastereoselectivity, which is first reported here on the photo- or thermal-reactions using chiral auxiliaries. The presented method needs 10 equiv of a naphthalene derivative as the additive, but the added naphthalenes were separated easily from the photoadducts by the standard column chromatographycally technique on silica gel. The mechanistic study of the additive effect is discussed based on the above experimental results and some spectral aspects (vide infra).

Isolation of the Optically Pure Bicyclo[4.2.0]-octanone 5. None of the isomers of **2a** could be separated by the standard column chromatographycally technique on silica gel or alumina. But recrystallization of the oily diastereomeric mixture (major/minor = 11/1) in CH$_2$Cl$_2$−hexane solution afforded a crystalline solid. When the major/minor ratio of the diastereomeric mixtures was less than 11/1, no solid was generated by the similar recrystallization technique. The repeated recrystallization of the obtained solid gave single crystals, which were confirmed to be the pure major isomer by NMR analysis (> 98% de). By adding a very small amount of the single crystal as a seed in the saturated solution, the crystals were afforded as the major isomer more effectively through a self-similar crystal-growth process. Three-times recrystallization in the presence of the single crystals afforded the pure major isomer of **2a** (> 98% de) in 56% yield from the diastereomeric mixture of **2a** (major/minor = 11/1). The pure isomer of **2a** was hydrolyzed to remove the chiral auxiliary and the esterification of the obtained bicyclo[4.2.0]octanone carboxylic acid **3** with diazomethane afforded methyl ester **5** in 75% yield (two steps) (Scheme 2). From the organic layer of the hydrolysis, 8-(2-naphthyl)menthol **4** was recovered in 97% yield, which suggests the possibility of the recycling **4** as a chiral auxiliary. GC analysis using a chiral column (CHIRALDEX G-TA) indicated that **5** was optically pure

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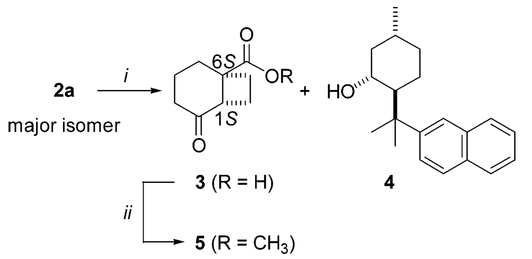
(7) (−)-8-(2-Naphthyl)menthol was prepared according to the literature procedure; see: (a) Ort, O. In *Organic Synthesis*; Freeman, J. P., Ed.; John Wiley & Sons: New York, 1993; Vol. 8, p 522. (b) Hagiwara, H.; Akama, T.; Okano, A.; Uda, H. *Chem. Lett.* **1989**, 2149. (c) Potin, D.; Dumas, F.; Maddaluno, J. *Synth. Commun.* **1990**, *20*, 2805.

SCHEME 2[a]



[a] Reagents: (i) NaOH, DMSO, 110 °C (**4**: 97%); (ii) CH_2N_2, Et_2O (75%, two steps).

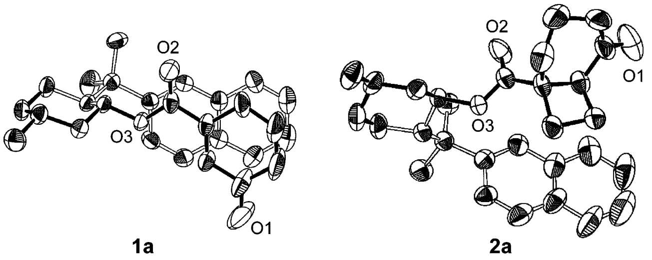


FIGURE 1. X-ray structures of **1a** and **2a**.

and a specific optical rotation could be measured ($[\alpha]^{22.2}_D$ = +169.8, c = 0.08 in CH_2Cl_2). The absolute configuration of **5** was not directly proven, but we confirmed the (1*S*,6*S*) stereochemistry of a bicyclic system from the X-ray crystallography analysis of **2a** (vide infra).

X-ray Crystallographic Analyses of 1a and 2a. A single-crystal X-ray crystallographic analysis of **1a** established the stacked conformation, where the cyclohexenone and the naphthyl ring are face-to-face (Figure 1, **1a**). Such a stacked conformation might imply a π-stacking interaction between the naphthyl ring and the cyclohexenone−ester moiety. The crystal structure of **1a** reveals the s-trans conformer between the ester carbonyl group and the double bond involved in the cyclohexane ring, which may be the most stable conformer in solution state. The absolute configuration of **2a** (major isomer) was proven by the single-crystal X-ray analysis (Figure 1, **2a**), which indicated that it has the (1*S*,6*S*) stereochemistry of a bicyclic system. The configuration of the chiral centers generated in the reaction is consistent with the addition to the *Si*-face of the cyclohexenone ring. From these X-ray structures, it is reasonable to assume that ethylene approaches from the less shielded *Si*-face of the cyclohexenyl group of **1a** to yield the major product **2a**. The experimental de's in Table 1 and the structural property reveal that the bulky and electron-rich naphthalene backbone is more efficient in diastereoface differentiation than the benzene one of **1b**.

Intermolecular Interaction between 1a and Added Naphthalenes. The higher induction requires both diastereoface selectivity and a fixed orientation of the cyclohexenone ring in the transition state. Supposing that the diastereoselectivity consists of the population of stacked conformation as shown in Figure 1, the additive effect might stabilize such a conformer. Since the additive effects were observed for **1a** but not for **1b**, the added naphthalenes interact with the naphthyl moiety attached to the menthyl group. We carried out UV−vis spectroscopy analyses for **1a**, 1-cyanonaphthalene, and a mixture of 1-cyanonaphthalene and **1a**, respectively. However, new absorption band, based on CT complex of 1-cyanonaphthalene and **1a**, was not observed (Figure 2). In addition, the CD spectrum of a mixture of 1-cyanonaphthalene and **1a** did not also show the interaction clearly by comparison with the spectrum of **1a** (Figure 3). We confirmed such interaction by fluorescence spectral analyses of **1a** and some components (Figure 4). Excitation (λ_{ex} = 297 nm)[8] of 1-cyanonaphthalene (0.05 M) in CH_2Cl_2 at −78 °C emitted fluorescences at 347 and 424 nm resulting from the monomer and the excimer, respectively (Figure 4f). The fluorescence at 424 nm was not observed clearly at 25 °C or for the 0.01 M solution. The intensity of the emissions of 1-cyanonaphthalene decreased as **1a** was added, but no new fluorescence,

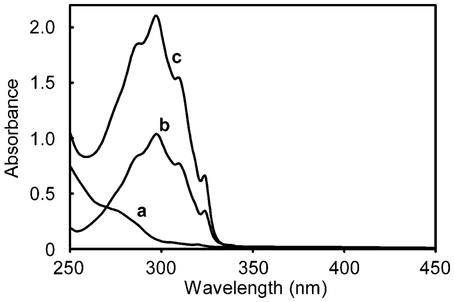


FIGURE 2. UV−vis spectra in CH_2Cl_2 at 25 °C (cell length: 1 cm): (a) **1a** (1.0×10^{-4} M); (b) 1-cyanonaphthalene (1.0×10^{-4} M); (c) 1-cyanonaphthalene (1.0×10^{-4} M) + **1a** (1.0×10^{-4} M).

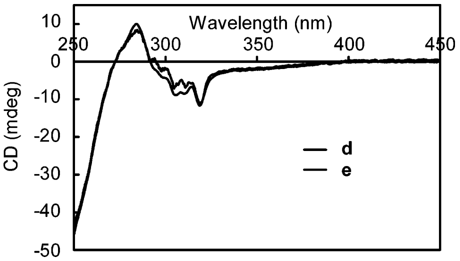


FIGURE 3. CD spectra in CH_2Cl_2 at −78 °C (cell length: 1 cm): (d) 1-cyanonaphthalene (1.0×10^{-4} M) + **1a** (1.0×10^{-4} M); (e) **1a** (1.0×10^{-4} M).

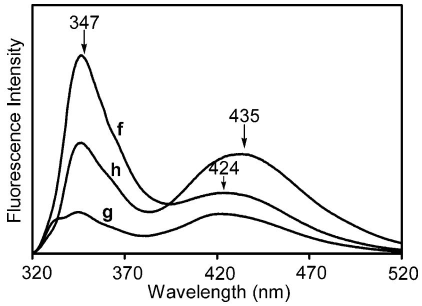


FIGURE 4. Fluorescence spectra upon excitation at 297 nm in CH_2Cl_2 at −78 °C: (f) 1-cyanonaphthalene (0.05 M); (g) 1-cyanonaphthalene (0.05 M) + **1a** (0.05 M); (h) 1-cyanonaphthalene (0.05 M) + (−)-8-(2-naphthyl)menthol (0.05 M).

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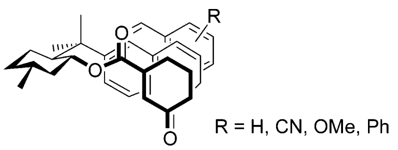
[8] The UV−vis spectra of 1-cyanonaphthalene in CH_2Cl_2 show the π,π^* aromatic absorption at 297 nm (ϵ = 8811), while for **1a** a weak absorption band was observed at 297 nm (ϵ = 885). See Figure 2.

CHART 1



based on the exciplex of 1-cyanonaphthalene and **1a**, was observed (Figure 4g). The emissions might have been quenched by the absorption of the excitation light at 297 nm by the added **1a** or by the intramolecular interaction between the naphthyl ring and the enone ester moiety.[9] In contrast, for the mixture of 8-(2-naphthyl)menthol and 1-cyanonaphthalene, a new exciplex fluorescence appeared at 435 nm (Figure 4h). These spectral results and the photocycloaddition might lead to a new understanding of the complex formation (naphthyl ring of **1a**/added naphthalene derivative) as illustrated in Chart 1. The increase of de's is considered the result of the fixed conformation and the increased steric hindrance for the approach of ethylene caused by such a complex formation.

Conclusion

In conclusion, we demonstrated that in the diastereoselective [2 + 2] photocycloaddition of chiral cyclohexenone carboxylates to ethylene, the (−)-8-(2-naphthyl)menthyl group was an effective chiral auxiliary in this reaction, proof of which was supported by X-ray analysis. We also discovered a novel and fairly efficient method of increasing diastereoselectivity by the addition of naphthalenes. The additive effect is attributed to the complex formation of **1a** and naphthalenes, which was supported by the fluorescence spectra. Moreover, recrystallization of the photoadduct **2a** afforded the diastereomerically pure major isomer (> 98% de). Removing the chiral auxiliary gave the optically pure bicyclo[4.2.0]octanone derivative **5**, of which the absolute configuration of the bicyclic system was elucidated from the X-ray analysis of the major cycloadduct.

Experimental Section

Synthesis of Materials. (−)-(1*R*,2*S*,5*R*)-5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexylcyclohexen-3-one-1-carboxylate (**1b**) and cyclohexen-3-one-1-carboxylic acid were prepared according to the literature procedure[7] and reported in ref 5. (1*R*,2*S*,5*R*)-(−)-8-(2-Naphthyl)menthol was prepared according to literature procedures.[7b,c]

(−)-(1*R*,2*S*,5*R*)-5-Methyl-2-[1-methyl-1-(2-naphthyl)ethyl]cyclohexylcyclohexen-3-one-1-carboxylate (1a). To a mixture of cyclohexen-3-one-1-carboxylic acid (0.43 g, 3.05 mmol), (−)-8-(2-naphthyl)menthol (0.86 g, 3.05 mmol, $[\alpha]^{20.0}_{D} = -2.5$, $c = 0.99$ in EtOH), and (dimethylamino)pyridine (0.37 mg, 3.05 mmol) in dry CH_2Cl_2 (4 mL) was added 1,3-dicyclohexylcarbodiimide (1.89 g, 9.14 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 5 min and at room temperature for 14 h. The precipitated dicyclohexylurea was removed by filtration through a glass filter, and the resulting filtrate was washed with 0.5 N HCl and an aqueous, saturated solution of $NaHCO_3$. During this procedure, additional precipitated dicyclohexylurea was again removed by the filtration of both layers to facilitate their separation. The organic solution was dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (AcOEt/hexane, 1/9) to give the ester **1a** (1.08 g, 88%) as a colorless solid: mp 118.0−119.7 °C; $[\alpha]^{20.0}_{D} = -61.2$, $c = 2.0$ in CH_2Cl_2; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, $J = 9.5$ Hz, 1H), 7.68 (d, $J = 8.8$ Hz, 2H), 7.50 (m, 2H), 7.36 (m, 2H), 5.87 (s, 1H), 5.06 (td, $J = 11.0$, 4.4 Hz, 1H), 2.25 (td, $J = 12.5$, 3.7 Hz, 1H), 2.04 (dd, $J = 13.9$, 3.7 Hz, 1H), 1.81−1.20 (m, 16H), 1.14−0.95 (m, 2H), 0.90 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.71 (s), 165.91 (s), 150.27(s), 148.38 (d), 134.25 (s), 132.47 (s), 132.16 (s), 128.47 (d), 128.36 (d), 128.12 (d), 126.58 (d), 125.95 (d), 125.90 (d), 122.74 (d), 75.12 (d), 50.53 (d), 42.52 (t), 40.26 (t), 37.62 (s), 35.20 (t), 32.07 (q), 31.36 (q), 26.77 (t), 24.54 (d), 22.55 (t), 22.13 (q), 22.01 (t); IR (KBr) 2949, 1714, 1685, 1252, 1227 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{27}H_{32}O_3$ 404.2351, found 404.2351; UV−vis (CH_2Cl_2) $\lambda = 320$ nm ($\epsilon = 393$, C═O), see Figure 2.

General Procedure for Photoreaction of 1 to Ethylene. Irradiation reactions were carried out using a Pyrex flask (>280 nm) in a water-cooled quartz immersion apparatus using a HALOS 500-W Hg high-pressure UV lamp as the light source. A 0.05 M solution of **1** and naphthalenes (0.05 M) in CH_2Cl_2 was purged with ethylene at 25 °C for 5 min and irradiated at each temperature without continuous purging until **1** was nearly completely consumed. The reaction was monitored by TLC and GLC. After the solvent evaporated, the residue was purified chromatographically to give a diastereomeric mixture of photoadduct **2** along with the recovery of naphthalenes. Each isomer of **2** could not be separated by standard chromatographic purification, and therefore the de value was not affected by this process. The de value of **2** was determined by ^1H NMR spectroscopy. The results are summarized in Table 1, along with reaction conditions.

(1*R*,2*S*,5*R*)-5-Methyl-2-[1-methyl-1-(2-naphthyl)ethyl]cyclohexyl (1*S*,6*S*)- and (1*R*,6*R*)-Bicyclo[4.2.0]octan-2-one-6-carboxylate (2a). The photoreaction of **1a** (40.5 mg, 0.10 mmol) in the presence of 1-phenylnaphthalene at −78 °C in CH_2Cl_2 for 1.5 h gave a diastereomeric mixture of **2a** (41.1 mg, 95%) after chromatography (AcOEt/hexane, 1/9). The de was determined to be 83% by ^1H NMR spectroscopy. **2a**: Colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ for the major diastereomer (values in parentheses are distinct signals assigned to the minor diastereomer) 7.75−7.69 (m, 3H), (7.60) 7.59 (s, 1H), 7.45 (d, $J = 8.5$ Hz, 1H), 7.38−7.31 (m, 2H), 4.93 (m, 1H), 2.70 (2.54) (dd, $J = 9.2$, 7.3 (9.2) Hz, 1H), 2.18−2.05 (m, 2H), 1.96−1.19 (m, 13H), (1.40) 1.39 (s, 3H), (1.22) 1.21 (s, 3H), 1.12−1.03 (m, 1H), 0.98−0.91 (m, 1H), 0.86−0.78 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ for the major diastereomer (values in parentheses are distinct signals assigned to the minor diastereomer) 212.46 (211.11) (s), 174.61 (174.48) (s), 148.61 (148.51) (s), 132.99 (s), (131.24) 131.13 (s), 127.44 (d), (127.25) 127.13 (d), 126.92 (d), 125.43 (d), 124.80 (d), 124.45 (d), 122.19 (d), (74.58) 74.54 (d), 48.93 (48.88) (d), 47.81 (47.72) (s), 45.21 (d), (41.37) 41.24 (t), (39.50) 39.47 (s), (38.16) 38.09 (t), 30.80 (d), (29.55) 28.96 (t), 27.73 (t), 27.55 (27.37) (q), (26.34) 26.30 (t), (25.13) 24.84 (q), 21.40 (q), 20.66 (20.30) (t), (20.25) 20.03 (t); IR (neat) 2952, 1712, 1239 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{29}H_{36}O_3$ 432.2664, found 432.2662.

(1*S*,6*S*)-Bicyclo[4.2.0]octan-2-one-6-carboxylic Acid Methyl Ester (5). Recrystallization of the diasteromeric mixture of **2a** (major/minor = 11/1) from CH_2Cl_2−hexane gave a crystalline solid, and similar recrystallizations of the obtained crystals were carried out several times to give a few pure major isomer of **2a** as colorless single crystals. In the presence of a small amount of the single crystals, 3× recrystallization of the diastereomeric mixture of **2a** (205.3 mg; major/minor = 11/1) from CH_2Cl_2−hexane afforded the diastereomerically pure major isomer (> 98% de, 108.6 mg, 53% yield). Optical rotation of the obtained major isomer was measured ($[\alpha]^{22.7}_{D} = +86.3$, $c = 0.02$ in CH_2Cl_2).

To a solution of the major isomer of **2a** (18.0 mg, 0.042 mmol) in 2.0 mL of degassed DMSO was added 0.10 mL of 1.0M NaOH aq, and the reaction mixture was stirred at 110

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[9] Similar photophysical intramolecular quenching of α-carbonyl 8-phenylmenthyl ester: Whitesell, J. K.; Younathan, J. N.; Hurst, J. R.; Fox, M. A. *J. Org. Chem.* **1985**, *50*, 5499.

°C under nitrogen atmosphere for 2 h. After removal of DMSO under reduced pressure, the reaction mixture was poured into 10 mL of H_2O and extracted with 3 × 20 mL of Et_2O. The aqueous layer was separated, and the combined organic layers were washed with saturated NaCl aq, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography (AcOEt/hexane, 1/9) to give (−)-8-(2-naphthyl)menthol (11.8 mg, 97%) as a colorless solid. The separated aqueous layer was treated with 10% HCl aq (pH 1) and extracted with 3 × 20 mL of Et_2O. The combined organic layers were washed with saturated NaCl aq, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was resolved in 0.5 mL of Et_2O and treated with an ethereal solution in diazomethane until a yellow color persisted. After 20 min, excess diazomethane was quenched by the addition of a few drops of AcOH. The reaction mixture was concentrated in vacuo, and the residue was purified by flash chromatography (AcOEt/hexane, 1/9) to afford 6.0 mg (75%; 2 steps) of **5** as a colorless oil: $[\alpha]^{22.2}_D = +169.8$, $c = 0.08$ in CH_2Cl_2; ^1H NMR (500 MHz, $CDCl_3$) δ 3.72 (s, 3H), 3.28 (t, $J = 9.15$ Hz, 1H), 2.52−2.22 (m, 4H), 2.18−1.80 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 212.17 (s), 176.42 (s), 52.31 (d), 48.45 (s), 46.43 (q), 38.99 (t), 30.62 (t), 28.80 (t), 21.29 (t), 20.97 (t); IR (neat) 2952, 1729 cm^{-1}; HRMS (EI) m/z calcd for $C_{10}H_{14}O_3$ 182.0943, found 182.0944.

Crystal Structure Analysis. Measurements were made on a Rigaku RAXIS-RAPID Imaging Plate diffractometer with Mo Kα radiation at 296 K. **1a**: $C_{27}H_{32}O_3$, yellow crystal (0.40 × 0.10 × 0.10 mm), orthorhombic, space group $P2_12_12_1$ (#19), $Z = 4$, $a = 15.5081(3)$ Å, $b = 21.0872(4)$ Å, $c = 7.0796(1)$ Å, $V = 2315.18(8)$ Å^3, $\rho_{calcd} = 1.161$ g cm^{-3}. Of 10 848 reflections up to $2\theta = 55.0°$, 2942 were independent ($R_{int} = 0.016$) and 2913 with $I > 2\sigma(I)$. The structure was solved with direct methods and refined with full matrix against all F^2 data. Hydrogen atoms were calculated in "riding" positions. $wR = 0.097$ and $R = 0.072$. **2a**: $C_{29}H_{36}O_3$, colorless crystal (0.25 × 0.25 × 0.17 mm), orthorhombic, space group $P2_12_12_1$ (#19), $Z = 4$, $a = 11.0801(9)$ Å, $b = 20.731(2)$ Å, $c = 10.8500(9)$ Å, $V = 2492.2(4)$ Å^3, $\rho_{calcd} = 1.153$ g cm^{-3}. Of 18 945 reflections up to $2\theta = 55.0°$, 3221 were independent ($R_{int} = 0.055$) and 3218 with $I > 2\sigma(I)$. The structure was solved and refined in an analogous manner to **1a**. $wR = 0.088$ and $R = 0.071$.

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Supporting Information Available: The crystallographic data for **1a** and **2a** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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