Synthesis of 2,6-Disubstituted Dihydronaphthalenes and Naphthalenes by Electrocyclic Reaction of *o*-Quinodimethane. A Synthesis of (±)-Naproxen

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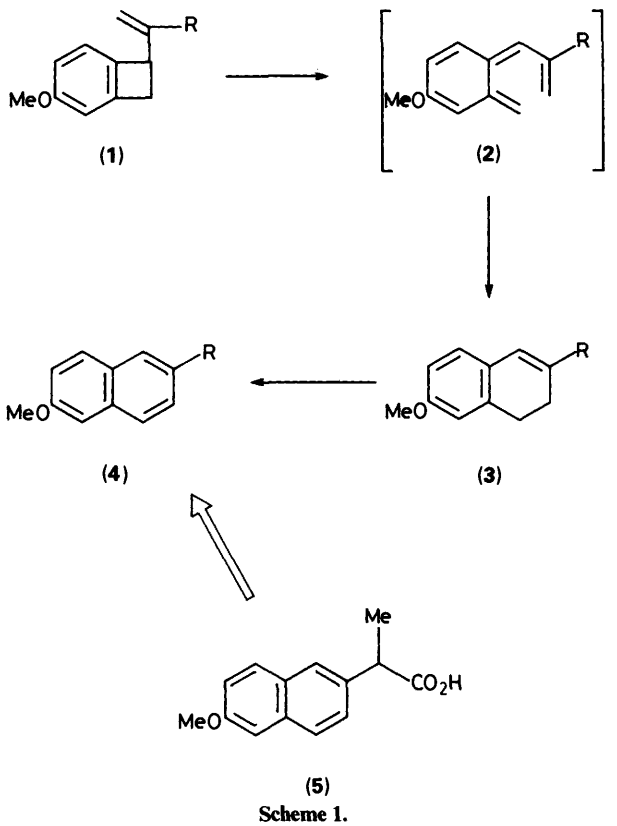
A survey of the electrocyclic reactions of *o*-quinodimethanes generated *in situ* by the thermolysis of dihydrobenzocyclobutenes with a variety of olefinic substituents at C-1 is reported. These reactions provide convenient access to the 2,6-disubstituted dihydronaphthalenes (**11**) and the naphthalenes (**12**). Thermolysis of the benzocylobutenes (**10**) at 180 °C in the presence of manganese dioxide affords in good yields the 2,6-di- and 2,3,6-tri-substituted naphthalenes (**12**) and (**16**). The naphthalenes (**12b,f,h**) thus obtained were easily converted into (±)-naproxen (**5**).

The electrocyclic reaction (ECR) of *o*-quinodimethane is one of the useful features of preparative benzocyclobutene chemistry.[1] It provides the chemist with a powerful tool for constructing nitrogen[2] or oxygen[3] containing six-membered heterocycles as well as naphthalene derivatives.[4] Recently, we have evaluated the ECR[5] from a standpoint of its competition with the [1,5]sigmatropic reaction[6] (or with different kind of ECR[7]). However, detailed study of the quite simple ECR *via* a hexatriene intermediate, which would be induced by the thermolysis of 1-alkenyl-substituted dihydrobenzocyclobutenes, has been rarely reported to date.[8] Particularly, the thermolysis of benzocyclobutenes with an *exo*-methylene moiety at C-1 has never been investigated at all. In this paper, we report the details of our survey of the ECR of *o*-quinodimethanes generated by the thermolysis of dihydrobenzocyclobutenes with olefinic substituents at C-1 and an application of the methodology developed here to the synthesis of (±)-naproxen (**5**), a non-steroidal anti-inflammatory agent.[9]

Results and Discussion

We envisaged that the ECR of the *o*-quinodimethane (**2**), generated *in situ* by the thermolysis of the dihydrobenzocyclobutene (**1**), would provide, after dehydrogenation of the resulting dihydronaphthalene (**3**), the 2,6-disubstituted naphthalene (**4**). Compound (**4**) could presumably be converted into (±)-naproxen (**5**) depending upon the choice of R (Scheme 1).

The thermolysis of dihydrobenzocyclobutenes with an *E*-alkene group at C-1, leading to the corresponding dihydronaphthalenes by ECR, has already been investigated by DeCamp.[8] However, this report did not mention the preparative value, but merely reported the reactivity. For the evaluation of the planned route [(**1**)→(**3**)→(**4**), Scheme 1], it was necessary for us to prepare the dihydrobenzocyclobutenes (**1**) with an *exo*-methylene moiety at C-1; these could in principle be derived from the corresponding 1-acyldihydrobenzocyclobutenes (**8**) by methylenation. According to the literature,[3a] 1-acyldihydrobenzocyclobutenes have been synthesized in low yields by the reaction of 1-cyanodihydrobenzocyclobutene with appropriate Grignard reagents. For investigation of the thermolysis using a variety of substrates, the development of a more flexible and convenient way of preparing (**8**) would be required. Thus the carboxylic acid (**6**), prepared from 1-cyano-1,2-dihydro-4-methoxybenzocyclobutene[10] by alkaline hydrolysis, was converted by treatment with 2.2 equiv. of lithium di-



Scheme 1.

isopropylamide (LDA) into the dianion; this was then treated with a variety of methyl esters (**7a–g**) in a one-pot operation, to produce in good yields the 1-acyl-1,2-dihydro-4-methoxybenzocyclobutenes (**8a–g**) through acylation and spontaneous decarboxylation.[11] We next attempted to prepare the *exo*-olefin (**10**) from (**8**) using methylenetriphenylphosphorane, and also Nozaki's procedure[12] employing $Zn–CH_2Br_2–TiCl_4$ or $Zn–CH_2I_2–AlMe_3$. In no case were we successful. The problem was nicely solved by using the conditions of Peterson olefination.[13] Thus, treatment of (**8a–g**) with trimethylsilylmethylmagnesium chloride provided the alcohols (**9a–g**), a mixture of diastereo-

† Deceased October 1988.

Table 1. Synthesis of (**10**) and its thermolysis

(7) R	(8) Yield%	Method[b]	(10) Yield%	Reaction time of thermolysis min	(11) Yield%
a Et	66	A	73	10	97
b i-Pr	76	A	99[a]	30	100
c cyclohexyl	83	A	83[a]	70	92
d t-Bu	69	A	65[a]	60	87
e $C(Me)_2SPh$	77	A	82[a]	120	84[(**11h**,) R = C(Me) = CH]
f $\overline{C(Me)CH_2OC(Me)_2O}$	91	A	26	10	94
		B	76		
g Ph	71	A	95	15	84

[a] Based on the consumed starting ketone (**8**). [b] Method A: BF_3·OEt_2; Method B: KH, 18-Crown-6

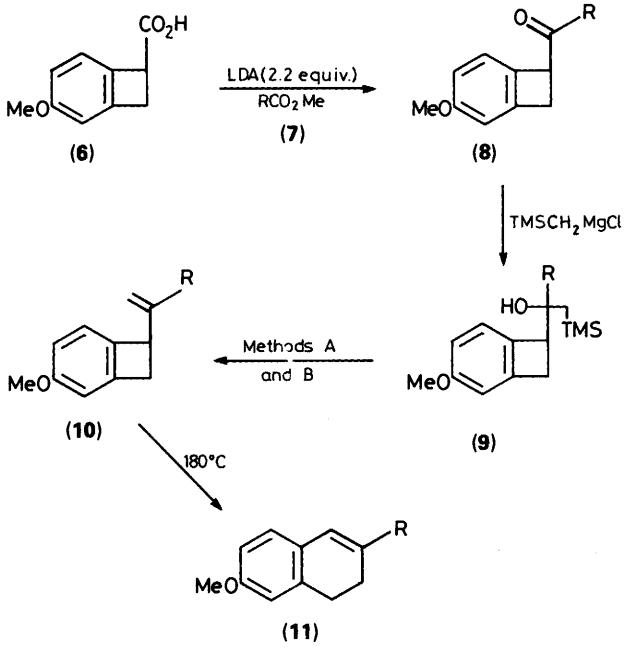
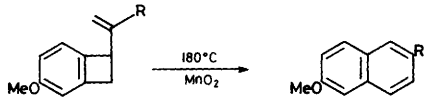


Table 2. Direct conversion of (**10**) into (**12**).



(**10**) (**12**)

(10) R	Reaction time (h)	(12) Yield (%)
a Et	20	66
b Pr^i	36	87
c cyclohexyl	15	77 + 6(**12g**)
d Bu^t	48	66
e $C(Me)_2SPh$	120	77[**12h**; R = C(Me) = CH_2]
f $\overline{C(Me)CH_2OC(Me)_2O}$	48	84
g Ph	24	97

isomers, which were exposed to boron trifluoride–ether (BF_3·OEt_2) to provide (**10a–e, g**) in good to excellent yields. When the alcohol (**9f**) was treated with potassium hydride and 18-crown-6 instead of BF_3·OEt_2, a greatly improved yield (26%→76%) was realized.

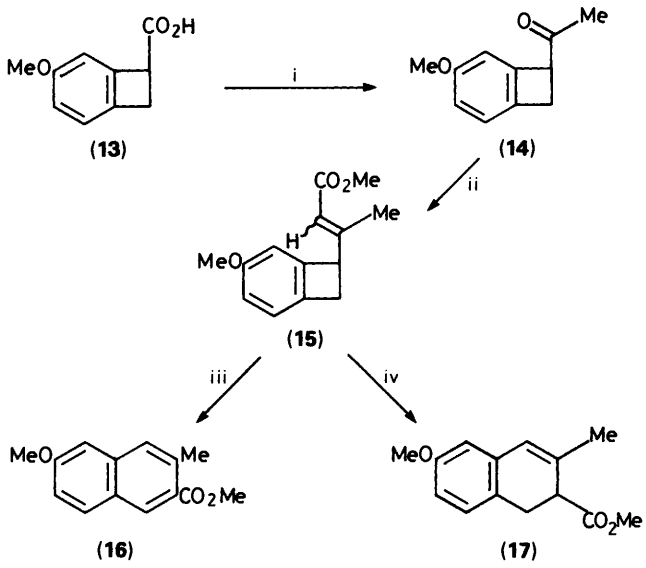
The achievement of an efficient three-step synthesis of (**10**) from (**6**) set the stage for the investigation of the thermolysis. On heating a solution of (**10a–g**) in *o*-dichlorobenzene (ODB) at 180 °C, the reaction was completed within *ca.* 1 h [except with (**10e**)] to provide excellent yields of the dihydronaphthalenes (**11a–d, f–h**) *via* the expected ECR. It should be noted that the thermolysis of (**10e**) required a longer reaction time and provided (**11h**) through elimination of thiophenol.

Having accomplished the successful conversion *via* ECR, we next examined the direct conversion of (**10**) into the naphthalenes (**12**). Since we had previously demonstrated that the thermolysis of 1-alkenyl-1-alkyl-1,2-dihydrobenzocyclobutenes in the presence of 10% palladium on carbon led to the formation of naphthalenes *via* successive ECR and dehydrogenation, we applied the same procedure to (**10**). When this reaction was conducted at 180 °C, several unidentified products were formed which complicated isolation of the naphthalene (less than 30% yield). After considerable experimentation, the conversion was nicely achieved by heating (**10**) at 180 °C in ODB in the presence of manganese dioxide[14] (ICS#22, Toho Zinc Co.) as dehydrogenating agent to produce the naphthalenes (**12a–d, f–h**) in good yields. When the substrate (**10c**) was thermolized, the fully aromatized product (**12g**) could be obtained in 6% yield as a by-product.

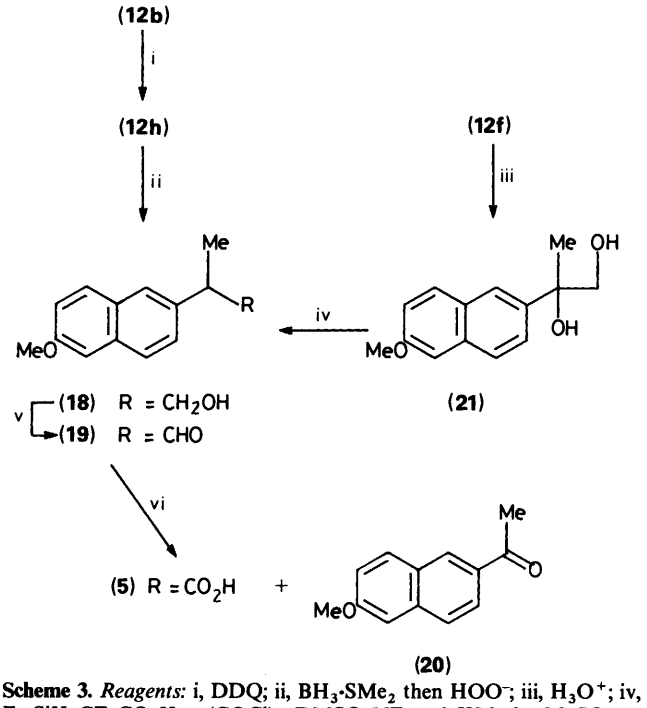
Another example of the convenient transformation (**10**)→(**12**) is the successful synthesis of the 2,3,6-trisubstituted naphthalene (**16**). Thermolysis of an inseparable mixture of two isomers (*E*/*Z* = 2.6:1 by ^1H NMR) of (**15**), prepared from the carboxylic acid (**13**) by sequential methylation[15] and Horner–Emmons reaction as shown in Scheme 2, with or without manganese dioxide provided (**16**) or (**17**), respectively, in good yield.

In order to explore the potential application of the present methodology to the synthesis of (±)-naproxen (**5**), we investigated the conversion of (**12h**) and (**12f**) to (**5**).[16] Since the resolution of (±)-naproxen has been established,[17] the development of a flexible and convenient synthetic route for racemic (**5**) and related compounds would be significant. As outlined in Scheme 3, the naphthalenes (**12h**) and (**12f**) were readily converted into the aldehyde (**19**) which was finally oxidized to (**5**) by the conditions of Stille.[18] The identity of the product was confirmed by comparison of its ^1H NMR, IR, and mass spectroscopic properties, as well as its TLC mobility, with those of an authentic sample of naproxen.[19]

In conclusion, we have investigated the ECR of *o*-quinodimethane and demonstrated that dihydrobenzocyclobutenes (**10**) with an *exo*-olefin moiety at C-1 are smoothly converted into the naphthalenes (**12**) and the dihydronaphthalenes (**11**) by thermolysis with or without manganese dioxide. Finally, the present transformation has been successfully applied to a novel synthesis of (±)-naproxen.



Scheme 2. *Reagents:* i, MeLi; ii, $(MeO)_2POCH_2CO_2Me$, NaH; iii, 180 °C, MnO_2, 3 days; iv, 180 °C, 1 h.



Scheme 3. *Reagents:* i, DDQ; ii, BH_3·SMe_2 then HOO^-; iii, H_3O^+; iv, Et_3SiH, CF_3CO_2H; v, $(COCl)_2$, DMSO, NEt_3; vi, $KMnO_4$, $MgSO_4$.

Experimental

M.p.s were determined on a Yanagimoto MP-22 apparatus and are uncorrected. IR spectra were recorded on a Hitachi 260-10 spectrophotometer. ^1H NMR spectra were recorded at 60 MHz on a JEOL JNM-PMX-60, at 90 MHz on a JEOL JNM-FX-90A, or at 500 MHz on a JEOL JNM-GX500 spectrometer. ^{13}C NMR spectra were recorded on a JEOL JNM-GX500 instrument, and all samples for NMR analyses were dilute solutions in deuteriochloroform unless otherwise stated. Mass spectra were recorded on a JOEL JMS-01SG-2 spectrometer, and microanalytical data were obtained on a JEOL JMS-DX303 spectrometer. All reactions were carried out under an atmosphere of dry argon or nitrogen. Column chromatography was carried out with silica gel (Kieselgel 60, 70-230 mesh, Merck). Thin-layer chromatography was carried out with E. Merck Silica gel 60F-254 (0.25 mm thickness) pre-coated TLC plates. The phrase 'residue upon work-up' refers to the residue obtained when the organic layer was separated, dried over magnesium sulphate ($MgSO_4$), and the solvent was evaporated under reduced pressure. All new compounds described in this Experimental section were homogeneous on TLC.

1,2-Dihydro-4-methoxybenzocyclobutene-1-carboxylic Acid (**6**).—A solution of 1-cyano-1,2-dihydro-4-methoxybenzocyclobutene[10] (7.27 g, 45.7 mmol) in ethanol (160 ml) was mixed with water (40 ml) containing potassium hydroxide (12.8 g, 227 mmol), and the mixture was heated at 100 °C for 5 h. After removal of the solvent *in vacuo*, the resulting aqueous layer was washed with diethyl ether. The aqueous phase was then acidified with 10% hydrochloric acid and extracted with chloroform. The extracts were washed with saturated brine and the residue upon work-up was recrystallized from benzene–hexane to afford the *carboxylic acid* (**6**) (8.0 g, 99%) as needles, m.p. 89–90 °C (Found: C, 67.3; H, 5.7. $C_{10}H_{10}O_3$ requires C, 67.4; H, 5.65%); $\nu_{max}(CHCl_3)$ 3 525 and 1 710 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 3.41 (2 H, d, *J* 4.2 Hz, ArCH_2), 3.76 (3 H, s, OMe), 4.23 (1 H, t, *J* 4.2 Hz, ArC*H*), 6.70–6.84 (2 H, m, ArH), 7.07 (1 H, d, *J* 10.2 Hz, ArH), and 11.40 (1 H, br, CO_2H, exchanges with D_2O); *m/z* 178 (M^+).

Methyl 2-Methyl-2-(phenylthio)propionate (**7e**).—Butyllithium solution (1.54 M in hexane; 20 ml, 30.8 mmol) was added dropwise to a stirred solution of di-isopropylamine (3.64 g, 34.3 mmol) in dry tetrahydrofuran (THF) (40 ml) at −78 °C. After being stirred at 0 °C for 30 min, the solution was cooled to −78 °C, and a solution of methyl isobutyrate (2.67 g, 26.2 mmol) in dry THF (15 ml) was added dropwise. The solution was stirred at 0 °C for a further 30 min, and then hexamethylphosphoramide (HMPA) (5.16 g, 28.8 mmol) was added at −78 °C. After being stirred at 0 °C for 30 min, a solution of diphenyl disulphide (6.30 g, 28.9 mmol) in dry THF (15 ml) was added dropwise at −78 °C. The reaction mixture was allowed to warm to 0 °C over 2.5 h, and was then quenched by addition of saturated aqueous ammonium chloride, and the solvent evaporated. The residue was extracted with chloroform and the extracts were washed with saturated brine. The residue upon work-up was chromatographed using hexane–ethyl acetate (19:1, v/v) as eluant to afford the *sulphide* (**7e**) (5.13 g, 93%) as an oil, which was further purified by distillation, b.p. 170–173 °C/18 mmHg, $\nu_{max}(CHCl_3)$ 1 725 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 1.49 (6 H, s, Me × 2), 3.66 (3 H, s, OMe), and 7.23–7.65 (5 H, m, ArH) (Found: M^+, 210.0711. $C_{11}H_{14}O_2S$ requires *M*, 210.0714).

Methyl 2,2,4-Trimethyl-1,3-dioxolane-4-carboxylate (**7f**).—Methyl methacrylate (11.2 g, 112 mmol) was added dropwise to a stirred solution of *N*-methylmorpholine *N*-oxide (1.44 g, 123 mmol) and osmium tetraoxide (0.084 g, 0.30 mmol) in a mixture of acetone (28 ml), t-butyl alcohol (14 ml), and water (70 ml) at 0 °C, and the mixture was stirred at room temperature for 22 h. To the mixture was added water (20 ml) and hydrated magnesium silicate (0.3 g), and the resulting mixture was filtered through Celite. The filtrate was adjusted to pH 7 with 10% aqueous sulphuric acid, then the organic solvent was evaporated to give a residue which was acidified with 10% aqueous sulphuric acid to pH 2. The mixture was extracted with ethyl acetate under salting-out conditions and the extracts were washed with saturated brine. The residue upon work-up was used in the next reaction without purification.

A solution of a mixture of the crude diol (4.7 g), 2,2-dimethoxypropane (7.28 g, 70 mmol), and a catalytic amount of toluene-*p*-sulphonic acid in 1,2-dichloroethane (140 ml) was heated under reflux for 13.5 h. Removal of the solvent gave an

oily residue which was distilled under reduced pressure to afford the *dioxolane* (**7f**) (4.47 g, 23%) as an oil, b.p. 67–69 °C/13 mmHg, ν_{max}($CHCl_3$) 1 740 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 1.43 (6 H, s, Mex2), 1.53 (3 H, s, Me), 3.78 (3 H, s, OMe), 3.81 (1 H, d, *J* 8.4 Hz, OC*H*H), and 4.39 (1 H, d, *J* 8.4 Hz, OCH*H*) (Found: $M^+ - CO_2Me$, 115.0739. $C_6H_{11}O_2$ requires *M*, 115.0759).

General Procedure for the Preparation of 1-*Acyl*-1,2-*dihydro*-4-*methoxybenzocyclobutenes* (**8a–g**).—Butyl-lithium (in hexane, 2.2 mmol) was added dropwise to a stirred solution of diisopropylamine (2.2 mmol) in dry THF (2 ml) at −78 °C. After being stirred at 0 °C for 30 min, the solution was cooled to −78 °C, and a solution of the carboxylic acid (**6**) (1.0 mmol) in dry THF (1 ml) was added dropwise. The solution was stirred at 0 °C for a further 30 min, and then HMPA (1.1 mmol) was added at the same temperature. After being stirred at 0 °C for 30 min, the solution was cooled again to −78 °C, and a solution of the ester (**7a–g**) (1.2 mmol) in dry THF (1 ml) was added dropwise to the mixture. The reaction mixture was allowed to warm to 0 °C over 1 h with stirring, and was then quenched with saturated aqueous ammonium chloride. After removal of the solvent, the residue was extracted with chloroform and the extracts were washed with saturated brine. The residue upon work-up was chromatographed to give the *ketones* (**8a–g**) in the yield indicated in Table 1.

For *ethyl* 1,2-*dihydro*-4-*methoxybenzocyclobuten*-1-*yl ketone* (**8a**): eluting solvent, hexane–ethyl acetate (9:1, v/v); oil (Found: C, 75.75; H, 7.5. $C_{12}H_{14}O_2$ requires C, 75.75; H, 7.4%); ν_{max}($CHCl_3$) 1 710 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 1.09 (3 H, t, *J* 7.2 Hz, CH_2CH_3), 2.59 (2 H, q, *J* 7.2 Hz, CH_2CH_3), 3.30–3.38 (2 H, m, $ArCH_2$), 3.77 (3 H, s, OMe), 4.21–4.32 (1 H, m, ArC*H*CO), 6.71–6.84 (2 H, m, ArH), and 7.05 (1 H, d, *J* 7.8 Hz, ArH); *m*/*z* 190 (M^+).

For *isopropyl* 1,2-*dihydro*-4-*methoxybenzocyclobuten*-1-*yl ketone* (**8b**): eluting solvent, hexane–ethyl acetate (9:1, v/v); oil (Found: C, 76.5; H, 7.9 $C_{13}H_{16}O_2$ requires C, 76.45; H, 7.9%); ν_{max}($CHCl_3$) 1 695 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 1.14 (3 H, d, *J* 7.2 Hz, $CHCH_3$), 1.22 (3 H, d, *J* 7.2 Hz, $CHCH_3$), 2.85–2.94 [1 H, m, C*H* $(CH_3)_2$], 3.25–3.39 (2 H, m, $ArCH_2$), 3.78 (3 H, s, OMe), 4.35–4.45 (1 H, m, ArC*H*CO), 6.64–6.82 (2 H, m, ArH), and 7.05 (1 H, d, *J* 8.8 Hz, ArH); *m*/*z* 204 (M^+).

For *cyclohexyl* 1,2-*dihydro*-4-*methoxybenzocyclobuten*-1-*yl ketone* (**8c**): eluting solvent, hexane– ethyl acetate (19:1, v/v); oil; ν_{max}($CHCl_3$) 1 700 cm^{-1}; δ_H(90 HMz, $CDCl_3$) 1.10–2.10 [10 H, m, $(CH_2)_5$], 2.00–2.30 [1 H, m, $COCH(CH_2)_5$], 3.28–3.35 (2 H, m, $ArCH_2$), 3.78 (3 H, s, OMe), 4.34–4.44 (1 H, m, ArC*H*CO), 6.67–6.84 (2 H, m, ArH), and 6.95–7.11 (1 H, m, ArH) (Found: M^+, 244.1472. $C_{16}H_{20}O_2$ requires *M*, 244.1463).

For *t-butyl* 1,2-*dihydro*-4-*methoxybenzocyclobuten*-1-*yl ketone* (**8d**): eluting solvent, hexane–ethyl acetate (19:1, v/v); oil (Found: C, 77.25; H, 8.3. $C_{14}H_{18}O_2$ requires C, 77.25; H, 8.3%); ν_{max}($CHCl_3$) 1 700 cm^{-1}; δ_H (90 MHz, $CDCl_3$) 1.26 [9 H, s, $C(CH_3)_3$], 3.24–3.36 (2 H, m, $ArCH_2$), 3.76 (3 H, s, OMe), 4.63–4.74 (1 H, m, ArC*H*CO), 6.68–6.81 (2 H, m, ArH), and 6.86 (1 H, d, *J* 10.1 Hz, ArH); *m*/*z* 218 (M^+).

For 1,2-*dihydro*-4-*methoxybenzocyclobuten*-1-*yl* 2-*phenylthiopropan*-2-*yl ketone* (**8e**): eluting solvent, hexane–ethyl acetate (97:3, v/v); prisms, m.p. 99–100 °C (from benzene–hexane); ν_{max}($CHCl_3$) 1 700 cm^{-1}; δ_H (90 MHz, $CDCl_3$) 1.46 (3 H, s, Me), 1.57 (3 H, s, Me), 3.25–3.38 (2 H, m, $ArCH_2$), 3.76 (3 H, s, OMe), 5.05–5.21 (1 H, m, ArC*H*CO), 6.65–6.82 (2 H, m, ArH), 6.88–7.01 (1 H, m, ArH), and 7.25–7.55 (5 H, m, SPh) (Found: M^+, 312.1188. $C_{19}H_{20}O_2S$ requires *M*, 312.1184).

For 1,2-*dihydro*-4-*methoxybenzocyclobuten*-1-*yl* 2,2,4-*trimethyl*-1,3-*dioxolan*-4-*yl ketone* (**8f**): eluting solvent, hexane–ethyl acetate (17:3, v/v); oil, as a mixture of two diastereoisomers; ν_{max}($CHCl_3$) 1 700 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 1.45 (3 H, s, Me), 1.53 (6 H, s, Me × 2), 3.05–3.65 (2 H, m, $ArCH_2$), 3.78 (3 H, s, OMe), 3.85 (1 H, d, *J* 9.1 Hz, OC*H*HC), 4.26 (1 H, d, *J* 9.1 Hz, OCH*H*C), 4.18–4.28 (1 H, m, ArC*H*CO), 6.62–6.82 (2 H, m, ArH), and 7.05–7.25 (1 H, m, ArH) (Found: M^+, 276.1344. $C_{16}H_{20}O_4$ requires *M*, 276.1361).

For 1,2-*dihydro*-4-*methoxybenzocyclobuten*-1-*yl phenyl ketone* (**8g**): eluting solvent, hexane–ethyl acetate (97:3, v/v); oil; ν_{max}($CHCl_3$) 1 680 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 3.47–3.77 (2 H, m, $ArCH_2$), 3.77 (3 H, s, OMe) 5.00–5.10 (1 H, m, ArC*H*CO), 6.68–6.80 (2 H, m, ArH), 6.69–7.05 (1 H, m, ArH), 7.39–7.65 (3 H, m, ArH), and 8.01–8.04 (2 H, m, ArH) (Found: M^+, 238.1004. $C_{16}H_{14}O_2$ requires *M*, 238.0994).

General Procedure for the Peterson Reaction of the Ketones (**8a–g**).—A solution of trimethylsilylmethylmagnesium chloride (prepared from trimethylsilymethyl chloride and magnesium; stored as a diethyl ether solution in a refrigerator; 1.8 mmol) was added dropwise to a stirred solution of the ketone (**8a–g**) (0.6 mmol) in dry diethyl ether (3 ml) at 0 °C. After being stirred at room temperature for 2 h, the reaction mixture was quenched with saturated aqueous ammonium chloride and was filtered through Celite. The filtrate was concentrated to give a residue which was diluted with water, and the resulting aqueous phase was extracted with chloroform. The extracts were washed with saturated brine and the residue upon work-up was subjected to the next step without purification (Method A).

Boron trifluoride–diethyl ether (0.65 mmol) was added dropwise to a stirred solution of this crude alcohol (**9**) in dry methylene dichloride (4 ml) at −78 °C. After being stirred at the same temperature for 30 min, the mixture was quenched with saturated aqueous sodium hydrogencarbonate and the resulting mixture was allowed to warm to 0 °C over 5 min. The organic layer was separated and was washed with saturated brine. The residue upon work-up was chromatographed to afford the exo-*methylene compounds* (**10a–g**) in the yield indicated in Table 1 (Method B).

A solution of the crude alcohol (**9f**), prepared from the ketone (**8f**) (0.1 mmol) by the same procedure as described above, in dry THF (2.2 ml) was added dropwise to a stirred mixture of potassium hydride (0.23 mmol) and a catalytic amount of 18-crown-6 in dry THF (2.2 ml) at 0 °C. The mixture was allowed to warm to 40 °C over 11 h with stirring and was quenched with saturated aqueous ammonium chloride at 0 °C. After being concentrated, the residue was extracted with chloroform and the extracts were washed with saturated brine. The residue upon work-up was chromatographed to give (**10f**) in the yield indicated in Table 1.

For 1-(*but*-1-*en*-2-*yl*)-1,2-*dihydro*-4-*methoxybenzocyclobutene*) (**10a**): eluting solvent, hexane–ethyl acetate (9:1, v/v); oil; δ_H(90 MHz, $CDCl_3$) 1.14 (3 H, t, *J* 7.8 Hz, CH_2CH_3), 2.09 (2 H, q, *J* 7.8 Hz, CH_2CH_3), 2.25–2.52 (1 H, m, ArC*H*H), 3.43 (1 H, dd, *J* 13.7 and 2.4 Hz, ArCH*H*), 3.82 (3 H, s, OMe), 3.95–4.13 (1 H, m, ArC*H*C=), 4.81–4.89 (1 H, m, =C*H*H), 4.88–4.93 (1 H, m, =CH*H*), 6.70–6.88 (2 H, m, ArH), and 7.07 (1 H, d, *J* 7.8 Hz, ArH) (Found: M^+, 188.1208. $C_{13}H_{16}O$ requires *M*, 188.1201).

For 1,2-*dihydro*-4-*methoxy*-1-(3-*methylbut*-1-*en*-2-*yl*)*benzocyclobutene* (**10b**): eluting solvent, hexane–ethyl acetate (24:1, v/v); oil; δ_H(90 HMz, $CDCl_3$) 1.11 [6 H, d, *J* 7.2 Hz, $CH(CH_3)_2$], 2.20–2.51 [1 H, m, $CH(CH_3)_2$], 2.82 (1 H, dd, *J* 13.8 and 2.7 Hz, ArC*H*H), 3.39 (1 H, dd, *J* 13.8 and 5.5 Hz, ArCH*H*), 3.76 (3 H, s, OMe), 3.95–4.15 (1 H, m, ArC*H*C=), 5.25–5.35 (2 H, m, $=CH_2$), 6.65–6.83 (2 H, m, ArH), and 7.03 (1 H, d, *J* 7.2 Hz, ArH) (Found: M^+, 202.1343. $C_{14}H_{18}O$ requires *M*, 202.1358). Recovered starting ketone (**8b**), 21%.

For 1-(1-*cyclohexylvinyl*)-1,2-*dihydro*-4-*methoxybenzocyclobutene* (**10c**): eluting solvent, hexane–ethyl acetate (19:1, v/v); oil; δ_H(90 MHz, $CDCl_3$) 0.90–2.20 [11 H, m, $=CCH(CH_2)_5$], 2.86 (1 H, dd, *J* 14.0 and 2.7 Hz, ArC*H*H), 3.42 (1 H, dd, *J* 14.0 and 5.7 Hz, ArCH*H*), 3.75 (3 H, s, OMe), 4.00–4.15 (1 H, m,

ArC*H*C=), 4.79–4.92 (2 H, m, =CH_2), 6.70–6.89 (2 H, m, ArH), and 7.07 (1 H, d, *J* 7.8 Hz, ArH) (Found: M^+, 242.1662. $C_{17}H_{22}O$ requires *M*, 242.1671). Recovered starting ketone (**8c**), 13%.

For 1-(3,3-*dimethylbut*-1-*en*-2-*yl*)-1,2-*dihydro*-4-*methoxybenzocyclobutene* (**10d**): eluting solvent, hexane–ethyl acetate (19:1, v/v), oil; δ_H(90 HMz, $CDCl_3$) 1.17 [9 H, s, $C(CH_3)_3$], 2.80 (1 H, dd, *J* 13.5 and 3.6 Hz, ArC*H*H), 3.42 (1 H, dd, *J* 13.5 and 5.4 Hz, ArCH*H*), 3.78 (3 H, s, OMe), 4.16 (1 H, dd, *J* 5.4 and 3.6 Hz, ArC*H*C=), 4.80 (1 H, m, =C*H*H), 4.85 (1 H, m, =CH*H*), 6.75–6.87 (2 H, m, ArH), and 6.99 (1 H, d, *J* 7.8 Hz, ArH) (Found: M^+, 216.1495. $C_{15}H_{20}O$ requires *M*, 216.1514). Recovered starting ketone (**8d**), 25%.

For 1,2-*dihydro*-4-*methoxy*-1-(3-*methyl*-3-*phenylthiobut*-1-*en*-2-*yl*)*benzocyclobutene* (**10e**); eluting solvent, hexane–ethyl acetate (97:3, v/v); oil; δ_H(90 MHz, $CDCl_3$) 1.48 [6 H, s, $C(CH_3)_2$], 2.75 (1 H, dd, *J* 13.8 and 2.7 Hz, ArC*H*H), 3.49 (1 H, dd *J* 13.8 and 5.4 Hz, ArCH*H*), 3.79 (3 H, s, OMe), 4.51–4.54 (1 H, m, =C*H*H), 4.55–4.69 (1 H, m, ArC*H*C=), 4.82–4.86 (1 H, m, =CH*H*), 6.65– 6.89 (2 H, m, ArH), 6.98 (1 H, d, *J* 7.8 Hz, ArH), and 7.20–7.55 (5 H, m, SPh) (Found: M^+, 310.1385. $C_{20}H_{22}O_3S$ requires *M*, 310.1392). Recovered starting ketone (**8e**), 51%.

For 1,2-*dihydro*-1-[1-(2,2,4-*trimethyl*-1,3-*dioxolan*-4-*yl*)*vinyl*]*benzocyclobutane* (**10f**): eluting solvent, hexane–ethyl acetate (19:1, v/v); oil, as a mixture of diastereoisomers; δ_H(500 MHz, $CDCl_3$) 1.34 (1.74 H, s, Me), 1.35 (1.26 H, s, Me), 1.41 (1.26 H, s, Me), 1.45 (3.48 H, s, Me), 1.47 (1.26 H, s, Me), 2.82 (1 H, m, ArC*H*H), 3.38 (1 H, m, ArCH*H*), 3.72 (3 H, s, OMe) 3.78 (0.58 H, d, *J* 7.2 Hz, C*H*HO), 3.87 (0.42 H, d, *J* 7.2 Hz, OC*H*H), 3.95 (0.42 H, d, *J* 7.2 Hz, OCH*H*), 3.97 (0.58 H, d, *J* 7.2 Hz, OCH*H*), 4.07 (1 H, m, ArC*H*C=), 4.85 (0.42 H, s, =C*H*H), 4.89 (0.58 H, s, =C*H*H), 5.03 (1 H, s, =CH*H*), and 6.92–6.96 (1 H, m, ArH) (Found: M^+, 274.1541. $C_{17}H_{22}O_3$ requires *M*, 274.1569).

For 1,2-*dihydro*-4-*methoxy*-1-(1-*phenylvinyl*)*benzocyclobutene* (**10g**): eluting solvent, hexane–ethyl acetate (97:3, v/v); oil; δ_H(90 MHz, $CDCl_3$) 2.89 (1 H, dd, *J* 13.5 and 2.7 Hz, ArC*H*H), 3.52 (1 H, dd, *J* 13.5 and 5.4 Hz, ArCH*H*), 3.79 (3 H, s, OMe), 4.48–4.61 (1 H, m, ArC*H*C=), 5.18 (1 H, m, =C*H*H), 5.21 (1 H, m, =CH*H*), 6.75–6.88 (2 H, m, ArH), and 7.09 (1 H, m, *J* 7.8 Hz, ArH) (Found: M^+, 236.1203. $C_{17}H_{16}O$ requires *M*, 236.1201).

General Procedure for the Thermolysis of Compounds (**10a–g**).—A solution of the olefinic dihydrobenzocyclobutene (**10a–g**) (1 mmol) in dry *o*-dichlorobenzene (5 ml) was sonicated for 5 min and the solution was heated at 180 °C for the period shown in Table 1. After removal of the solvent, the residue was chromatographed to give the *dihydronaphthalenes* (**11a–d, f–h**) in the yield indicated in Table 1.

For 2-*ethyl*-3,4-*dihydro*-6-*methoxynaphthalene* (**11a**): eluting solvent, hexane–ethyl acetate (9:1, v/v); oil; δ_H(90 MHz, $CDCl_3$) 1.15 (3 H, t, *J* 7.5 Hz, CH_2CH_3), 2.08–2.42 (4 H, m, CH_2CH_3 and $ArCH_2CH_2$), 2.70–2.95 (2 H, m, $ArCH_2$), 3.83 (3 H, s, OMe), 6.20 (1 H, br s, ArC*H*=), and 6.65–7.03 (3 H, m, ArH) (Found: M^+, 188.1207. $C_{13}H_{16}O$ requires *M*, 188.1201).

For 3,4-*dihydro*-2-*isopropyl*-6-*methoxynaphthalene* (**11b**): eluting solvent, hexane–ethyl acetate (19:1, v/v); oil; δ_H(90 MHz, $CDCl_3$) 1.15 [6 H, d, *J* 6.8 Hz, $CH(CH_3)_2$], 2.10–2.41 (4 H, m, $ArCH_2CH_2$), 3.83 (3 H, s, OMe), 6.22 (1 H, br s, ArC*H*=), 6.62–6.83 (2 H, m, ArH), and 6.90–7.08 (1 H, m, ArH) (Found: M^+, 202.1356. $C_{14}H_{18}O$ requires *M*, 202.1358).

For 2-*cyclohexyl*-3,4-*dihydro*-6-*methoxynaphthalene* (**11c**): eluting solvent, hexane–ethyl acetate (97:3, v/v); oil; δ_H(90 MHz, $CDCl_3$) 1.10–2.33 [13 H, m, $CH(CH_2)_5$ and $ArCH_2CH_2$], 2.66–2.83 (2 H, m, $ArCH_2$), 3.88 (3 H, s, OMe), 6.15 (1 H, br s, ArC*H*=), and 6.55–6.99 (3 H, m, ArH) (Found: M^+, 242.1665. $C_{17}H_{22}O$ requires *M*, 242.1671).

For 2-*t*-*butyl*-3,4-*dihydro*-6-*methoxynaphthalene* (**11d**): eluting solvent, hexane–ethyl acetate (97:3, v/v); oil; δ_H(90 MHz, $CDCl_3$) 1.14 [9 H, s, $C(CH_3)_3$], 3.10–3.89 (4 H, m, $ArCH_2CH_2$), 3.79 (3 H, s, OMe), 6.23 (1 H, br s, ArC*H*=), and 6.60–7.01 (3 H, m, ArH) (Found: M^+, 216.1510. $C_{15}H_{20}O$ requires *M*, 216.1514).

For 3,4-*dihydro*-2-*isopropenyl*-6-*methoxynaphthalene* (**11h**): eluting solvent, hexane–ethyl acetate (97:3, v/v); δ_H(90 MHz, $CDCl_3$) 2.05 (3 H, s, $=CCH_3$), 2.35–2.95 (4 H, m, $ArCH_2CH_2$), 3.81 (3 H, s, OMe), 5.00 (1 H, br s, =C*H*H), 5.17 (1 H, m, =CH*H*), 6.65 (1 H, br s, ArC*H*=), and 6.60–7.09 (3 H, m, ArH) (Found: M^+, 200.1167. $C_{14}H_{16}O$ requires *M*, 200.1202).

For 3,4-*dihydro*-2-(2,2,4-*trimethyl*-1,3-*dioxolan*-4-*yl*)-6-*methoxynaphthalene* (**11f**): eluting solvent, hexane–ethyl acetate (9:1, v/v); oil; δ_H(90 MHz, $CDCl_3$) 1.43 (3 H, s, Me), 1.45 (3 H, s, Me), 2.00 (3 H, s, Me), 2.12–2.38 (2 H, m, $ArCH_2CH_2$), 2.68–2.90 (2 H, m, $ArCH_2$), 3.79 (3 H, s, OMe), 3.85 (1 H, d, *J* 9.0 Hz, OC*H*H), 4.06 (1 H, d, *J* 9.0 Hz, OCH*H*), 6.50 (1 H, br s, ArC*H*C=), 6.60–6.82 (2 H, m, ArH), and 6.99 (1 H, d, *J* 8.7 Hz, ArH) (Found: M^+, 274.1573. $C_{17}H_{22}O_3$ requires *M*, 274.1569).

For 3,4-*dihydro*-6-*methoxy*-2-*phenylnaphthalene* (**11g**): eluting solvent, hexane–ethyl acetate (97:3, v/v), prisms, m.p. 115–116 °C (from diethyl ether–hexane) (Found: C, 86.4; H, 7.0. $C_{17}H_{16}O$ requires C, 86.4; H, 6.85%); δ_H(90 MHz, $CDCl_3$) 2.56–3.05 (4 H, m, $ArCH_2CH_2$), 3.82 (3 H, s, OMe), 6.61–7.15 (4 H, m, ArC*H*= and ArH), and 7.18–7.62 (5 H, m, ArH); *m*/*z* 236 (M^+).

General Procedure for the Thermolysis of Compounds (**10a–g**) *in the Presence of Manganese Dioxide.*—Manganese dioxide (ICS#22, Toho Zinc Co., 5 mmol) was added to a degassed solution of the benzocyclobutene (**10a–g**) (1 mmol) in dry *o*-dichlorobenzene (15 ml) and the mixture was heated at 180 °C for the period depicted in Table 2. After filtration through Celite, the filtrate was concentrated *in vacuo* to give a residue which was chromatographed to give the naphthalene (**12a–d, f–h**) in the yield in Table 1.

For 2-*ethyl*-6-*methoxynaphthalene* (**12a**): eluting solvent, chloroform–hexane (1:2, v/v); prisms, m.p. 61 °C (from hexane) (Found: C, 83.85; H, 7.4. $C_{13}H_{14}O$ requires C, 83.85; H, 7.6%); δ_H(90 MHz, $CDCl_3$) 1.30 (3 H, t, *J* 7.5 Hz, CH_2CH_3), 2.77 (2 H, q, *J* 7.5 Hz, CH_2CH_3), 3.90 (3 H, s, OMe), 7.00–7.19 (2 H, m, ArH), 7.29 (1 H, dd, *J* 8.4 and 1.7 Hz, ArH), and 7.50–7.78 (2 H, m, ArH): *m*/*z* 186 (M^+) and 171 (100%).

For 2-*isopropyl*-6-*methoxynaphthalene* (**12b**): eluting solvent, hexane–ethyl acetate (97:3, v/v); needles, m.p. 60–61 °C (from diethyl ether–hexane); δ_H(90 MHz, $CDCl_3$) 1.32 [6 H, d, *J* 6.8 Hz, $CH(CH_3)_2$], 2.85–3.21 (1 H, m, ArC*H*), 3.90 (3 H, s, OMe), and 7.02–7.78 (6 H, m, ArH) (Found: M^+, 200.1208. $C_{14}H_{16}O$ requires *M*, 200.1201).

For 2-*cyclohexyl*-6-*methoxynaphthalene* (**12c**): eluting solvent, hexane–ethyl acetate (95:5, v/v); prisms, m.p. 95–95.5 °C (from hexane) (Found: C, 85.0; H; 8.4. $C_{17}H_{20}O$ requires C, 84.95; H, 8.4%); δ_H(90 MHz, $CDCl_3$) 1.02–2.13 [10 H, m, $(CH_2)_5$], 2.61 (1 H, m, ArC*H*), 3.94 (3 H, s, OMe), and 7.00–7.79 (6 H, m, ArH); *m*/*z* 240 (M^+, 100%).

For 2-*t*-*butyl*-6-*methoxynaphthalene* (**12d**): eluting solvent, chloroform–hexane (1:3, v/v); needles, m.p. 76.5–77 °C (from hexane) (Found: C, 83.95; H, 8.65. $C_{15}H_{18}O$ requires C, 84.05; H, 8.45%); δ_H(90 MHz, $CDCl_3$) 1.40 [9 H, s, $C(CH_3)_3$], 3.91 (3 H, s, OMe), 7.00–7.20 (2 H, m, ArH), 7.51 (1 H, dd, *J* 8.4 and 1.7 Hz), and 7.60–7.75 (2 H, m, ArH); *m*/*z* 214 (M^+) and 199 (100%).

For 2-*methoxy*-6-(2,2,4-*trimethyl*-1,3-*dioxolan*-4-*yl*)*naphthalene* (**12f**): eluting solvent, hexane–ethyl acetate (97:3, v/v); prisms, m.p. 85–86 °C (from diethyl ether–hexane); δ_H(90 MHz, $CDCl_3$) 1.42 (3 H, s, Me), 1.58 (3 H, s, Me), 1.62 (3 H, s, Me), 3.91 (3 H, s, OMe), 4.61 (2 H, s, OCH_2), 7.05–7.23 (2 H, m, ArH), 7.43 (1 H, dd, *J* 8.6 and 1.7 Hz, ArH), and 7.63–7.83 (3 H, m, ArH) (Found: M^+, 272.1407. $C_{17}H_{20}O_3$ requires *M*, 272.1413).

For 2-*methoxy*-6-*phenylnaphthalene* (**12g**): eluting solvent,

hexane–ethyl acetate (95:5, v/v); leaflets, m.p. 150–151 °C (from hexane) (Found: C, 87.0; H, 6.25. $C_{17}H_{14}O$ requires C, 87.15; H, 6.0%); δ_H(90 MHz, $CDCl_3$) 3.94 (3 H, s, OMe), 7.01–7.90 (10 H, m, ArH), and 7.97 (1 H, br s, ArH); *m/z* 234 (M^+, 100%).

For *2-isopropenyl-6-methoxynaphthalene* (**12h**): eluting-solvent, hexane–ethyl acetate (97:3, v/v); leaflets, m.p. 85–86 °C (diethyl ether–hexane) (Found: C, 84.7; H, 7.3. $C_{14}H_{14}O$ requires C, 84.8; H, 7.1 %): δ_H(90 MHz, $CDCl_3$) 2.27 (3 H, br s, $=CCH_3$), 5.15 (1 H, m, $=CHH$), 5.49 (1 H, br s, $=CHH$), 7.09–7.20 (3 H, m, ArH), and 7.65–7.81 (3 H, m, ArH); *m/z* 198 (M^+, 100%).

1,2-Dihydro-5-methoxybenzocyclobutene-1-carboxylic Acid (**13**).—1-Cyano-1,2-dihydro-5-methoxybenzocyclobutene[20] (2.09 g, 13.1 mmol) was hydrolysed by the same procedure as described for preparing (**6**) to yield the *carboxylic acid* (**13**) (2.37 g, 100%) as prisms after recrystallization from diethyl ether–hexane, m.p. 93–94 °C (Found: C, 67.05; H, 5.6. $C_{10}H_{10}O_3$ requires C, 67.4; H, 5.65%); ν_{max}($CHCl_3$) 3 525 and 1 710 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 3.40 (2 H, d, *J* 4.2 Hz, $ArCH_2$), 3.77 (3 H, s, OMe), 4.27 (1 H, t, *J* 4.2 Hz, ArC*H*), 6.76 (1 H, br s, ArH), 6.81 (1 H, dd, *J* 8.7 and 2.1 Hz, ArH), 7.02 (1 H, d, *J* 8.7 Hz, ArH), and 10.87 (1 H, br s, CO_2H, exchange with D_2O); *m/z* 178 (M^+, 100%).

1-Acetyl-1,2-dihydro-5-methoxybenzocyclobutene (**14**).—Methyl-lithium solution (1.5M in diethyl ether; 17.6 ml, 26.4 mmol) was added in one portion to a stirred solution of the carboxylic acid (**23**) (1.57 g, 8.82 mmol) in dry THF (20 ml) at 0 °C. After being stirred at 0 °C for 2 h, trimethylsilyl chloride[22] was added and the resulting mixture was allowed to warm to room temperature over 10 min. The reaction mixture was then quenched by addition of 5% hydrochloric acid and extracted with diethyl ether. The extracts were washed successively with 5% aqueous sodium hydroxide and saturated brine. The residue upon work-up was chromatographed using hexane–ethyl acetate (9:1, v/v) as eluant to afford the *ketone* (**14**) (1.22 g, 79%) as an oil, ν_{max}($CHCl_3$) 1 710 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 2.23 (3 H, s, $COCH_3$), 3.32 (2 H, d, *J* 4.1 Hz, $ArCH_2$), 3.78 (3 H, s, OMe), 4.26 (1 H, t, *J* 4.1 Hz, ArC*H*CO), 6.75 (1 H, br s, ArH), 6.80 (1 H, dd, *J* 9.1 and 2.2 Hz, ArH), and 7.02 (1 H, d, *J* 9.1 Hz, ArH) (Found: M^+, 176.0834. $C_{11}H_{12}O_2$ requires *M*, 176.0837).

Methyl 3-(*1,2-Dihydro-5-methoxybenzocyclobuten-1-yl*)-(E *and* Z)-*crotonate* (**15**).—Trimethyl phosphonoacetate (135 mg, 0.74 mmol) was added dropwise to a stirred suspension of sodium hydride (60% in oil; 36 mg, 0.9 mmol) in dry THF (3 ml) at 0 °C. After being stirred at room temperature for 40 min, a solution of the ketone (**14**) (88 mg, 0.5 mmol) in dry dimethoxyethane (2 ml) was added dropwise and the resulting mixture was stirred at 55 °C for 2 h. Water was added to the mixture under ice–water cooling, and the solvent was evaporated *in vacuo* to give a residue which was extracted with methylene dichloride. The extracts were washed with saturated brine, and the residue upon work-up was chromatographed using hexane–ethyl acetate (92:8, v/v) as eluant to afford the *ester* (**15**) (106 mg, 91%), a mixture of *E* and *Z* isomers, as an oil, ν_{max}($CHCl_3$) 1 710 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 1.76 (0.83 H, d, *J* 1.7 Hz, $=CCH_3$ of *Z*-isomer), 2.19 (2.17 H, d, *J* 1.2 Hz, $=CCH_3$ of *E*-isomer), 2.75–3.05 (1 H, m, ArC*H*H), 3.27–3.68 (1 H, m, ArCH*H*), 3.68 (2.17 H, s, OMe of *E*), 3.72 (0.83 H, s, OMe of *Z*), 3.76 (0.83 H, s, OMe of *Z*), 3.78 (2.17 H, s, OMe of *E*), 3.94–4.20 (0.72 H, m, ArC*H*C= of *E*), 5.43–5.62 (0.28 H, m, ArC*H*C= of *Z*), 5.70–5.91 (1 H, m, $=CH$), 6.55–6.90 (2 H, m, ArH), and 7.00 (1 H, br d, *J* 9.0 Hz, ArH) (Found: M^+, 232.1090. $C_{14}H_{16}O_3$ requires *M*, 232.1100).

6-Methoxy-2-methoxycarbonyl-3-methylnaphthalene (**16**).—According to the general procedure for the thermolysis of (**10**) in the presence of manganese dioxide, the benzocyclobutene (**15**) (38.4 mg, 0.17 mmol) was converted by heating at 180 °C for 3 days into the *naphthalene* (**16**) (27 mg, 71%) as prisms after recrystallization from diethyl ether–hexane, m.p. 96–97 °C (Found: C, 72.9; H, 6.2. $C_{14}H_{14}O_3$ requires C, 73.0; H, 6.15%); ν_{max}($CHCl_3$) 1 715 cm^{-1}; δ_H(90 HMz, $CDCl_3$) 2.71 (3 H, br s, $=CCH_3$) 3.92 (3 H, s, OMe), 3.93 (3 H, s, OMe), 7.05 (1 H, s, ArH), 7.09 (1 H, dd, *J* 8.6 and 2.4 Hz, ArH), 7.55 (1 H, br s, ArH), 7.78 (1 H, d, *J* 9.6 Hz, ArH), and 8.43 (1 H, s, ArH); *m/z* 230 (M^+, 100%).

1,2-Dihydro-6-methoxy-2-methoxycarbonyl-3-methylnaphthalene (**17**).—According to the general procedure for the thermolysis of (**10**), (**15**) (104 mg, 0.45 mmol) was converted by heating at 180 °C for 1 h into the *dihydronaphthalene* (**17**) (101 mg, 96%) as prisms after recrystallization from hexane, m.p. 56–57 °C (Found: C, 72.1; H, 6.9. $C_{14}H_{16}O_3$ requires C, 72.4; H, 6.95%); ν_{max}($CHCl_3$) 1 735 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 1.98 (3 H, d, *J* 0.9 Hz, $=CCH_3$), 2.85–3.32 (3 H, m, $ArCH_2CH$), 3.65 (3 H, s, OMe), 3.69 (3 H, s, OMe), 6.30 (1 H, br s, ArC*H*=), 6.58 (1 H, br s, ArH), 6.63 (1 H, dd, *J* 7.8 and 2.4 Hz, ArH), and 7.03 (1 H, d, *J* 7.8 Hz, ArH); *m/z* 232 (M^+) and 173 (100%).

Dehydrogenation of (**12b**).—A solution of (**12b**) (51.3 mg, 0.26 mmol) and DDQ (64 mg, 0.28 mmol) in dry benzene (3 ml) was heated under reflux for 4.7 h. The reaction mixture was diluted with benzene and was washed successively with 10% aqueous sodium hydroxide and saturated brine. The residue upon work-up was chromatographed using hexane–ether acetate (19:1, v/v) as eluant to give (**12h**) (27 mg, 53%) as needles after recrystallization from diethyl ethyl–hexane, m.p. 85–86 °C, identical with the authentic sample prepared above.

2-(6-Methoxy-2-naphthyl)propan-1-ol (**18**).—Borane–methyl sulphide complex (10M; 1.02 ml, 10.2 mmol) was added dropwise to a stirred solution of (**12h**) (0.84 g, 4.22 mmol) in dry THF (25 ml) at 0 °C. After being stirred for 1 h at 0 °C, 10% aqueous sodium hydroxide (2.5 ml) and 30% hydrogen peroxide (0.5 ml) were added and the resulting mixture was stirred for 6 h at room temperature. The reaction mixture was quenched with saturated aqueous ammonium chloride and the solvent was evaporated *in vacuo* to give a residue which was extracted with ethyl acetate. The extracts were washed with saturated brine and the residue upon work-up was recrystallized from diethyl ether–hexane to give the *alcohol* (**18**) (0.73 g, 80%) as prisms, m.p. 95–96 °C (Found: C, 77.45; H, 7.45. $C_{14}H_{16}O_2$ requires C, 77.75; H, 7.45%); ν_{max}($CHCl_3$) 3 560 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 1.35 (3 H, d, *J* 6.8 Hz, $CHCH_3$), 1.53 (1 H, br s, OH, exchange with D_2O), 3.03–3.13 (1 H, m, CH_2CHCH_3), 3.76 (2 H, d, *J* 6.8 Hz, $CHCH_2OH$), 3.91 (3 H, s, OMe), 7.05–7.21 (2 H, m, ArH), 7.33 (1 H, dd, *J* 8.6 and 1.8 Hz, ArH), and 7.56–7.79 (3 H, m, ArH); *m/z* 216 (M^+).

2-(6-Methoxy-2-naphthyl)propanal (**19**).—Oxalyl chloride (0.88 g, 6.9 mmol) was added to a stirred solution of dimethyl sulphoxide (1.1 g, 14.1 mmol) in dry methylene dichloride (12 ml) at −78 °C and the stirring was continued for 30 min. A solution of the alcohol (**18**) (0.74 g, 3.43 mmol) in dry methylene dichloride (10 ml) was then added dropwise to the solution at −78 °C. The mixture was stirred at the same temperature for 30 min, after which triethylamine (1.74 g, 17.3 mmol) was added dropwise; stirring was continued at −78 °C for 30 min. The reaction mixture was diluted with water and extracted with methylene dichloride. The extracts were washed with saturated brine and the residue upon work-up was chromatographed using benzene as eluant to afford the aldehyde (**19**)[18] (0.69 g, 94%) as an oil.

2-(6-*Methoxy*-2-*naphthyl*)*propane*-1,2-*diol* (**21**).—A solution of the dioxolane (**12f**) (58.2 mg, 0.21 mmol) and 5% hydrochloric acid (0.9 ml) in THF (5 ml) was stirred at room temperature for 19 h. After removal of the solvent, the residue was extracted with ethyl acetate, and the extracts were washed successively with saturated aqueous sodium hydrogen carbonate and saturated brine. The residue upon work-up was chromatographed using hexane–ethyl acetate (1:1, v/v) as eluant to give the *diol* (**21**) (37.2 mg, 75%) as prisms after recrystallization from diethyl ether–hexane, m.p. 114–115 °C (Found: C, 72.3; H, 6.9. $C_{14}H_{16}O_3$ requires C, 72.4; H, 6.95%); $\nu_{max}(CHCl_3)$ 3 600 cm^{-1}; δ_H(90 MHz, $CDCl_3$) 1.59 (3 H, s, Me), 1.80–2.60 (2 H, br s, OH × 2, exchange with D_2O), 3.66 (1 H, d, *J* 11.3 Hz, C*H*HOH), 3.88 (1 H, d, *J* 11.3 Hz, CH*H*OH), 3.91 (3 H, s, OMe), 7.05–7.22 (2 H, m, ArH), 7.47 (1 H, dd, *J* 8.6 and 1.9 Hz, ArH), and 7.60–7.90 (3 H, m, ArH); *m/z* 232 (M^+).

Ionic Hydrogenation of (**21**).—Trifluoroacetic acid (118 mg, 1.04 mmol) was added dropwise to a stirred solution of the diol (**21**) (24.4 mg, 0.11 mmol) and triethylsilane (14.6 mg, 0.13 mmol) in dry methylene dichloride (1.2 ml) at room temperature.[21] After being stirred for 30 min, a solution of sodium carbonate (22.0 mg, 0.21 mmol) in water (0.5 ml) was added to the mixture and the solvent was evaporated *in vacuo* to give a residue which was taken up into methanol (1 ml). Potassium carbonate (72 mg, 0.52 mmol) was added to the methanol solution and the mixture was stirred for 40 min at room temperature. After removal of the solvent, the residue was extracted with chloroform and the extracts were washed with saturated brine. The residue upon work-up was chromatographed using hexane–ethyl acetate (4:1, v/v) as eluant to afford the alcohol (**18**) (20.7 mg, 91%) as prisms after recrystallization from diethyl ether–hexane, m.p. 95–96 °C. The alcohol thus obtained was identical with an authentic sample in all respects.

(±)-*Naproxen* (**5**).—A solution of potassium permanganate (110 mg, 0.70 mmol) in dry acetone (5 ml) was slowly added dropwise to a stirred solution of the aldehyde (**19**) (103 mg, 0.48 mmol) and magnesium sulphate (116 mg, 0.97 mmol) in dry acetone (25 ml) for 65 min. After being stirred for 2 h, the solvent was evaporated *in vacuo*, water was added, and the resulting aqueous phase was filtered. The filtrate was washed with chloroform, the aqueous layer was acidified with 10% hydrochloric acid at 0 °C, and the resulting mixture was extracted with chloroform. The extracts were washed with saturated brine and the residue upon work-up was recrystallized from acetone–hexane to give (±)-naproxen (**5**) (56 mg, 50%) as prisms, m.p. 160–161 °C (lit.,[22] m.p. 152–153 °C). The initial chloroform extracts were washed with saturated brine and the residue upon work-up was chromatographed using hexane–ethyl acetate (4:1, v/v) to afford the ketone (**20**) (34 mg, 35%) as prisms, m.p. 104–105 °C (lit.,[23] m.p. 106.5–108 °C).

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