oxide with the peak due to the *E* isomer. The results (Table I) represent mean values of at least two experimental runs and at least two GC determinations with standard deviation: 2–3. The remainder of the solution was concentrated and subjected to column chromatography[4] using benzene or chloroform to elute the column. The major fraction containing both isomers was concentrated and the (*E*)-stilbene was isolated by fractional crystallization.[4] The *Z* isomer was subsequently isolated from the mother liquor by preparative GC. In the majority of cases separation by fractional crystallization failed; thus the two isomers were separated by preparative GC as white solids or viscous colorless liquids. Reagents and quantities used are listed in Table II (see paragraph at the end of the paper about supplementary material). All the *E* isomers thus isolated were cleaved to the corresponding stilbenols, which had similar melting points and IR characteristics with those previously obtained.[4] Exceptions to the above are noted.

Acknowledgment. We are indebted to G. Barbaratsas (Chemistry Department, University of Thessaloniki) for carrying out the elemental microanalyses.

Registry No. **1**, 115032-58-1; **2**, 110983-36-3; **3a**, 100-52-7; **3b**, 104-87-0; **3c**, 939-97-9; **3d**, 3218-36-8; **3e**, 105-07-7; **3f**, 1571-08-0; **3g**, 100-10-7; **3h**, 555-16-8; **3i**, 123-11-5; **3j**, 6515-21-5; **3k**, 878-00-2; **3l**, 459-57-4; **3m**, 104-88-1; **3n**, 1122-91-4; **3o**, 15164-44-0; **4a**, 16721-45-2; **4b**, 39110-21-9; **4c**, 115032-59-2; **4d**, 115032-60-5; **4e**, 59625-61-5; **4f**, 115032-61-6; **4g**, 115032-62-7; **4h**, 6933-17-1; **4i**, 21960-26-9; **4j**, 115032-63-8; **4l**, 59625-60-4; **4m**, 38897-99-3; **4n**, 59625-59-1; **5a**, 1449-46-3; **5b**, 2378-86-1; **5c**, 65413-33-4; **5d**, 36908-37-9; **5e**, 26104-68-7; **5f**, 1253-46-9; **5g**, 115032-56-9; **5h**, 2767-70-6; **5i**, 3462-97-3; **5j**, 115032-57-0; **5l**, 51044-11-2; **5m**, 1530-39-8; **5n**, 51044-13-4; **5o**, 61130-13-0; **6**, 5533-04-0; **7a**, 115032-31-0; **7b**, 115032-33-2; **7c**, 115032-35-4; **7d**, 115032-37-6; **7e**, 115032-39-8; **7f**, 115032-41-2; **7g**, 115032-42-3; **7h**, 115032-43-4; **7i**, 115032-45-6; **7j**, 115032-47-8; **7k**, 115032-48-9; **7l**, 115032-49-0; **7m**, 115032-51-4; **7n**, 115032-53-6; **7o**, 115032-55-8; **8a**, 115032-32-1; **8b**, 115032-34-3; **8c**, 115032-36-5; **8d**, 115032-38-7; **8e**, 115032-40-1; **8f**, 110983-46-5; **8g**, 110983-47-6; **8h**, 115032-44-5; **8i**, 115032-46-7; **8j**, 110983-48-7; **8k**, 110983-49-8; **8l**, 115032-50-3; **8m**, 115032-52-5; **8n**, 115032-54-7; **8o**, 110983-50-1; **9**, 115032-65-0; **10**, 115032-66-1; *p*-carbomethoxybenzyl bromide, 2417-72-3; *p*-(dimethylamino)-benzyl alcohol, 1703-46-4; *p*-(methoxymethoxy)benzyl bromide, 115032-64-9; *p*-iodobenzyl bromide, 16004-15-2.

Supplementary Material Available: General experimental, melting point, IR, NMR, and microanalytical data for phosphonium salts **5f,g,j,o**; table of reagents and conditions for the Wittig reactions (Table II); UV (Table III), melting point, IR, NMR, and microanalytical data for stilbenes **7a–o**, **8a–o**, **9**, and **10** (10 pages). Ordering information is given on any current masthead page.

Notes

Convenient Route to 1,3-Disubstituted Cyclobutanes: An Inexpensive Synthesis of 3-Oxocyclobutanecarboxylic Acid

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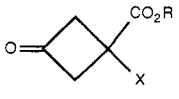
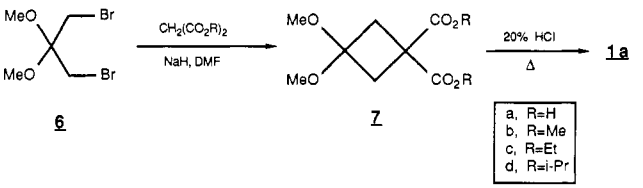
The formation of carbocycles is a common requirement in organic synthesis, and cyclobutanes are undoubtedly the most difficult of the small to medium sized rings to prepare. Although there are good procedures available for the preparation of cyclobutane,[1,2] methylenecyclobutane,[2] and 1,1-disubstituted cyclobutanes,[3,4] routes to 1,3-disubstituted derivatives with functionality amenable to further elaboration are not as plentiful. The title compound **1a** is a very useful precursor in the preparation of the substituted bicyclo[1.1.1]pentane skeleton[5] and is currently under investigation in these laboratories as an intermediate to higher bicyclo[*n*.1.1]alkanes. Other 1,3-disubstituted cyclobutanes have been found useful in the syntheses of thromboxane analogues.[6–9]



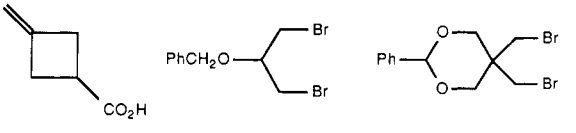
1, X=H
2, X=CO_2R

a, R=H
b, R=Me
c, R=Et
d, R=i-Pr

Scheme I



Previously **1a** has been prepared by the cycloaddition of allene and acrylonitrile[10,11] followed by hydrolysis to the carboxylic acid **3**[12] and subsequent oxidation of the alkene.[13] This is a useful route to **1** and is suited to large-scale preparations; however, it is not without limitation. The cycloaddition requires specialized equipment, and caution must be exercised with the potentially hazardous operation.[12,14] Furthermore, allene is expensive and not a commercially available feedstock in all localities.



3 **4** **5**

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Table I. Product Distribution for the Reaction of 6 with Dialkyl Malonates

R	temp, °C	time, h	% yield[a] 6[b]	$RCH(CO_2R)_2$[b]	10[b]	7[c]
Et	130	40	43	29	13	30 (53)[d]
i-Pr	140	48	40 (27)[c]	nd[e]	<2	56 (77)[d]

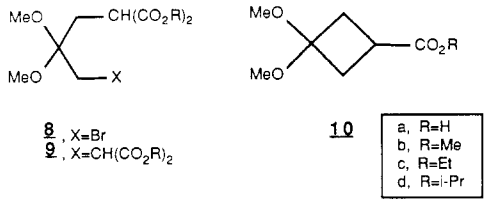
[a] Yields with respect to **6**. [b] ^1H NMR and GC analysis of distilled fraction, bp 82–88 °C (5 mm) (R = Et), 68–85 °C (3 mm) (R = *i*-Pr). [c] Isolated yield. [d] Yield based on recovered **6**. [e] nd = not detected.

In the earlier method of Avram et al.,[15] the key ring-forming condensation between diethyl malonate and **4** proceeds in only 36% yield and is a considerably longer sequence to **1a**. Similar attempts by Applequist and Roberts[16] to prepare cyclobutanes by malonate substitution on neopentyl halides were unsuccessful. However, under comparable conditions, **5** was successfully condensed with malonate to deliver the expected cyclobutane derivative in good yield (70%)[17] and, after several further steps, cyclobutane-1,3-dicarboxylic acid.

The success of the above method in achieving malonate substitution at the neopentyl centers encouraged us to investigate a similar reaction on 1,3-dibromo-2,2-dimethoxypropane (**6**) (Scheme I). This route would result in a cyclobutane (**1**) with dissimilar 1,3-substituents, each of which is independently available for further elaboration. Another advantage of the proposed method is the relatively inexpensive nature of all the reagents, including **6**, which is readily available from the bromination of acetone in methanol.[18]

Initial experiments employing the solvents isoamyl alcohol, 1,4-dioxane, diglyme, *tert*-butyl alcohol and mixtures of 1,4-dioxane/HMPA were unsuccessful. However, *N,N*-dimethylformamide (DMF) proved to be very effective, allows the volume of the reaction mixture to be kept to a minimum, and to date has been the solvent of choice.

Preliminary work was carried out by using diethyl malonate, which gave useful yields of the diester **7c**, although the conversion was not as effective as hoped. The initial displacement of halogen appears to be the rate-determining step as neither **8c** nor **9c** was observed in the reaction mixture, even though 2 molar equiv of malonate is used. Due to the sluggish nature of the substitution, elevated reaction temperatures are necessary, and the range 120–130 °C was found to be the most useful. Temperatures greater than this promoted excessive decarboethoxylation of the diesters, primarily of diethyl malonate, but also of **7c**. Evidence for this comes directly from isolation of the monoester **10c**, as well as diethyl ethylmalonate and ethyl acetate from the product mixture. The identity of **10c** was confirmed by deketalization in aqueous acetone, which furnished the known keto ester **1c**. Although decarboethoxylation to **10c** is ultimately required, its occurrence at this stage is undesirable as isolation of the diester **7c** from the reaction mixture is much more convenient.



Not unexpectedly, dimethyl malonate was not useful in this reaction as decarbomethoxylation was overwhelming. However, the bulkier diisopropyl malonate proved to be advantageous as the appearance of **10d** was essentially eliminated and reaction temperatures of 145 °C could be tolerated.

The subsequent conversion of **7d** to **1a** by concomitant ester hydrolysis, deketalization, and decarboxylation (Scheme I) proceeds smoothly in high yield (97%). Overall the method is quite efficient, 54% over four steps in two pots (74% with respect to recovered **6**), inexpensive, and easily scaled up to accommodate the reaction of 1 kg of **6**.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer 237 grating spectrometer. ^1H and ^{13}C NMR spectra were obtained on Varian EM-360A and JEOL FX90Q instruments respectively. Mass spectra were determined on an HP 5980A spectrometer. Analytical GC was performed on a Perkin-Elmer 8410 chromatograph using a 3 m × 3 mm stainless steel column packed with 5% SE-30 on Chromosorb W. Elemental analysis was carried out by The Australian Microanalysis Service, Melbourne.

Diisopropyl malonate was prepared by standard azeotropic esterification of malonic acid in benzene/isopropyl alcohol. 1,3-Dibromo-2,2-dimethoxypropane (**6**) was prepared as reported,[18] and DMF was dried over 4A molecular sieves before use.

Preparation of Dialkyl 3,3-Dimethoxycyclobutane-1,1-dicarboxylates (7c,d). In a typical experiment, the dialkyl malonate (2.0 mol) was added in a dropwise manner, under nitrogen, to a stirred suspension of sodium hydride (2.2 mol) in dry DMF (750 mL) at a rate such that the temperature was maintained below 70 °C. On cessation of hydrogen evolution, the dibromide **6** (267 g, 1.0 mol) was added in one portion and the mixture heated (see Table I) for 24–48 h. The conversion becomes very slow after the first 30 h, and reaction times in excess of 2 days are not warranted.

The cooled mixture was poured into an aqueous solution of ammonium chloride (100 g in 1.6 L), to prevent emulsion formation, and extracted with hexane. The combined extracts were then washed with water and sodium hydrogen carbonate solution and dried over magnesium sulfate, and the solvent was evaporated. Distillation of the residue through a short Vigreux column afforded a mixture of products in the more volatile fraction as shown in Table I. An air condenser was used to prevent clogging by **6** (mp[19] 62.5 °C), which could be recovered by filtration of the cooled distillate followed by recyrstallization from methanol. Continued distillation then gave the required diester **7c** or **7d** as a colorless oil.

Physical Data. 7c: bp 92 °C (0.05 mm); IR (CCl_4) 1735 cm^{-1}; ^1H NMR (CCl_4) δ 4.19 (4 H, q, J = 7 Hz), 3.13 (6 H, s), 2.62 (4 H, s), 1.27 (6 H, t, J = 7 Hz); ^{13}C NMR (CCl_4) 169.68 (C=O), 98.28 (C_3, s), 60.79 (OCH_2, t), 48.00 (OCH_3, q), 44.48 (C_1, s), 39.44 ($C_{2,4}$, t), 13.93 (CH_2CH_3, q) ppm; mass spectrum, m/e 260 (M^+, 2), 229 (45), 215 (52), 187 (74), 183 (18), 169 (19), 167 (10), 155 (100).

7d: bp 92–94 °C (0.01 mm); IR (neat) 1722 cm^{-1}; ^1H NMR (CCl_4) δ 5.00 (2 H, sept, J = 6.5 Hz), 3.08 (6 H, s), 2.55 (4 H, s), 1.23 (12 H, d, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) 170.08 (C=O), 98.35 (C_3), 68.77 (OCH), 48.29 (OCH_3), 44.88 (C_1), 39.46 ($C_{2,4}$), 21.26 ($CHCH_3$) ppm; mass spectrum, m/e 288 (M^+, 1), 257 (44), 233 (25), 231 (49), 229 (85), 215 (19), 202 (19), 201 (100), 184 (19), 183 (68). Anal. Calcd for $C_{14}H_4O_6$: C, 58.3; H, 8.4. Found: C, 58.1; H, 8.3.

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10c. Preparative GLC of a portion of the more volatile distillate [bp 82–88 °C (5 mm)] gave a sample of **10c**: ^{1}H NMR (CCl_4) δ 4.10 (2 H, q, J = 7 Hz), 3.10 (6 H, s), 2.38 (3 H, br s), 2.27 (2 H, br s), 1.23 (3 H, t, J = 7 Hz).

3-Oxocyclobutanecarboxylic Acid (1a). Diisopropyl 3,3-dimethoxycyclobutane-1,1-dicarboxylate (**7d**) (287.5 g, 1.0 mol) was stirred with 20% hydrochloric acid (750 mL) at reflux for 60 h.

After cooling, the solution was continuously extracted with ether for 18 h. The ether was removed at reduced pressure, leaving a yellow oil, which crystallized on standing and proved to be the title acid (111 g, 97%), which was characterized by conversion to its ethyl ester, whose physical properties were in accord with literature data:[15] ^{1}H NMR (CCl_4) δ 4.17 (2 H, q, J = 7 Hz), 3.27 (5 H, m), 1.27 (3 H, t, J = 7 Hz); ^{13}C NMR (CCl_4) 201.48 (C_3), 173.21 (CO_2), 60.57 (OCH_2), 51.20 ($C_{2,4}$), 27.09 (C_1), 14.09 (CH_3).

Acknowledgment. We thank the Flinders University of South Australia for financial support, the National Research Fellowships Advisory Committee for a Queen Elizabeth II Award (to P.E.P.), and Dr. E. W. Della for valuable discussions.

Registry No. **1a**, 23761-23-1; **6**, 22094-18-4; **7c**, 115118-67-7; **7d**, 115118-68-8; **10c**, 115118-69-9; $CH_2(CO_2Et)_2$, 105-53-3; $CH_2(CO_2Pr\text{-}i)_2$, 13195-64-7; $EtCH(CO_2Et)_2$, 133-13-1.

A Highly Versatile Synthesis of 2,2-Dimethyl-3-(2,2-dichlorovinyl)cyclopropane-1-carboxylic Acid Esters

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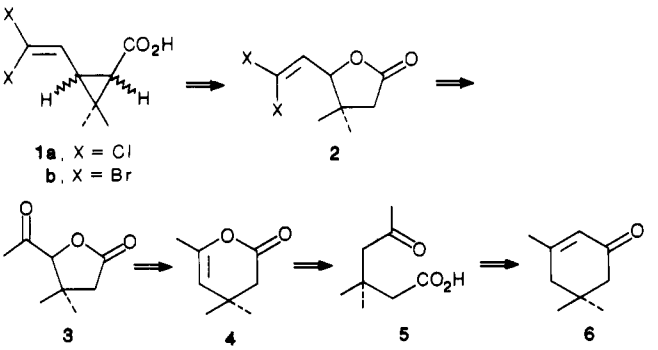
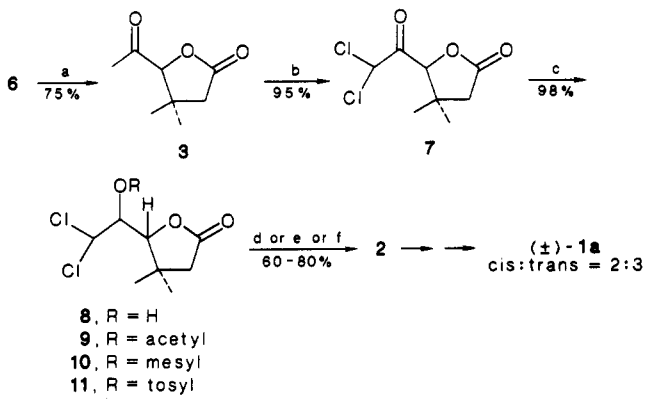
The esters of 2,2-dimethyl-3-(2,2-dihalovinyl)cyclopropane-1-carboxylic acids, which are structurally similar to naturally occurring chrysanthemates, have emerged as one of the most important classes of agricultural insecticides in recent years.[1] These compounds, known as pyrethroids, possess extraordinarily high insecticidal activity, low mammalian toxicity, biodegradability, and considerable increased photostability compared to the natural chrysanthemates.[2] Consequently, much research and development activity were put forward to develop elegant and cost-effective routes to the most potent precursor, 2,2-dimethyl-3-(2,2-dihalovinyl)cyclopropane-1-carboxylic acid (**1**).[3] As part of a general program to develop newer synthetic methodologies to **1** based on readily available and inexpensive raw materials, we reported recently two independent approaches for the syntheses of (1*R*)-*cis*-(+) acids **1a** and **1b** from (+)-3-carene.[4] Further to this work we report herein a short synthesis of *cis*/*trans*-(±)-**1a**, an important precursor for commercial permethrin and cypermethrin, from a readily available and inexpensive raw material, isophorone (**6**).[5]

Scheme I



Scheme II[a]



[a] Reagents: (a) 3.5 mol of $KMnO_4$, 30% aqueous AcOH; (b) SO_2Cl_2, *p*-TsOH·$2H_2O$ (cat.), 60 °C, 2 h or Cl_2, *N*-formylpyrrolidine hydrochloride (cat.), 25 °C, 3 h; (c) 0.3 mol of $NaBH_4$, MeOH, 25 °C, 1 h; (d) *p*-TsCl, 20% aqueous NaOH, 80 °C, 2 h; (e) $SOCl_2$, pyridine, 80 °C, 24 h; (f) DBU, 100 °C, 3 h.

In formulating our synthetic strategy to *cis*/*trans*-(±)-**1**, we viewed the retrosynthetic pathway (Scheme I) with particular attention. It occurred to us that isophorone (**6**) possesses a molecular geometry that is tailor-made for the synthesis of the key intermediate **2**[6] via the lactone **3**. The synthesis of **3** could be conceivable from the enol lactone **4** by the recently reported bromolactonization technique.[7] The enol lactone **4** in turn could be obtained from isophorone (**6**) via its oxidation product **5**.

The synthesis is outlined in Scheme II. With a view to obtain enol lactone precursor **5**, the oxidation of isophorone (**6**) was attempted with potassium permanganate. Thus, when the oxidation was carried out in aqueous acetic acid, to our surprise, lactone **3** was directly obtained as the major product in addition to keto acid **5**. The best yield of **3** was, however, obtained when the oxidation was carried out in 30% aqueous acetic acid. Purification by simple acid–base extraction followed by distillation furnished **3** and **5** in 75% and 10% yields, respectively. Thus, it was possible to achieve three different reaction sequences (Scheme I) in just one pot!

Conversion of **3** to the corresponding dichloro derivative **7** proceeded in near-quantitative yield, either with sulfuryl chloride or with chlorine in the presence of a catalyst.

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