(Z)-5-Acetoxy-5-methyl-2-phenylhex-2-en-4-one ((Z)-32d): IR (neat) 3058, 2983, 1739, 1700, 1617, 1371, 1099, 815, 764, 699 cm^{-1}; ^1H NMR (300 MHz) δ 1.48 (s, 6 H), 2.13 (s, 3 H), 2.21 (s, 3 H), 6.40 (s, 1 H), 7.27–7.36 (overlapping m, 5 H); ^{13}C NMR (75 MHz) δ 21.3, 23.6, 27.9, 83.8, 118.8, 126.8, 127.7, 128.0, 141.0, 156.5, 170.1, 197.0; HRMS calcd for $C_{15}H_{18}O_3$ 246.1256, found 246.1258.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work. We also thank the National Institutes of Health for a Biomedical Research Support grant.

Supplementary Material Available: ^1H NMR spectra of all new compounds (52 pages). Ordering information is given on any current masthead page.

Functional Group Hybrids. Reactivity of α'-Nucleofuge α,β-Unsaturated Ketones. 2. Reactions with Malonate Anion. Concerning the Mechanism of the Favorskii Rearrangement

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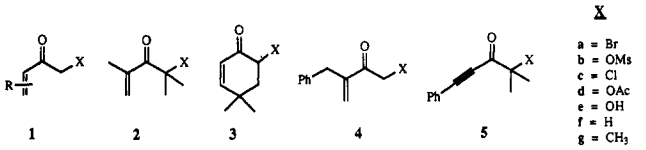
The scope and limiations of the reaction of α'-nucleofuge α,β-unsaturated ketones with sodium dimethyl malonate has been studied systematically. The substrates with good nucleofuges (halides, mesylate) give cyclopropanols upon reaction with malonate anion by way of a conjugate Favorskii reaction. In reactions with substrates containing the poorer nucleofuge (acetoxy) conjugate addition proceeded without entering the Favorskii manifold. Concerning the mechanism of the Favorskii reaction, it is suggested that the loss of the nucleofuge occurs to give a 2-oxyallyl cation, but that disrotatory ring closure is facile and the only products observed result from nucleophilic trapping of cyclopropanones to yield cyclopropanols in fair to good yield.

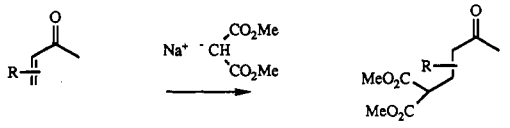
The 1,4-conjugate addition of active methylene compounds to the β-carbon of an α,β-unsaturated ketone is a widely utilized method for the formation of carbon–carbon bonds.[2] In a project designed to develop a sequential conjugate addition–cycloaddition process for carbocycle synthesis (Scheme I, previous paper), we examined the reaction of α'-nucleofuge α,β-unsaturated ketones with a variety of agents which were anticipated to undergo conjugate addition to 1 as the triggering reaction to such a sequential process. In the previous article, we described the synthesis of substrates of general structure 1 in the form of **2–5 (a–d)** and their reactions with Me_2CuLi and MeCu. Herein we present our results of the reactions of **2–5** with dimethyl malonate anion, which should proceed via a different mechanistic pathway than either Me_2CuLi or MeCu.



Results

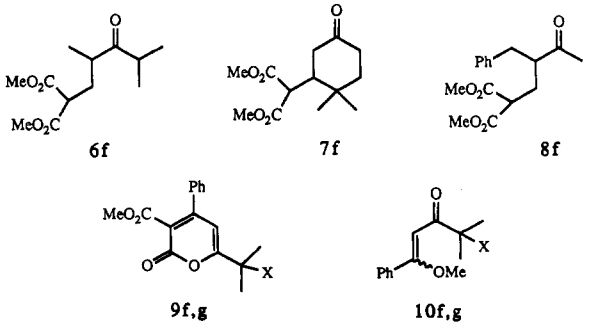
Given the many possible reaction pathways envisioned for the substrates under study, it was necessary to show that "simple" conjugate addition to the enone portion of these substrates was viable. As control experiments, each of the parent α,β-unsaturated ketones **2f–5f** was treated with sodium dimethyl malonate. The dimethyl ester of malonic acid was selected for study since this choice conveniently minimized the number of ^1H and ^{13}C NMR resonances and avoids unnecessary spectral complexity. Two sets of standard reaction conditions were employed for these conjugate additions. Method A involved the generation of the sodium anion of dimethyl malonate with NaH in THF followed by the addition of a solution of the unsaturated ketone in furan. After 2 h, the reaction was quenched and acidified with 1 M HCl. Method B utilized

Scheme I. Reactions of 2f–5f,g with Dimethyl Malonate Anion[a]



Substrate	Product	Method A	Method B
2f	6f	40	52
3f	7f	0	28
4f	8f	70	41
5f	9f	77[b]	24[b,c]
5g	10g	71[b]	19[b,d]

[a] Yields represent chromatographically isolated products; [b] Conjugate addition leads to formation of pyrones **9f** or **g**; [c] Also gives 11% **10f**; [d] Also gives 16% **10g**.



(1) Author to whom correspondence should be addressed concerning the X-ray analyses.

(2) (a) Bergman, E. D.; Ginsburg, D.; Pappo, R. *Org. React.* **1959**, *10*, 179. (b) Oare, D.; Heathcock, C. *Top. Stereochem.* **1991**, *20*, 87.

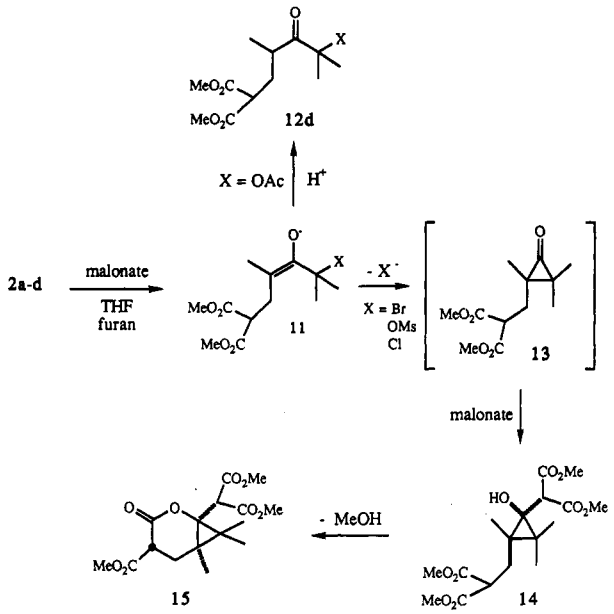
0022-3263/91/1956-6773$02.50/0

Table I. Reaction of 2a–d with Malonate Anion

substrate		14[a]	12	15
2a (Br)	method A	44[b]	0	0
b (OMs)		10[c]	0	25
c (Cl)		12[d]	0	25
d (OAc)		0[e]	55	0
2a (Br)	method B	12[f]	0	0
b (OMs)		0[g]	0	0
c (Cl)		11[4]f	0	0
d (OAc)		0	38[h]	0

[a] Obtained as a single diastereomer, yields are based on malonate. [b] 33% **2a** recovered. [c] 20% **2b** recovered. [d] 12% **2c** recovered. [e] 16% **2d** recovered. [f] No other detectable products. [g] 63% **2e** recovered due to sulfonate saponification. [h] **12e** was the isolated product.

Scheme II. Reaction Pathways of 2a–d



the classical Michael conditions of an alkoxide base in an alcohol. Thus, the sodium anion of dimethyl malonate was generated with sodium methoxide in methanol followed by the addition of a solution of the α,β-unsaturated ketone in furan, with workup as in method A. The results are summarized in Table I. Under the conditions of Method A, the acyclic enones **2f** and **4f** underwent conjugate addition to give **6f** and **8f** but cyclic enone **3f** returned only unchanged starting material. The ynones **5f** and **5g** did not react with sodium dimethyl malonate to give the expected conjugate adducts, but instead gave good yields of the 2-pyrones **9f** and **9g**, respectively.[3] In contrast to the results of method A, under the conditions of method B all of the parent substrates gave conjugate addition products. While the yield of conjugate adduct **6f** was improved slightly, the yield of **8f** from **4f** dropped off considerably. Under these conditions, even the cyclic enone **3f** afforded conjugate adduct **7f**. Reaction of the ynones under these conditions led again to 2-pyrone formation although yields decreased at least in part due to competitive methanol addition to give **10f** and **g**. So that the reactivity could be compared both within and between substrate series, the standard conditions were adhered to, even though methods A and B were not optimal for all substrates.

(3) The reaction of ynones with malonate anions is one of the more common methods for the synthesis of 2-pyrones. See: Shusherina, N. P.; Dmitrieva, N. D. Luk'yanets, E. A.; Levina, R. Y. *Russ. Chem. Rev.* **1967**, *36*, 175.

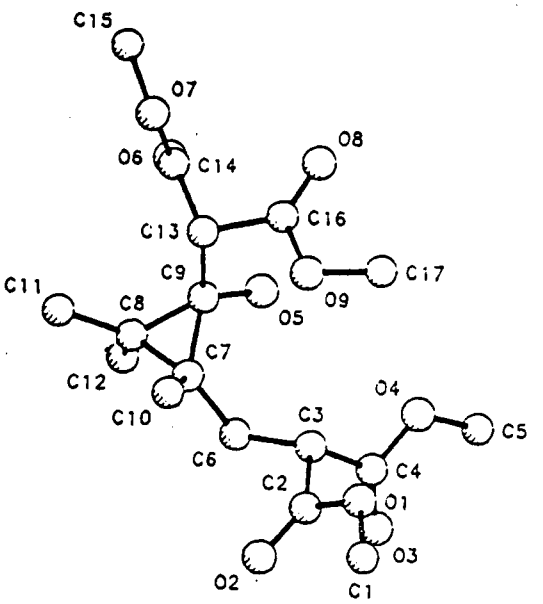


Figure 1. Pluto plot of X-ray coordinates of cyclopropanol **14**.

When **2a** was treated with the sodium dimethyl malonate (method A), the only product observed was the cyclopropanol **14**, which was isolated as a single diastereomer in 44% yield (Scheme II and Table I). Cyclopropanol **14** is most likely formed by conjugate addition of malonate anion followed by loss of the bromide to give the cyclopropanone **13** which then adds a second equivalent of malonate anion resulting in **14**. Replacement of bromide by mesylate or chloride also resulted in formation of cyclopropanol **14**, and in no case was an intermediate adduct (**12a–c**) isolated from the reactions of substrates **2a–c**. The gross structure of cyclopropanol **14** was assigned from the standard spectral data; the relative stereochemistry was determined by X-ray crystallographic analysis from which the trans relationship of the malonate groups was readily apparent (Figure 1).[4] In contrast to the results obtained with **2a–c**, the α-acetoxy enone **2d** reacted under the same conditions to give only the 1,4-conjugate addition product **12d**. Once the reactivity of the substrates in the **2** series had been uncovered, some further studies were carried out to optimize the yields of cyclopropanol **14**. By varying the number of equivalents of base and ratio of dimethyl malonate to substrate, it was found that the reaction of 1.5 equiv of the sodium anion of dimethyl malonate and 1.5 equiv of dimethyl malonate with either **2a** or **c** leads to **14** in yields of 60 or 57%, respectively.

When substrates **2b** and **c** were treated under the conditions of Method A, similar results were obtained (Table I). Upon acidic, methanolic workup, lactonization was apparently facile and the δ-lactone **15** was produced in addition to cyclopropanol **14**. Under the conditions of method B, the sulfonate ester **2b** was hydrolyzed to the α-hydroxy enone **2e**. With the acetate **2d**, conjugate addition was also accompanied by acetate hydrolysis to give hydroxy ketone **2e**.

When hybrids **4a–d**, possessing nucleofuges at primary sites, were treated with the sodium dimethyl malonate, processes involving 1,2-addition and direct displacement (at least formally) of the nucleofuge were prevalent as might be expected due to the reduced steric hindrance around the carbonyl and α carbons. In this series of substrates, differences in reactivity as a result of nucleofuge

(4) Full crystallographic parameters on both cyclopropanols mentioned in this article can be found in the supplementary material.

Scheme III. Reaction Pathways of 4a–d with Malonate Anion

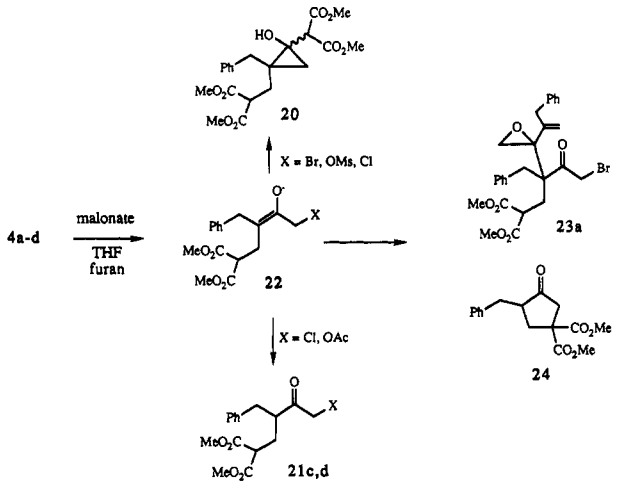
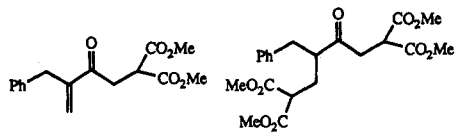


Table II. Reactions of 4a–d with Malonate

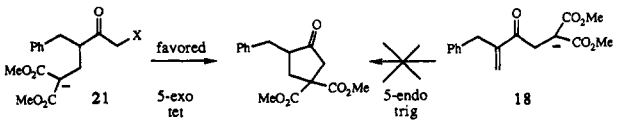
		20[a]	21
4a (Br)	method A	20[b]	0
b (OMs)		56[c]	0
c (Cl)		8[d]	14
d (OAc)		0	30[e]

[a] Isolated as a 2:1 mixture of diastereomers. [b] Also **24** (22%), **23a** (12%), **18** (5%), and **19** (3%). [c] 6% **4b** recovered. [d] 47% **4c** recovered. [e] 42% **4d** recovered.



18 19

variation were more pronounced (Scheme III and Table II). When treated under the conditions of method A, bromide **4a** gave many products arising from several different reaction modes. The major products were the diastereomeric cyclopropanols **20**, cyclopentanone **24**, and the epoxide **23a**, along with smaller amounts of the simple displacement product **18** and the displacement and conjugate addition adduct **19**. Most of these products can be explained (Scheme III) by an initial conjugate addition leading to the enolate **22**, which has several fates. One of these is loss of bromide leading to a cyclopropanone which is then trapped by malonate anion to give the cyclopropanols **20**. Conjugate addition–induced aldol condensation followed by collapse of the bromohydrin gives epoxide **23a**. Based on Baldwin's empirical rules,[5] ring closure of the simple displacement product (**18** → **17**) should be a disfavored 5-*endo-trig* process, but ring closure occurring as a 5-*exo-tet* intramolecular displacement (**21** → **17**) or by trapping of an oxyallyl cation (5-*exo-trig*) should be favored. While the simple protonated form of **18** was obtained, the protonated form of anion **21** was not observed.



21 favored 5-exo tet 17 5-endo trig 18

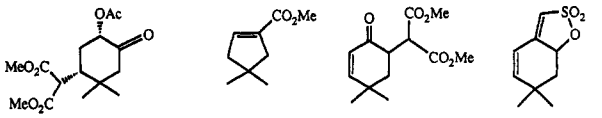
Fortunately, the other members of this series were a little more controlled in their reactivity. The mesylate **4b**

(5) Baldwin, J. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

Table III. Reaction of 3a–d with Malonate Anion

		32/33	27	26
3a (Br)[a]	method A	19	21	0
b (OMs)[b]		14	15	0
c (Cl)[f]		20	22	0
d (OAc)		0	0	48[d]
		36	**37**	**35**
3a (Br)[e]	method B	8	7	8
b (OMs)[f]		18	17	0
c (Cl)[g]		14	13	14
d (OAc)[h]		0	0	25[i]

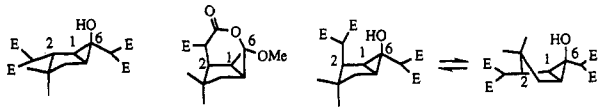
[a] Traces of **3j** and 32% **3a** recovered. [b] Also **44** (3%) and 26% **3b** recovered. [c] 33% **3c** recovered. [d] Obtained as an 11:1 mixture of **38** and **26d**, 33% **3d** recovered. [e] **27** (3%) and **43** (5%). [f] **27** (7%) and **44** (3%). [g] Also obtained **27** (4%). [h] Also obtained **3e** (35%). [i] Isolated as saponification product **26e**.



38 42 43 44 (16h in preceding article)

gave the diastereomeric cyclopropanols **20** as the only products, while the chloride gave a mixture of the cyclopropanols **20** and the simple 1,4-adduct **21c**. The only product formed from acetate **4d** was the 1,4-adduct **21d**. Under the conditions of method B, these substrates each gave rise to an intractable mixture.

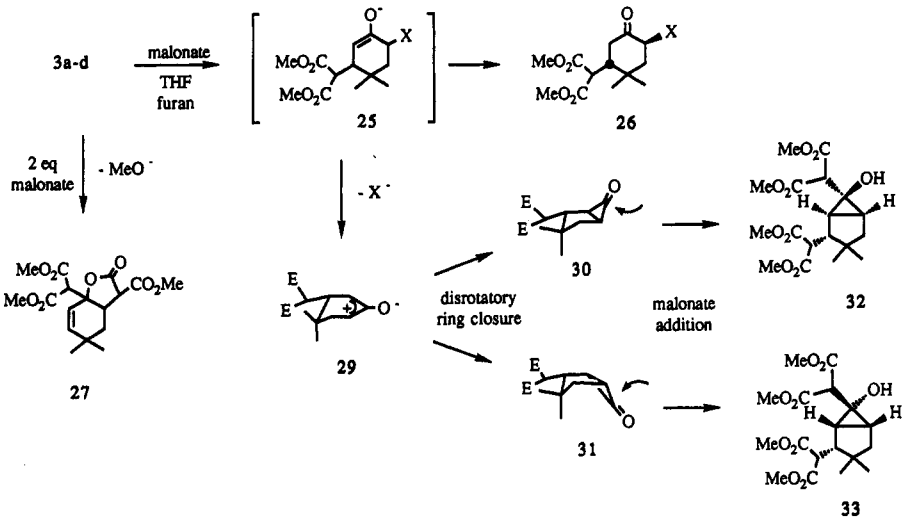
The cyclic series of substrates **3** with nucleofuges at secondary sites was expected to give less competing 1,2-addition and displacement chemistry than was observed with the series **4a–d**. By comparison to the substrate series **4a–d**, the effect of nucleofuge variation was somewhat attenuated in the **3a–d** series. The results are shown in Table III. Reaction of **3a–c** under the conditons of method A gave rise to a mixture of the diastereomeric cyclopropanols **32** and **33**, γ-lactone **27** (Scheme IV), and only traces of the Favorskii esters **36** and **37**. The cyclopropanols **32** and **33** are thought to arise by conjugate



32 (X-ray) 35 33-I 33-II

addition followed by ionization of the nucleofuge to give the oxyallyl cation **29**. Disrotatory ring closure of the oxyallyl cation can then occur to give the diastereomeric cyclopropanones **30** and **31** which are trapped with malonate on the convex face to give **32** and **33**. The structural assignment of these compounds was aided by X-ray crystallography (vide infra). The γ-lactone **27** results from malonate displacement of the nucleofuge, 1,2-addition of malonate, and lactonization with loss of methoxide. The formation of this product did not reflect any unique reactivity of the hybrid aside from that of the component α-nucleofuge functionality. The methoxide thus generated played a role in the formation of some of the reaction products. Some of the cyclopropanones **30**/**31** generated as outlined above reacted with methoxide ion and underwent subsequent fragmentation to give the ring contracted Favorskii esters **36** and **37** as mixtures of cis and trans isomers. The acetate of this series of substrates (**3d**) was also interesting. As expected, the acetate was not ionized after conjugate addition, but only a small amount of the simple 1,4-adduct **26d** was obtained. The major product isolated was instead the isomeric α-acetoxy ketone

Scheme IV. Reaction Pathways in the Reaction of 3a–d with Malonate Anion



Scheme V. Reaction Pathways of 5a–d with Malonate Anion

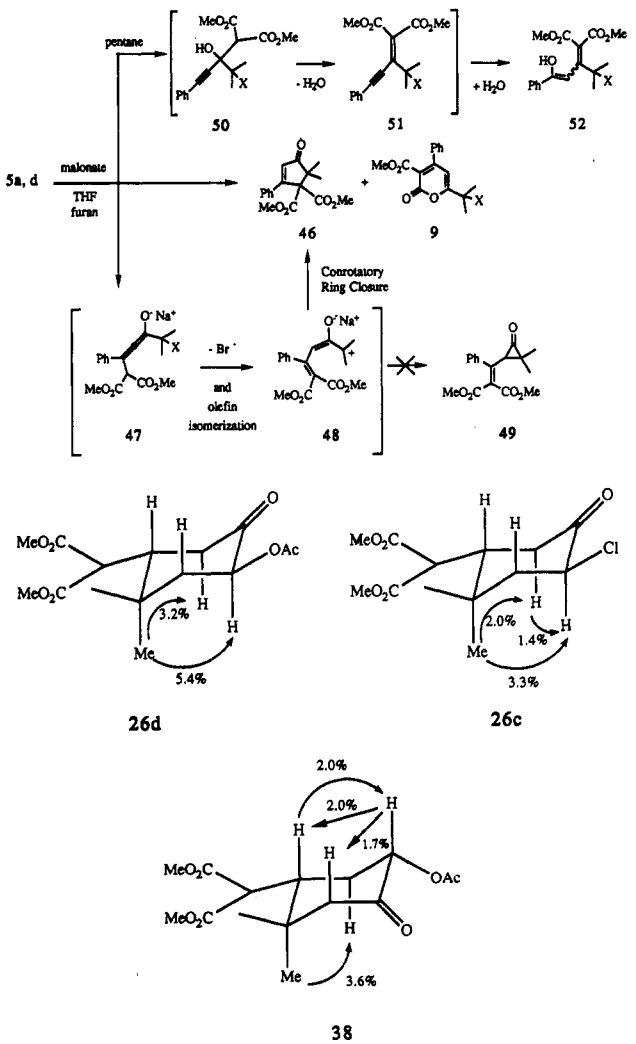
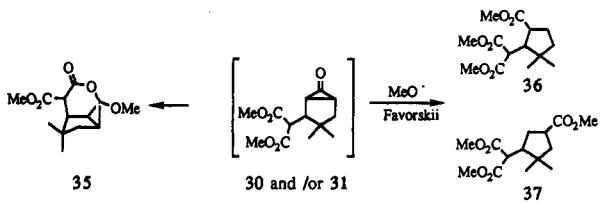


Figure 2. NOE data on **26d**, **26c** and **38**.

38, where the carbonyl and acetate have been transposed. The different connectivity pattern of these isomers was readily established by decoupling experiments and their existence as chair-like conformers was supported by the NOE data shown in Figure 2. This transposition presumably takes place by acyl transfer through an enediolate-like intermediate by analogy to the well known α-ketol rearrangement.

By varying the number of equivalents of base and dimethyl malonate to substrate, it was found that the reaction of 1.5 equiv of the sodium anion of dimethyl malonate and 1.5 equiv of dimethyl malonate with **3a** led to the diastereomeric cyclopropanols **32**/**33** in 64% yield with <5% of the γ-lactone **27** as the only other product observed. The chloroenone **3c** under the same conditions, also gave improved yields **32**/**33** (34%) along with the formation of conjugate adduct **26c** in 19% yield.

When **3a–c** were treated under the conditions of method B, the major products were tricyclic acetal **35**, the cis and trans Favorskii esters **36** and **37**, and lactone **27**. The bromoenone **3a** also gave a 5% yield of the known ring contracted unsaturated ester **42**, presumably arising via a pathway similar to that previously described by Takeda.[6]



The gross structure of the cyclopropanols was established by evaluation of the standard spectroscopic data, with the connectivity relationships coming from 1-D decoupling experiments. The relative configuration of one of the diastereomers (**32**) was determined by X-ray crystallographic analysis. The PLUTO plot (Figure 3), clearly shows that the six-membered ring of the bicyclo[3.1.0]-hexane adopts a chairlike conformation with both of the malonate moieties occupying more or less equatorial positions with respect to the six-membered ring. Diastereomer **33** is thought to be epimeric at C-2 and exists either in a chair-like conformation with the C-2 malonate in a pseudoaxial position or in a twist-boat conformation with the C2 malonate oriented pseudoequatorially, with the C6 malonate moiety in either case occupying a pseudoequatorial position. The rationale for this assignment is 2-fold. First, the $J_{1,2}$ coupling constants of the two diastereomers are 4 Hz for **32** and 7 Hz for **33**. This suggests that the dihedral angles for **32** and **33** are fairly different. Indeed,

(6) Tsuboi, S.; Nagae, H.; Yamoto, H.; Takeda, A. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 836.

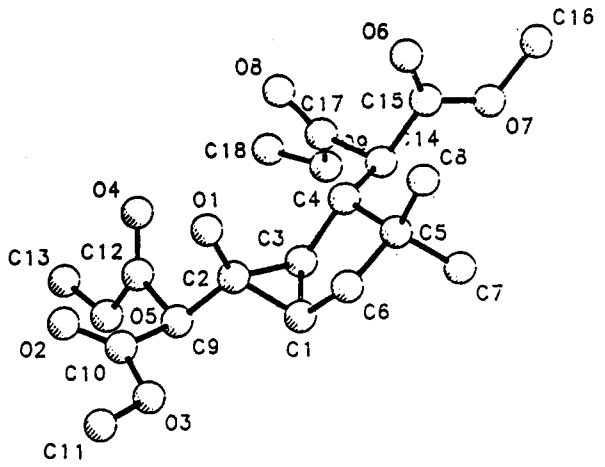


Figure 3. Pluto plot of X-ray coordinates of cyclopropanol **32**.

Table IV. Reaction Products of 5a–d with Malonate Anion

		46	9	52
5a (Br)[a]	method A	30	7	0
d (OAc)	pentane as solvent	0	5	36
a (Br)[b]		9	10	26

[a] 5% recovered **5a**. [b] 6% recovered **5a**.

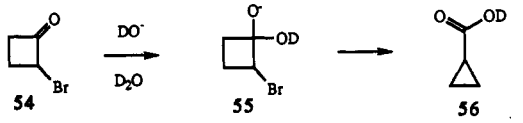
on examination of Drieding models, it can be seen that the dihedral angle H1–C1–C2–H2 for **32** is ≅110° while the corresponding angle in the **33** is ≅15° or 40° depending on whether the relatively flat 5-membered ring of the bicyclo[3.1.0]hexane is deformed towards a chair- (**33-I**) or boatlike (**33-II**) conformation.

This assignment is further supported by the 8-Hz coupling constant found in **35**, which, by virtue of its tricyclic skeleton, must be epimeric to **32** at C-2 and possesses the same dihedral relationship for H1–H2 ($J \cong 15$ Hz) as that proposed for the chairlike conformer of **32**. Second, examination of Drieding models indicates that for a configuration in which the C-6 malonate is pseudoaxial and on the concave side of the bicyclo[3.1.0]hexane ring system considerable steric interaction in either a chair- or a boatlike conformation would be present. This seems mechanistically reasonable since conjugate addition may occur followed by ionization of X^- from the resulting enolate to give a planar 2-oxyallyl cation (**29**, Scheme IV). This can then undergo disrotatory ring closure to give diastereomeric cyclopropanones which are trapped with malonate in an equatorial manner to give the diastereomeric cyclopropanols **32** and **33**.

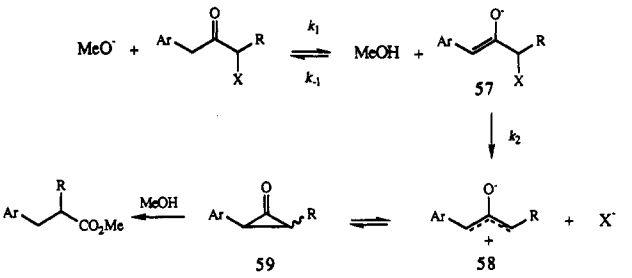
The reaction of bromo ynone **5a** with malonate anion under the conditions of method A gave the cyclopentenone **46** and bromopyrone **9a** (Scheme V and Table IV). We speculate that conjugate addition of the malonate anion gives an enolate **47** which can subsequently lose bromide ion to give a pentadienyl cation **48**, which undergoes conrotatory ring closure to cyclopentenone **46**. Prior to the loss of bromide, **47** can close to bromopyrone **9a** as a competitive process. Inadvertently, a reaction of the bromoynone was run utilizing pentane as a solvent. This change in solvent led to a change in product formation with the major product being the conjugated enol **52**. Under these conditions, the acetoxy ynone **5d** also led to formation of pyrone **9d**, but the major product was **52**. 1,2-Addition of malonate anion followed by dehydration could give an enyne **51** which can then rehydrate to give the fully conjugated enol **52**.

In summary, it has been shown that the reaction of α-nucleofuge α',β'-unsaturated ketones with anions of malonic esters generally leads to the formation of cyclopropanols with the better nucleofuges (Br, OMs, and Cl), while the simple conjugate adduct is obtained with the acetates and sometimes the chlorides. The formation of the cyclopropanols in these reactions represents an interruption of a "conjugate" Favorskii reaction.

Scheme VI. Semibenzylic Mechanism



Scheme VII. Dewar Mechanism for the Favorskii Rearrangement



Discussion

It is appropriate to address the relationship of this work to the "normal" Favorskii rearrangement. Originally described in 1894,[7] the Favorskii rearrangement[8] has been the subject of many studies, and yet, controversy over the mechanism of this reaction persists. While at least five mechanisms have been proposed, two have been supported by most of the evidence and remain as the accepted mechanisms. In cases where α' hydrogens are available, the Loftfield cyclopropanone mechanism is generally preferred.[9] The second accepted mechanism is usually operative in cases where the Loftfield mechanism is prohibited either due to an absence of α' hydrogens or structural features that prevent cyclopropanone formation (Scheme VI).[10] The controversy about the mechanism of the Favorskii reaction is not centered upon the differences between these two mechanisms but on the details of how the symmetrical intermediate is reached in the cyclopropanone mechanism. Shortly after the Loftfield mechanism appeared, Dewar[11] proposed the detailed mechanism shown in Scheme VII, including the intermediacy of a dipolar ion. Considerable support for this has been provided, primarily by Bordwell.[12] The first step has (→**57**) been shown to be reversible for R = H by deuterium exchange studies and there is a moderate nucleofuge effect ($k_{Br/Cl} \cong 10^2$). Positive charge character at the transition state was demonstrated by a large negative ρ value of −2.37, and rate acceleration was observed with increasing ionic strength of the medium. While this model has been fairly well supported and accepted, there is evidence which suggests that not all Favorskii rearrangements proceed through a delocalized intermediate.[13]

(7) Favorskii, A. E. *J. Russ. Phys. Chem. Soc.* **1894**, *26*, 559.
(8) For the most recent reviews and leading references to the older literature see: (a) Kende, A. S. *Org. React.* **1960**, *11*, 261. (b) Akhrem, A. A.; Ustynyuk, T. K.; Titov, Y. A. *Russ. Chem. Rev.* **1970**, *39*, 732. (c) Chenier, P. J. *J. Chem. Educ.* **1978**, *55*, 286.
(9) (a) Loftfield, R. B. *J. Am. Chem. Soc.* **1950**, *72*, 632. (b) Loftfield, R. B. *Ibid.* **1951**, *73*, 4707.
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In the conjugate Favorskii reactions of the hybrid substrates described herein, several trends have appeared. The reactions involving bromides (**2a**, **3a**, **4a**, or **5a**) or mesylates (**2b**, **3b**, or **4b**) did not produce products of conjugate addition without loss of the nucleofuge, regardless of the degree of substitution at the α' carbon. In reactions of the acetates (**2d**, **3d**, **4d**, or **5d**), conjugate addition was not accompanied by loss of the nucleofuge. Looking to the chlorides (**2c**, **3c**, or **4c**), intermediate reactivity was observed. When the chloride was at a tertiary center as in **2c**, conjugate addition and loss of chloride occurred, but with the secondary chloride **3c**, traces of the conjugate adduct were obtained and the yield increased under the optimized conditions. Finally, reaction of substrate **4c** with the chloride at a primary center yields more of the conjugate adduct than of the products resulting from loss of the nucleofuge **20**.

These results seem to fit Bordwell's mechanism quite well, where the first step involving reversible deprotonation has now been replaced with reversible conjugate addition. This generates enolate **60** which can proceed on to cyclopropanone **61** by either ionizing to a dipolar ion (S_N1-like) (k_2) or by internal S_N2 displacement (k_3). Once formed, the cyclopropanone rapidly accepts a nucleophile to give the observed cyclopropanol **62**. Assuming that halide loss is involved in the rate-determining step on the pathway to cyclopropanols and drawing upon analogy to standard nucleophilic substitution trends, as the steric hindrance surrounding an alkyl halide increases the relative ease of solvolysis versus displacement should also increase. In the conjugate addition reactions, the chloride was the only nucleofuge that both was lost and also not lost after conjugate addition. Qualitatively following the ratio of conjugate addition with loss of chloride to conjugate addition without loss of chloride, the ratio decreases going from tertiary to secondary to primary. In other words, the tertiary chloride is lost more readily than the secondary chloride which is lost more readily than the primary chloride, suggesting that halide loss more closely resembles ionization to the dipolar ion.

Conclusion

The scope and limitations of the reaction of α-nucleofuge α',β'-unsaturated ketones with nucleophiles as new methodology for the generation of 2-oxyallyl cations has been examined. The substrates with good nucleofuges give cyclopropanols upon reaction with sodium dimethyl malonate by way of a conjugate Favorskii reaction. In reactions with substrates containing the poorer nucleofuge (acetoxy), conjugate addition proceeded without entering the Favorskii manifold. The conjugate addition reactions involving the hybrid substrates have also shed some light on the release of the nucleofuge in Favorskii reactions, and it is suggested that loss occurs to give a 2-oxyallyl cation but that disrotatory ring closure is facile and the only products observed result from nucleophilic trapping of cyclopropanones to yield cyclopropanols in fair to good yield.

Experimental Section

General Methods. See the preceding paper in this issue.

General Procedures for the Reaction of α'-Nucleofuge α,β-Unsaturated Ketones with Sodium Dimethyl Malonate. Method A. To a stirred suspension of 50.4 mg (2.1 mmol) of NaH (from 50% dispersion) in 2 mL of THF at 0 °C was added 228 μL (264 mg, 2.0 mmol) of dimethyl malonate. After 15 min, 726 μL (680 mg, 10 mmol) of furan was added (furan addition was accompanied by the solution turning a faint rose color and a decrease in malonate salt solubility), followed 10 min later by 2.0 mmol of enone. After 2 h, the reaction was quenched by the addition of 2 mL of 7% HCl. The reaction mixture was extracted with ether, washed with dilute aqueous HCl and then with saturated NaCl solution, dried, and evaporated.

Method B. To 2.5 mL of methanol in an addition funnel was added 46 mg (2.0 mmol) of sodium. After hydrogen evolution stopped, 228 μL (264 mg, 2.0 mmol) of dimethyl malonate was added. After 10 min, this mixture was added dropwise over 1 h to a room-temperature solution of 2.0 mmol enone in 2.0 mL of furan at room temperature. The reaction was quenched and worked up after 2 h. The reaction was quenched with dilute aq HCl, extracted with ether, washed with dilute HCl and then with saturated NaCl solution, dried, and evaporated. Purification of the reaction products was accomplished by semipreparative HPLC on silica using hexane/EtOAc mixtures as eluants.

Methyl 2-(methoxycarbonyl)-4,6-dimethyl-5-oxoheptanoate (6f): IR (neat) 2971, 2879, 1755, 1737, 1711 cm^{-1}. ^1H NMR (300 MHz) δ 1.06 (overlapping d, 9 H), 1.87 (m, 1 H, J = 14, 9, 6 Hz), 2.27 (m, 1 H, J = 14, 8, 7 Hz), 2.27 (overlapping m, 2 H), 3.35 (dd, 1 H, J = 9, 7 Hz), 3.73 (s, 3 H), 3.73 (s, 3 H); ^{13}C NMR (75 MHz) δ 16.9, 17.8, 18.2, 31.0, 39.1, 41.4, 49.1, 52.3, 169.2, 169.5, 216.6; MS isobutane chemical ionization 245 (M^+ + 1); HRMS calcd for $C_{11}H_{17}O_4$ 213.1127, found 213.1130 (M^+ - OCH_3).

(1*S,2*R**)-2-[2,2-Bis(methoxycarbonyl)ethyl]-1,1-bis(methoxycarbonyl)-2,3,3-trimethylcyclopropanol (14)**: mp 123–124 °C; IR (melt) 3514, 3000, 2956, 1735 (broad), 1437, 1326, 1282, 1198, 1154 cm^{-1}; ^1H NMR (300 MHz) δ 0.97 (s, 3 H), 0.98 (s, 3 H), 1.10 (s, 3 H), 2.14 (dd, 1 H, J = 15, 6 Hz), 2.23 (dd, 1 H, J = 15, 6 Hz), 3.44 (s, 1 H), 3.51 (t, 1 H, J = 6 Hz) 3.61 (s, 1 H), 3.72 (s, 3 H), 3.73 (s, 3 H), 3.77 (s, 3 H), 3.79 (s, 3 H); ^{13}C NMR (75 MHz) δ 15.0, 16.0, 18.6, 26.1, 27.3, 29.7, 49.8, 52.8, 64.0, 169.5, 169.7, 170.5; MS isobutane chemical ionization 375 (M^+ + 1); HRMS calcd for $C_{16}H_{23}O_8$ 343.1393, found 343.1388 (M^+ - OCH_3).

Optimization Experiments. A series of reactions were carried out with **2a** and **2c** where the ratio of malonate anion to substrate was varied. It was found that the reaction of 1.5 equiv of sodium dimethyl malonate and 1.5 equiv of dimethyl malonate with 1 equiv of the substrate gave, from **2a** and **2c**, 60 and 57% yield of cyclopropanol **14**, respectively. Compound **15**: IR (melt) 2957, 1756, 1740, 1164, 916, 733 cm^{-1}; ^1H NMR (300 MHz) δ 1.13 (s, 3 H), 1.14 (s, 3 H), 1.20 (s, 3 H), 1.98 (dd, 1 H, J = 14, 5 Hz), 2.29 (t, 1 H, J = 14 Hz), 3.52 (s, 1 H), 3.79 (s, 6 H), 3.81 (s, 3 H), 3.85 (dd, partly obscured, J = 14, 5 Hz); ^{13}C NMR (75 MHz) δ 16.5, 17.2, 18.3, 22.9, 27.6, 29.8, 44.7, 51.1, 52.4, 52.8, 53.0, 70.6, 167.0, 168.2, 168.9, 169.6; HRMS calcd for $C_{16}H_{23}O_8$ 343.1393, found 343.1399 (M^+ + H).

Methyl 6-acetoxy-2-(methoxycarbonyl)-4,6-dimethyl-5-oxoheptanoate (6d): IR (neat) 2987, 2956, 1738 (broad), 1256, 1156, 1020 cm^{-1}; ^1H NMR (300 MHz) δ 1.04 (d, 3 H, J = 7 Hz),

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1.44 (s, 3 H), 1.46 (s, 3 H), 1.83 (m, 1 H), 1.99 (s, 3 H), 2.15 (m, 1 H), 2.94 (t, 1 H, J = 7 Hz), 3.36 (m, 1 H, J = 7 Hz), 3.66 (s, 3 H), 3.67 (s, 3 H); ^{13}C NMR (75 MHz) δ 17.5, 20.9, 23.7, 24.0, 32.1, 37.1, 48.7, 52.2, 83.4, 169.3, 169.4, 170.0, 211.6; HRMS calcd for $C_{14}H_{23}O_7$ 303.1443, found 303.1447 (M^+ + H).

Methyl 6-hydroxy-2-(methoxycarbonyl)-4,6-dimethyl-5-oxoheptanoate (6e): IR (neat) 3507, 3424, 2977, 1754, 1737, 1711, 1198 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.07 (d, 3 H, J = 6 Hz), 1.30 (s, 3 H), 1.31 (s, 3 H), 1.92 (m, 1 H), 2.17 (m, 1 H), 3.10 (m, 1 H, J = 7 Hz), 3.28 (t, 1 H, J = 7 Hz), 3.67 (s, 3 H), 3.68 (s, 3 H); ^{13}C NMR (75 MHz) δ 17.7, 26.1, 32.1, 36.7, 49.1, 52.4, 76.6, 169.2, 169.3, 217.2; HRMS calcd for $C_{12}H_{21}O_6$ 261.1338, found 261.1342 (M^+ + H).

3-[Bis(methoxycarbonyl)methyl]-4,4-dimethylcyclohexanone (7f): mp 56–58 °C; IR (neat) 2960, 1754, 1737, 1717, 1437, 1152 cm^{-3}; ^{1}H NMR (300 MHz) δ 1.04 (s, 3 H), 1.05 (s, 3 H), 1.67 (overlapping m, 2 H), 2.26–2.68 (overlapping m, 5 H), 3.62 (d, 1 H, J = 5 Hz), 3.72 (s, 3 H), 3.74 (s, 3 H); ^{13}C NMR (75 MHz) δ 19.9, 28.5, 33.0, 37.7, 39.9, 40.3, 45.3, 51.8, 52.3, 52.8, 168.9, 169.1, 209.8; HRMS calcd for $C_{13}H_{20}O_5$ 256.1311, found 256.1308.

(1*R,2*R**,5*R**,6*R**)-2,6-Bis[bis(methoxycarbonyl)methyl]-3,3-dimethylbicyclo[3.1.0]hexan-6-ol (32)**: mp 87–88.5 °C; IR (melt) 3510, 2958, 1737, 1437, 1254, 1160 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.87 (s, 3 H), 0.99 (s, 3 H), 1.36 (dd, 1 H, J = 8, 4 Hz), 1.46 (dd, 1 H, J = 13, 7 Hz), 1.56 (ddd, 1 H, J = 8, 7, 3 Hz), 1.67 (td, 1 H, J = 13, 3 Hz), 2.41 (dd, 1 H, J = 11, 4 Hz), 2.88 (s, 1 H), 3.48 (d, 1 H, J = 11 Hz), 3.69 (s, 1 H), 3.71 (s, 3 H), 3.72 (s, 3 H), 3.76 (s, 3 H), 3.80 (s, 3 H); ^{13}C NMR (75 MHz) δ 23.0, 25.2, 28.3, 34.2, 39.2, 45.3, 52.3, 52.4, 52.5, 52.6, 52.7, 53.0, 58.8, 62.5, 168.4, 168.7, 168.9, 169.2; MS isobutane chemical ionization 387 (M^+ + H); HRMS calcd for $C_{18}H_{27}O_9$ 355.1393, found 355.1387 (M^+ – OCH_3).

(1*R,2*S**,5*R**,6*R**)-2,6-Bis[bis(methoxycarbonyl)methyl]-3,3-dimethylbicyclo[3.1.0]hexan-6-ol (33)**: mp 89–90 °C; IR (melt) 3501, 2957, 1750, 1736, 1435, 1256, 1239, 1160 cm^{-1}; ^{1}H NMR (300 MHz) (C_6D_6) δ 0.88 (s, 3 H), 1.17 (s, 3 H), 1.22 (td, 1 H, J = 8, 8, 2 Hz), 1.55 (dd, 1 H, J = 13, 7 Hz), 1.67 (t, 1 H, J = 7.5 Hz), 1.85 (dd, 1 H, J = 13, 2 Hz), 2.70 (s, 1 H), 3.19 (s, 3 H), 3.24 (s, 3 H), 3.28 (dd, 1 H, J = 12, 7 Hz), 3.42 (s, 3 H), 3.49 (s, 3 H), 4.04 (s, 1 H), 4.24 (d, 1 H, J = 12 Hz); ^{13}C NMR (75 MHz) (C_6H_6) δ 23.6, 28.8, 34.0, 34.1, 40.5, 40.7, 48.3, 50.1, 51.8, 52.0, 52.2, 52.7, 59.1, 63.0, 168.5, 168.8, 169.4, 170.1; MS isobutane chemical ionization 387 (M^+ + H); HRMS calcd for $C_{18}H_{27}O_9$ 355.1393, found 355.1394 (M^+ – OCH_3).

1-[Bis(methoxycarbonyl)methyl]-4,4-dimethyl-7-(methoxycarbonyl)-9-oxabicyclo[4.3.0]non-2-en-8-one (27): mp 131–132 °C; IR (KBr) 3546, 3457, 2970, 2850, 1783, 1734, 1314, 1199, 1165 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.93 (s, 3 H), 1.07 (s, 3 H), 1.99 (br dd, 1 H, J = 19, 5 Hz), 2.16 (br d, 1 H, J = 19 Hz), 3.05 (dd, 1 H, J = 12, 7 Hz), 3.38 (d, 1 H, J = 12 Hz), 3.76 (s, 6 H), 3.82 (s, 3 H), 4.23 (s, 1 H), 5.19 (d, 1 H, J = 7 Hz), 5.95 (dd, 1 H, J = 5, 2 Hz); ^{13}C NMR (75 MHz) δ 26.4, 27.4, 31.5, 34.9, 48.0, 48.7, 52.6, 52.8, 52.9, 53.9, 76.9, 127.0, 130.9, 167.9, 168.1, 168.7, 171.1; HRMS calcd for $C_{17}H_{22}O_8$ 354.1315, found 354.1317.

6-[Bis(methoxycarbonyl)methyl]-4,4-dimethylcyclohex-2-en-1-one (43): IR (KBr) 2959, 1753, 1736, 1682 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.17 (s, 3 H), 1.25 (s, 3 H), 1.78 (ddd, 1 H, J = 13, 5, 2 Hz), 1.99 (t, 1 H, J = 14 Hz), 3.36 (m, 1 H), 3.76 (s, 3 H), 3.79 (s, 3 H), 3.87 (d, 1 H, J = 7 Hz), 5.86 (d, 1 H, J = 10 Hz), 6.64 (dd, 1 H, J = 10, 2 Hz); ^{13}C NMR (75 MHz) δ 25.1, 30.5, 33.8, 39.2, 43.4, 51.4, 52.6, 52.7, 125.8, 159.1, 168.7, 169.0, 197.6; HRMS calcd for $C_{13}H_{18}O_5$ 254.1154, found 254.1158.

2-[Bis(methoxycarbonyl)methyl]-3,3-dimethyl-1-(methoxycarbonyl)cyclopentane (36-I). The higher R_f vicinally substituted isomer: R_f 0.65; IR (neat) 2954, 2878, 1758, 1735, 1437, 1193, 1166 cm^{-1}; ^{1}H NMR (300 MHz) (C_6D_6) δ 0.91 (s, 3 H), 1.11 (s, 3 H), 1.23 (m, 1 H), 1.42 (m, 1 H), 1.63 (m, 1 H), 1.85 (m, 1 H), 2.68 (dd, 1 H, J = 12, 9 Hz), 3.26 (s, 3 H), 3.30 (s, 3 H), 3.32 (s, 3 H), 3.42 (m, 1 H), 4.15 (d, 1 H, J = 12 Hz); ^{13}C NMR (75 MHz) (C_6H_6) δ 21.7, 26.7, 28.8, 40.4, 42.4, 46.3, 50.0, 50.6, 51.4, 51.5, 169.0, 169.3, 175.3; MS isobutane chemical ionization 287 (M^+ + H); HRMS calcd for $C_{13}H_{19}O_5$ 255.1232, found 255.1230 (M^+ – OCH_3).

2-[Bis(methoxycarbonyl)methyl]-3,3-dimethyl-1-(methoxycarbonyl)cyclopentane (36-II). The lower R_f vicinally substituted isomer: R_f 0.54; IR (neat) 2956, 2878, 1758, 1738, 1436, 1153 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.85 (s, 3 H), 1.00 (s, 3 H), 1.45 (m, 1 H), 1.59–1.77 (overlapping m, 2 H), 1.97 (m, 1 H), 2.71 (t, 1 H, J = 9 Hz), 2.91 (m, 1 H), 3.39 (d, 1 H, J = 9 Hz), 3.64 (s, 6 H), 3.70 (s, 3 H); ^{13}C NMR (75 MHz) δ 22.2, 27.6, 28.0, 41.6, 42.2, 46.7, 51.0, 51.7, 52.3, 52.3, 52.5, 169.1, 176.6; MS isobutane chemical ionization 287 (M^+ + H); HRMS calcd for $C_{13}H_{19}O_5$ 255.1232, found 255.1230 (M^+ – OCH_3).

4-[Bis(methoxycarbonyl)methyl]-3,3-dimethyl-1-(methoxycarbonyl)cyclopentane (37-I). The higher R_f 1,3-disubstituted isomer: R_f 0.60; IR (neat) 2956, 2876, 1760, 1737, 1436, 1205, 1159 cm^{-1}; ^{1}H NMR (300 MHz) (C_6H_6) δ 0.82 (s, 3 H), 0.86 (s, 3 H), 1.54 (dd, 1 H, J = 13, 10 Hz), 1.75 (dd, 1 H, J = 13, 6 Hz), 1.87 (m, 1 H), 2.19 (m, 1 H), 2.44 (m, 1 H), 2.55 (m, 1 H), 3.28 (s, 3 H), 3.29 (s, 3 H), 3.34 (s, 3 H), 3.40 (d, 1 H, J = 10 Hz); ^{13}C NMR (75 MHz) (C_6H_6) δ 22.8; 28.8, 33.9, 40.4, 45.5, 48.4, 51.2, 51.8, 51.9, 53.4, 169.0, 175.8; MS isobutane chemical ionization 287 (M^+ + H); HRMS calcd for $C_{13}H_{19}O_5$ 255.1232, found 255.1229 (M^+ – OCH_3).

4-[Bis(methoxycarbonyl)methyl]-3,3-dimethyl-1-(methoxycarbonyl)cyclopentane (37-II). The lower R_f 1,3-disubstituted isomer: R_f 0.56; mp 36–37 °C; IR (neat) 2956, 2876, 1761, 1736, 1436, 1197, 1163 cm^{-1}; ^{1}H NMR (300 MHz) (C_6H_6) δ 0.66 (s, 3 H), 0.85 (s, 3 H), 1.52 (dd, 1 H, J = 13, 8 Hz), 1.61 (m, 1 H), 1.77 (dd, 1 H, J = 13, 10 Hz), 2.51–2.72 (overlapping m, 3 H), 3.25 (s, 3 H), 3.26 (s, 3 H), 3.33 (s, 3 H), 3.33 (d, 1 H, J = 10 Hz); ^{13}C NMR (75 MHz) (C_6H_6) δ 20.6, 26.9, 32.7, 39.0, 41.2, 46.1, 47.2, 50.9, 51.3, 51.4, 53.3, 168.4, 168.6, 175.6; MS isobutane chemical ionization 287 (M^+ + H); HRMS calcd for $C_{13}H_{19}O_5$ 255.1232, found 255.1234 (M^+ – OCH_3).

Lactone (35): IR (neat) 2960, 2874, 1758, 1739, 1146, 1131 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.92 (s, 3 H), 1.10 (s, 3 H), 1.50 (dd, 1 H, J = 14, 3 Hz), 1.72 (ddd, 1 H, J = 14, 7, 1 Hz), 1.97 (td, 1 H, J = 8, 8, 3 Hz), 2.14 (t, 1 H, J = 8 Hz), 2.58 (br d, 1 H, J = 8 Hz), 3.40 (d, 1 H, J = 2 Hz), 3.42 (s, 3 H), 3.75 (s, 3 H); ^{13}C NMR (75 MHz) δ 23.0, 27.3, 30.7, 31.5, 38.3, 48.0, 49.5, 50.1, 52.9, 55.0, 98.0, 165.5, 168.8; HRMS calcd for $C_{13}H_{18}O_5$ 254.1154, found 254.1157.

Optimization Experiments. A series of reactions were run utilizing **3a** and **3c** to see if one reaction mode could be favored over the others. As was found with the acyclic enones **2a** and **2c**, the yield of cyclopropanols **32** and **33** could be considerably improved by reaction of 1.5 equiv of sodium dimethyl malonate and 1.5 equiv of dimethyl malonate with 1 equiv of the substrate. Under these conditions, **3a** yielded 69% **32**/**33** (3:1) with <5% **27** and 12% recovered **3a**. Also under these conditons, **3b** gave 34% **32**/**33** (3:1), 29% recovered **3c**, and 19% **26c**.

***trans*-2-Chloro-4,4-dimethyl-5-[bis(methoxycarbonyl)methyl]cyclohexanone (26c)**: mp 78–80 °C; IR (thin film) 2959, 1734 br, 1440, 1157, 853 cm^{-1}; ^{1}H NMR (300 MHz) (C_6D_6) δ 0.58 (s, 3 H), 0.62 (s, 3 H), 1.46 (t, 1 H, J = 13 Hz), 1.69 (dd, 1 H, J = 13, 6 Hz), 2.36 (dt, 2 H, J = 14, 4, 4 Hz), 2.56 (t, 1 H, J = 14 Hz), 2.70 (dd, 1 H, J = 14, 4 Hz), 3.25 (s, 3 H), 3.28 (s, 3 H), 3.39 (d, 1 H, J = 4 Hz), 4.10 (dd, 1 H, J = 13, 6 Hz); ^{13}C NMR (75 MHz)(C_6D_6) δ 19.4, 28.2, 35.5, 40.1, 45.9, 51.4, 51.9, 51.9, 52.4, 61.2, 168.6, 168.7, 199.1; MS isobutane chemical ionization 291 (M^+ + H); HRMS calcd for $C_{12}H_{16}ClO_4$ 259.0737, found 259.0734 (M^+ – OCH_3).

***cis*-2-Acetoxy-5,5-dimethyl-4-[bis(methoxycarbonyl)methyl]cyclohexanone (38)**: mp 125–127 °C; IR (melt) 3461, 3443, 2962, 1744, 1728, 1435, 1370, 1149, 1062 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.79 (s, 3 H), 1.03 (s, 3 H), 2.00 (q, 1 H, J = 13), 2.10 (s, 3 H), 2.18 (overlapping m, 2 H), 2.43 (d, 1 H, J = 13 Hz), 2.71 (dt, 1 H, J = 13, 4, 4 Hz), 3.59 (d, 1 H, J = 5 Hz), 3.69 (s, 3 H), 3.73 (s, 3 H), 5.19 (dd, 1 H, J = 13, 7 Hz); ^{13}C NMR (75 MHz) δ 20.2, 20.7, 28.9, 35.1, 39.4, 46.1, 46.4, 51.3, 52.5, 53.0, 73.5, 168.7, 168.9, 202.6; HRMS calcd for $C_1{}^5H_{23}O_7$ 315.1444, found 315.1438 (M^+ + H).

***trans*-2-Acetoxy-4,4-dimethyl-5-[bis(methoxycarbonyl)methyl]cyclohexanone (26d)**: IR (neat) 2959, 1747, 1733, 1437, 1240, 1156, 916, 733 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.07 (s, 3 H), 1.15 (s, 3 H), 1.75 (t, 1 H, J = 13 Hz), 1.94 (dd, 1 H, J = 13, 6 Hz), 2.14 (s, 3 H), 2.48 (overlapping m, 2 H), 2.82 (t, 1 H, J = 15 Hz), 3.61 (d, 1 H, J = 4 Hz), 3.74 (s, 6 H), 5.29 (dd), 1 H, J = 13, 7 Hz); ^{13}C NMR (75 MHz) δ 20.2, 20.5, 29.0, 30.8, 38.9, 43.5, 51.1, 52.4, 52.9, 54.6, 75.6, 168.7, 169.2, 169.7, 202.4; MS isobutane chemical ionization 315 (M^+ + H); HRMS calcd for $C_{13}H_{20}O_6$ 272.1260, found 272.1255 (M^+ + H – $OCCH_3$).

6-Isopropyl-3-(methoxycarbonyl)-4-phenyl-2-pyrone (9f): mp 83.5–85 °C; IR (melt) 2977, 2874, 1745, 1701, 1630, 1539, 1106, 1021, 772, 702 cm^{-1}; ^1H NMR (300 MHz) δ 1.25 (d, 6 H, J = 7 Hz), 2.78 (m, 1 H, J = 7 Hz), 3.62 (s, 3 H), 6.12 (s, 1 H), 7.39 (m, 5 H); ^{13}C NMR (75 MHz) δ 19.8, 32.7, 52.2, 102.8, 115.6, 126.9, 128.6, 130.0, 135.9, 155.2, 159.8, 165.3, 171.0; HRMS calcd for $C_{16}H_{16}O_4$ 272.1049, found 272.1054.

1-Methoxy-4-methyl-1-phenyl-1-penten-3-one (10f): IR (neat) 2968, 1688, 1683, 1588, 1245, 1060, 919, 848, 776, 756, 696 cm^{-1}; ^1H NMR (300 MHz) δ 1.11 (d, 6 H, J = 7 Hz), 2.61 (m, 1 H, J = 7 Hz), 3.84 (s, 3 H), 5.66 (s, 1 H), 7.42 (br s, 5 H); ^{13}C NMR (75 MHz) δ 18.9, 41.4, 56.3, 99.9, 128.0, 128.9, 129.9, 135.6, 170.3, 202.9; HRMS calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1146.

6-*tert*-Butyl-3-(methoxycarbonyl)-4-phenyl-2-pyrone (9g): mp 139.5–141 °C; IR (melt) 2974, 1745, 1703, 1628, 1034, 1017, 773, 702 cm^{-1}; ^1H NMR (300 MHz) δ 1.32 (s, 9 H), 3.67 (s, 3 H), 6.18 (s, 1 H), 7.44 (m, 5 H); ^{13}C NMR (75 MHz) δ 27.8, 36.4, 52.3, 101.8, 115.8, 127.0, 128.8, 130.0, 136.4, 155.2, 159.8, 165.4, 173.3; HRMS calcd for $C_{17}H_{18}O_4$ 286.1205, found 286.1201.

4,4-Dimethyl-1-methoxy-1-phenyl-1-penten-3-one (10g): IR (neat) 3060, 2968, 1681, 1608, 1589, 1570, 799, 758, 696 cm^{-1}; ^1H NMR (300 MHz) δ 1.22 (s, 9 H), 3.83 (s, 3 H), 5.91 (s, 1 H), 7.40 (br s, 5 H); ^{13}C NMR (75 MHz) δ 26.9, 43.7, 56.0, 95.9, 127.7, 128.4, 129.4, 135.6, 170.7, 203.3; HRMS calcd for $C_{14}H_{18}O_2$ 218.1307, found 218.1307.

4,4-Bis(methoxycarbonyl)-5,5-dimethyl-3-phenylcyclopent-2-en-1-one (46): IR (neat) 2972, 1782, 1751, 1731, 1600, 1065, 756, 697 cm^{-1}; ^1H NMR (300 MHz) δ 1.34 (s, 6 H), 3.74 (s, 6 H), 6.66 (s, 1 H), 7.40 (m, 3 H), 7.50 (m, 2 H); ^{13}C NMR (75 MHz) δ 24.4, 51.3, 53.2, 73.1, 126.5, 128.3, 128.4, 133.1, 136.7, 138.4, 165.9, 207.8; HRMS calcd for $C_{17}H_{18}O_5$ 302.1154, found 302.1157.

6-[2-(2-Bromopropyl)]-3-(methoxycarbonyl)-4-phenyl-2-pyrone (9a): mp 118–120 °C; IR (neat) 3008, 2951, 1744, 1713, 1639, 1550, 1255, 1199, 1140, 1107, 1084, 839, 806, 769, 743, 732, 703, 693 cm^{-1}; ^1H NMR (300 MHz) δ 2.08 (s, 6 H), 3.67 (s, 3 H), 6.45 (s, 1 H), 7.38–7.47 (m, 5 H); ^{13}C NMR (75 MHz) δ 31.5, 52.6, 55.6, 102.6, 117.8, 127.1, 129.0, 130.4, 135.6, 154.3, 158.5, 164.9, 165.5; HRMS calcd for $C_{16}H_{15}BrO_4$ 350.0154, found 350.0158.

Methyl 3-[2-(2-bromopropyl)]-2-(methoxycarbonyl)-5-hydroxy-5-phenyl-1,3-pentadienoate (52a): mp 125–126.5 °C; IR (melt) 2951, 2929, 1742, 1679, 1609, 1576, 1298, 1151, 1067, 780 cm^{-1}; ^1H NMR (300 MHz) δ 1.94 (s, 6 H), 3.67 (s, 6 H), 5.59 (s, 1 H), 7.16 (s, 1 H), 7.38–7.52 (m, 5 H); ^{13}C NMR (75 MHz) δ 29.6, 52.7, 55.3, 63.7, 124.6, 127.4, 128.4, 129.3, 139.8, 140.8, 151.1, 168.0, 195.3; MS isobutane chemical ionization 383 (M^+ + H); HRMS calcd for $C_{17}H_{19}O_5$ 303.1232, found 303.1236 (M^+ – Br).

6-[2-(2-Acetoxypropyl)]-3-(methoxycarbonyl)-4-phenyl-2-pyrone (9d): IR (neat) 3062, 2992, 2851, 1743, 1721, 1637, 1581, 1247, 1131, 1021 cm^{-1}; ^1H NMR (300 MHz) δ 1.71 (s, 6 H), 2.07 (s, 3 H), 3.67 (s, 3 H), 6.30 (s, 1 H), 7.41–7.46 (m, 5 H); ^{13}C NMR (75 MHz) δ 21.6, 25.5, 52.6, 77.8, 102.9, 116.7, 127.2, 128.9, 130.3, 136.1, 154.9, 159.0, 165.2, 166.1, 169.6; HRMS calcd for $C_{18}H_{18}O_6$ 330.1103, found 330.1098.

Methyl 3-[2-(2-acetoxypropyl)]-2-(methoxycarbonyl)-5-hydroxy-5-phenyl-1,3-pentadienoate (52d): mp 100–103 °C; IR (melt) 3457, 3364, 2985, 1738, 1691, 1606, 1147, 1077, 1020, 777, 699 cm^{-1}; ^1H NMR (300 MHz) δ 1.51 (s, 6 H), 2.09 (s, 3 H), 3.60 (s, 6 H), 5.56 (s, 1 H), 6.69 (s, 1 H), 7.32–7.42 (m, 5 H); ^{13}C NMR (75 MHz) δ 21.0, 23.3, 52.4, 55.2, 83.6, 123.5, 127.3, 128.2, 128.9, 139.7, 150.3, 168.1, 169.9, 198.5; MS isobutane chemical ionization 363 (M^+ + H); HRMS calcd for $C_{14}H_{13}O_5$ 261.0763, found 261.0768 (M^+ – $CH_3CO_2C(CH_3)_2$).

Methyl 4-benzyl-2-(methoxycarbonyl)-5-oxohexanoate (8f): IR (neat) 3066, 2956, 1754, 1737, 1715, 1604, 1158, 738, 702 cm^{-1}; ^1H NMR (300 MHz) δ 1.99 (s, 3 H), 2.02 (partly obscured m, 1 H), 2.25 (m, 1 H), 2.71 (m, 1 H), 2.88 (m, 1 H), 3.34 (dd, 1 H, J = 9, 6 Hz), 3.69 (s, 6 H), 7.11–7.30 (overlapping m, 5 H); ^{13}C NMR (75 MHz) δ 29.6, 30.4, 38.3, 49.3, 51.5, 52.5, 126.6, 128.5, 128.7, 138.3, 169.2, 169.4, 210.8; HRMS calcd for $C_{16}H_{20}O_5$ 292.1311, found 292.1308.

2-Benzyl-2-[2,2-bis(methoxycarbonyl)ethyl]-1-[bis(methoxycarbonyl)methyl]cyclopropanol (20, major isomer): R_f 0.20; IR (neat) 3506, 3033, 1738, 1604, 1436, 1198, 1156, 1021, 703 cm^{-1}; ^1H NMR (300 MHz) δ 0.67 (d, 1 H, J = 6 Hz), 0.77 (d, 1 H, J = 6 Hz), 1.62 (dd, 1 H, J = 15, 11 Hz), 2.13 (dd, 1 H, J = 15, 4 Hz), 2.93 (d, 1 H, J = 15 Hz), 3.01 (d, 1 H, J = 15 Hz), 3.44 (s, 1 H), 3.60 (partially obscured dd, 1 H), 3.64 (s, 3 H), 3.64 (s, 3 H), 3.72 (s, 3 H), 3.80 (s, 3 H), 4.13 (s, 1 H), 7.17–7.30 (overlapping m, 5 H); ^{13}C NMR (75 MHz) δ 23.3, 29.8, 30.3, 35.7, 48.6, 52.5, 52.6, 55.0, 61.7, 126.1, 128.1, 129.3, 138.6, 168.7, 169.2, 169.6, 169.9; HRMS calcd for $C_{21}H_{27}O_9$ 423.1655, found 423.1651 (M^+ + H).

2-Benzyl-2-[2,2-bis(methoxycarbonyl)ethyl]-1-[bis(methoxycarbonyl)methyl]cyclopropanol (20, minor isomer): R_f 0.17; IR (neat) 3504, 3029, 2957, 1752, 1734, 1604, 1155, 1028, 703 cm^{-1}; ^1H NMR (300 MHz) δ 0.92 (d, 1 H, J = 6 Hz), 0.96 (d, 1 H, J = 6 Hz), 2.18 (dd, 1 H, J = 15, 7 Hz), 2.34 (dd, 1 H, J = 15, 6 Hz), 2.41 (d, 1 H, J = 15 Hz), 2.92 (d, 1 H, J = 15 Hz), 3.38 (s, 1 H), 3.64 (partially obscured dd, 1 H, J = 8, 6 Hz), 3.66 (s, 3 H), 3.75 (s, 3 H), 3.81 (s, 3 H), 3.83 (s, 3 H), 4.26 (s, 1 H), 7.19–7.32 (overlapping m, 5 H); ^{13}C NMR (75 MHz) δ 25.3, 29.6, 29.7, 37.4, 49.5, 52.5, 52.7, 52.8, 55.7, 61.0, 126.6, 128.4, 128.9, 138.0, 168.9, 169.1, 170.0, 170.5; HRMS calcd for $C_{21}H_{27}O_9$ 423.1655, found 423.1660 (M^+ + H).

2-Benzyl-4,4-bis(methoxycarbonyl)cyclopentanone (17): IR (neat) 3032, 2958, 1745, 1736, 1456, 1437, 1249, 1166, 703 cm^{-1}; ^1H NMR (300 MHz) δ 2.08 (dd, 1 H, J = 15, 9 Hz), 2.59 (dd, 1 H, J = 13, 9 Hz), 2.60–2.72 (overlapping m, 2 H), 2.71 (d, 1 H, J = 19 Hz), 3.01 (d, 1 H, J = 19 Hz), 3.18 (dd, 1 H, J = 13, 3 Hz), 3.73 (s, 3 H), 3.75 (s, 3 H), 7.14–7.31 (overlapping m, 5 H); ^{13}C NMR (75 MHz) δ 35.5, 35.8, 45.0, 49.2, 53.1, 53.2, 54.6, 126.4, 128.6, 128.8, 138.8, 171.3, 214.1; HRMS calcd for $C_{16}H_{18}O_5$ 290.1154, found 290.1156.

Compound 23a: IR (neat) 3029, 2953, 1755, 1735, 1682, 1604, 1150, 736, 705 cm^{-1}; ^1H NMR (300 MHz) δ 1.65 (m, 1 H), 1.81 (m, 2 H), 2.18 (m, 1 H), 2.93 (d, 1 H, J = 14 Hz), 3.02 (d, 1 H, J = 14 Hz), 3.33 (d, 1 H, J = 16 Hz), 3.41 (d, 1 H, J = 16 Hz), 3.63 (d, 1 H, J = 16 Hz), 3.75 (s, 3 H), 3.76 (s, 3 H), 3.83 (t, 1 H, J = 8 Hz), 4.03 (d, 1 H, J = 16 Hz), 7.08–7.32 (overlapping m, 10 H); ^{13}C NMR (75 MHz) δ 21.9, 28.7, 30.0, 35.5, 37.5, 43.9, 49.1, 52.7, 52.8, 85.9, 109.4, 126.2, 127.2, 128.2, 128.4, 128.5, 130.2, 134.6, 139.5, 143.3, 169.2, 169.4, 205.0; HRMS calcd for $C_{27}H_{29}BrO_6$ 528.1148, found 528.1151.

Methyl 5-benzyl-2-(methoxycarbonyl)-4-oxohex-5-enoate (18): IR (neat) 3031, 2955, 1755, 1737, 1680, 1630, 1605, 1273, 1158, 751, 701 cm^{-1}; ^1H NMR (300 MHz) δ 3.37 (d, 2 H, J = 7 Hz), 3.59 (s, 2 H), 3.75 (s, 6 H), 3.94 (t, 1 H, J = 7 Hz), 5.69 (t, 1 H, J = 1 Hz), 6.19 (s, 1 H), 7.14–7.32 (overlapping m, 5 H); ^{13}C NMR (75 MHz) δ 36.8, 37.2, 46.7, 52.8, 126.3, 126.6, 128.5, 129.1, 138.6, 147.5, 169.4, 197.4; HRMS calcd for $C_{16}H_{18}O_5$ 290.1154, found 290.1155.

Tetraester 19: IR (neat) 3027, 3007, 1753, 1735, 1715, 1602, 1438, 1275, 1030, 738, 703 cm^{-1}; ^1H NMR (300 MHz) δ 1.99 (m, 1 H), 2.25 (m, 1 H), 2.64 (dd, 1 H, J = 16, 10 Hz), 2.77 (dd, 1 H, J = 19, 7 Hz), 2.94 (dd, 1 H, J = 16, 7 Hz), 2.94 (obscured m, 1 H), 3.02 (dd, 1 H, J = 19, 7 Hz), 3.34 (dd, 1 H, J = 9, 7 Hz), 3.69 (s, 6 H), 3.69 (s, 3 H), 3.72 (s, 3 H), 3.78 (t, 1 H, J = 7 Hz), 7.10–7.30 (overlapping m, 5 H); ^{13}C NMR (75 MHz) δ 29.6, 38.2, 41.9, 46.3, 49.1, 50.7, 52.6, 52.7, 52.9, 126.7, 128.6, 128.8, 138.0, 168.9, 169.2, 169.3, 209.4; HRMS calcd for $C_{21}H_{26}O_9$ 422.1576, found 422.1580.

Methyl 4-benzyl-6-chloro-2-(methoxycarbonyl)-5-oxohexanoate (21c): IR (neat) 3064, 3031, 2956, 2853, 1753, 1735, 1605, 1585, 1438, 1269, 1158, 1032, 739, 703 cm^{-1}; ^1H NMR (300 MHz) δ 2.10 (m, 1 H, J = 13, 9, 4 Hz), 2.35 (m, 1 H, J = 14, 9, 6 Hz), 2.76 (dd, 1 H, J = 13, 6 Hz), 2.86 (dd, 1 H, J = 13, 9 Hz), 3.16 (m, 1 H), 3.35 (dd, 1 H, J = 9, 6 Hz), 3.64 (s, 6 H), 3.93 (d, 1 H, J = 16 Hz), 7.12–7.34 (overlapping m, 5 H); ^{13}C NMR (75 MHz) δ 30.0, 39.2, 48.4, 49.1, 49.2, 52.7, 127.0, 128.8, 128.9, 137.7, 169.1, 169.3, 204.5; HRMS calcd for $C_{16}H_{20}ClO_5$ 327.0999, found 327.0996 (M^+ + H).

Methyl 6-acetoxy-4-benzyl-2-(methoxycarbonyl)-5-oxohexanoate (21d): IR (neat) 3031, 2955, 1752, 1734, 1604, 1439, 1233, 1155, 736, 704 cm^{-1}; ^1H NMR (300 MHz) δ 2.06 (m, 1 H), 2.12 (s, 3 H), 2.31 (m, 1 H), 2.72 (dd, 1 H, J = 13, 5 Hz), 2.86–2.98 (overlapping m, 2 H), 3.41 (dd, 1 H, J = 10, 6 Hz), 3.71 (s, 3 H), 3.72 (s, 3 H), 4.16 (d, 1 H, J = 17 Hz), 4.58 (d, 1 H, J = 17 Hz), 7.13 (d, 2 H, J = 7 Hz), 7.14–7.33 (overlapping m, 3 H); ^{13}C NMR (75 MHz) δ 20.3, 29.9, 38.6, 47.3, 48.9, 52.6, 68.7, 126.9, 128.8, 128.9, 137.9, 169.2, 169.4, 170.1, 206.1; MS isobutane chemical ionization 351 (M^+ + H); HRMS calcd for $C_{16}H_{18}O_5$ 290.1154, found 290.1150 (M^+ – CH_3CO_2H).

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Supplementary Material Available: ^{1}H NMR spectra of all new compounds as well as X-ray parameters for cyclopropanols **14** and **32** (72 pages). Ordering information is given on any current masthead page.

The Gymnochromes: Novel Marine Brominated Phenanthroperylenequinone Pigments from the Stalked Crinoid *Gymnocrinus richeri*†

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Five novel brominated phenanthroperylenequinone pigments, gymnochromes A–D (**1–4**) and isogymnochrome D (**5**), were isolated from the stalked crinoid *Gymnocrinus richeri*. The structures of the compounds were inferred from their spectra (IR, UV–vis, ^{1}H and ^{13}C NMR, FABMS). The presence of both bulky hydroxy groups at positions 10 and 11 and side chains at positions 3 and 4 causes sufficient crowding to force the octacyclic phenanthroperylenequinone system into a nonplanar helical shape. This helicity generates axial chirality in the molecules. The presence of chiral carbon atoms in the side chains gives rise to diastereomers. The absolute configurations of the chiral carbons and the axial chirality of the natural pigments was inferred from CD and NMR data and by correlations made with cercosporin and other naturally occurring perylenequinones. The configurations assigned to the chiral carbons in the side chains of compounds **4** and **5** were confirmed by the results of the application of Horeau's method of kinetic resolution.

Quinoid pigments occur widely in microorganisms and plants.[1] In the animal kingdom they are found in certain insects and in echinoderms,[2] often in echinoids and crinoids. At present, four groups of polyketide-derived pigments are known to occur in crinoids:[3] linear and angular naphtopyrones; 4-acylanthraquinones; 3-alkylanthraquinones; and dimeric bianthrones, bianthraquinones and phenanthroperylenequinones.[4] Apparently, quinoid pigments were biosynthesized many millions of years ago. In support of this belief is the observation that fringelites, described by Blumer[5] as hydroxylated phenanthroperylenequinones, were found in the fossilized remains of a Jurassic crinoid (*Apiocrinus*) discovered near Fringeli in northwestern Switzerland.

We recently had the opportunity to examine a deep-water stalked fossil crinoid, *Gymnocrinus richeri*, discovered by one of us (B.R.F.) at a depth of 520 m during the CHALCAL 2 oceanographic campaign of 1986. The campaign was directed toward the exploration of the bathial zone off the coast of New Caledonia, which is particularly rich in so-called "living fossils". *Gymnocrinus richeri* is one of the best examples of those species to which it is appropriate to apply the description "living fossil".[6] The body of the live crinoid is saffron yellow, whereas its stalk is a darker yellow and the inside of its tentacles is dark yellow-green. However, within a few minutes of collection, outside salt water, the animal turns dark green.

Extraction with hexane and dichloromethane did not remove any pigment from a freeze-dried green sample. Extraction with methanol gave a dark green solution, which on very mild acidification turned violet.

Herein we describe the isolation, structure, and stereochemistry of five violet pigments [gymnochrome A (**1**), gymnochrome B (**2**), gymnochrome C (**3**), gymnochrome D (**4**) and isocymnochrome D (**5**)] which constitute a novel

† Dedicated to Professor G. B. Marini Bettolo on the occasion of his 75th birthday.

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(4) (Hydroxypropyl)propylphenanthroperylenequinone (1% of the total pigment components) was detected in extracts of *Lamprometra palmata*. It may have been formed in very small amounts by air oxidation of the structurally related bianthrone during the extraction. Dipropylphenanthroperylenequinone was found to be a very minor component in extracts of *Himerometra robustipinna*, but in this case bianthroquinones and bianthrones were not present.[3]

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