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Bromomalonates as Synthetic Reagents. Transfer Alkylations[1]

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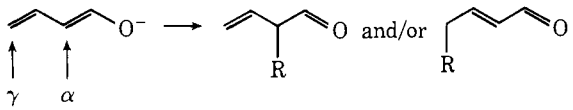
Abstract: A procedure for site selectivity in the alkylation of polyenolates is developed. The substrates examined, alkylidene succinates, were prepared by an Emmons–Wadsworth–Horner modification of the Stobbe condensation. The "alkylating" agents were bromomalonates of which cyclic isopropylidene 2-bromo-2-methylmalonate was the most useful. It can also serve as a general source of Br^+ toward carbanions. Reaction of the enolates of the alkylidene succinates with the bromomalonates leads initially to bromine transfer and malonate anion. Recombination of the two parts by conjugate addition–elimination leads to the product of remote alkylation. The regioselectivity of the reaction with polyenolates is discussed.

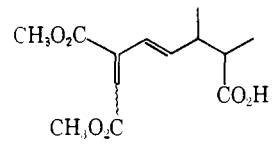
Introduction

The position of alkylation of a polyenolate is an intriguing and important problem. Normally, it is expected and observed that reaction occurs at the α position, at least in a kinetic process.[3,4] In several instances, the initial product



arising by alkylation at the α position has been rearranged to isomers which correspond to a net γ attack.[5,6] Direct attack at the γ (or more remote position) has been observed in a few cases. For example, allylation of a copper enolate of an α,β-unsaturated ester has led to an approximately 1:1 mixture of the α and γ alkylation products.[7] The alkylation of the dianion of 2-butynoic acid gives a 2.2:1 ratio of γ vs. α attack.[8] Alkylation of β-dialkylamine α,β-unsaturated ketones apparently gives only products of γ attack.[9]

In conjunction with a problem in sesquiterpene synthesis we developed a need for large quantities of acid **1**. One approach involves the alkylation of the polyenolate **2** at the ϵ



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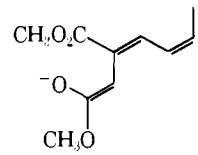
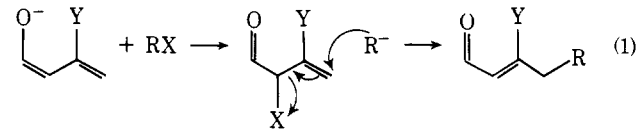


2

position. A potential solution to this problem takes advantage of the intrinsic preference for reaction at the α position by choosing an "alkylating" agent, RX, that reacts at the X group rather than at carbon. Recombination of the thus-formed R^- in a SN2′-type process with **3** would yield the product of net γ or ϵ, etc., attack (see eq 1). This process will be aided by the presence of polarizing groups on the enolate (e.g., Y in **3**) which will facilitate SN2′ attack. Con-



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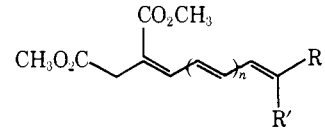
sidering our interest in the synthesis of **1**, we restricted our study to an examination of alkylidene succinates of general formula **4**. As a result of this investigation, we have uncov-



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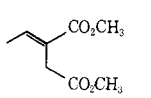
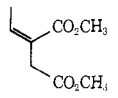
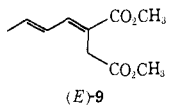
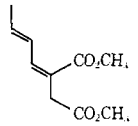
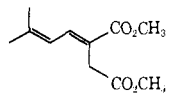
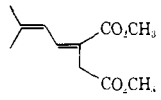
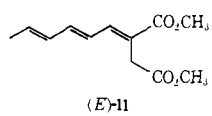
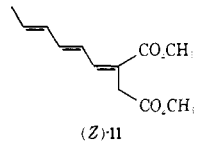
ered a new positive brominating agent, *O,O*-isopropylidene 2-bromo-2-methylmalonate, which serves as an excellent reagent for bromination of anions.

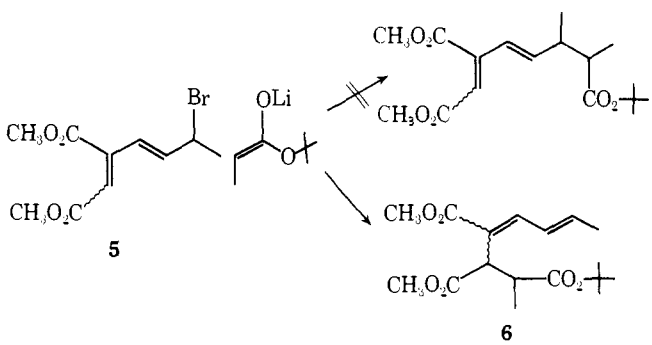
The need for such a route was underscored by the failure of a conceptually more direct path to **1**. Alkylation of the bromoester **5** with *tert*-butyl 2-lithiopropionate would be expected to give the *tert*-butyl ester of the desired carboxylic acid. Instead, it underwent reaction by a net SN2″ alkylation to give **6**, presumably by a Michael addition followed by elimination.[10]

Preparation of Alkylidenesuccinates

The Stobbe condensation is the most direct approach to alkylidene succinates; however, the yields in this reaction with aldehyde partners are generally low.[11] Considering the

Table I. Preparation of Alkylidene Succinates

Aldehyde	Product		E/Z	Yield, %
Acetaldehyde	 (E)-8	 (Z)-8	1.0	81
Crotonaldehyde	 (E)-9	 (Z)-9	2.0	76
β,β-Dimethylacrolein	 (E)-10	 (Z)-10	3.8	60
Sorbaldehyde	 (E)-11	 (Z)-11	3.7	77



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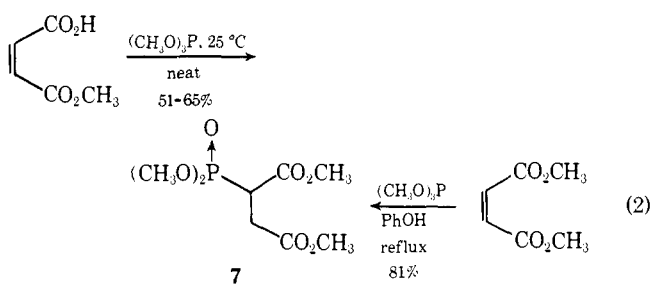
base sensitivity of the α,β-unsaturated aldehydes to be employed in this study, an alternative which involves more neutral conditions was sought. The success of the Emmons–Wadsworth–Horner reaction for the synthesis of α,β-unsaturated esters,[12] as well as the ready accessibility of the requisite phosphonate **7** (eq 2),[13] suggested this approach. For



(2)

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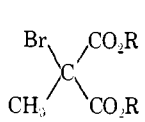
large-scale preparations, we found the direct condensation of trimethyl phosphite with monomethyl maleate to be preferred.

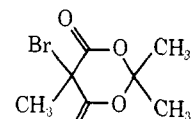
Utilizing the standard conditions for the Emmons–Wadsworth–Horner reaction of sodium hydride in DME at room temperature or below, the alkylidene succinates **8–11** were prepared (see Table I). In each case, a mixture of *E* and *Z* isomers was obtained as determined by NMR spectroscopy. For **8** the lower field absorption for the vinyl methyl group at δ 2.01 was assigned to the *Z* isomer and the higher field one at δ 1.78 to the *E* isomer. The methylene group α to the ester appears at δ 3.27, 3.35, 3.35, and 3.38 for the *E* isomers and at δ 3.17, 3.20, 3.23, and 3.24 for the *Z* isomers of **8–11**, respectively. For **9**, the *E* and *Z* isomers were separated chromatographically. The methylene group at lower field (δ 3.35) correlated with the lower field vinyl proton at C-4 (δ 7.24); this substantiates the conclusion that the lower field absorptions of the α-methylene groups correspond to the *E* isomers.

Preparation of Bromomalonates

The choice of "alkylating" agent for the process visualized in eq 1 is crucial. The fact that cyanogen chloride serves as a cyanating agent whereas cyanogen bromide frequently serves to transfer bromine as Br^+ indicated the desirability of X = Br.[14] Bromomalonates appeared to be ideal choices for our goal since they would introduce an acetic acid unit directly. Indeed, the debromination of diethyl bromomalonate with heteroatom nucleophiles[15] and the cyclization of 1,3-dibromo-1,1,3,3-tetracarboethoxypropane with malonate anion[16] suggests that these compounds can serve as sources of Br^+. Three bromomalonates **12**,[17] **13**,



12, R = C_2H_5
13, R = *t*-C_4H_9



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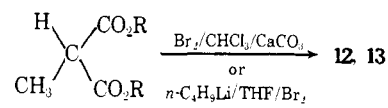
and **14** were examined. The ability of these substances to serve as sources of Br^+ depends on the electronegativity of the malonate unit. We may use the pK_a of the parent malonates as a measure of the polarizing influence of this unit. The pK_a of **15** (R = CH_3), may be estimated to be about 15



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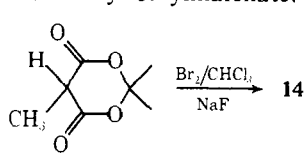
from the value for diethyl ethylmalonate.[18] The pK_a of **16**



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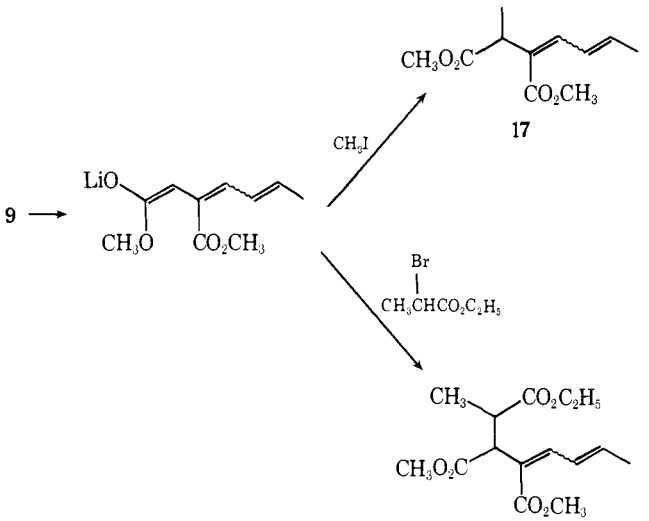
has been determined to be 4.77.[19] This ΔpK_a of more than 10 indicates that **14** should be an exceptionally good brominating agent, an expectation that has been subsequently verified. Indeed, the steric rigidity of **14**, as well as the unfavorable dipole–dipole interaction of the two carbonyl groups, factors which may account in part for its high acidity, reinforce the above conclusion.

Bromination of **15** (R = C_2H_5) was performed by the usual methods for forming bromomalonates.[20] However, the preparation of **13** required quenching of the preformed lithium enolate of di-*tert*-butyl malonate[21] with bromine to avoid the acid-catalyzed cleavage of the sensitive *tert*-butyl esters. The preparation of **14** involved bromination of the methyl Meldrum's acid **16**[22] in the presence of solid sodium fluoride as a mild scavenger for hydrogen bromide under aprotic conditions. Whereas **12** and **13** are liquids, **14** is a beautifully crystalline compound, mp 86 °C. The crystallinity of **14** enhances its shelf-life relative to **12** and **13.** We have been able to store it for over a year without any signs of decomposition.

Transfer Alkylations

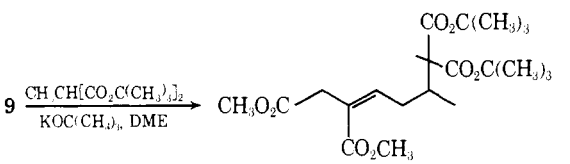
The expectation that alkylations of the alkylidene succinates (**4**) would alkylate at C-2 was confirmed in the case of **9**. The polyenolate of **9**, generated with lithium diisopropylamide in THF,[23] is alkylated with methyl iodide or ethyl 2-bromopropionate to yield **17** and **18,** respectively, as the



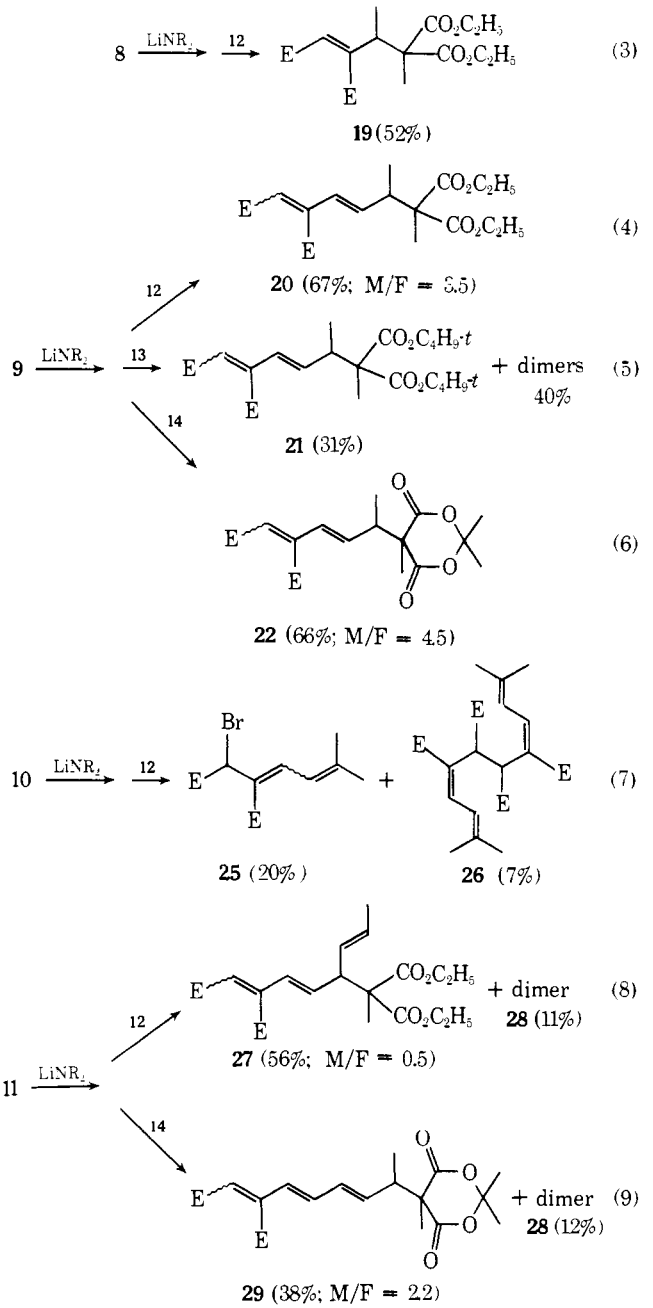
17

18

only products of alkylation. These alkylation products are characterized by a vinyl methyl resonance in their NMR spectra at δ 1.88 (**17**) and 1.94 (**18**), as well as a C-4 vinyl proton resonance at α 4.12 in **17** and a C-5 proton resonance at δ 7.30 in **18.** Another feature of these polyenolates is their susceptibility toward the conjugate addition of nucleophiles. The Michael addition of di-*tert*-butyl methylmalonate to alkylidene succinate **9** proceeds in 88% yield.



In general, the transfer alkylations were carried out under a standard set of conditions. The enolates of **8–11** were generated by the addition of the neat alkylidene succinate to a −78 °C THF–hexane solution of lithium diisopropylamide. Enolate generation is rapid and nearly quantitative. No problem was encountered with conjugate addition of the amide base as has been reported for acrylate derivatives.[4a,b] The cold solution of the enolate is added to an equally cold (−78 °C) solution of the bromomalonate in THF via a cannula. Use of this siphon is quite convenient for transfers of solutions of enolates even on a 1-mol scale. The reaction is then allowed to warm to room temperature. In the case of the cyclic bromomalonate **14,** HMPA, Me_2SO, or DMF is added to solubilize the lithiomalonate. Equations 3–9 summarize the results where the symbol E is used to represent the CO_2CH_3 unit, and M/F represents the ratio of the maleate to the fumarate isomer. The yields represent material isolated by chromatography.



19 (52%)

20 (67%; M/F = 3.5)

21 (31%)

22 (66%; M/F = 4.5)

25 (20%)

26 (7%)

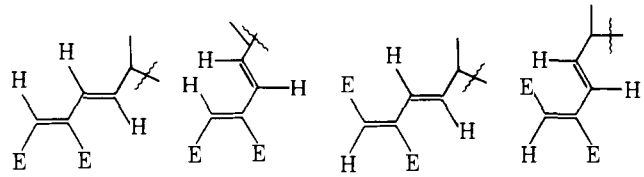
27 (56%; M/F = 0.5)

29 (38%; M/F = 2.2)

The stereochemistry of **19** is characterized by the resonance of a vinyl proton at δ 5.88 in its ^1H NMR spectrum. In comparison, the vinyl proton of dimethyl methylmaleate occurs at δ 5.77, whereas that of dimethyl methylfumarate occurs at δ 6.71.

The stereochemistry of **20–22** was assigned on the basis of the ^1H NMR and uv spectral data as well as chemical reactivity. As an example, the structures of the isomers of **20** will be discussed in detail since the others exhibit analogous

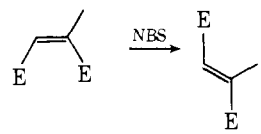
characteristics. In all cases the C-3–C-4 double bond possessed the E configuration as determined by the 16-Hz coupling constant. However, the assignment of the maleate (M) or fumarate (F) geometry is more complicated. In the NMR spectrum of **20M**, the vinyl protons appear at δ 6.29 (s), 7.25 (d, J = 16 Hz), and 6.32 (dd, J = 16, 9 Hz), whereas the corresponding absorptions for **20F** are δ 6.12 (s), 6.48 (d, J = 16 Hz), and 6.18 (dd, J = 16, 9 Hz). All corresponding vinyl protons of the fumarate isomer resonate at higher field than those of the maleate isomer. This result may be explained by studying the possible conformers of **20M** and **20F**. For the former, while the transoid conformation **23t** suffers a bad 1,3-E–H interaction, the cisoid



23t **23c** **24t** **24c**

conformation **23c** only suffers from the normal 1,4-H–H interaction. The difference may lead to **23c** becoming the more favorable conformation. In such a case, the C-2 and C-4 vinyl protons would be deshielded by the adjacent double bond and carbomethoxy group, respectively, causing the low-field resonances observed. On the other hand, neither planar conformation for **20F** (i.e., **24t** or **24c**) appears reasonable because of the severe steric interactions. Thus, it would be expected to exist in a twisted form which removes the deshielding effects of the vinyl protons relative to the maleate isomer. Such a twisted conformation for **20F** relative to **20M** is supported by a λ_{max} at 254 nm for the former, but at 267 nm for the latter.

In addition, maleate isomers are normally isomerized to fumarate isomers upon treatment with NBS in carbon tetrachloride (see eq 10 and 11).[10] Indeed, such treatment



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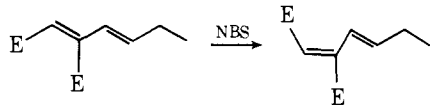


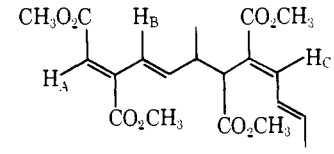
(11)

converts the compound assigned as **20M** to **20F**. Compound **20F** is more polar than **20M**; **20F** is crystalline, and **20M** is an oil. These properties are suggestive of the stereochemistry assigned. Similar arguments apply to the assignment of the stereochemistry of **21** and **22**.

Compound **10** did not produce any products of transfer alkylation. Compound **25**, only obtained admixed with starting diester, was tentatively identified as the bromide expected from bromination. In particular, a singlet at δ 5.62 in the ^{1}H NMR is characteristic of the C*H*Br group. It is interesting to note that only a single saturated methine resonance at δ 3.98 (s) is present for **26**, suggesting that it is a single stereoisomer.

The formation of **27** rather than a positional isomer in the reaction of the enolate of **11** with **12** was first suggested by the uv data where **27F** has a λ_{max} at 249 nm and **27M** at 271 nm compared with 254 and 267 nm for **20F** and **20M**, respectively. The presence of the propenyl group was confirmed by the vinyl methyl doublets at δ 1.72 (d, J = 4.5 Hz) and 1.77 (d, J = 6 Hz) for the M and F isomers. The stereochemistry of the double bonds of **27** was assigned on the basis of the NMR data as described for **20**.

A clear distinction existed for the products of transfer alkylation of **11** with bromomalonate **14**. In this case, the much longer wavelength of the uv maxima (304 nm for **29M** and 300 nm for **29F**) indicated a more highly conjugated system than **27**. The presence of methyl doublets (J = 7 Hz) at δ 1.12 and 1.13 for **29M** and **29F**, respectively, confirmed that carbon–carbon bond formation occurred at C-8. Assignment of stereochemistry of the double bonds is based upon the interpretation of the spectral data as discussed above. In several cases, oxidative dimers of the enolates were obtained (see eq 4, 6–8). The structures of these compounds must be considered tentative where assigned. From **9**, one dimer which could be obtained pure was assigned structure **30**. The presence of a methyl doublet on



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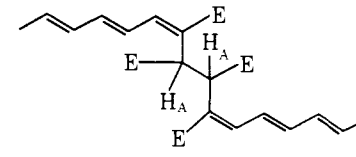
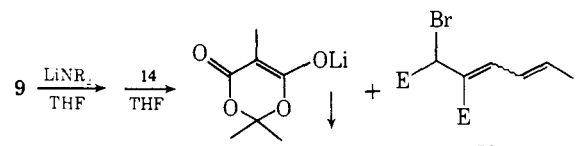


28

saturated carbon (δ 1.5, J = 5 Hz) and on unsaturated carbon (δ 1.95, J = 6 Hz), as well as a uv maximum at 263.5 (ϵ 21 200), indicated coupling between C-2 and C-6 (head-to-tail dimer). The appearance of H_A at δ 6.78 (s), H_B at δ 6.76 (d, J = 15 Hz), and H_C at δ 7.35 (d, J = 10 Hz) indicates the E, E, E stereochemistry for these double bonds. The dimer isolated from **10** (i.e., **26**, see above) and **11** (i.e., **28**) have been assigned the head-to-head structure. Like in **10**, this assignment rests heavily on the presence of only a single doublet for a methyl group on unsaturated carbon (1.83, d, J = 5.5 Hz) and the characteristic singlet at δ 3.99 for H_A (see formula **28**). The stereochemistry of the double bonds is uncertain.

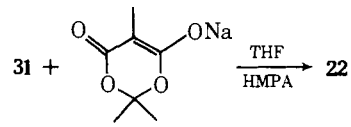
The occurrence of dimeric alkylidene succinates in the products of transfer alkylation is probably due to insufficient mixing during the quenching of the polyenolate with a bromomalonate. For the case of compound **9**, the production of dimer can be almost eliminated by adding the enolate slowly to a vigorously mixed solution of a slight excess of bromomalonate. The maleate/fumarate ratio is not controlled in this sequence. Use of the pure *E* or *Z* isomer of alkylidene succinate **9** with transfer alkylating agent **14** leads to the same M/F ratio of **22**.

That the course of reaction proceeds as envisioned is supported by several observations. As previously stated, use of bromo Meldrum's acid **14** requires the use of a cosolvent like DMF, Me_2SO, or HMPA to solubilize the lithiomalonate. If only THF is used, inverse quenching of the enolate solution into a solution of the bromomalonate **14** also in THF leads to a thick precipitate. Addition of pentane to complete the precipitation and filtration allows nearly quantitative recovery of the lithium salt of Meldrum's acid. Chromatography of the filtrate allows isolation of the reactive bromide **31** in 87% yield. Indeed, this ability to bromi-



31

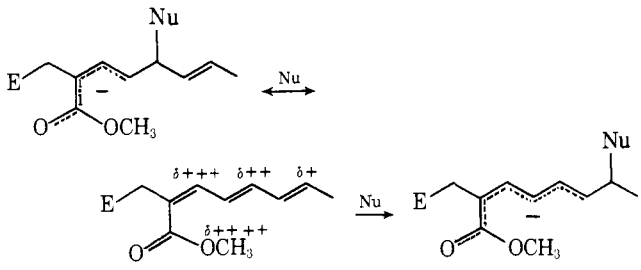
nate the enolate cleanly and in high yield suggests the utility of this new reagent for the halogenation of anions. Treatment of **31** with the sodium salt of methyl Meldrum's acid leads cleanly to the product of transfer alkylation, **22.** The question can be raised as to whether bromide **31** isomerizes to **5** followed by normal SN2 alkylation. The previous demonstration that **5** undergoes displacement by a net SN2″ process rules out this pathway.[10]



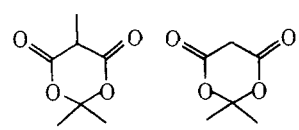
Steric hindrance plays an important role in these reactions as expected for a Michael type addition.[24] For example, the gem dimethyl substitution of **10** leads to a modest yield of the expected brominated product **25,** but no conjugate addition to this system occurs. The problem of steric hindrance also resides in the Michael donor. Thus, di-*tert*-butyl 2-bromo-2-methylmalonate produces only low yields, if any, of transfer alkylation. Both approach to the bromomalonate by the polyenolate and subsequent Michael addition of the malonyl enolate are impeded by the bulky *tert*-butyl ester functionality.

The most intriguing aspect of this work is the regioselectivity observed in the case of **11** as a function of the nature of the bromomalonate. A rationalization of this result invokes Hammond's postulate[25] which relates the position of the transition state along the reaction coordinate to the reactivity of the reagents. Thus, it predicts that the transition state for bonding of a reactive nucleophile with a substrate will yield products which, to a certain extent, reflect the stabilities of the starting materials. However, the transition state for less reactive nucleophiles is predicted to yield products reflecting relative product stability.

The polarization of alkylidene succinate **11** is depicted in a manner to reflect the decrease in positive character at the more distal positions from the polarizing carbonyl group. Reaction of such a system with a reactive enolate would be expected to yield products arising from reaction at one of the more highly polarized sites (but not necessarily leading to the product enolate of greatest stability). Conversely, a



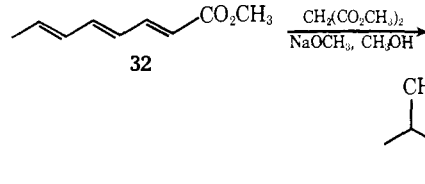
less reactive enolate is expected to react such as to yield the product enolate of greater thermodynamic stability. The reactivity of the enolates used in transfer alkylation can be implied from the pK_a values of their respective acids using



			$CH_2(CO_2CH_3)_2$	$CH_3CH(CO_2CH_3)_2$
pK	4.77	4.97	13	15
ref	19	19	18	18

the notion that the more stable the anion, the less reactive it is. The fact that Meldrum's acids are about 10 pK_a units more acidic than acyclic malonates accounts for the large differences in reactivity of these two systems. Thus, the more stable anion gives the product reflecting enolate stability, whereas the less stable anion gives a product which reflects charge distribution in the polyenoate slightly more.

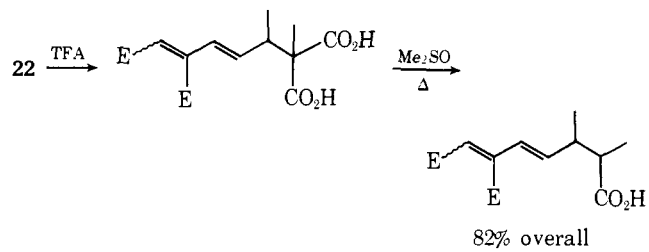
It is known that triene **32** undergoes Michael addition with dimethyl malonate giving a high yield of the terminal



addition product. This result is not anomalous with respect to the above discussion since the first step of the Michael reaction is reversible. The product **33** may simply reflect the thermodynamic equilibrium. On the other hand, such equilibration would not be expected to be seen in transfer alkylation because the initial Michael addition would be made irreversible by bromide expulsion. The clean regiospecificity seen suggests that, by picking the appropriate nucleophile, transfer alkylation may be used to specifically substitute any position of a polyenoate.

Conclusions

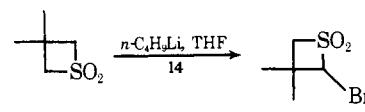
The transfer alkylation process as described is a synthetically useful means for homologating a polyenoate with a propionate unit. Thus, **22** undergoes chemospecific transes-



82% overall

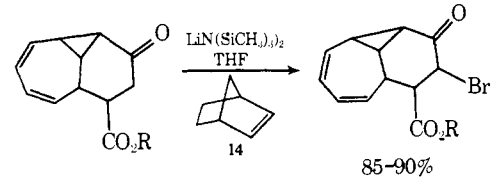
terification with trifluoroacetic acid, and the resultant malonic acid undergoes decarboxylation in hot Me_2SO. The potential of this chain homologation is unexplored, but should prove to be quite general for a range of nucleophiles. The fact that **14** only serves as a positive brominating agent when THF is used as solvent with full recovery of lithiomalonate would allow addition of other nucleophiles at this point.

The last point reemphasizes the utility of bromo Meldrum's acid **14** as a source of positive bromine, especially with respect to carbanions. It does not react rapidly with alcohols or amines which would indicate selectivity. Indeed, based upon our work, Marino has pointed out the superiority of this reagent for the bromination of sulfone anions (eq 12)[27] and Vedejs has carried out a selective bromination of



(12)

85%



(13)

85-90%

a ketone enolate (eq 13).[28] Further work along these lines is clearly desirable.

Experimental Section

All reactions were done under an atmosphere of nitrogen or argon gas. Ethereal solvents were dried by distillation from sodium benzophenone ketyl. Diisopropylamine was distilled from potassium hydroxide. Unless otherwise stated, evaporations were done on a Büchi Rotovapor at water aspirator pressure. The silica gel for preparative-layer chromatography (PLC) and thin-layer chromatography (TLC) was Merck Silica Gel PF-254. The silica gel for column chromatography was MCB Grade 62, 60–200 mesh. Proton magnetic resonance (^{1}H NMR) spectra were obtained on a Varian Associates A60A, T60, XL100, or a Jeol MH100 spectrometer. Infrared (ir) spectra were obtained on a Beckman IR8 spectrometer. Ultraviolet (uv) spectra were obtained on a Cary 15 spectrometer. Mass spectra (70 eV) were obtained on an AEC MS-902 spectrometer using samples which were known to be of high purity of ^{1}H NMR and TLC analysis. Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.

Diethyl 2-Bromo-2-methylmalonate (12). To a solution of 8.10 g (46.5 mmol) of diethyl methylmalonate in 50 ml of chloroform was added 9.30 g (93.0 mmol) of calcium carbonate. To this mixture 2.54 ml (46.5 mmol) of bromine was added slowly and the resultant mixture heated to reflux to discharge the bromine color. The reaction was cooled and filtered, and the filtrate was evaporated to an oil. This oil was fractionally distilled to yield 10 g (85%), bp (0.2) 56–59 °C (lit.[17] bp (2) 84 °C) of **12:** ^{1}H NMR (CCl_4) δ 1.31 (t, O-C-CH_3, J = 7 Hz), 2.01 (s, BrCCH_3), and 4.27 (q, O-CH_2-C, J = 7 Hz).

Di-*tert*-butyl 2-Bromo-2-methylmalonate (13). To a solution of 8.70 g (37.8 mmol) of di-*tert*-butyl methylmalonate[21] in 125 ml of dry tetrahydrofuran at −78 °C was added dropwise 23.6 ml of a 1.6 M solution of *n*-butyllithium *in* hexane. The resulting solution was stirred 30 min at −78 °C and then 2.38 ml (43.4 mmol) of bromine was added. The reaction was warmed to 25 °C, evaporated, and redissolved in carbon tetrachloride. This solution was washed once with 5% sodium bicarbonate solution, dried over magnesium sulfate and sodium carbonate, and evaporated to an oil. This oil was distilled from sodium bicarbonate through a base washed distilling apparatus to yield 7.19 g (61%) of **13:** bp (0.1) 62.4 °C; ir C=O 1735 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.48 (s, *tert*-butyl) and 1.92 (s, CH_3).

Cyclic Isopropylidene 2-Bromo-2-methylmalonate (14). Preparation A. To a mixture of 6.51 g (41.2 mmol) of cyclic isopropylidene methylmalonate[22] and 4.90 g (0.117 mol) of anhydrous sodium fluoride in 50 ml of chloroform was added 7.25 g (45.3 mmol) of bromine in 10 ml of chloroform. The reaction was stirred 30 min at 25 °C, 45 min at reflux (caution: a violent reaction may occur), and finally 45 min at 25 °C yielding a white mixture. This mixture was filtered and the filtrate evaporated to yield 9.2 g (100%) of **15** as white crystals: mp 77–81°. If the product is completely crystalline and of this high mp, then it is suitable for use in the transfer alkylation reactions. If not, it must be recrystallized from 2-propanol.

Preparation B. To a solution of 135 g (0.855 mol) of cyclic isopropylidene methylmalonate in 1 l. of chloroform was added 108 g (2.56 mol) of sodium fluoride and the mixture heated to 50–60 °C. A solution of 54.6 ml (1 mol) of bromine in 100 ml of chloroform was slowly dripped into the hot reaction. After approximately 2 min, the bromine color instantly disappears. External heating is removed and the remainder of the bromine solution added to the reaction over a period of approximately 1 h which maintains the reaction at 40–50 °C. The reaction is then refluxed 30 min, cooled, and filtered, and the filtrate was evaporated. Recrystallization of the solid obtained from the filtrate first from hexane and then 2-propanol yielded 121.7 g (mp 86 °C), 20.3 g (mp 73–83 °C), and 6 g (mp 83–86 °C) of **14** (73%): ir (CCl_4) C=O 1770 and 1750 cm^{-1}; ^{1}H NMR (CCl_4) α 1.78, 2.02, and 2.20 (s, CH_3); mass spectrum *m/e* (rel intensity) 223 (1.8), 221 (1.8), 194 (0.8), 192 (0.8), 176 (23), 134 (23), 108 (6), 106 (6), 44 (10), 43 (100), 42 (5), and 41 (5). Anal. ($C_7H_9BrO_2$): C, H, Br. *Note.* Attempts to perform this reaction under extremely anhydrous conditions always failed. A small amount of water is apparently needed for a successful reaction.

Dimethyl Dimethylphosphonosuccinate (2). Preparation A. Phenol Method. A mixture of 11.6 g (0.0806 mol) of dimethyl maleate, 12.5 g (0.101 mol) of trimethyl phosphite (distilled from CaH_2), and 19.0 g (0.202 mol) of phenol was heated at 105 °C for 24 h. The reaction was then distilled at a pressure of 10 Torr to yield 12 ml of liquid, bp 50–90 °C. The residue was fractionally distilled to yield 16.5 g (81%) of **7**, bp (0.2) 115–124 °C (lit.[13b] bp (0.25) 122 °C).

Preparation B. To 1326 g (10.2 mol) of monomethyl maleate in a mechanically stirred 5-l. three-neck flask was added dropwise over an 18 h period (via a 2-mm Teflon tube directly siphoning under nitrogen atmosphere from the reagent bottle) 1322 ml (11.2 mol) of trimethyl phosphite. The rate of addition was such that the reaction remained at 32–38 °C. The reaction was stirred an additional 18 h at 25 °C, and then the volatile materials were removed by high vacuum evaporation at 25 °C. The remaining residue was fractionally distilled from 1 3-l. three-neck flask through a 35-cm Vigreux column and a vacuum distilling head to yield 776 g: bp 127–135 °C (ca. 0.2–0.3 mm), and 1167 g, bp 135 °C (ca. 0.3 mm) (75%); GLC (8 ft × ¼ in. 20% SE-30 Chromosorb W 60/80, 185 °C, 60 ml/min) 21.3 min retention time; ir (CCl_4) C=O 1735, P-O-C 1250 and 1050; ^{1}H NMR (CCl_4) δ 2.6–3.2 (m, methylene and methine) and 3.6–3.9 (m, methyls). ^{1}H NMR (approximately 60 mol % Eu(thd)$_3$ in CCl_4) δ 3.64 (s, $COOCH_3$), 5.23 (s, $COOCH_3$), 7.80 (dd, one proton of methylene, J = 10 and 7.3 Hz), 8.01 (dd, one proton of methylene, J = 9 and 4.5 Hz), 9.31 and 9.41 (d, both $POOCH_3$, J = 11 Hz), and 10.94 (ddd, methine, J = 25, 10.5, and 4.25 Hz); mass spectrum *m/e* (rel intensity) 254 (3), 223 (100), 195 (95), 163 (89), 113 (55), 110 (40), 109 (58), 93 (48), 59 (25), and 55 (52). Anal. Calcd for $C_8H_{15}O_7P$: *m/e* 254.0602. Found: 254.0555.

Methyl 3-Carbomethoxy-3-pentenoate (8). To a slurry of 699 mg (29.1 mmol) of sodium hydride (57% dispersion in mineral oil) in 75 ml of 1,2-dimethoxyethane was added dropwise 7.92 g (31.2 mmol) of dimethyl dimethylphosphonosuccinate (**7**). The reaction was stirred 1.5 h at 10–25 °C yielding a clear solution followed by the rapid addition of 1.7 ml (30 mmol) of acetaldehyde. The resulting mixture was stirred 1 h at 25 °C poured into ether–water, and extracted twice with ether. The ether extracts were washed once with saturated sodium chloride solution, dried over magnesium sulfate, and evaporated to an oil. This oil was vacuum distilled to yield 4.04 g (81%) of 8, bp 60–65 °C (ca. 0.2 mm) (lit.[29] bp (0.2) 56–7 °C). GLC (8 ft × ¼ in. 20% SE-30 Chromosorb W 60/80, 180 °C, 60 ml/min) indicated two peaks with retention times for (*Z*)- and (*E*)-**8** of 5.2 and 5.8 min in a ratio of 5:6.5.

Methyl 3-Carbomethoxy-3,5-heptadienoate (9). As described above, 2.36 g (98.5 mmol) of sodium hydride (57% in mineral oil), 25.0 g (98.5 mmol) of dimethyl dimethylphosphonosuccinate, and 8.1 ml (98.5 mmol) of crotonaldehyde were reacted for 2 h in 160 ml of DME. After work-up, the oil was vacuum distilled to yield 14.7 g (76%) of **9**: bp 68–70 °C (ca. 0.2 mm); GLC (8 ft × ¼ in. 20% SE-30 Chromosorb W 60/80, 205 °C, 60 ml/min) showed peaks at 8 and 8.25 min for (*Z*)- and (*E*)-**9** in the ratio of 1:2; ir (CCl_4) C=O 1740, 1720 and C=C 1645 cm^{-1}; ^{1}H NMR (*E*, CCl_4) δ 1.88 (d, vinyl CH_3, J = 5.5 Hz), 3.35 (s, methylene), 3.63 and 3.71 (s, OCH_3), 6.2 (m, C-5,6 vinyl H), and 7.24 (bd, C-4 vinyl H, J = 10.5 Hz); ^{1}H NMR (*Z* CCl_4) δ 1.88 (d, vinyl CH_3, J = 5.5 Hz), 3.20 (s, methylene), 3.63 and 3.71 (s, OCH_3), 5.6–6.6 (m, C-4,6 vinyl H), and 6.90 (bd, C-4 vinyl H, J = 11 Hz); uv (ethanol) 272 nm, ϵ 24 300; mass spectrum *m/e* (rel intensity) 195 (65), 183 (42), 167 (38), 166 (25), 149 (25), 148 (24), 147 (24), 107 (25), 79 (100), 77 (25), and 59 (43). Anal. Calcd for $C_{10}H_{14}O_4$: *m/e* 198.0892. Found: 198.0892.

Methyl 3-Carbomethoxy-6-methyl-3,5-heptadienoate (10). As described above, 699 mg (29.1 mmol) of sodium hydride (57% in mineral oil), 7.63 g (30.0 mmol) of dimethyl dimethylphosphonosuccinate, and 2.44 g (29.1 mmol) of 3-methylcrotonaldehyde were reacted for 1 h in 75 ml of DME. After work-up, the oil was vacuum distilled to yield 3.68 g (60%) of **10:** bp 99–102 °C (ca. 0.2 mm); GLC (8 ft × ¼ in. 20% SE-30 Chrom W 60/80, 200 °C, 60 ml/min) showed only one broad peak at 13 min with no isomer separation; ir (CCl_4) C=O 1725 and C=C 1630 cm^{-1}; ^{1}H NMR (CCl_4, (*E*)-**10**) 1.91 and 1.93 (s, *gem* dimethyl), 3.35 (s, methylene), 3.62 and 3.72 (3, OCH_3), 6.02 (dm, C-5 vinyl H, J = 12 Hz), and 7.51 (d, C-4 vinyl H, J = 12 Hz); (*E*)-**10**:(*Z*)-**10** is 3.8:1 by ^{1}H NMR; uv (ethanol) 275 nm, ϵ = 21 300; mass spectrum *m/e* (rel intensity) 212 (37), 197 (20), 181 (23), 180 (15), 148 (60), 137 (37), 93 (100), 77 (34), and 59 (26). Anal. Calcd for

$C_{11}H_{16}O_4$: *m/e* 212.1049. Found: 212.1028.

Methyl 3-Carbomethoxy-3,5,7-nonatrienoate (11). As described above, 720 mg (30.0 mmol) of sodium hydride (57% in mineral oil), 8.05 g (31.6 mmol) of dimethyl dimethylphosphonosuccinate, and 2.88 g (30.0 mmol) of 2,4-hexadienal were reacted for 1 h in 75 ml of DME. After work-up, the oil was vacuum distilled to yield 5.18 g (77%) of **10**: bp 105–10 °C (ca. 0.2 mm); GLC (8 ft × ¼ in., 20% SE-30 Chromosorb W 60/80, 215 °C, 60 ml/min) showed one broad peak at 17.2 min with no isomer separation; ir (CCl_4) C=O 1740, 1710 and C=C 1615 cm^{-1}; ^1H NMR (CCl_4, (*E,E,E*)-**11**), δ .82 (d, vinyl methyl, J = 6 Hz), 3.38 (s, methylene), 3.65 and 3.74 (s, OCH_3), 5.4–6.7 (m, C-5,6,7,8 vinyl H), and 7.30 (m, C-4, vinyl H); (*E,E,E*)-**11**:(*Z,E,E*)-**11** is 3.7:1 by ^1H NMR; uv (ethanol) 303 nm, ϵ 31 900; mass spectrum *m/e* (rel intensity) 224 (24); 193 (15), 192 (15), 165 (15), 164 (15), 133 (35), 132 (26), 11105 (100), 104 (52), 91 (60), 79 (35), 77 (48), and 59 (41). Anal. Calcd for $C_{12}H_{16}O_4$: *m/e* 224.1048. Found: 224.1048.

Methyl 3-Carbomethoxy-5,5-dicarboethoxy-4-methyl-*trans*-2-hexenoate (19). To a solution of 1.71 mmol of lithium diisopropylamide in 7 ml of dry tetrahydrofuran prepared in the usual way was added dropwise 259 mg (1.50 mmol) of methyl 3-carbomethoxy-3-pentenoate. The resulting orange solution was stirred 35 min at −78 °C and then poured via a stainless steel tube into a solution of 512 mg (2.00 mmol) of diethyl 2-bromo-2-methylmalonate in 7 ml of dry tetrahydrofuran at −78 °C. The resulting orange solution was stirred 10 min at −78 °, 1 h at 25 °C, poured into ether–water, and extracted twice with ether. The ether extracts were washed with saturated sodium chloride solution, dried over magnesium sulfate, and evaporated to an oil. This oil was purified by PLC on silica gel eluted twice with 40% ether–pentane to yield 262 mg (51%) of **19** (R_f 0.35): ir (CCl_4) C=O 1730 and C=O 1640 cm^{-1}; ^1H NMR (CCl_4) δ 1.21 (d, C-4 methyl, J = 7 Hz), 1.25 (t, O-C-CH_3, J = 7 Hz), 1.36 (s, terminal methyl), 3.36 (q, C-4 methine, J = 7 Hz), 3.70 (s, OCH_3), 4.15 (q, O-CH_2, J = 7 Hz), and 5.88 (s, vinyl H); mass spectrum *m/e* (rel intensity) 344 (7), 313 (17), 299 (29), 211 (32), 174 (56), 171 (100), 139 (58), 128 (43), and 59 (33). Anal. Calcd for $C_{16}H_{24}O_8$: *m/e* 344.1471. Found: 344.1438.

Reaction of Lithio Methyl 3-Carbomethoxy-6-methyl-3,5-heptadienoate (10) with Diethyl 2-Bromo-2-methylmalonate (12). In a similar manner to the above, the enolate from 325 mg (1.53 mmol) of methyl 3-carbomethoxy-6-methyl-3,5-heptadienoate, prepared utilizing 1.71 mmol of lithium diisopropylamide in 7 ml of THF, was reacted with 468 mg (1.83 mmol) of diethyl 2-bromo-2-methylmalonate (**12**) in 10 ml of dry THF. After work-up, the oil was purified by PLC on silica gel eluted twice with 1:1 ether:hexane to yield 208 mg of a mixture (R_f 0.44) (by ^1H NMR) representing 38% recovery of starting material and a yield of 20% of methyl 2-bromo-3-carbomethoxy-6-methyl-3,5-heptadienoate (**25**): ^1H NMR (CCl_4, of the mixture) δ 1.97 (m, vinyl CH_3), 3.23 and 3.25 (s, methylene of *trans*- and *cis*-**10**), 3.62, 3.72, and 3.77 (s, OCH_3), 5.62 (s, Br-C-H of **25**), 6.28 (dm, C-5 vinyl H, J = 12 Hz), and 7.54 (d, C-4 vinyl H, J = 12 Hz). There was also obtained 22.5 mg (7%) of 2,11-dimethyl-5,6,7,8-tetracarbomethoxy-2,4,8,10-dodecatetraene (**26**): ir (CCl_4) C=O 1745 (broad), C=C 1640 and 1590 cm^{-1}; ^1H NMR (CCl_4) δ 1.82 and 1.90 (s, vinyl CH_3), 3.75 (s, OCH_3), 3.98 (s, C-6,7 methines), and 6.72 (m, vinyl H); uv (ethanol) 279 nm, ϵ 9210; mass spectrum *m/e* (rel intensity) 422 (0.4), 211 (100), 180 (50), 179 (61), 169 (56), 151 (52), 82 (35), and 59 (33). Anal. Calcd for $C_{22}H_{30}O_8$: *m/e* 422.1939. Found: 422.1939.

Methyl 3-Carbomethoxy-2-methyl-3,5-heptadienoate (17). A solution of 240 μl (1.71 mmol) of diisopropylamine in 7 ml of dry tetrahydrofuran was cooled to −20 °C followed by the dropwise addition of 1 ml (1.6 mmol) of a 1.6 M solution of *n*-butyllithium in hexane. The resulting solution was stirred 15 min at −20 °C and cooled to −78 °C, and 294 mg (1.48 mmol) of methyl 3-carbomethoxy-3,5-heptadienoate (**9**) was added dropwise. The resulting orange solution was stirred 35 min at −78 °C and then poured via a stainless steel tube into a −78 °C solution of 185 μl (2.97 mmol) of methyl iodide in 10 ml of dry tetrahydrofuran. The resulting orange solution was stirred 5 min at −78 °C and 1 h at 25 °C. The resulting red solution was poured into ether–water and extracted twice with ether. The combined ether fractions were washed with saturated sodium chloride solution, dried over magnesium sulfate, and evaporated to an oil. This oil was purified by PLC on silica gel eluted with 1:1 ether:hexane to yield 275 mg (87%) of **17** (R_f 0.38): ir (CCl_4) C=O 1740, 1720 and C=C 1645 cm^{-1}; ^1H NMR (CCl_4) δ 1.29 (d, C-2 methyl, J = 7 Hz), 1.88 (d, vinyl CH_3, J = 5 Hz), 3.25–3.85 (C-2 methine), 3.59, 3.69, and 3.71 (s, OCH_3), 5.75–6.60 (m, C-5,6 vinyl H), and 7.12 (bd, C-4 vinyl H, J = 10.5). Compound **17** is actually a mixture of approximately (by ^1H NMR) 86% cis,trans and 14% trans,trans. Uv (ethanol) 266 nm, ϵ 19 000; mass spectrum *m/e* (rel intensity) 212 (48), 153 (40), 121 (21), 93 (100), 79 (25), 77 (24), and 59 (25). Anal. Calcd for $C_{11}H_{16}O_4$: *m/e* 212.1048. Found: 212.1048.

Ethyl 3,4-Dicarbomethoxy-2-methyl-*cis,trans*-4,6-octadienoate (18). A solution of 234 μl (1.67 mmol) of diisopropylamine in 3 ml of dry THF was cooled to −20 °C followed by the dropwise addition of 0.95 ml (1.53 mmol) of a 1.6 M solution of *n*-butyllithium in hexane. The resulting solution was stirred 15 min at −20 °C and cooled to −78 °C, and 306 mg (1.54 mmol) of methyl 3-carbomethoxy-3,5-heptadienoate (**9**) was added dropwise. The resulting orange solution was stirred 35 min at −78 °C and then poured via a stainless steel tube into a −78 °C solution of 400 μl (3.08 mmol) of ethyl 2-bromopropionate in 5 ml of dry tetrahydrofuran. The reaction was stirred at 25 °C for 2 h, poured into water–ether, and extracted twice with ether. The ether extracts were dried over magnesium sulfate and evaporated to an oil. This oil was initially purified by PLC on silica gel eluted with 1:1 ether:hexane. The one main broad band (R_f 0.6) was removed and purified via PLC on silica gel six times with 30% ether–hexane yielding the following compounds: R_f 0.62, **18**, 109 mg (24%, a pure diastereomer); ir (CCl_4) C=C 1725 and C-C 1640 cm^{-1}; ^1H NMR (CCl_4) δ 0.91 (d, C-2 methyl, J = 7.5 Hz), 1.28 (t, O-C-CH_3, J = 7 Hz), 1.94 (d, vinyl CH_3, J = 5.5 Hz), 3.02 (dq, C-2 methine, J = 10 and 7.5 Hz), 3.5–4.2 (C-3 methine), 3.59 and 3.71 (s, OCH_3), 4.13 (q, OCH_2, J = 7 Hz), 6.0–6.7 (m, C-6,6 vinyl H), and 7.30 (d, C-5 vinyl H, J = 10.5); R_f 0.65, 54 mg (12%) of a mixture of diastereomers of **18**; ^1H NMR (CCl_4) 0.91 and 1.00 (d, C-2 methyl, J = 7 Hz), 1.25 and 1.27 (t, O-C-CH_3, J = 7 Hz), 1.90 (six-line multiplet, vinyl CH_3), 2.6–4.3 (apparently the region of the C-2,3 methines), 3.60, 3.69, and 3.73 (s, OCH_3), 4.10 (m, O-CH_2), and 5.8–7.4 (m, vinyl H); R_f 0.82, 31.7 mg (14%) yield of ethyl 3-carboethoxy-3,5-heptadienoate; ir (CCl_4) C=O 1735 (shoulder), 1715 and C=C 1640 cm^{-1}; ^1H NMR (CCl_4) δ 1.23 and 1.28 (t, O-C-CH_3, J = 7.0 Hz), 1.89 (d, vinyl CH_3, J = 5 Hz), 3.32 (s, methylene), 4.09 and 4.17 (q, O-CH_2, J = 7 Hz), 6.2 (m, C-5,6 vinyl H), and 7.20 (d, C-4 vinyl H, J = 10); R_f 0.76, 41.4 mg (20%) of recovered starting material. Together these products represent an 85% yield.

Methyl 3-Carbomethoxy-7,7-dicarboethoxy-6-methyl-2,4-octadienoate (20). In a manner similar to the previous transfer alkylations, the enolate from 286 mg (1.44 mmol) of methyl 2-carbomethoxy-3,5-heptadienoate (**9**), prepared utilizing 1.51 mmol of lithium diisopropylamide in 5 ml of THF, was reacted with 828 mg (3.23 mmol) of diethyl 2-bromo-2-methylmalonate in 2 ml of dry tetrahydrofuran at −78 °C. After work-up, the resultant oil was purified by PLC eluting with 1:1 ether:hexane to yield 276 mg (52%) of **20M** (R_f 0.37): ir (CCl_4) C=O 1725, C=C 1640 and 1595 cm^{-1}; ^1H NMR (CCl_4) δ 1.11 (d, C-6 methyl, J = 7 Hz), 1.24 (t, O-C-CH_3, J = 7 Hz); 1.32 (s, terminal methyl), 3.08 (quintet, C-6 methine, J = 7 Hz), 3.72 and 3.79 (s, OCH_3), 6.40 (dd, C-5 vinyl H, J = 16 and 8 Hz), 6.21 (s, C-2-vinyl H), and 7.25 (d, C-4 vinyl H, J = 16 Hz); uv (ethanol) 267 nm, ϵ 12 000; mass spectrum *m/e* (rel intensity) 370 (0.4), 196 (100), 169 (36), and 59 (18). Anal. Calcd for $C_{18}H_{26}O_8$: *m/e* 270.1628. Found: 370.1630. Also obtained was a mixture (R_f 0.29, 131 mg) representing at least an additional 15% of **20F**: ^1H NMR (CCl_4) δ 1.25 (m, terminal methyl and O-C-CH_3), 3.00 (quintet, methine, J = 7 Hz), 3.70 and 3.80 (s, OCH_3), 4.11 (q, O-CH_2, J = 7 Hz) and 5.90 (m, C-2,4,5 vinyl H).

Methyl 3-Carbomethoxy-7,7-dicarbo-*tert*-butoxy-6-methyl-*trans,trans*-2,4-octadienoate (21). In a manner similar to the above, the enolate from 210 mg (1.06 mmol) of methyl 3-carbomethoxy-3,5-heptadienoate, generated utilizing 1.06 mmol of lithium diisopropylamide in 3 ml of THF, was reacted with 401 mg (1.30 mmol) of di-*tert*-butyl 2-bromo-2-methylmalonate in 3 ml of tetrahydrofuran. After work-up, the oil was purified by PLC eluting with 1:1 ether:hexane to yield 140 mg (31%) of **21**: R_f 0.53; ir (CCl_4) C=O 1727, C=C 1630 and 1591 cm^{-1}; ^1H NMR (CCl_4) δ 1.10 (d, C-6 methyl, J = 7 Hz), 1.22 (s, terminal methyl), 1.41

and 1.43 (s, *tert*-butyl), 3.00 (quintet, C-6 methine, J = 7.5 Hz), 3.72 and 3.78 (s, OCH_3), 6.18 (s, C-2 vinyl H), 6.42 (dd, C-5 vinyl H, J = 16 and 8 Hz), and 7.29 (d, C-4 vinyl H, J = 16 Hz); uv (ethanol) 269 nm, ϵ 10 200; mass spectrum m/e (rel intensity) 314 (3), 69 (20), 59 (18), 58 (11), 57 (100), and 56 (19). Anal. Calcd for $C_{22}H_{34}O_8$ minus C_8H_{16}: m/e 314.1002. Found: 314.0965. Also obtained was 90.5 mg (40%) of a mixture of dimers one of which appears to be methyl 6-methyl-3,7,8-tricarbomethoxy-2,4,8,10-dodecatetraenoate: R_f 0.21; ^{1}H NMR (CCl_4) δ 1.55 (d, C-6, CH_3, J = 4.75 Hz), 1.97 (d, terminal vinyl CH_3, J = 6.0 Hz), 3.53 (s, β,γ-unsaturated methyl ester), 3.72, 3.80, and 3.82 (s, α,β-unsaturated methyl esters), 4.2–5.6 (m, C-6,7 methines and two vinyl H), 5.8–6.8 (m, a vinyl H), 6.68 (s, C-2 vinyl H), 6.75 (bd, C-4 vinyl H, J = 14 Hz), 7.22 (d, C-9 vinyl H, J = 11 Hz).

Methyl 3-Carbomethoxy-7,7-dicarbo-cyclic-isopropoxy-6-methyl-2,4-octadienoate (22). In a similar manner, the enolate from 4.72 g (23.8 mmol) of methyl 3-carbomethoxy-3,5-heptadienoate, generated utilizing 25.3 mmol of lithium diisopropylamide in 25 ml of dry THF, was reacted with 5.73 g (24.1 mmol) of cyclic isopropylidene 2-bromo-2-methylmalonate in 25 ml of tetrahydrofuran at −78 °C. The resulting mixture was stirred 10 min at −78 °C, warmed to 10 °C, 12.6 ml (72 mmol) of dry hexamethylphosphoramide added, and then stirred 6 h at 25 °C. The reaction was poured into ether–water and extracted twice with ether. The ether extracts were washed with saturated sodium chloride solution, dried over magnesium sulfate, and evaporated to an oil. This oil was dissolved in ether–pentane causing the crystallization of 773 mg (9%) of **22F** which was recrystallized from carbon tetrachloride yielding 514 mg of **22F** as white crystals, mp 151–152 °C. The remaining oil was purified by column chromatography on 450 g of silica gel eluted with 20–50% ether–hexane and collected in 500-ml fractions. Fractions 8–17 yielded 407 mg (9%) of **9**. Fractions 22–39 yielded 4.30 g (51%) of **22M**. Fractions 40–48 yielded 480 mg (6%) of a 1:1 mixture of **22M** and **F. 22M:** ir (CCl_4) C=O 1780, 1740, C=C 1635 and 1620 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.15 (d, C-6 methyl, J = 7 Hz), 1.51 (s, terminal methyl), 1.71 (s, isopropyl methyls), 2.91 (quintet, C-6 methine, J = 7 Hz), 3.75 and 3.83 (s, OCH_3), 6.29 (s, C-2 vinyl H), 6.32 (dd, C-5 vinyl H, J = 16 and 9 Hz), and 7.25 (d, C-4 vinyl H, J = 16 Hz); uv (ethanol) 267 nm, ϵ 13 900; mass spectrum m/e (rel intensity) 354 (0.9), 323 (2), 210 (22), 192 (35), 185 (35), 169 (48), 83 (47), 59 (51), and 43 (100). Anal. Calcd. for $C_{17}H_{22}O_8$: m/e 354.1315. Found: 354.1295. **22F:** ir ($CHCl_3$) C=O 1775, 1735, C=C 1625 and 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.18 (d, C-6 methyl, J = 7 Hz), 1.55 (s, terminal methyl), 1.70 and 1.72 (s, isopropyl methyls), 2.98 (quintet, C-6 methine, J = 7 Hz), 3.75 and 3.95 (s, OCH_3), 5.88 (s, C-2 vinyl H), and 5.7–6.4 (m, C-4, 5 vinyl H); uv (ethanol) 254 nm, ϵ 30 800; mass spectrum m/e (rel intensity) 354.1315 (calcd. M^+ 354.1315, 0.5), 297 (16), 296 (25), 265 (35), 220 (30), 192 (64), 185 (65), 169 (72), 165 (75), 133 (46), 105 (50), 83 (100), 59 (68), and 43 (95). Anal. ($C_{17}H_{22}O_8$): C,H.

Methyl 3-Carbomethoxy-6-(1′,1′-dicarboethoxyethyl)-2,4,7-nonatrienoate (27). In a similar manner, the enolate from 338 mg (1.51 mmol) of methyl 3-carbomethoxy-3,5,7-nonatrienoate (**11**), generated utilizing 1.60 mmol of lithium diisopropylamide in 7 ml of dry THF, was reacted with 463 mg (1.81 mmol) of diethyl 2-bromo-2-methylmalonate in 10 ml of tetrahydrofuran at −78 °C. After work-up, the oil was purified by PLC eluting with 1:1 ether: hexane to yield three fractions. The first consisted of 111 mg (18%) of **27M:** ir (CCl_4) C=O 1740, C=C 1635 and 1600 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.23 (t, O-C-CH_3, J = 7 Hz), 1.35 (s, malonyl methyl) 1.71 (d, terminal methyl, J = 4.5 Hz), 3.2–4.2 (apparently the region of the C-6 methine), 3.72 and 3.80 (s, OCH_3), 4.12 (q, O-CH_2, J = 7 Hz), 5.5 (m, C-7,8 vinyl H), 6.21 (s, C-2 vinyl H), 6.48 (dd, C-5 vinyl H, J = 16 and 8 Hz), and 7.22 (d, C-4 vinyl H, J = 16 Hz); uv (ethanol) 272 nm, ϵ 12 600; mass spectrum m/e (rel intensity) 396 (0.2), 365 (1.6), 364 (0.8), 324 (0.7) 323 (3), 191 (27), and 169 (100). Anal. Calcd for $C_{20}H_{28}O_8$: m/e 396.1784. Found: 396.1784. The second consisted of 231 mg (38%) of **27F:** ir (CCl_4) C=O 1735 and C=C 1645 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.22 (t, O-C-CH_3, J = 7 Hz), 1.41 (s, malonyl methyl) 1.74 (d, terminal methyl, J = 5.5 Hz), 3.5–4.0 (apparently the region of C-6 methine), 3.68 and 3.71 (s, OCH_3), 4.11 (q, diastereotopic O-CH_2, J = 7 Hz) and 5.3–6.5 (m, C-2,4,5,7,8 vinyl H); uv (ethanol) 226 nm, ϵ 21 900; 249 nm, ϵ 5790; mass spectrum m/e (rel intensity) 396 (5), 366 (7), 365 (19), 351 (5), 350 (12), 336 (13), 324 (7), 323 (20), 304 (7), 303 (20), 263 (37), 191 (80), 169 (22), 163 (100), 105 (53), 91 (44), 69 (53), and 59 (45). Anal. Calcd for $C_{20}H_{28}O_8$: m/e 396.1784. Found: 396.1784. The third, 36.1 mg (11%), was tentatively identified as 7,8,9,10-tetracarbomethoxy-2,4,6,10,12,14-hexadecahexane (**28**): ^{1}H NMR (CCl_4) δ 1.81 (d, terminal methyls, J = 5.5 Hz), 3.67 (s, OCH_3), 3.98 (s, C-8,9 methines), and 5.5–7.3 (m, vinyl H).

Methyl 3-Carbomethoxy-9,9-dicarbo-cyclic-isopropoxy-8-methyl-2,4,6-decatrienoate (29). In a similar manner, the enolate from 224 mg (1.00 mmol) of methyl 3-carbomethoxy-3,5,7-nonatrienoate (**11**), generated utilizing 1.1 mmol of lithium diisopropylamide in 5 ml of dry THF, was reacted with 237 mg (1.00 mmol) of cyclic isopropylidene 2-bromo-2-methylmalonate in 5 ml of dry tetrahydrofuran. The resulting yellow solution was stirred 5 min at −78 °C, warmed to 25 °C with the formation of a white precipitate, 4 ml of hexamethylphosphortriamide added, and then stirred 12 h at 25 °C. After work-up, the oil was purified via PLC eluting five times with 50% ether–hexane to yield three fractions. The first consisted of 99.4 mg (26%) of **29M** (R_f 0.62): ir ($CHCl_3$) C=O 1730 and C=C 1600 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.11 (d, C-8 methyl, J = 7 Hz), 1.50 (s, C-10 protons), 1.71 (s, isopropoxy methyls), 2.90 (quintet, C-8 methine, J = 7 Hz), 3.74 and 3.83 (s, OCH_3), 5.4–6.8 (m, C-5,6,7 vinyl protons), 6.23 (s, C-2 vinyl proton) and 7.50 (d, C-4 vinyl proton, J = 16 Hz); uv (ethanol) 304 nm; mass spectrum m/e (rel intensity) 365 (0.20), 350 (0.17), 349 (0.40), 323 (2), 322 (7), 169 (18), 163 (14), 105 (12), 91 (11), 83 (19), 59 (22), 58 (45), and 43 (100). The second consisted of 46 mg (12%) of **29F** (R_f 0.41): ir ($CHCl_3$) 1735 and C=C 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.11 (d, C-8 methyl, J = 7 Hz), 1.53 (s, C-10 protons), 1.72 (s, isopropoxy methyls), 2.94 (quintet, C-8 methine, J = 7 Hz), 3.75 and 3.93 (s, OCH_3), 5.8–6.5 (m, C-4,5,6,7 vinyl protons), and 5.88 (s, C-2 vinyl proton); uv (ethanol) 300 nm, ϵ 35 700; mass spectrum m/e (rel intensity) 380 (1.8), 365 (0.50), 350 (0.30), 349 (0.60), 323 (10), 322 (30), 291 (20), 208 (25), 203 (17), 191 (27), 190 (27), 169 (100), 163 (30), 131 (30), 94 (44), 83 (78), 59 (50), 43 (76). Anal. Calcd for $C_{19}H_{24}O_8$: m/e 380.1471. Found: 380.1471. The third consisted of 42 mg (12%) of a mixture of **29M** and 7,8,9,10-tetracarbomethoxy-2,4,-6,10,12,14-hexadecahexane (**28**).

Methyl 2-Bromo-3-carbomethoxy-3,5-heptadienoate (31). In a similar manner, the enolate from 26.6 g (0.134 mol) of methyl 3-carbomethoxy-3,5-heptadienoate, generated utilizing 0.153 mol of lithium diisopropylamide in 500 ml of dry THF at −78 °C, was siphoned via a 2-mm Teflon tube into a vigorously stirred cold (−78 °C) solution of 38.4 g (0.162 mol) of cyclic isopropyl 2-bromo-2-methylmalonate in 150 ml of dry THF over a period of 10 min. The resultant yellow mixture was stirred 1 h at −78 °C followed by warming to 15 °C. Pentane (200 ml) was added to the light-yellow reaction mixture, and after 5 min the reaction was filtered. The filtrate was redissolved in 75% ether–pentane and filtered. This second filtrate was evaporated to an orange oil which was purified via column chromatography on 1 kg of silica gel eluted with methylene chloride to yield: (fraction, 1 l. each, weight of evaporated fraction) 1–4, -; 5, 21.8 g; 6, 9.1 g; 7, 1.7 g; 6–7, -. Fractions 5–7 represent an 87% (32.6 g) yield of **31** as a mixture of isomers: ir (CCl_4) C=O 1725, C=C 1640 and 1608 cm^{-1}; ^{1}H NMR (CCl_4) 1.95 (d, vinyl CH_3, J = 5.5 Hg) 3.79 and 3.83 (s, OCH_3), 5.73 and 5.92 (s, BrCH), 6.2–7 (m, C-5,6 vinyl protons), and 7.40 (bd, C-4 vinyl proton, J = 11 Hz). Anal. ($C_{10}H_{13}BrO_4$): C, H.

Acknowledgment. We wish to thank the National Institutes of Health and the National Science Foundation for their generous support of our programs.

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Electronic States of Organic Molecules. I. Potential Functions for the Deformation of Methane[1,2]

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Abstract: The energy changes for four angle deformation modes of methane have been calculated using three different basis sets. A double-ζ basis set reproduced experimental results satisfactorily and gave values which agreed well with those for a larger basis set and large angular deformations. The deformation modes are related to those which are involved in the formation of several types of small ring compounds.

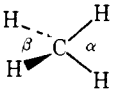
Saturated compounds which possess distorted bond angles have been of particular interest to organic chemists over the past decade. Despite the many studies which have been carried out, relatively little is known about the potential functions for bond angle bending.[3] Most of the calculations which have been carried out have concentrated on small angular deformations which are of interest in connection with studies of molecular vibrations.[4] A few calculations, however, have been carried out for the planar methane configuration.[5]

We have carried out a series of calculations on the potential functions for the deformation of methane.[2] Methane was chosen since it is a prototype for the effects which can be studied, and it is small enough to permit a detailed study of the potential surface. Most of the calculations were carried out at the minimal STO-3G[6] or double-ζ 4-31G level,[7] and a few selected points were studied using a double-ζ plus polarization (DZP) basis set.[8]

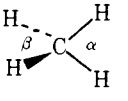
Before considering the angular deformation modes, we present a comparison of the equilibrium geometry and symmetric stretching force constants derived from the basis sets used herein with the results obtained using other basis sets (Table I). It can be seen that all basis sets give essentially the same equilibrium geometry, which is in good agreement with the experimentally determined value.[11] The STO-3G basis set gives a relatively high stretching force constant, whereas the 4-31G set gives a value close to the experimental result. The extensive summary of Meyer and Pulay[4] suggests that the 4-31G basis set should be adequate for the calculation of the relative energies of all but possibly the more highly deformed methane configurations. Although the calculated energies are still considerably higher than the Hartree–Fock limit, the relative energies do not appear to change significantly when larger basis sets are used.

Knowing that at least the 4-31G basis set gives reasonable deformation energies, we have examined the modes in Chart I. The symmetric and antisymmetric bending modes

Chart I

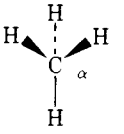


I $\Delta\alpha = \Delta\beta$ symmetric bend



II $\Delta\alpha = -\Delta\beta$ antisymmetric bend

III $\Delta\alpha \neq -\Delta\beta$ unsymmetric bend



IV C_{3v} or umbrella mode

correspond to the E and F_2 vibrational modes for methane. The relationship between these bending modes and the types of angular deformation present in several types of small ring compounds has been presented elsewhere.[2]