The Addition of Methanol to Hexynedioic Esters. The Synthesis of Cyclopentanediones and Muconates

J. M. Landesberg and D. Kellner[1]

Adelphi University, Garden City, New York 11530

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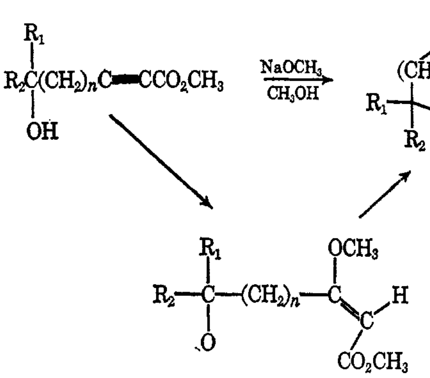
Sodium methoxide reacts with hexynedioic esters in a manner that is determined by the structure of the ester and by the solvent medium. Treatment of 4,4-dimethyl-2-hexynedioic acid dimethyl ester (**2a**) with sodium methoxide in dry tetrahydrofuran gives 4,4-dimethyl-3-methoxy-2-carbomethoxy-2-cyclopenten-1-one (**5**), an over-all *trans* addition to the triple bond. In methanol ester **2a** reacts to give *trans*-4,4-dimethyl-3-methoxy-2-hexenedioic acid dimethyl ester (**9**), *cis*-4,4-dimethyl-3-methoxy-2-hexenedioic acid dimethyl ester (**10**), and 4,4-dimethyl-3-methoxy-5-carbomethoxy-2-cyclopenten-1-one (**8**); a net *cis* addition occurs. The distribution of these products varies with time. Hydrolysis and decarboxylation of esters **5** and **8** lead to 4,4-dimethylcyclopentane-1,3-dione (**6**). For 4-*n*-propyl-2-hexynedioic acid diethyl ester (**2b**) and 2-hexynedioic acid dimethyl ester (**2c**), rearrangement to muconates competes with base-catalyzed alcohol addition and is the principal reaction pathway. The structures of all products are proven by a combination of analysis, spectral identification, and chemical transformation and synthesis. The mechanisms of these reactions are discussed.

The reaction of nucleophiles with the acetylenic bond has been examined from a number of viewpoints.[2] As a synthetic method nucleophilic additions to acetylenic compounds have found use in the synthesis of aliphatic compounds,[2d] natural products,[3] and heterocyclic systems.[2b,4] Studies aimed at determining the stereochemistry of these additions have shown that nucleophilic agents add primarily in a *trans* fashion.[5-15] Deviations from *trans* additions are observed, however, when the nucleophile is an amine[16-18] and when the solvent medium is varied in polarity.[17,18]

The synthetic usefulness of base-catalyzed addition of alcohols to α,β-acetylenic esters has been demonstrated by the preparation of β-alkoxy-α,β-ethylenic esters[19,20] and β-keto esters.[20] The steric course of the reaction may be other than a *trans* addition. Jones and Whiting[16] previously had demonstrated that γ- and δ-hydroxyacetylenic esters in methanol with sodium methoxide yield lactones, a result that could be interpreted as a net *cis* addition of methanol followed by cyclization of the unstable *cis* adduct (eq 1), whereas Eaton and Stubbs[21] have shown that α,β-acetylenic ketones add methanol in base with an over-all *cis* result.



(1)

a, $R_1 = CH_3; R_2 = H; n = 0$
b, $R_1, R_2 = \text{-}(CH_2)_5\text{-}; n = 0$
c, $R_1 = R_2 = CH_3; n = 0$

The study described in this paper establishes the stereochemical course of the base-catalyzed addition of methanol to hexynedioic esters. Our particular choice of substituted hexynedioic esters **2** is for the following reasons: (a) the ready availability of the substrates (*vide infra*); (b) the possibility of trapping the vinyl carbanion, arising from a facile *trans* attack by methoxide,[10,22] by a subsequent cyclization; (c) the possibility of observing competing rearrangements to muconates.[23]

Synthesis of Hexynedioic Esters 2.—Outlined in Chart I are schemes used to synthesize the hexynedioic esters **2**. Pentynoic acids **1a** and **b** are obtained by Whitehead's method.[24] Over-all yields of 16% (for **1a**) and 35% (for **1b**) are obtained. Although the over-all yields may be low, the starting materials are inexpensive and the synthetic steps are well known. Large-scale reactions can be carried out thereby making acids **1a** and **1b** readily available.

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(1) Abstracted in part from the M.S. Thesis of D. K., Adelphi University 1968.

(2) Reviews of this subject may be found in (a) A. W. Johnson, "Chemistry of the Acetylenic Compounds," Vol. II, Longmans, Green and Co., New York, N. Y., 1950, pp 101–138 and 199–266; (b) R. A. Raphael, "Acetylenic Compounds in Organic Synthesis," Academic Press, New York, N. Y., 1955, pp 37–40, 44–45, and 170–191; (c) W. E. Truce in "Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press Inc., New York, N. Y., 1961, pp 112–120; (d) E. D. Bergmann, D. Ginsburg, and R. Pappo, *Org. Reactions*, **10**, 179 (1959).

(3) G. Stork and M. Tomasz, *J. Amer. Chem. Soc.*, **86**, 471 (1964).

(4) J. B. Hendrickson, R. Rees, and J. F. Templeton, *ibid.*, **86**, 107 (1964).

(5) W. E. Truce and R. Kassinger, *ibid.*, **80**, 6450 (1958), and earlier papers in this series.

(6) W. E. Truce and J. A. Simms, *ibid.*, **78**, 2756 (1956).

(7) W. E. Truce, H. G. Klein, and R. B. Kruse, *ibid.*, **83**, 4636 (1961).

(8) W. E. Truce and R. F. Heine, *ibid.*, **81**, 592 (1959).

(9) F. Montanari, *Tetrahedron Lett.*, 18 (1960).

(10) S. I. Miller, *J. Amer. Chem. Soc.*, **78**, 6091 (1956), and references cited therein.

(11) G. S. Krishnamurthy and S. I. Miller, *ibid.*, **83**, 3961 (1961).

(12) J. B. Hendrickson, *ibid.*, **84**, 653 (1962).

(13) W. E. Truce and R. F. Heine, *ibid.*, **79**, 5311 (1957).

(14) W. E. Truce, D. L. Goldhamer, and R. B. Kruse, *ibid.*, **81**, 4931 (1959).

(15) W. E. Truce, W. Bannister, B. Groten, H. Klein, R. Kruse, A. Levy, and E. Roberts, *ibid.*, **82**, 3799 (1960).

(16) E. R. H. Jones and M. C. Whiting, *J. Chem. Soc.*, 1423 (1949).

(17) J. E. Dolfini, *J. Org. Chem.*, **30**, 1298 (1965).

(18) R. Huisgen, B. Giese, and H. Huber, *Tetrahedron Lett.*, 1883 (1967); B. Giese and R. Huisgen, *ibid.*, 1889 (1967).

(19) (a) C. K. Ingold and E. H. Ingold, *J. Chem. Soc.*, **127**, 870 (1925); (b) E. H. Ingold, *ibid.*, **127**, 1199 (1925); (c) W. Wislicenus and K. Schollkopf, *J. Prakt. Chem.*, **95**, 269 (1917).

(20) (a) C. Moureu, *Bull. Soc. Chim. Fr.*, **31**, 493 (1904); *Compt. Rend.*, **137**, 259 (1903); **138**, 206 (1904). (b) L. N. Owen, *J. Chem. Soc.*, 385 (1945).

(21) P. E. Eaton and C. E. Stubbs, *J. Amer. Chem. Soc.*, **89**, 5722 (1967).

(22) S. I. Miller and G. Shkapenko, *ibid.*, **77**, 5038 (1955).

(23) E. R. H. Jones, G. H. Mansfield, and M. C. Whiting, *J. Chem. Soc.*, 3208 (1954).

(24) C. W. Whitehead, *J. Biol. Chem.*, **175**, 788 (1948).

CHART I

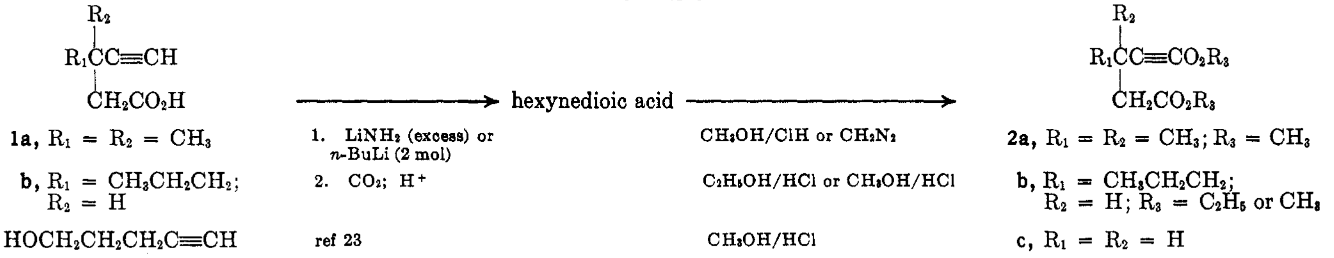
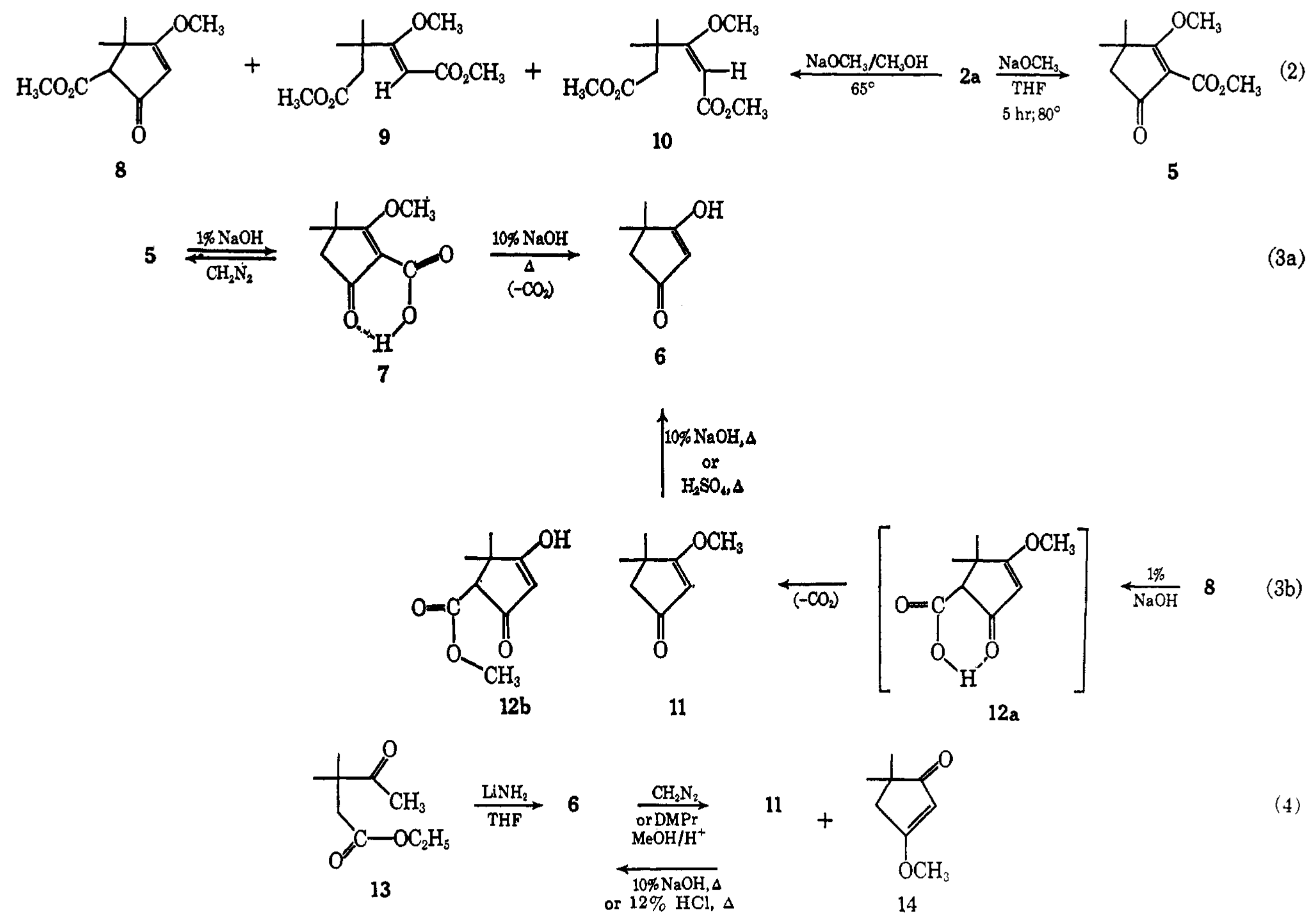
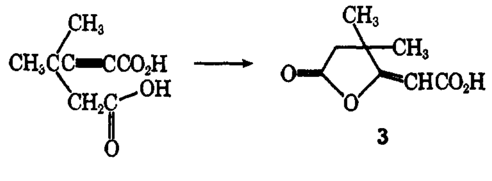


CHART II



Conversion into the hexynedioic esters is accomplished *via* the dilithium salt of 1 using the sequences shown. The hexynedioic acids are never purified since isolation procedures generally result in lactone formation (*e.g.*, **3**).



Unsubstituted 2-hexynedioic acid is prepared by the procedures of Jones, *et al.*;[23,25] esterification affords **2c**.

Reactions of Hexynedioic Esters. A. 4,4-Dimethyl-2-hexynedioic Acid Dimethyl Ester (2a).—The reactions of ester **2a** with sodium methoxide are summarized by eq 2 of Chart II. Identification of the products is based on combustion analyses, spectral characteristics, and chemical transformations (eq 3 and 4 of Chart II).

Treatment of **2a** with sodium methoxide in dry tetrahydrofuran gives only 4,4-dimethyl-3-methoxy-2-carbomethoxy-2-cyclopenten-1-one (**5**). Confirmation of the cyclic nature is provided by the hydrolysis and decarboxylation to 4,4-dimethylcyclopentane-1,3-dione (**6**), identical with material from base-catalyzed cyclization of ethyl β,β-dimethyl levulinate.

Stepwise loss of functionality from **5** can be demonstrated. With dilute sodium hydroxide (1%), only the ester is hydrolyzed and crystalline carboxylic acid **7** is isolated upon neutralization. Treatment of this acid with diazomethane re-forms **5**. Heating **7** in stronger base (10% NaOH) yields **6** upon acidification. If the last reaction is stopped before decarboxylation takes place, a white solid can be isolated after acidification. This material appears to be 4,4-dimethylcyclopentane-1,3-dione-2-carboxylic acid. However, any purification procedure only gives rise to crystalline **6**. In addition, the crude carboxylic acid melts with gas evolution and quantitatively yields **6**.

The reaction of **2a** with sodium methoxide in methanol gives products identified as 4,4-dimethyl-3-me-

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[25] G. Eglinton, E. R. H. Jones, and M. C. Whiting, *J. Chem. Soc.*, 2873 (1952).

thoxy-5-carbomethoxy-2-cyclopenten-1-one (**8**), *trans*-4,4-dimethyl-3-methoxy-2-hexenedioic acid dimethyl ester (**9**), and *cis*-4,4-dimethyl-3-methoxy-2-hexenedioic acid dimethyl ester (**10**).

Product distribution is found to vary with time and methanol concentration. Experimental data is presented in Tables I and II (see Experimental Section for details). The results indicate that (a) **9** and **10** are initial reaction products; (b) *cis* addition of methanol (**10**) is favored over *trans* addition (**9**); (c) loss of **10** coincides with the appearance of **8**; (d) neither **9** nor **10** isomerizes to the other; (e) the presence of water retards methanol addition and gives rise to lower yields of recovered materials.

Table I

Relative Per Cent[a] of Compounds with Time

Time, hr	Volatile[b] products	2a	9	10	8
0	. .	100	. .	. .	. .
0.5	2	35	27	34	2
1.0	4	15	37	38	6
2.5	11	8	37	28	16
4.0	16	9	37	17	21
12[c]	22	6	26	3	43

[a] Determined by vpc (column 2D; 180°; 200°) relative to an internal standard and are accurate to ±5%; the solvent is anhydrous methanol. [b] A multicomponent envelope which was eluted before starting material and products. [c] Reactions carried beyond 12 hr showed an increase in volatile products and corresponded to an over-all decrease in reaction products.

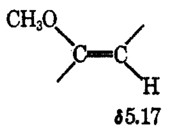
Table II

Distribution of Compounds in Varying Methanol Concentrations[a-c]

Solvent (%)	2a	9	10	Yield, % of recovered material
CH_3OH, H_2O (70, 30)	33	7	7	47
CH_3OH, H_2O (90, 10)	54	8	8	70
CH_3OH (100)	39	23	30	92
CH_3OH, THF (50, 50)[d]	22	26	40	88
CH_3OH, C_6H_6 (50, 50)[d,e]	47	18	29	94

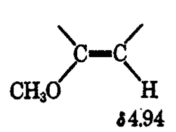
[a] Reactions stopped after 0.5 hr. [b] Vpc determined as in Table I. [c] Less than 2% **8** found in any run. [d] No **5** was found. [e] Reaction stopped after 1 hr.

Differentiation between the isomeric esters **9** and **10** rests upon the nmr spectrum of a 50:50 mixture which shows two vinyl singlets. The chemical shift upfield in the vinyl region, assigned to *cis* **10**, is consistent with an olefinic proton shielded by a neighboring *cis*-methoxyl group.[26]



trans **9**

and



cis **10**

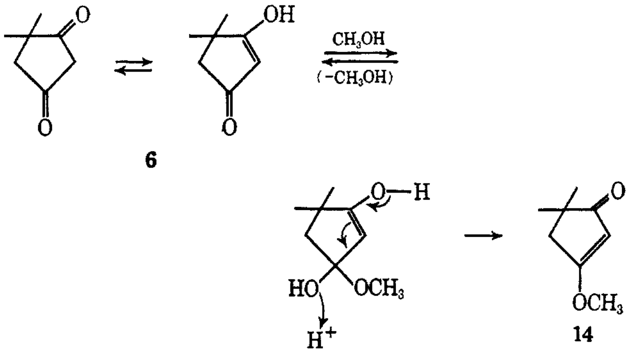
The loss of **10** in the reaction mixture on continued heating coinciding with the appearance of **8** also lends weight to the *cis* orientation of the methoxyl group and the proton about the double bond. The nmr spectrum of a pure sample of **9** confirms that this is the material with the vinyl signal at δ 5.17.

Ester **8** is isomeric with **5**. The cyclic nature of **8** is provided by its hydrolysis and decarboxylation to **6**.

Attempts at a stepwise hydrolysis of **8** only leads to 4,4-dimethyl-3-methoxy-2-cyclopenten-1-one (**11**). This probably arises from ester hydrolysis to the β-keto acid **12a** which then rapidly decarboxylates (eq 3b). The structure of **11** is authenticated by synthesis[27] and by its hydrolysis to **6**.

Treatment of **6** with excess diazomethane gives an equimolar mixture of enol ethers. These are separable by vpc; one of the enol ethers is identical with **11**. Its isomer **14** is spectrally similar to **11** (see Experimental Section) but can be differentiated by examination of the nmr spectra: the two-proton singlet at δ 2.32 for **11** belongs to the $-CH_2-$ adjacent to the carbonyl, while the two-proton singlet at δ 2.47 for **14** belongs to an allylic $-CH_2-$ adjacent to a methoxyl.[28]

Additional support for the assignments in 5,5-dimethyl-3-methoxy-2-cyclopenten-1-one (**14**) comes from the reaction of **6** with methanolic HCl in the presence of 2,2-dimethoxypropane (DMPr); **14** predominates over **11** by 19-fold. This is the expected result from acid-catalyzed hemiketal formation of the least hindered carbonyl followed by loss of water.



6

14

Thus, it is conclusive that the hydrolysis and decarboxylation of **8** yields **11** (*via* **12a**) and precludes any unusual rearrangements (such as decarboxylation with methyl migration to **14** from **12b**).

Cyclization of **2a** to esters **5** and **8** provides a relatively facile route to substituted cyclopentane-1,3-diones. Selective hydrolysis and decarboxylation of these esters represents a new method of synthesis for the enol ether **11** or the cyclopentanedione **6**.

B. 4-*n*-Propyl-2-hexynedioic Acid Diethyl Ester (2b).—The reaction of **2b** with sodium ethoxide in

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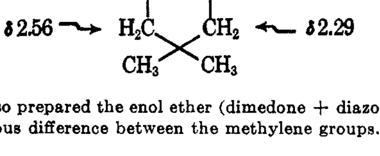
[26] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, pp 119–125.

[27] B. Eistert and W. Reiss, *Chem. Ber.*, **87**, 108 (1954).

[28] N. S. Bhacca, D. P. Hollis, L. F. Johnson, and E. A. Pier, "NMR Spectra Catalog," Vol. II, Varian Associates, Palo Alto, Calif., 1963; this interpretation draws analogy from the enolic form of dimedone (spectrum no. 512). We also prepared the enol ether (dimedone + diazomethane) and found an analogous difference between the methylene groups.



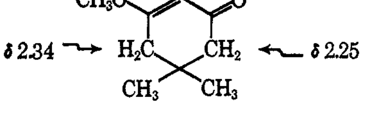
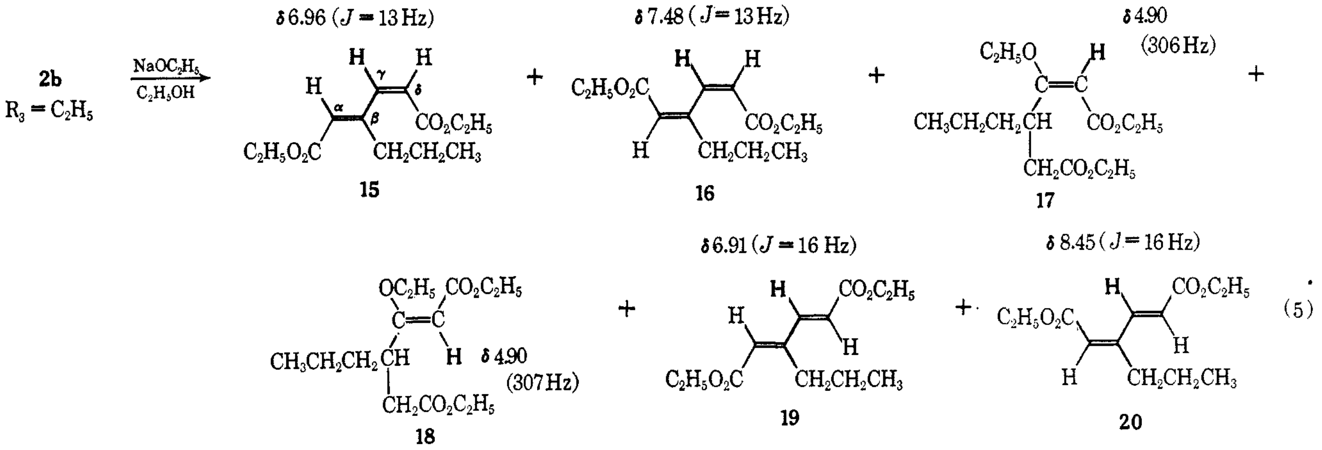


CHART III



ethanol gives mostly muconates. All possible muconic esters are formed in addition to the isomeric *cis*- and *trans*-β-ethoxy hexenedioic esters. Preparative vpc is useful in separating the products, but the columns available to us could not give single-component mixtures. Fortunately, the components are separated into isomeric pairs, thus permitting characterization and identification. The results are summarized in Chart III and are detailed in the Experimental Section.

Equation 5 shows the approximate order in which the compounds are eluted. The two-component mixtures are identified as I, ethyl *trans,cis*-β-*n*-propylmuconate (**15**) and ethyl *cis,cis*-β-*n*-propylmuconate (**16**); II, *cis*- and *trans*-3-ethoxy-4-*n*-propylhexenedioic acid diethyl esters (**17** and **18**); and III, ethyl *trans,-trans*-β-*n*-propylmuconate (**19**) and ethyl *cis,trans*-β-*n*-propylmuconate (**20**).

I is present in the least amount, 12%. The assignment of the geometry about the double bonds of these muconates is permitted by the nmr spectrum. Two lowfield vinyl doublets, δ 6.96 (J = 13 Hz) and 7.48 (J = 13 Hz), totaling one proton are present along with other signals. From the spin–spin coupling constants of these doublets, a cisoid geometry is established[7,29] for one double bond of each isomer. Therefore, the isomerism is caused by the geometry about the remaining double bond. The low field doublet is assigned to the all-*cis* muconate **16**; this assignment is in agreement with a deshielding effect due to the diamagnetic anisotropy of the cisoid ester carbonyl.[26] The remaining doublet belongs to **15** since the transoid nature of the second double bond precludes any deshielding effects. Integration gives a relative concentration of **15** to **16** as 2 to 1.

Mixture II makes up 40% of the isolated oil. Evidence for the assigned geometry in **17** and **18** is found in the nmr spectrum; two singlets of equal intensity are exhibited at δ 4.90 with a separation of 1 Hz. By analogy to compounds **9** and **10**, the higher field singlet belongs to **17** (*cis*) and the remaining lower field singlet is assigned to **18** (*trans*).

Compounds **19** and **20** make up the major portion of the reaction mixture (44% of the vpc volatile material). The compounds are isomeric to **15** and **16** and their respective geometrical assignments is provided by the nmr spectrum. The olefinic region exhibits two doublets at low field: δ 8.45 (J = 16 Hz; 0.4 protons), 6.91 (J = 15.5 Hz; 0.6 protons). The spin–spin coupling constants conclusively establish the presence of a *trans* double bond in each isomer.[7,29] This is in agreement with the generalization that *trans* isomers have higher coupling constants than their corresponding *cis* isomers. That the doublet at δ 8.45 belongs to **20**, the *cis,trans* isomer, follows from the δ 1.54 shift to lower field for the γ hydrogen, a result consistent with it being deshielded by two carbonyls.[26] Similar results are observed for the β-methyl muconic esters[30] and the parent muconic esters.[26] The all-*trans* isomer **19**, therefore, has the absorption at δ 6.91 (60% of the mixture by integration).

No cyclized material is found in the mixture.

C. 2-Hexynedioic Acid Dimethyl Ester (2c).—While the isolation of adducts **17** and **18** from **2b** was expected, the presence of all the possible muconic esters was not. Jones, Mansfield, and Whiting[23] rearranged 2-hexynedioic acid with base and observed a 23% yield (spectroscopic) of *trans,trans*-muconic acid; only 8% was isolated from work-up. No adduct was found, nor was any attempt made to detect or to isolate any *cis,trans* or *cis,cis* isomer, although it was suggested that they might be present. Considering the results from the reaction of **2b** with sodium ethoxide in ethanol, an investigation was carried out with **2c** in order to determine whether this ester would parallel our observations or those of Jones.

The reaction of **2c** with sodium methoxide in methanol yields methyl *trans,trans* muconate (**21**, 59%) and 3-methoxy-2-hexenedioic acid dimethyl ester (**22**, 41%) (Chart IV). A careful examination of the nuclear magnetic resonance spectrum and the vapor phase chromatogram of the crude material reveals no other products.

Compound **22** is easily isolated free from **21**. The nmr spectrum exhibits only a singlet at δ 4.95 and totals one vinyl hydrogen. The geometry about the double bond is uncertain; the presence of only one peak on vpc and a possible ambiguity in the chemical shift of a *cis*-vinyl proton *vs.* a *trans*-vinyl proton (*cf.* **17** and **18**) do not allow any conclusive assignment.

Some additional information for the rearrangement to the muconate is gained by carrying out the reaction in deuteriomethanol. The isolated product is *trans,-*

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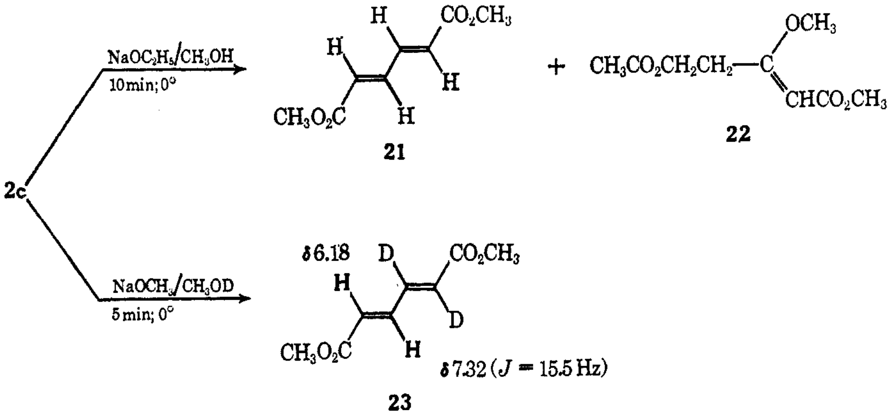
(29) See ref 26, p 85.

(30) J. Elvidge, *J. Chem. Soc.*, 474 (1959).

CHART IV



(6)

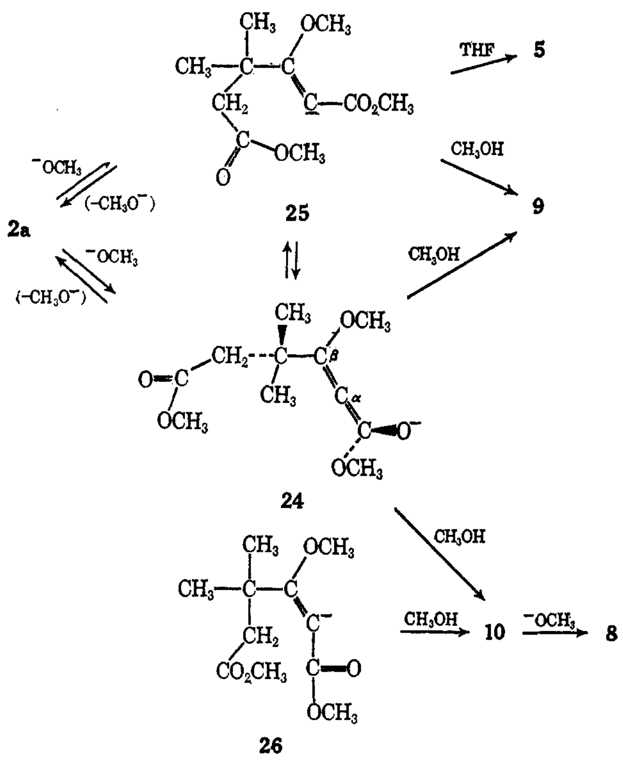
(7)

trans-α,β-d_2-muconate (**23**); a mixture melting point with **21** was undepressed (eq 7). The presence of deuterium is confirmed by the C–D stretch in the infrared spectrum (4.43 μ) and the presence of doublets in the vinyl region of the nmr spectrum: δ 7.32 (1.02 protons) and 6.18 (1.00 proton), J = 15.5 Hz, respectively.

Discussion

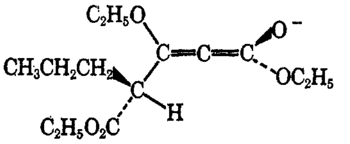
One rationalization for the products derived from **2a** is presented in Chart V. From the experimental results the reaction is a solvent dependent process. A deviation from a *trans*-nucleophilic addition to triple bonds is observed. When an external proton is lacking, *i.e.*, anhydrous tetrahydrofuran, the carbanion resulting from methoxide attack is trapped in a cyclization step;[4] thus, only **5** is isolated and *trans* addition is ostensively followed. In a solvent bearing a labile proton, *i.e.*, methanol, external protonation is kinetically faster, **9** forms in preference to cyclized material, but the *cis* adduct **10**, also arising from external protonation, predominates; thus, a deviation results.

CHART V



It is reasonable to assume that a stepwise process occurs in the methanolic medium. Attack of methoxide by Michael addition[2d] leads to the α,β-unsaturated enolate ion **24**.[17,18,31] In methanol the enolate would be solvated. Proton transfer from the solvated enolate anion leads to product. If **24** interconverts to **25** and **26**,[13] development of the sterically favored *trans* product should predominate, all other factors being equal, and *trans* adduct should result. A preference for the *cis* adduct probably results from a steric-approach controlled protonation step rather than a product-development controlled process. Models show that the bulky, alkyl side chain should hinder protonation from the side of attachment. Approach of solvent in the less hindered direction of the methoxy group should be favored and is the observed experimental result.

This argument is supported by the results from ethanol addition to ester **2b**; equimolar amounts of *cis* and *trans* adduct are found. A model of the enolate derived from **2b** shows that the favored conformation is sterically hindered equally on either side of the unsaturated system. Thus, protonation is equally probable from either direction. Unfortunately, a similar reaction with ester **2c** offers little support. The "single isomer" could also be a mixture of adducts, not separable by vpc and not distinguishable by nmr spectroscopy.



The source of ester **8** is simply from Dieckmann cyclization of **10**. In light of these results, the original

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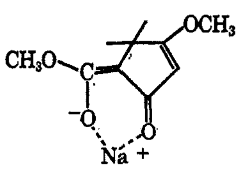
[31] E. H. Farmer, S. C. Ghosal, and G. A. R. Kon [*J. Chem. Soc.*, 1804 (1936)] have isolated the sodio derivative from ethyl phenylpropiolate and sodium malonate; they identified the adduct as the enolate by subsequent C alkylation. In our work-up procedures, isolation of **8** required strong acid conditions; this suggests that a similar type of sodio derivative was formed from cyclized product.



observations of Jones and Whiting[16] may also involve a net *cis* addition of methanol followed by lactonization (eq 1).

Finally, the change in the ratio of *trans* to *cis* adducts with time (Table I) eliminates the possibility that either isomer isomerizes to the other under the reaction conditions.

It is not certain whether a stepwise or a concerted process is involved with tetrahydrofuran as solvent. A concerted process gives **5** directly: coulombic repulsions between attacking methoxide and the displaced pair of electrons favors a *trans* orientation,[8] *i.e.*, anion **25**; attack of the electron-deficient carbonyl by the carbanion results in cyclization. However, arguments based on a stepwise sequence through **24** also leads to **5** since the anhydrous conditions preclude formation of either **9** or **10**.

Rearrangement to muconates is the principal reaction pathway for esters **2b** and **2c**. This competition with the addition reaction results from the availability of a labile propargylic proton. The first step probably is a base-catalyzed conversion of the α,β-acetylenic ester into an allenic system; this type of transformation is well known.[23,32] A proton of the methylene group, coplanar with the π cloud of the adjacent olefinic unit, is then lost giving the conjugated diene. The source of proton for both rearrangements is solvent. Further comment on the muconate distributions must await additional studies.

Experimental Section

General.—All melting points were taken in soft glass capillary tubes and are uncorrected; all boiling points are uncorrected. The ir spectra were measured on a Perkin-Elmer spectrophotometer, Model 237 or Model 337, and are recorded in microns; bands in the 5.0–7.0-μ region were calibrated against the 6.24-μ band of polystyrene. The uv spectra were run on a Cary Model 14 recording spectrophotometer and are recorded in mμ. Nuclear magnetic resonance spectra were taken on a Varian A-60 spectrometer; measurements are expressed in parts per million (δ) downfield from tetramethylsilane used as an internal standard. Vpc were carried out isothermally on equipment as follows: (1) an F & M Model 720 thermal conductivity gas chromatograph[33a] using (A) a column 4 ft × 0.25 in. packed with 20% Carbowax 1540 on Chromosorb P, regular (column 1A); (2) a Varian Aerograph Model A-700 thermal conductivity gas chromatograph[33] using (B) a column 6 ft × 0.25 in. packed with 5% Carbowax 20M on Chromosorb W, acid washed (column 2B), (C) a column 20 ft × 0.25 in. packed with 30% SE-30 Chromosorb W, acid washed (column 2C), or (D) a column 8 ft × 0.25 in. packed with 5% Carbowax 20M on Anakrom ABS (column 2D). Compound ratios were calibrated against mixtures of known composition and were found to be accurate to ±5%. Microanalyses were performed by Micro-Tech Laboratories, Inc., Skokie, Ill. Mass spectra were obtained on a Perkin-Elmer Hitachi Model RMU-6D mass spectrometer.

3,3-Dimethyl-4-pentynoic Acid (1a).—This acid was prepared according to the method of Whitehead[24] in 16% over-all yield starting from 3-methyl-1-butyn-3-ol:[34] bp 75–76° (2 mm) [lit.[24] bp 75–77° (2 mm)].

4,4-Dimethyl-2-hexynedioic Acid Dimethyl Ester (2a).—The dimethyl ester **2a** could be obtained from acid **1a** by using two different procedures.

Procedure A.—3,3-Dimethyl-4-pentynoic acid (15.0 g, 0.118 mol) in 50 ml of tetrahydrofuran was slowly added to a stirred slurry of lithium amide[35] (16.0 g, 0.652 mol) in 500 ml of tetrahydrofuran. The mixture was then heated at reflux for 48 hr. After cooling to room temperature, the mixture was then poured over a large excess of crushed Dry Ice and kept at room temperature for 1 hr. The solvent was removed *in vacuo*, and the residue was diluted with 300 ml of ether. A saturated aqueous sodium chloride solution was slowly added while the reaction mixture temperature was cooled below 15°. The heterogeneous solution was then acidified with 8 *N* H_2SO_4 to pH 2 at ice-bath temperature. The ethereal layer was separated and the aqueous layer was washed twice with 100-ml portions of ether. The combined ethereal layers were dried (anhydrous $MgSO_4$) and concentrated *in vacuo* giving 15 g of crude 4,4-dimethyl-2-hexynedioic acid.[36] The diacid was taken up in 200 ml of methanol containing 10 ml of H_2SO_4 and was refluxed for 3 hr. Isolation by standard procedures yielded **2a** (14 g, 61%), a clear liquid: bp 82° (0.2 mm); $n^{28.5}D$ 1.4525.

Procedure B.—To a tetrahydrofuran solution (500 ml) of 4,4-dimethyl-2-pentynoic acid (15.0 g, 0.118 mol), *n*-butyllithium in hexane (Foote Chemical Co.; 150 ml, 1.67 *M*) was added dropwise. The mixture was stirred for 15 min at room temperature before pouring onto crushed Dry Ice. Work-up as in procedure A gave 18 g of crude hexynedioic acid.[36] An ether solution of the diacid when treated with excess diazomethane gave 17 g (74%) of pure **2a** after distillation.

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.94; H, 7.35.

The spectral characteristics of **2a** are as follows: ir (film), 4.48 (C≡C), 5.75 (saturated ester C═O), 5.83 μ (unsaturated ester C═O); nmr (neat), δ 3.65 (s, 3), 3.60 (s, 3), 4.15 (s, 2), and 1.35 (s, 6).

3-*n*-Propyl-4-pentynoic Acid (1b).—This acid was prepared in a similar manner as 4, 4-dimethyl-2-pentynoic acid (**1a**) using the procedures described by Whitehead.[24] Starting from 1-hexyn-3-ol[34] an over-all yield of 35% of **1b** was obtained as a water-white liquid: bp 76–78° (0.2 mm); $n^{28.5}D$ 1.4438.

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.42; H, 8.67.

The spectral characteristics of **1b** are as follows: ir (film), 3.04 (C≡C—H, s), 4.73 (C≡C, vw), 5.85 μ (acid C═O, s); nmr (CCl_4), δ 11.92 (s, 1), 3.00–2.40 [m, 3, made up of a m, broad, at 2.77 (center); s, sharp, at 2.57; d, J = 3 Hz, at 2.43 (center), -(**H**)CC**H**$_2$CO$_2$H], 2.01 (d, J = 2.5 Hz, 1, C≡C**H**), 1.70–1.20 (m, 4), and 1.10–0.80 (m, 3).

4-*n*-Propyl-2-hexynedioic Acid Diethyl Ester (2b).—Using procedure B (*vide supra*), 3-*n*-propyl-4-pentynoic acid (14 g, 0.1 mol) was converted into 23 g of crude 4-*n*-propyl-2-hexynedioic acid. The diethyl ester **2b** was prepared by azeotropic distillation of water from a solution of 70 ml of ethanol, 400 ml of benzene, and 4 ml of concentrated sulfuric acid with a Dean–Stark apparatus. Using standard isolation methods, 15 g (62% over-all) of **2b**, a colorless liquid, was obtained: bp 91–93° (0.2 mm); $n^{28.5}D$ 1.4515.

Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.86; H, 8.46.

The spectral characteristics of **2b** are as follows: ir (film), 4.47 (C≡C), 5.77 (saturated ester C═O), 5.85 μ (unsaturated ester C═O); nmr (CCl_4), δ 4.14 (q, J = 7 Hz, 4), 3.15–2.63 (m, 1, ⩾C—**H**), 2.53 and 2.43 [s and d (J = 2 Hz), 2, -C**H**$_2$—CO$_2$Et], and 1.70–0.70 [m, 13, made up of a multiplet at 1.53 (center); t, J = 7 Hz at 1.28; m, at 0.97 (center)]. The methyl ester was prepared by the same method: bp 94–96° (0.3 mm); $n^{28.5}D$ 1.4543.

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.09; H, 7.48.

2-Hexynedioic Acid.—This diacid was prepared in 8% over-all yield according to the method of Jones, *et al.*,[23,25] starting from tetrahydrofurfuryl alcohol: mp 140° (lit.[23] mp 139–140°).

2-Hexynedioic Acid Dimethyl Ester (2c).—2-Hexynedioic acid (15.0 g, 0.102 mol) was refluxed in 200 ml of methanol containing 2 ml of concentrated H_2SO_4. Isolation by standard techniques gave 10 g (58%) of **2c**, a clear liquid: bp 116° (0.2 mm); $n^{30}D$ 1.4586.

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[32] (a) G. Eglinton, E. R. H. Jones, G. H. Mansfield, and M. C. Whiting, *J. Chem. Soc.*, 3197 (1954); (b) K. Shingir, S. Hagishita, and M. Nakagawa, *Tetrahedron Lett.*, 4371 (1967).

[33] (a) Flow rate adjusted to 60 cc of He/min. (b) Use of this instrument was generously provided by the Revlon Research Center, Inc., New York, N. Y.

[34] We wish to thank Airco Chemicals and Plastics, Calvert City, Ky., for generous samples of this compound.

[35] Obtained from Matheson Coleman and Bell.

[36] The acid was not purified as further manipulations generally gave lactone **3** (*vide infra*).

Anal. Calcd for $C_8H_{10}O_4$: C, 56.46; H, 5.92. Found: C, 56.54; H, 5.91.

The spectral characteristics of **2c** are as follows: ir (film), 4.46 (C≡C), 5.75 (saturated ester C═O), 5.83 μ (unsaturated ester C═O); nmr (CCl_4), δ 3.70 and 3.68 (s and s, 6), and 2.63 (s, 4).

Reaction of 4,4-Dimethyl-2-hexynedioic Acid Dimethyl Ester (2a) with Sodium Methoxide. A. In Tetrahydrofuran.—4,4-Dimethyl-2-hexynedioic acid dimethyl ester (3.0 g, 15 mmol) was heated for 5 hr at 80° in a sealed tube with sodium methoxide[37] (2.3 g, 41 mmol) and tetrahydrofuran (35 ml). Upon cooling, solvent was removed *in vacuo* and the colored, solid residue was taken up in 50 ml of ether. Methanolic H_2SO_4 was added to the slurry, with cooling and good agitation, to give pH 2. Solid salts were removed by filtration and the filtrate was concentrated to a viscous oil, 2.6 g. Vpc (column 2C, 225°, retention time, 6 min) showed a single product; preparative vpc provided an analytical sample of 4,4-dimethyl-3-methoxy-2-carbomethoxy-2-cyclopenten-1-one (**5**).

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.58; H, 7.20.

The spectral characteristics of **5** are as follows: ir (film), 5.80 (unsaturated ester C═O), 5.90 (unsaturated C═O), 6.20 (enol ether C═C) μ; uv, λ_{max} (95% ethanol) 240 mμ (ε 9900); nmr ($CDCl_3$), δ 4.03 (s, 3), 3.82 (s, 3), 2.18 (s, 2) and 1.27 (s, 6).

B. In Methanol.—The data in Tables I and II was obtained by the following procedure. Ester **2a** (freshly distilled; 0.123 g, 0.622 mmol) in methanol (2.0 ml) with sodium methoxide[37] (0.069 g, 1.24 mmol) was heated at 65° in a sealed tube. At the indicated times, aliquots were withdrawn through a septum and worked up with a stock solution of 0.32 *M* H_2SO_4 in methanol. Two work-up procedures were used for each time interval and are illustrated by the following examples. (a) After heating for 1 hr, a 25-μl aliquot was withdrawn and the solution brought to a pH of 8 using 5 μl of the stock sulfuric acid solution. The composition of the solution was then determined by vpc (column 2D, 180°). (b) A second 20-μl aliquot was brought to a pH of 3 using 10 μl of the stock solution of sulfuric acid. The acidified mixture was warmed for 30 min at 50° [31] before determining its composition by vpc (column 2D, 200°).

Using these procedures only three products were found with retention times greater than **2a** (Table III); these were *trans*-4,4-dimethyl-3-methoxy-2-hexenedioic acid dimethyl ester (**9**), *cis*-4,4-dimethyl-3-methoxy-2-hexenedioic acid dimethyl ester (**10**), and 4,4-dimethyl-3-methoxy-5-carbomethoxy-2-cyclopenten-1-one (**8**).

TABLE III

Compd	Column temp, °C	Retention time, min	Work-up procedure
2a	180	5.4	a
9	180	7.8	a
10	180	8.8	a
8	200	7.8	b

Analytical samples were obtained by modifying reactions of the above scale to a single reaction time and work-up procedure. Using procedure a, a reaction was acidified after heating 1 hr (65°) and the 50:50 mixture of **9** and **10** was recovered by preparative vpc. Separation of the individual components by reinjection of the mixture and collection of each isomer in separate tubes was not successful; one isomer was generally contaminated by the other. An analysis of the isomeric mixture was obtained.

Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.57; H, 7.74.

Acidification of a 12-hr reaction (65°) according to procedure a yielded uncontaminated **9** after preparative vpc.

Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.26; H, 7.88.

The spectral characteristics of **9** are as follows: ir (film), 5.77 (saturated ester C═O), 5.82 (unsaturated ester C═O), 6.24 μ (enol ether C═C); uv, λ_{max} (95% ethanol), 241 mμ (ε 10,200); nmr ($CDCl_3$), δ 5.17 (s, 1), 3.84 (s, 3), 3.67 and 3.62 (two s, 6), 2.48 (s, 2), and 1.27 (s, 6).

Subtracting these absorptions from spectra of a mixture of 13% **9** and 87% **10**, the spectral characteristics of **10** are as follows: ir (film), 5.77 (saturated ester C═O), 5.82 (unsaturated ester C═O), 6.24 μ (enol ether C═C); nmr ($CDCl_3$), δ 4.94 (s, 1), 3.50 (two s), 2.95 (s, 2) and 1.35 (s). An analytical sample of **8** was obtained from a reaction similar to the last one but acidified according to procedure b.

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.52; H, 7.18.

The spectral characteristics of **8** are as follows: ir (film), 5.75 (saturated ester C═O), 5.90 (unsaturated C═O), 6.25 μ (enol ether C═C); uv, λ_{max} (95% ethanol) 237 mμ (ε 13,900); nmr ($CDCl_3$), δ 5.34 (s, 1), 3.88 (s, 3), 3.74 (s, 3), 3.50 (s, 1), 1.27 (s, 3) and 1.07 (s, 3).

Hydrolysis of 4,4-Dimethyl-3-methoxy-2-carbomethoxy-2-cyclopenten-1-one (5).—Hydrolysis of compound **5** (0.50 g, 2.5 mmol) with 10 ml of 1% NaOH at 70° for 20 min gave 4,4-dimethyl-3-methoxy-2-carboxy-2-cyclopenten-1-one (**7**) (0.31 g, 65%) after acidification and extraction with ether. Recrystallization from 30–60° petroleum ether–ether solution gave white needles: mp 90–92°.

Anal. Calcd for $C_9H_{12}O_4$: C, 58.68; H, 6.57; mol wt, 184. Found: C, 58.44; H, 6.63; mol wt, 184 (mass spectrometry).

The spectral characteristics of **7** are as follows: ir (Nujol), 3.7–4.3 (broad, OH), 5.83 (unsaturated acid C═O), 6.03 (unsaturated C═O), 6.35 μ (enol ether C═C); uv, λ_{max} (95% ethanol) 243 mμ (ε 19,100); nmr ($CDCl_3$), δ 11.37 (s, 1), 3.85 (s, 3), 2.50 (s, 2) and 1.25 (s, 6). Treatment of **7** with excess diazomethane in ether quantitatively gave **5**.

Compound **7** (0.20 g, 1.1 mmol) was hydrolyzed further in 10 ml of 10% NaOH when it was heated on a steam bath for 30 min. Following acidification and ether extraction, solid 4,4-dimethylcyclopentane-1,3-dione-2-carboxylic acid (0.11 g, 57%) was obtained: mp 110° dec; ir (Nujol), 5.83, 6.10 μ; no satisfactory analysis was obtained.

Decarboxylation at the melting point quantitatively gave 4,4-dimethylcyclopentane-1,3-dione (**6**), white needles from ligroin, mp 95–97° (lit.[29] 97°); the mixture melting point with authentic material was undepressed (*vide infra*).

Hydrolysis of 4,4-Dimethyl-3-methoxy-5-carbomethoxy-2-cyclopenten-1-one (8).—Hydrolysis of compound **8** (0.50 g, 2.5 mmol) with 1% NaOH, by the procedure described for compound **5**, gave an oil (0.27 g, 75%). This oil was identical with 4,4-dimethyl-3-methoxy-2-cyclopenten-1-one (**11**) in all respects (*vide infra*).

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63; mol wt, 141. Found: C, 68.53; H, 8.67; mol wt, 141 (mass spectrometry).

The spectral characteristics of **11** are as follows: ir (film), 5.95 (unsaturated C═O), 6.30 μ (enol ether C═C); uv, λ_{max} (95% ethanol) 237 mμ (ε 19,800); nmr ($CDCl_3$), δ 5.18 (s, 1), 3.85 (s, 3), 2.32 (s, 2) and 1.25 (s, 6). Compound **8** (0.50 g, 2.5 mmol) when heated with 10% NaOH, as described for compound **7**, gave a solid upon acidification and ether extraction. Recrystallization from ligroine gave **6**, white needles: mp 95–97° (lit.[27] 97°; does not depress melting point of material derived from **7** or of authentic material).

4,4-Dimethylcyclopentane-1,3-dione (6).—Ethyl β,β-dimethyl levulinate[38,39] (15.4 g, 0.100 mol) in tetrahydrofuran (45 ml) was refluxed for 7 hr with lithium amide[35] (15.6 g, 0.68 mol). Solvent was then removed *in vacuo* and replaced with 100 ml of ether. Saturated aqueous sodium chloride (100 ml) was added to the resulting slurry at a temperature below 10°. Following acidification with 6 *N* HCl, the ethereal layer was separated, dried (anhydrous $MgSO_4$), and concentrated to an oil. Crystallization from ligroin gave white needles: 6.2 g (49%); mp 97–99° (lit.[27] mp 97°); nmr ($CDCl_3$), δ 12.97 (s, 1), 5.18 (s, 1), 2.42 (s, 2), and 1.20 (s, 6); uv, as reported by Eistert and Reiss.[27]

The 2-bromo derivative was also prepared[39] and gave needles from chloroform: mp 202–202.5° (lit.[39] mp 203°).

4,4-Dimethyl-3-methoxy-2-cyclopenten-1-one (11) and 5,5-Dimethyl-3-methoxy-2-cyclopenten-1-one (14). A.—The enol ethers **11** and **14** were prepared from 4,4-dimethylcyclopentane-1,3-dione and diazomethane using the method of Eistert and Reiss.[29] Preparative vpc (column 2B, 160°) separated the equimolar mixture into the individual components (see Table IV). The faster moving compound was identical in all respects with **11**. The slower moving component of the mixture was the isomer **14**, a clear oil.

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[37] Obtained from Matheson Coleman and Bell containing a minimum of 98% sodium methoxide.

[38] N. R. Easton and R. D. Dillard [*J. Org. Chem.*, **27**, 3602 (1962)] describe a convenient preparation of β,β-dimethyl levulinic acid from **1a**; the ethyl ester[39] was prepared from this acid by standard techniques.

[39] E. Rothstein and J. F. Thorpe, *J. Chem. Soc.*, 2011 (1926).

TABLE IV

Compd	Retention time, min	Rel % in mixture Method A	Rel % in mixture Method B
11	14.2	48	5
14	16.8	52	95

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.35; H, 8.65.

The spectral characteristics of **14** are as follows: ir (film), 5.93 (unsaturated C=O), 6.28 μ (enol ether C=C); uv, λ_{max} (95% ethanol) 237 mμ (ε 17,100); nmr ($CDCl_3$), δ 5.18 (s, 1), 3.85 (s, 1), 2.47 (s, 2) and 1.15 (s, 6).

B.—Heating 4,4-dimethylcyclopentane-1,3-dione (0.63 g, 5.0 mmol) in methanol (3 ml) and 2,2-dimethoxypropane (10 ml) containing 1 ml of ethereal HCl (*ca.* 15% solution) for 3 hr at reflux gave an oil (0.63 g, 90%) after solvent removal and short-path distillation. Vpc (column 2B, 160°) showed primarily **14** to be present.

Hydrolysis of 4,4-Dimethyl-3-methoxy-2-cyclopenten-1-one (11). A.—Enol ether **11** (0.35 g, 2.5 mmol) in 10 ml of 10% NaOH was heated for 30 min at 75°. Neutralization followed by ether extraction gave **6** (0.2 g, 67%) identical with authentic material.

B.—Enol ether **11** (0.35 g, 2.5 mmol) heated in 10 ml of 12% HCl for 30 min at 75° gave **6** (0.18 g, 61%) when isolated, identical with authentic material.

3-Hydroxy-4,4-dimethyl-2-hexenedioic Acid γ-Lactone (3).—Crude 4,4-dimethyl-2-hexynedioic acid when allowed to stand at room temperature deposited white needles. This solid was separated from the oil by triturating with ether. Recrystallization from isopropyl alcohol gave **3** as needles, mp 184–185°.

Anal. Calcd for $C_8H_{10}O_4$: C, 56.46; H, 5.92. Found: C, 56.70; H, 6.00.

The spectral characteristics of **3** are as follows: ir ($CHCl_3$), 3.4–3.6 (broad, OH), 5.48 (γ-lactone C=O; γ-exocyclic C=C), 5.88 (unsaturated acid C=O), 6.02 μ (C=C); uv, λ_{max} (95% ethanol) 224 mμ (ε 9,700); nmr ($CDCl_3$), δ 11.50 (s, 1), 5.05 (s, 1), 2.38 (s, 2), and 1.30 (s, 6). The methyl ester **4** was quantitatively obtained by treating **3** with diazomethane. A single recrystallization from chloroform–carbon tetrachloride gave **4** as white plates, mp 57–58°.

Anal. Calcd for $C_9H_{12}O_4$: C, 58.68; H, 6.57. Found: C, 58.51; H, 6.47.

The spectral characteristics of **4** are as follows: ir ($CHCl_3$), 5.48 (γ-lactone C=O; γ-exocyclic C=C), 5.85 (unsaturated ester C=O), 5.96 μ (C=C); uv, λ_{max} (95% ethanol) 224 mμ (ε 10,700); nmr ($CDCl_3$), δ 4.98 (s, 1), 3.68 (s, 3), 2.37 (s, 2) and 1.32 (s, 6).

Reaction of 4-*n*-Propyl-2-hexynedioic Acid Diethyl Ester (2b)[40] **with Sodium Ethoxide.**—A solution of **2b** (5.0 g, 0.021 mol) in ethanol (70 ml) containing sodium ethoxide [from Na metal (0.98 g, 0.042 g-atom) and ethanol (10 ml)] was stirred at room temperature for 12 hr. The solution was concentrated to 35 ml, diluted with 35 ml of ether, and mixed with 35 ml of saturated aqueous sodium chloride. The ethereal layer was separated, dried (anhydrous $MgSO_4$), and concentrated; an oil resulted (4.5 g). Vpc analysis showed a mixture; column 1A and column 2B gave comparable results; the data is listed in Table V.

Separation of the components for characterization purposes was carried out using column 1A (185°); 96% of the recovered oil was identified by analyzing the isomeric mixtures.

Mixture I, composed of ethyl *trans,cis*-β-*n*-propylmuconate (**15**) and ethyl *cis,cis*-β-*n*-propylmuconate (**16**), was a clear oil: ir (film), 5.83 (unsaturated ester C=O), 6.22 μ (C=C); nmr (CCl_4), δ 7.48 and 6.96 (d, *J* = 13 Hz for **16**, and d, *J* = 13 Hz for **15**, respectively; total 1 proton), 5.9–5.4 (m, 2), 4.4–3.8 (m, 4), 2.5–2.1 (m, 2), and 1.8–0.66 (m, 11).

Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39; mol wt, 240. Found: C, 65.15; H, 8.73; mol wt, 240 (mass spectrometry).

Mixture II, composed of *cis*- and *trans*-3-ethoxy-4-*n*-propylhexenedioic acid diethyl esters (**17** and **18**), was a colorless oil: ir (film), 5.77 (saturated ester C=O), 5.86 (unsaturated ester C=O), 6.15 μ (enol ether C=C); nmr (CCl_4), δ 4.90 (two singlets separated by 1 Hz, equal intensity, 1), 4.5–3.4 (m, 6), 3.1–2.1 (m, 3) and 2.1–0.66 (m, 16).

TABLE V

DISTRIBUTION OF PRODUCTS FROM **2b**

Mixture	Compound	Column 1A (185°) Retention time,^{a} min	Column 1A (185°) Rel %	Column 2B (185°) Retention time,^{a} min	Column 2B (185°) Rel %
	volatile unknowns	4.5	4^b	5.2	3
I	**15**	7.8	$(66)^c$	6.8	9
			12^b		
	16		(34)	8	5
II	**17**	13	$(50)^c$	10.2	39^b
			40^b		
	18		(50)	11.2	
III	**19**	20	$(60)^c$	13.6	44^b
			44^b		
	20		(40)	14.3	

^{a} Retention times refer to the point of maximum height for the chromatogram peaks. ^{b} Peak areas are for pairs of compounds; the vpc columns available were unable to separate the components completely for accurate estimates of per cent composition. ^{c} Relative per cent obtained from the nmr of the crude mixture, accurate to ±5%.

Anal. Calcd for $C_{15}H_{26}O_5$: C, 62.91; H, 9.15. Found: C, 63.19; H, 9.08.

Mixture III, composed of ethyl *trans,trans*-β-*n*-propylmuconate (**19**) and ethyl *cis,trans*-β-*n*-propylmuconate (**20**), was a clear oil: ir (film), 5.85 (unsaturated ester C=O), 6.15 and 6.25 μ (C=C); nmr (CCl_4), δ 8.45 and 6.91 (d, *J* = 16 Hz for **20**, and d, *J* = 15.5 Hz for **19**, respectively; total 1 proton), 6.2–5.7 (m, 2), 4.4–3.8 (m, 4), 2.6–2.1 (m, 2), and 1.9–0.7 (m, 11).

Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.82; H, 8.44.

Treatment of 2-Hexynedioic Acid Dimethyl Ester (2c) with Sodium Methoxide. A. In Anhydrous Methanol.—Sodium metal (0.059 g) was treated with anhydrous methanol (1.5 ml) in the cold under a nitrogen atmosphere. The ester **2c** (0.508 g, 3.0 mmol), in 2.0 ml of anhydrous methanol, was quickly added to the sodium methoxide solution at ice-bath temperature. A white solid formed after 2 min. The solution was stirred an additional 8 min before collecting the solid by filtration. Following a wash with 5 ml of cold methanol, the methyl *trans,trans*-muconate (**21**) was air dried: 0.178 g; white needles from chloroform; mp 156.5–157.5° (lit.[23] 157–158°). The filtrate was acidified (to pH 5) with methanolic HCl (*ca.* 5%), and insoluble salts were separated. Methanol was removed *in vacuo*. The residue was taken up in chloroform (5 ml), dried (anhydrous $MgSO_4$), and finally concentrated to an oil (0.287 g). Vpc (column 1A, 185°) showed the presence of two compounds (Table VI). Preparative vpc (column 1A, 185°) removed the muconate **21** from 3-methoxy-2-hexenedioic acid dimethyl ester (**22**), a colorless oil.

TABLE VI

Compd	Retention time, min	Rel % in mixture
21	7.5	33 (0.095 g)
22	12.5	67 (0.192 g)

Anal. Calcd for $C_9H_{14}O_5$: C, 53.47; H, 6.97. Found: C, 53.57; H, 7.12.

The spectral characteristics for **22** are as follows: ir (film) 5.78 (saturated ester C=O), 5.88 (unsaturated ester (C=O), 6.18 μ (enol ether C=C); nmr (CCl_4), δ 4.95 (s, 1), 3.62 (s, 9), 3.23–2.75 (m, 2), and 2.63–2.16 (m, 2).

B. In Methanol-d_1.[41]—Ester **2c** (0.310 g, 1.8 mmol) in methanol-d_1 (1.5 ml) was added to a cold sodium methoxide solution [from 0.084 g (3.6 g-atoms) of sodium metal and 4.0 ml of methanol-d_1]. The mixture was stirred an additional 5 min before the methyl *trans,trans*-α,β-d_2-muconate (**23**) was isolated: 0.062 g; mixture melting point with **21** was undepressed; ir (KBr),

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[40] The diethyl ester was used because the reaction products could be separated by vpc; a similar reaction mixture was obtained when the methyl ester was used, but vpc could not suitably separate the products for identification.

[41] Obtained from Stohler Isotope Chemicals, Montreal, Canada, 99% D.

4.43 μ (C-D str); nmr ($CDCl_3$), δ 7.32 (d, J = 15.5 Hz, 1.02), 6.18 (d, J = 15.5 Hz, 1.00), and 3.78 (s, 6)

Registry No.—Methanol, 67-56-1; **1b**, 17038-07-2; **2a**, 17037-89-7; **2b** ($R_3 = C_2H_5$), 17037-90-0; **2b** ($R_3 = CH_3$), 17037-91-1; **2c**, 3402-60-6; **3**, 17038-08-3; **4**, 17037-93-3; 4,4-dimethylcyclopentane-1,3-dione-2-carboxylic acid, 17037-94-4; **5**, 17037-95-5; **7**, 17037-97-7; **8**, 17037-96-6; **9**, 17038-09-4; **10**, 17038-10-7; **11**, 17037-98-8; **14**, 5921-03-9; **15**, 17038-00-5; **16**, 17038-01-6; **17**, 17038-02-7; **18**, 17038-03-8; **19**, 17038-04-9; **20**, 17038-05-0; **22**, 17038-06-1.

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The Synthesis and Stereochemical Assignment of *cis*- and *trans*-2-Methyl-2-pentenoic Acid and the Corresponding Esters, Aldehydes, and Alcohols[1a]

K. C. Chan,[1b] Richard A. Jewell, William H. Nutting, and Henry Rapoport

Department of Chemistry, University of California at Berkeley, Berkeley, California 94720

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The title compounds were prepared by standard procedures. The *trans* acid, ester, and alcohol are distinguished from the corresponding *cis* isomers in the nmr spectrum by the chemical shift of the β-vinyl proton which lies at lower field by 0.82, 0.82, and 0.10 ppm, respectively, in $CDCl_3$. In the aldehydes, however, the β-vinyl proton signals are separated by only 0.01 ppm and cannot be used to distinguish the isomers. Differentiation can be made *via* the aldehydic proton signal which lies 0.73 ppm downfield in the *cis* isomer. The difference in chemical shift of the β-vinyl protons increases to 0.98, 1.08, and 0.15 ppm in C_6D_6 for the acid, ester, and alcohol, respectively, but remains essentially unchanged in the aldehydes. Solvent shifts, $\Delta = \delta_{CDCl_3} - \delta_{C_6D_6}$, were calculated and found useful for the stereochemical assignment of the acids and esters but not for the aldehydes and alcohols for which one must rely upon the chemical shift of the appropriate protons.

Several methods for assigning the stereochemistry of *cis–trans* carbon–carbon double-bond isomers are available.[2] Of these the application of nmr spectroscopy is well suited to the problem of trisubstituted ethylenes and has been applied with respect to isoprenoids of the type alkyl-$CH_2(CH_3)C{=}CH(CH_2OH)$,[3a] -(CHO),[3b] -($COOCH_3$).[3c] On the other hand, there are an increasing number of diversified[4] natural products containing the partial structure $RCH{=}C(CH_3)R'$ where R = dialkyl -CH- or most often alkyl $-CH_2-$ and R′ = CH_2OH,[4] CHO,[5] COOH,[6] and $COOCH_3$.[7] Although studies have been made for the acids and esters,[8] no model compound studies of the application of nmr spectra to the stereochemistry of such aldehydes and alcohols have been reported.

We therefore decided to synthesize the *cis* and *trans* isomers of 2-methyl-2-penten-1-ol since they would serve as models for a number of sesquiterpene alcohols recently characterized.[4b,9] In addition, these isomers would have the advantage[10] of being homologs of angelic and tiglic acid. Preparation of the corresponding aldehydes was also desirable since the assignment of their stereochemistry is not well documented.[11] The acids and esters were also prepared for comparison with previous studies and thus provide an additional basis for the assignment of stereochemistry to the aldehydes and alcohols.

Synthesis.—The synthesis of any one pair of isomers would afford the other pairs of isomers by standard transformations. Since the synthesis and separation of the isomeric acids had been reported,[12] these were the starting materials for the syntheses outlined in Scheme I. Hydrolysis of 2-pentanone cyanohydrin yielded the expected 2-hydroxy-2-methylpentanoic acid (**1**). Pyrolysis of **1** afforded a product from which the isomerically pure (*E*)-2-methyl-2-pentenoic acid[13] (**2**) was obtained after spinning-band distillation. However, the fraction containing the *cis* isomer, (*Z*)-2-methyl-2-pentenoic acid (**3**), was contaminated with an impurity exhibiting nmr vinyl proton signals at δ 5.61 (q, $J \sim 1.5$ Hz) and 6.28 (d, $J \sim 1.5$ Hz)[14] which is consistent with the formation of 2-methylene-

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[1] (a) Supported in part by the National Science Foundation. (b) On leave from the Department of Chemistry, University of Malaya, Kuala Lumpur.

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