The Carboxylation of Cyclooctatetraene Dianion. Structures and Reactions of the Dicarboxylic Acids Produced[1]

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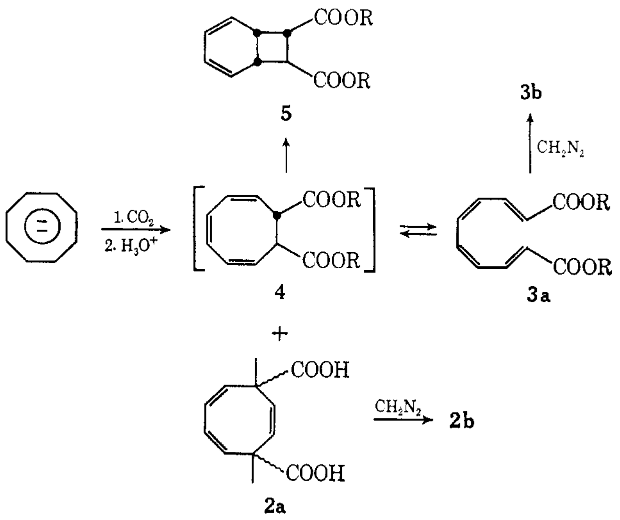
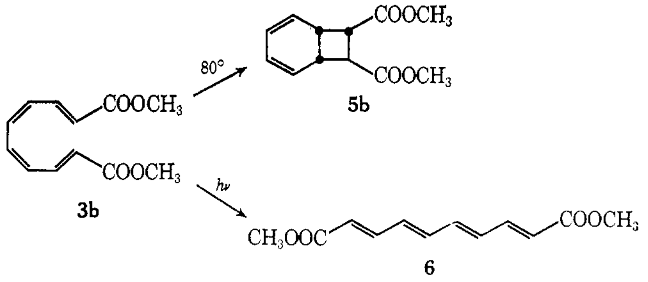
Abstract: The carboxylation of cyclooctatetraene dianion gives chiefly 2,4,6,8-decatetraene-1,10-dioic acid, accompanied by minor amounts of 2,5,7-cyclooctatriene-1,4-dicarboxylic acid. The major product, isolated as its dimethyl ester, evidently arises by electrocyclic ring opening of an initially produced 1,3,5-cyclooctatriene-7,8-dicarboxylic acid. The linear ester undergoes thermal isomerization *via* electrocyclic closure to *trans*-7,8-dicarbomethoxybicyclo[4.2.0]octadiene. Photolysis of the linear ester results in *cis–trans* isomerization to the stable all-*trans*-dimethyl-2,4,6,8-decatetraene-1,10-dioate. The factors governing the course of the observed transformations are discussed.

Considerable recent interest has centered about cyclooctatetraene dianion (**1**) because of its aromatic character[2] and chemical behavior.[3] The chemistry of **1** has proven to be much more varied and interesting than originally suspected;[4] intramolecular reactions occur in its alkylation[3a] and acylation.[3b] In the latter and in its condensation reactions with aldehydes and ketones[3c] diverse products are formed whose chemistry leads to a variety of classes of compounds.

The carboxylation of cyclooctatetraene dianion was originally reported by Reppe, in his early survey of cyclooctatetraene chemistry,[4] to lead to 2,5,7-cyclooctatriene-1,4-dicarboxylic acid (**2**). Reppe's finding that the protonation of **1** gave 1,3,6-cyclooctatriene was shortly thereafter confirmed by Cope[5] and there seemed no reason to doubt the structure assignment given by Reppe to the carboxylation product of **1**. However, in view of the results of our recent investigations of the chemistry of cyclooctatetraene dianion, in which many of the structures reported by early workers in the chemistry of **1** were shown to be erroneous,[6] it seemed worthwhile to establish the structure of the carboxylation product of **1** with certainty.



2a,3a,4a, R = H
2b,3b,4b, R = CH_3



5b $\xrightarrow{H_2-Pd}$ **7**

2b $\longrightarrow$ **8**

It has presently been found that carboxylation of lithium or potassium cyclooctatetraenide in ether–tetrahydrofuran gives *trans,cis,cis,trans*-2,4,6,8-decatetraene-1,10-dioic acid (**3a**, 50–65%), accompanied by small amounts of 2,5,7-cyclooctatriene-1,4-dicarboxylic acid (**2a**, 2–3%) (eq 1). Thus, addition of solutions of **1** (*ca.* 0.5 *M*) in ether–tetrahydrofuran to powdered solid carbon dioxide gave after acidification a dull yellow solid, mp 270–282° dec. This material, evidently a mixture of dicarboxylic acids, could be recrystallized only with difficulty and for convenience in handling was converted to the corresponding dimethyl ester mixture by treatment with excess diazomethane. By direct crystallization there was isolated pure **3b** as golden yellow blades, mp 114–115°. The gross structure of **3b** was proved by its conversion on hydrogenation over palladium–charcoal to dimethyl sebacate, identified by comparison with authentic material. The geometry of the double bonds of **3b** was assigned on the basis of the following evidence: (1) the nmr signals for the vinyl hydrogens comprise a pattern very similar to that shown in the spectrum of the known *trans,cis,-cis,trans*-dodecatetraene-2,11-dione,[3b] including *inter*

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[1] Preliminary report: *Tetrahedron Lett.*, 5635 (1968).

[2] (a) D. Lloyd, "Nonbenzenoid Aromatic Compounds," Elsevier, Amsterdam, 1966, Chapter VII; (b) T. J. Katz, *J. Amer. Chem. Soc.*, **82**, 3784, 3785 (1960).

[3] (a) T. J. Katz and P. J. Garrett, *ibid.*, **86**, 5194 (1964); (b) T. S. Cantrell and H. Shechter, *ibid.*, **89**, 5868 (1967); (c) T. S. Cantrell and H. Shechter, *ibid.*, **89**, 5877 (1967); (d) K. H. Conrow and D. A. Bak, *J. Org. Chem.*, **31**, 3958 (1966); (e) T. J. Katz, C. R. Nicholson, and C. A. Reilly, *J. Amer. Chem. Soc*, **88**, 3832 (1966).

[4] W. Reppe, O. Schlichting, K. Klager, and T. Toepel, *Justus Liebigs Ann. Chem.*, **560**, 1 (1948).

[5] A. C. Cope and F. A. Hochstein, *J. Amer. Chem. Soc.*, **72**, 2512 (1950).

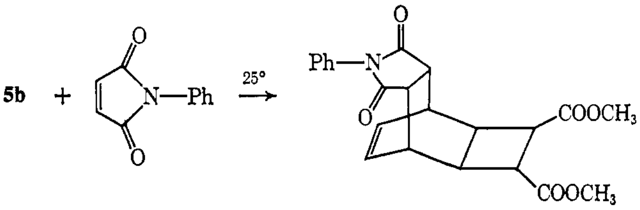
[6] Compare ref 3b and c and V. Azatyan, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **14**, 451 (1961).

alia, a doublet at τ 4.02 ($J = 16.0$) and a pair of doublets at τ 2.24 ($J = 16.0, J' = 11.8$), due to the hydrogens α and β to the carbomethoxyls, respectively; from the magnitude of $J_{\alpha,\beta}$ the outer double bonds are clearly *trans*; (2) the ultraviolet spectrum, which shows one broad maximum at long wavelength ($\lambda_{max}^{CH_3OH}$ 338 nm (36,000)), a characteristic of polyenes containing at least one *cis* double bond;[7] (3) the efficient photoisomerization (3500 Å) of **3b** to dimethyl all-*trans*-2,4,6,8-decatetraene-1,10-dioate (**6**), identified by comparison with an authentic sample.[8] Previously we had reported that **6** was produced thermally from **3b**;[1] it appears that our earlier observations were in error and that the presence of **6** in reaction mixtures from heating of **3b** was due to adventitious room light. We now find that irradiation of **3b** at $-5°$ gives a near-quantitative yield of **6** and no **5b**.

Chromatography on silica gel of the mother liquors from crystallization of **3b** gave fractions whose nmr spectra indicated they were composed mainly of **2b**, 5,8-dicarbomethoxy-1,3,6-cyclooctatriene, plus some **5b**, *trans*-7,8-dicarbomethoxybicyclo[4.2.0]octa-2,4-diene. Pure diester **5b** was subsequently obtained by thermal isomerization of **3b** (see below); it seems likely that the **5b** present in the carboxylation–esterification mixture may be an artifact formed from **3a** or **3b** during work-up. Diester **2b**, the product of condensation of **1** at C-1 and C-4, was heat and air sensitive, like **5b**, and was not obtained in pure form. The nmr spectra of certain chromatographic fractions [τ 3.9–4.2 (multiplets, 6 H), 6.21 and 6.25 (3 H each, singlets), and 6.3–6.4 (2 H)] indicated they were composed mainly of **2b**, contaminated with some **5b** (singlets at 6.28 and 6.31). The presence of **2b** in the reaction mixture from carboxylation of **1** was firmly established, and the amounts present of the sensitive compounds **2b** and **5b** were determined by hydrogenation of the mother liquors remaining after removal of most of the acyclic ester **3b** by crystallization, and analysis and separation of the resulting mixture of saturated esters. This mixture contained dimethyl sebacate (25%) from reduction of **3b** still present, as well as *trans*-7,8-dicarbomethoxybicyclo[4.2.0]octane (**7**, 20%) and *cis*- and *trans*-1,4-dicarbomethoxycyclooctane (**8**, 25%, 3% yield). Saturated diester **7** was identified by comparison with a sample obtained by hydrogenation of pure **5b** obtained from thermal isomerization of **3b** (see below). The cyclooctanedicarboxylic esters **8a** and **8b** were identical with samples synthesized by an unambiguous route.[9]

Heating oxygen-free solutions of tetraenic ester **3b** in benzene (5 hr at 80°) resulted in isomerization to *trans*-7,8-dicarbomethoxybicyclo[4.2.0]octa-2,4-diene (**5b**), mp 35–36°. The structure of **5b** was deduced from analytical and spectral data, including infrared bands at 1726 and ~1190 cm^{-1} indicative of saturated ester functions, and an ultraviolet spectrum ($\lambda_{max}^{CH_3OH}$ 270 nm, ϵ 3000) characteristic of the bicyclo[4.2.0]octa-2,4-diene chromophore.[10]

The nmr spectrum of **5b** exhibited signals for four vinyl hydrogens at τ 4.0–4.7, for two methine hydrogens at 6.05–6.24, two three-hydrogen singlets at 6.28 and 6.31 for the methoxyls, and multiplets worth two hydrogens at τ 6.5–7.0, assignable to the tertiary allylic hydrogens at C-1 and C-6. Further evidence in support of structure **5b** was its facile Diels–Alder addition to N-phenylmaleimide (20°, 4 hr) to give adduct **9**, mp 185°.



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Esterification of **3a** in refluxing methanol containing a trace of sulfuric acid led to a somewhat different product, although erratically. In addition to considerable amounts of esters **3b** and **5b** there was isolated, after chromatography on silica gel, a product assigned the structure 2,5-dicarbomethoxybicyclo[4.2.0]octa-2,4-diene (**10**). The structural assignment is supported by infrared bands in the spectrum of **10** characteristic of α,β-unsaturated ester (1708 cm^{-1}) and conjugated double bond functions (1572 cm^{-1}), by the nmr spectrum [τ (CCl_4) 2.28 (2 H, singlet, vinyl H), 6.20 (6 H, singlet, OCH_3), ~6.3 (2 H, multiplet, methine H), and 7.1–7.4 (4 H, multiplets, methylenes)], and by the ultraviolet spectrum, λ_{max}^{EtOH} 327 nm (ϵ 9200). The wavelength of the ultraviolet absorption maximum of **10** is exactly that predicted by adding an increment of 18 nm for the fused four-membered ring (the difference in λ_{max} of the parent hydrocarbons 1,3-cyclohexadiene and bicyclo[4.2.0]octadiene, 256 and 274 nm, respectively) to the position of the absorption maximum of the model system 1,4-dicarbomethoxy-1,3-cyclohexadiene, 309 nm.[11] The transformation of **3a** to **10** can be rationalized by an extensive series of thermal- and acid-catalyzed reorganizations. Pertinent here is the observation that, although some of the linear ester **3b** could be isolated, it was not converted to **10** by subsequent acid treatment.

Hydrolysis of esters **3b** and **5b** with cold aqueous base gave the corresponding free acids **3a** and **5a**, respectively, with no isomerization observed during the hydrolysis. The acids were identified by their infrared spectra and by the nmr spectra of their sodium salts (see Experimental Section).

Discussion

The condensation of cyclooctatetraene dianion with carbon dioxide has presently been found to occur almost exclusively at C-1 and C-2 of **1**, in contrast to its reactions with aldehydes and ketones, which give appreciable amounts of products resulting from re-

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(7) For discussions of this point see ref 3b and L. Zechmeister and J. H. Pinckard, *J. Amer. Chem. Soc.*, **76**, 4144 (1954).

(8) (a) R. Kuhn and C. Grundmann, *Ber.*, **69**, 1757 (1936); (b) J. R. Schenk, M. P. Hargie, D. S. Tarbell, and P. Hoffman, *J. Amer. Chem. Soc.*, **75**, 2274 (1953). We are grateful to Dr. Tarbell for furnishing a sample of the all-*trans* acid.

(9) The ester mixture **8** was prepared by hydrogenation of 1,6-dicarbomethoxy-1,3,5-cyclooctatriene; E. Vogel, O. Roos, and K.-H. Disch, *Justis Liebigs Ann. Chem.*, **653**, 55 (1962). (b) We thank Dr. J. J. Bloomfield for furnishing a sample of the ester mixture **8** prepared by another route; see footnote 10 in J. S. McConaghy, Jr., and J. J. Bloomfield, *Tetrahedron Lett.*, 1121 (1969).

(10) Known bicyclo[4.2.0]octadienes with substituents on C-7 and/or C-8 exhibit λ_{max} 269–275 nm (ϵ 2500–4000); (a) ref 3c; (b) A. C. Cope, A. C. Haven, Jr., F. L. Ramp, and E. R. Trumbull, *J. Amer. Chem. Soc.*, **74**, 4867 (1952); (c) A. C. Cope and M. Burg, *ibid.*, **74**, 168 (1952); (d) J. L. Kice and T. S. Cantrell, *ibid.*, **85**, 2298 (1963).

(11) G. Smith, C. L. Warren, and W. R. Vaughan, *J. Org. Chem.*, **28**, 3323 (1963).

action at C-1 and C-4.[3c] A further surprise was the observation that the presumed primary product, acid **4a**, underwent electrocyclic ring opening to the *linear* acid **3a**, rather than closure to the bicyclic isomer **5a**. The isolated products of condensation of **1** at C-1 and C-2 with aldehydes and ketones all possess the bicyclo[4.2.0]octadiene structure, with the single exception of the benzophenone adduct from **1** which is a linear decatetraene analogous to **3**. It seems unlikely that the preference shown by **4a** for opening to **3a** could be attributable to steric effects, such as are probably important in the case of the **1**-benzophenone product, in view of the much smaller size of the carboxyl group as compared to α-hydroxybenzhydryl. An explanation which seemed attractive, *a priori*, considers the electrostatic repulsion between the carboxylate functions of the dilithium salt of **4a**, which exists before protonation of the reaction mixture. The repulsion between the nearby carboxylate groups of the salt of **4** might be best relieved by ring opening to the salt of **3a**, in which the distance between negative charges would be much greater. This explanation seems unlikely to be correct however, in view of the observation that careful basic hydrolysis of **5b** gave acid **5a**, and not **3a**, which could be obtained from **5a** by two consecutive electrocyclic ring openings.

The opening of **4a** is most reasonably accounted for on the basis of the increased stability, relative to **4a**, of the linear structure **3a**, in which the carboxyl groups are in conjugation with the olefinic double bonds. Precedent exists for this behavior, in that previous attempts to prepare 1,3,5-cyclooctatrienes bearing unsaturated substituents at C-7 and/or C-8 have led to the corresponding octatetraenes.[3b,12]

The reasons for the thermal conversion of **3b** to **5b** at higher temperatures are not known; however this is apparently a general phenomenon for octatetraenes, since thermal equilibration of octatetraenes bearing alkyl and alkoxyl groups leads to mixtures in which bicyclo[4.2.0]octadienes predominate.[13,14]

The thermal and photochemical transformations observed here proceed in a manner predicted by the Woodward–Hoffman orbital symmetry correlations. Diacid **3a** evidently arises *via* a conrotatory ring opening on an initially formed 3,5,7-cyclooctatriene-*trans*-1,2-dicarboxylic acid.[2a] The linear diester **3b** undergoes thermal closure to **5b**, probably by way of the *trans* diester **4b**. The *trans* disposition of the carbomethoxy groups in **5b** supports the hypothesis that they are also *trans* in the monocyclic compounds **2a** and **2b**.

The photochemical conversion of **3b** to the all-*trans* ester **6** is somewhat surprising, since in hydrocarbon carotenoid polyenes large amounts of various isomers containing one or more *cis* double bonds are produced on irradiation. This behavior may be due to the absorption characteristics of the respective isomers.

Experimental Section

General. Infrared spectra were obtained in a Beckmann Model IR-8 grating instrument and ultraviolet spectra were recorded on a Cary Model 14 spectrophotometer. Nmr spectra were obtained on a Varian A-56/60A instrument operating at 46°. Mass spectral data were determined on a CEC Model 21-110B instrument at 70 eV. Gas chromatographic analyses and separations were performed on a Varian Aerograph Model 202-1 instrument, employing the following columns: column A, 5 ft × $^1/_4$ in. 15% SE-30 on 60–80 mesh Chromosorb W; column B, 5 ft × $^1/_4$ in. 15% Carbowax 20M on 60–80 mesh Chromosorb W; column C, 10 ft × $^1/_8$ in. 10% Carbowax 20M on 60–80 Chromosorb W; column D, 6 ft × $^3/_8$ in. 25% Carbowax 20M on 30–50 mesh Chromosorb P. Magnesium sulfate was used for all drying operations. Analyses were by the Elek Co., Torrance, Calif.

Carboxylation of Cyclooctatetraene Dianion (1). Dilithium cyclooctatetraenide was prepared by the general procedure previously described[3b] with the modification that the solvent employed was a 90:10 mixture of ether and tetrahydrofuran which had been freshly distilled from sodium and lithium aluminum hydride, respectively. A solution of **1** thus prepared (300 ml, *ca.* 0.3 *M*) was added rapidly to excess powdered Dry Ice, with vigorous stirring. A further 100-ml portion of ether was added, and after 20 min, water (200 ml). The layers were separated and the water washed once with ether (40 ml). The aqueous layer was carefully acidified by cooling to 0–5° and adding cold concentrated hydrochloric acid. Filtration and air drying of the lemon-yellow precipitate gave the crude acids (10.5 g, 57%). Recrystallization of a portion of this material from *n*-propyl alcohol or absolute ethanol gave a poor recovery (*ca.* 30%) of somewhat purer *trans,cis,cis,trans*-2,4,6,8-decatetraenedioic acid (**3a**) as a yellow powder, mp 271–280° dec. *Anal.* Calcd for $C_{10}H_{10}O_4$: C, 61.87; H, 5.5. Found: C, 60.02; H, 4.96. For separation and purification of the components, the acid mixture was directly converted to the corresponding methyl esters, as described below.

The crude acid mixture from carboxylation of **1** (10 g) was ground in a mortar to a fine powder and was added as a slurry in ether, in portions, to cold (0°) ethereal diazomethane prepared from N-nitrosomethylurea (12 g). The reaction mixture was stirred overnight while the excess diazomethane was allowed to evaporate. The ether was then removed under reduced pressure and the residue was extracted three times with warm ethyl acetate which had been flushed with nitrogen. The combined extracts were filtered and concentrated under reduced pressure. Cooling gave two crops of dimethyl-*trans,cis,cis,trans*-2,4,6,8-decatetraene-1,10-dioate (**3b**) as golden yellow blades: mp 113–114° (8.5 g); ir (KBr) 1701 (C=O), 1612 and 690 (C=C) cm^{-1}; uv (CH_3OH) max 338 nm (ϵ 36,000); nmr ($CDCl_3$) τ 2.24 (2 H, 2 doublets, J = 16.0, J' = 11.8 Hz, H-3 and H-8), 3.12 (2 H, m, H-5 and H-6), 3.60 (2 H, m, H-4 and H-7), 4.02 (2 H, doublet, J = 16.0 Hz, H-1 and H-9), 6.22 (6 H, s, OCH_3); mass spectrum *m/e* (parent) 222.

Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.88; H, 6.30. Found: C, 64.60; H, 6.39.

Evaporation of the solvent from the mother liquors from crystallization of **3b** left a golden-yellow oil (3.5 g) which was chromatographed on a 2.5 × 35 cm column of silica gel. Elution with mixtures of 5, 10, 20, and 40% chloroform in hexane gave first, additional **3b** (0.68 g) (total yield 51%), and then two fractions, which gave on evaporation a golden yellow oil, exhibited infrared bands at 1730 and ~1200 cm^{-1}, characteristic of ester C–O double and single bond stretching vibrations, respectively, and at 700 cm^{-1}. The nmr showed signals at τ 3.9–4.2 (6 H), 6.3 (0.4 H, m, impurity), 6.5 (2 H, m), and 6.1, 6.21, and 6.25 (~7 H, singlets, OCH_3). The ultraviolet spectrum [λ_{max} 244 (ϵ ~2000) and 270 (shoulder) nm] is that expected for a 1,3,6-cyclooctatriene derivative contaminated with *ca.* 20% of a bicyclo[4.2.0]octadiene, such as **5b**. This viscous oily material, believed to be **2b** containing some **5b** as an impurity, decomposed on standing to high molecular weight materials with higher oxygen content than **2b**, **3b**, or **5b**.

From a carboxylation–esterification sequence similar to that described above, the material remaining after removal of most acyclic ester **3b** by crystallization was dissolved in ethyl acetate (75 ml) and hydrogenated at 15 psig hydrogen pressure. When hydrogen uptake had ceased (3 hr) the solution was filtered and evaporated to give a pale yellow oil which was evaporatively distilled to give an almost colorless oil (3.8 g). Analysis of this material on column C at 220° showed the presence of six components, of retention times 16.2, 18.5, 19.6, 24.4, 25.6, and 32 min. Peak 2 was identified as dimethyl sebacate by identity of retention times of columns A, B, and C. Peak 1 was identified as 7 in a similar manner. Peaks 4 and 5 were identified as *cis*- and *trans*-1,4-dicarbomethoxycyclooctane by comparison of retention times on columns B and C, and by comparison in infrared spectra of material (peaks 4 and 5) collected from column B and of an authentic sample of the ester mixture.

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(12) (a) A. C. Cope and D. J. Marshall, *J. Amer. Chem. Soc.*, **75**, 3208 (1953); (b) H. Hover, *Tetrahedron Lett.*, 256 (1962).

(13) R. Huisgen, A. Dahmen, and H. Huber, *J. Amer. Chem. Soc.*, **89**, 7130 (1967).

(14) H. Meister, *Ber.*, **96**, 1688 (1963).

Photoisomerization of Diester 3b. Freshly recrystallized *trans,-cis,cis,trans* diester **3b** (0.50 g) was dissolved in cold (0°) ethyl acetate (60 ml) and the solution was flushed with nitrogen for 30 min. The solution was then irradiated (Srinivasan-Griffin chamber reactor, 3500-Å lamps) for 20 min at 0 to −10°. The solution was concentrated under reduced pressure to a volume of *ca.* 8 ml and chilled. Filtration gave the all-*trans* ester **6** (0.48 g, 95%), mp 210–213°. Recrystallization gave the pure all-*trans* dimethyl 2,4,6,8-decatetraene-1,10-dioate as tiny yellow prisms: mp 212–213°; ir (KBr) 1700 (C=O), 1617 (C=C), and 1302 (C—O) cm^{-1}. A mixture melting point with an authentic sample[8] was undepressed.

Thermal Isomerization of Diester 3b to Bicyclic Ester 5b. A solution of freshly recrystallized diester **3b** (0.50 g) in dry benzene (50 ml) was flushed with nitrogen for 1 hr and was then refluxed under nitrogen for 8 hr, all in a darkened room. Evaporation of the solvent under reduced pressure and trituration of the residue with ether-pentane gave the crude product as a very pale yellow semisolid. Recrystallization from ether-pentane at −20° gave **5b**, *trans*-7,8-dicarbomethoxybicyclo[4.2.0]octa-2,4-diene, as colorless prisms (0.31 g, 62%): mp 34–35°; ir (CCl_4) 1726 (C=O) and 1170–1200 (C—O) cm^{-1}; uv (CH_3OH) max 270 nm (ϵ 3000); nmr ($CDCl_3$) τ 4.0–4.7 (4 H, multiplets, vinyl hydrogens), 6.05–6.24 (2 H, multiplets, H-7 and H-8) 6.28 and 6.31 (3 H each, singlets, OCH_3); mass spectrum parent ion at *m/e* 222. Evaporation of the mother liquors left an oily residue whose spectral properties suggested it contained dimers of **5b**.

Diels-Alder Reaction of Diester 5b with N-Phenylmaleimide. A solution of diester **5b** (0.30 g, 1.5 mmol) and N-phenylmaleimide (0.25 g, 1.5 mmol) in tetrahydrofuran (5 ml) was allowed to stand in the dark at room temperature for 10 hr. The solution was treated with a few drops of hexane, chilled, and filtered. The white solid thus obtained (0.44 g, 77%) was almost pure adduct. A portion was recrystallized from ethyl acetate to give the analytical sample: mp 185–186° dec; ir (KBr) 1733 (ester C=O) and 1705 (amide C=O) cm^{-1}.

Anal. Calcd for $C_{22}H_{21}NO_6$: C, 66.84; H, 5.32. Found: C, 66.73; H, 5.62.

Hydrolysis of 5b. Isolation of Diacid 5a. A mixture of freshly prepared diester **5b** (0.20 g) and 10% aqueous sodium hydroxide (10 ml) was stirred at room temperature for 36 hr. The solution was extracted once with ether and then cooled and acidified with concentrated hydrochloric acid. The precipitated acid was filtered and washed with cold water and then reprecipitated from basic solution. The off-white solid thus obtained, **5a** (0.11 g, 60%), decomposed at 245–260° without a definite melting point: ir (KBr) 1695 (COOH) and 1245 and 1310 (C–O) cm^{-1}; nmr (0.5 *M* NaOD in D_2O) τ 4.0–4.3 (4 H, m, vinyl hydrogens), 6.2–6.4 (2 H, m, H- and H), and 6.5–6.9 (2 H, m, H-1 and H-6).

Anal. Calcd for $C_{10}H_{10}O_4$: C, 61.87; H, 5.53. Found: C, 61.10; H, 5.14.

Isolation of Ester 10. A mixture of diacid **3a** (5 g), methanol (50 ml), and sulfuric acid (4 drops) was refluxed under nitrogen for 2 hr. Most of the methanol was removed by evaporation under reduced pressure. The residue was taken up in ether, washed once with 5% sodium bicarbonate and with water, and dried. Evaporation of the solvent gave a brown oil which was chromatographed on silica gel (2.5 × 300 nm). Elution with 4:1 and 2:1 hexane-methylene chloride gave several fractions containing colorless oils; the first three of these crystallized on standing. Recrystallization from hexane gave colorless chunky prisms (0.68 g, 11%) of diester **10**: mp 69–70°; ir (KBr) 1708 (C=O) and 1572 (C=C) cm^{-1}; nmr (CCl_4) τ 2.28 (2 H, S, vinyl H), 6.20 (6 H, s, OCH_3), 6.3 (2 H, M, CH), and 7.1–7.4 (4 H, M, $-CH_2-$); uv (EtOH) max 327 nm (ϵ 9200).

Later fractions contained somewhat impure diester **5b**; in three of five runs under these conditions, only **5b** was obtained.

Acknowledgments. The author wishes to thank the Robert A. Welch Foundation for financial support of this work and the Badsiche Anilin-und-Soda Fabrik Co. for a generous gift of cyclooctatetraene. Thanks are also due to Professor Elliott N. Marvell for helpful discussions.

Structure and Chemistry of Antibiotic LL-Z1271α, an Antifungal Carbon-17 Terpene

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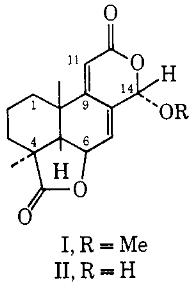
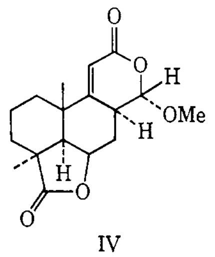
Abstract: The structure of a novel $C_{17}H_{20}O_5$ terpenoid antifungal agent I, labeled LL-Z1271α, is elucidated. In addition, the chemistry of some interesting base hydrolysis products of this mold metabolite is discussed.

In a continuing search for biologically useful fungal metabolites we had occasion to examine the metabolic products from fermentations of an unidentified *Acrostalagmus* species. From this investigation we isolated a novel C_{17} terpenoid I, labeled LL-Z1271α,[1] which exhibited *in vitro* and *in vivo* antifungal activity against several experimental fungal infections. However, later test results indicated considerable toxic side effects as well. Though the structure was determined primarily by physical methods in conjunction with biogenetic considerations, several intriguing base-catalyzed transformations were encountered giving rise to products which at first tended to obscure rather than aid our structural deductions. But as seen below, the structures of these derivatives, as well as their genesis, are singularly consistent with I.



I, R = Me
II, R = H
III, R = Ac



IV

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[1] A portion of this work was reported in preliminary form: G. A. Ellestad, R. H. Evans, Jr., and M. P. Kunstmann, *J. Amer. Chem. Soc.*, **91**, 2134 (1969).