Table VII. Solubilities of Cuprous Acetylides at 25°

Acetylide, CuC≡C—R	Solvent	Solubility, mol/l.
n-Propyl	Pyridine	10^{-5}
n-Propyl	DMF	0
n-Pyridyl	Pyridine	10^{-5}
β-Ethanolyl	Pyridine	10^{-5}
Phenyl	Pyridine	7.5×10^{-3}

results of three successive shots. This tedious procedure was supplanted with a direct potentiometric determination of iodide. An Orion iodide ion specific working electrode and a double jacketed calomel reference electrode were employed in conjunction with a Beckman Research potentiometer. For kinetic analysis, 1.00 ml of reaction solution was injected into a solution of 8.50 ml of distilled water and 0.50 ml of concentrated ammonium hydroxide. The electrode was calibrated under these conditions. A 10-fold change in concentration amounted to a potential difference of 59.16 mV.

Solubilities of Cuprous Acetylides. The solubilities of some acetylides as determined from atomic absorption analysis for copper are presented in Table VII. Solutions for analysis were prepared by warming at 100°, allowing to cool, and filtering.

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The Total Synthesis of Fulvoplumierin

G. Buchi and John A. Carlson[1]

Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139.
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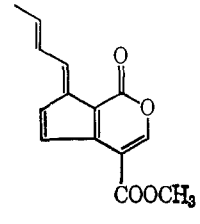
Abstract: Condensation of dimethyl penta-2,3-dienedioate (**3**) with butadiene gave the Diels–Alder adduct **4** which, on oxidation with potassium chlorate–osmium tetroxide, was transformed to the diol **5**. Treatment of the diol with dimethylformamide dimethyl acetal followed by acid hydrolysis yielded the α-pyrone **9**. Cleavage with periodate and aldol condensation of the resulting dialdehyde **10** gave the hydroxyfulvene **12** from which the chloride **15** was prepared with oxalyl chloride. Coupling of this chloride (**15**) with lithium di(*trans*-1-propenyl)cuprate (**16**) gave fulvoplumierin (**1**). The stereochemical outcome of coupling a vinyl cuprate with a vinyl halide is discussed.

Fulvoplumierin, an antibacterial pigment from the bark of *Plumiera acutifolia* and *Plumiera rubra var. alba*, was first isolated in 1952[2] and subsequent structural investigations led to formula **1**.[3,4] The total synthesis of fulvoplumierin described in this paper confirms this structural assignment and represents the first synthesis of a naturally occurring fulvene.[5] Condensation of dimethyl penta-2,3-dienedioate (**3**)[6] prepared from dimethyl β-chloroglutaconate (**2**)[7] and triethylamine in tetrahydrofuran with butadiene gave a mixture of the *cis*- and *trans*-α,β-unsaturated esters **4**. Potassium chlorate in the presence of a catalytic amount of osmium tetroxide[8] in aqueous tetrahydrofuran did differentiate satisfactorily between the two double bonds in **4** and led to a mixture of diastereomeric diols **5** characterized further by transformation to acetonides. Attempts to convert the diol **5** to the α-hydroxymethylene ester **6** with methyl formate and sodium hydride were unpromising and led to methyl 1-oxo-1H-2-benzopyran-4-carboxylate (**7**),[9] the latter probably originating from the desired diol **6**.



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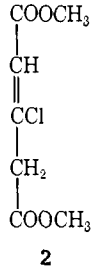

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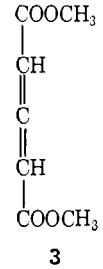

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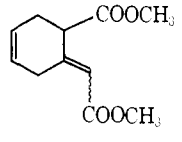

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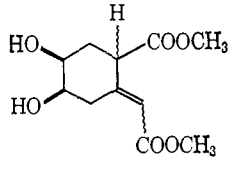

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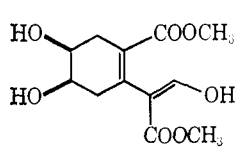

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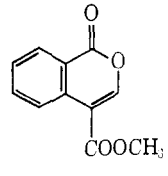

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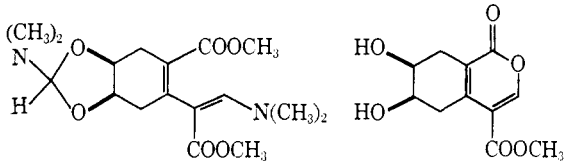
We then hoped that the mild conditions used in the condensation of active methylene compounds with dimethylformamide dimethyl acetal[10] would allow the

(1) National Institutes of Health Predoctoral Fellow, 1966–1969.
(2) H. Schmid and W. Bencze, *Experientia*, **8**, 224 (1952).
(3) H. Schmid and W. Bencze, *Helv. Chim. Acta*, **36**, 205, 1468 (1953).
(4) G. Albers-Schönberg, W. v. Phillipsborn, L. M. Jackman, and H. Schmid, *ibid.*, **45**, 1406 (1962).
(5) D. J. Bertelli and J. H. Crabtree, *Tetrahedron*, **24**, 2079 (1968), determined the structures of two other natural fulvenes.
(6) E. R. H. Jones, G. H. Mansfield, and M. C. Whiting, *J. Chem. Soc.*, 3208 (1954).
(7) J. M. van der Zanden, *Rec. Trav. Chim. Pays-Bas*, **54**, 289 (1935).
(8) M. F. Clark and L. N. Owen, *J. Chem. Soc.*, 319 (1949).
(9) We are indebted to Dr. R. S. Schneider of these laboratories for a sample of **7** prepared by the method of W. Dieckmann and W. Meiser, *Ber.*, **41**, 3253 (1908).
(10) H. Meerwein, W. Florian, N. Schon, and G. Stopp, *Ann.*, **641**, 1 (1961).

isolation of a nonaromatized product and indeed when the glutaconate **5** was treated with this reagent in dimethylformamide solution the dimethylaminomethylene ester **8** derived from the glutaconate anion was produced. Hydrolysis of the crude product with dilute hydrochloric acid afforded the crystalline α-pyrone **9**. As anticipated this diol was smoothly cleaved to the dialdehyde **10** by sodium periodate. No extensive effort was made to purify this highly reactive dialdehyde **10** but the corresponding bisdimethylacetal was fully characterized.



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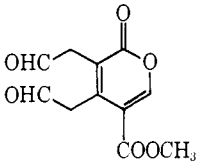
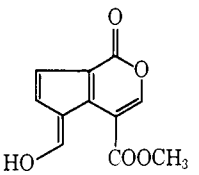


10

The next phase of the synthesis was concerned with the construction of the five-membered ring. We anticipated that intramolecular aldol condensation in **10** would lead mainly if not exclusively to the desired hydroxyfulvene **12** rather than its isomer **11**. Scale molecular models indicate that the hydroxyfulvene **11** and its two precursors, the α,β-unsaturated aldehyde and the corresponding aldol, are crowded molecules due to steric interaction between the carbomethoxy group and the substituent in the *peri* position. It therefore seemed reasonable to predict that cyclization would proceed *via* less crowded intermediates to the more stable hydroxyfulvene **12** and earlier experiences in a similar situation is in full accord with this.[11] In fact, the crude dialdehyde **10** was converted to a single hydroxyfulvene **12** by Amberlite IR-120 in dimethoxyethane. Contrary to 6-hydroxyfulvene, which is less stable in carbon tetrachloride solution than the tautomeric cyclopentadienecarboxaldehydes,[12] compound **12** in chloroform solution exists entirely in the hydroxyfulvene form. Its nuclear magnetic resonance spectrum in $CDCl_3$ is characterized by two doublets (J = 14 Hz at δ 14 and 7.65) caused by the enolic and the adjacent vinylic hydrogen atoms, respectively.[13] The hydroxy group in the enol **12** was readily exchanged for methoxy or isopropoxy when the compound was allowed to reflux in the appropriate alcohol with a catalytic amount of Amberlite IR-120. These exchanges, undoubtedly proceeding by an addition–elimination mechanism, should lead to the thermodynamically more stable ethers with the stereochemistries portrayed in **13** and **14**. The vinyl protons in these ethers give rise to a one-proton singlet in the δ 8.1–8.3 region of the nmr spectra and comparison with the chemical shifts of the corresponding protons in the hydroxyfulvene **12** (δ 7.65) and 6-ethylfulvene[4] (δ 6.6) suggest that the hydroxyfulvene has the stereochemistry already incicated in formula **12**.



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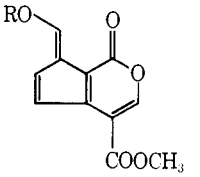
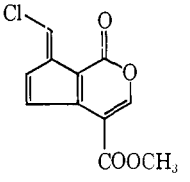


12, R = H
13, R = CH_3
14, R = CH_3CHCH_3

To complete the synthesis of fulvoplumierin (**1**) three additional carbon atoms had to be introduced and in one scheme this was to be accomplished by coupling a three-carbon organometallic reagent with a halofulvene. The highly reactive chlorofulvene **15** was readily available from the corresponding enol **12** and oxalyl chloride. Efforts to condense this chloride with *trans*-1-propenyl lithium were not promising but recent reports on the successful coupling of lithium diorganocuprates with organic halides[14,15] led us to investigate such a coupling. In the event, condensation of the chloride **15** with lithium di(*trans*-1-propenyl)cuprate (**16**)[16] in ether–dimethoxyethane at $-35°$ gave a dark red mixture of products from which an orange colored, crystalline substance could be isolated by chromatography in 27% yield. Infrared,[3] ultraviolet,[3] and nuclear magnetic resonance[4] spectra were indistinguishable from those of natural fulvoplumierin (**1**) and since the appearance of our preliminary communication[17] Professor H. Schmid has kindly compared synthetic and natural fulvoplumierin and found that a mixture of the two showed no melting point depression.



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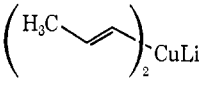

16

In conclusion we wish to comment on the stereochemistry of the two side-chain double bonds in synthetic fulvoplumierin. First, it seems clear that the chloride **15** has the stereochemistry indicated because in the other isomer the chlorine atom and the α-pyrone carbonyl oxygen atom occupy essentially the same space. Second, the reaction of lithium diphenylcuprate with *cis*- and *trans*-β-bromostyrene has been shown to result in high conversions to *cis*- and *trans*-stilbenes, respectively.[15] Retention of stereochemistry in the coupling reaction with vinyl halides thus demands the trisubstituted double bond to have the configuration indicated in structure **1**. Third, there is no experimental evidence available demonstrating that the conversion of a vinyl halide

(11) G. Büchi, B. Gubler, R. S. Schneider, and J. Wild, *J. Amer. Chem. Soc.*, **89**, 2776 (1967).
(12) K. Hafner, H. E. A. Kramer, H. Musso, G. Ploss, and G. Schulz, *Chem. Ber.*, **97**, 2066 (1964).
(13) *Cf.* E. W. Garbisch, Jr., *J. Amer. Chem. Soc.*, **85**, 1696 (1963).
(14) The coupling of lithium dialkylcuprates with alkyl and vinyl halides has been described by E. J. Corey and G. H. Posner, *ibid.*, **89**, 3911 (1967); **90**, 5615 (1968).
(15) For a carefully detailed study on the reaction of lithium dialkyl- and diarylcuprates with organic halides see G. M. Whitesides, W. F. Fischer, Jr., J. San Filippo, Jr., R. W. Bashe, and H. O. House, *ibid.*, **91**, 4871 (1969). We are indebted to Professor G. Whitesides and Mr. San Filippo for unpublished information.
(16) G. M. Whitesides, J. San Filippo, Jr., C. P. Casey, and E. J. Panek, *ibid.*, **89**, 5302 (1967).
(17) G. Büchi and J. A. Carlson, *ibid.*, **90**, 5336 (1968).

to an olefin *via* a vinyl cuprate proceeds with retention of the vinyl halide stereochemistry. However, the fact that *endo*-2-norbornyl cuprate on methylation with methyl tosylate gives exclusively *endo*-2-methylnorbornane strongly suggests that this should be the case.[18] Since the cuprate **16** was prepared from *trans*-1-bromopropene the disubstituted side-chain double bond in synthetic fulvoplumierin should have the *trans* geometry. Consequently, this synthesis confirms not only the structure but also the stereochemistry proposed for fulvoplumierin (**1**).

Experimental Section

Microanalyses were performed in the Massachusetts Institute of Technology Microchemical Laboratory. Melting points and boiling points are uncorrected. The following spectrometers and solvents were used: nuclear magnetic resonance (nmr), Varian A-60 and HA-100 (CCl_4 and $CDCl_3$, TMS as internal standard); infrared (ir), Perkin-Elmer Model 237 (CCl_4, $CHCl_3$); ultraviolet (uv), Cary Model 14 (EtOH, pentane); mass spectra, Hitachi Perkin-Elmer RMU-6D. Brinkmann silica gel PF_{254}, Fisher Florisil (100–200 mesh), and Mallinckrodt silicic acid (100 mesh) were used for column chromatography.

Dimethyl Penta-2,3-dienedioate (3). A solution of dimethyl 2-chloroglutaconate[7] (**2**) (30 g, 0.15 mol) in tetrahydrofuran (300 ml, freshly distilled from $LiAlH_4$) and triethylamine (21.5 ml, 0.16 mol) was maintained at 5° for 15 hr. The mixture was then diluted with 300 ml of ether and filtered. The filtrate was washed with ether and the combined organic phases were washed thoroughly with 0.1 *N* HCl and with NaCl solutions. After drying (Na_2SO_4) and evaporation, distillation yielded 20 g (63%) of allene **3**: bp 67–71° (0.08 mm) (lit.[6] bp 90° (0.2 mm)).

Dimethyl 2-Carboxymethylenecyclohex-4-enecarboxylate (4). A solution of allene **3** (63.0 g, 0.4 mol) in butadiene (100 ml), benzene (65 ml), and phenyl sulfide (1 ml) was heated at 80° for 15 hr in a glass-lined autoclave. The reaction mixture was evaporated and extracted four times with 100 ml of hot methanol. The methanol solution was concentrated and distilled giving 51.7 g (62%) of adduct **4**: bp 78–80° (0.3 mm); ir ($CHCl_3$) 1740–1700, 1650, 1440 cm^{-1}; uv max (EtOH) 214 mμ (ε 11,200).

Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.84; H, 6.71. Found: C, 62.70; H, 6.79.

Dimethyl 2-Carboxymethylene-4,5-dihydroxycyclohexanecarboxylate (5). To a stirred solution of potassium chlorate (50 g, 0.475 mol) in water (300 ml) was added the Diels–Alder adduct **4** (51 g, 0.24 mol) and osmium tetroxide (2 g) dissolved in tetrahydrofuran (300 ml). After 0.5 hr the ice bath was removed and stirring continued until the reaction mixture became nearly colorless (~40 hr). The tetrahydrofuran was evaporated, *in vacuo*, and the aqueous solution was saturated with sodium chloride and extracted with five 500-ml portions of ethyl acetate. The ethyl acetate layer was subsequently washed with water, concentrated *in vacuo*, and diluted with tetrahydrofuran. The resulting solution was saturated with hydrogen sulfide, filtered through Celite, and evaporated *in vacuo* giving 52 g (81%) of crude diol **5**.

The acetonide was prepared by treating the diol **5** (100 mg) in acetone (2 ml, distilled from $KMnO_4$, dried over K_2CO_3, and redistilled) with anhydrous copper sulfate (100 mg) at room temperature for 15 hr. After filtration the filtrate was evaporated *in vacuo* and distilled in a molecular still yielding 103 mg (81%) of acetonide: bp 170° (0.05 mm); ir ($CHCl_3$) 1730, 1710, 1630, 1440 cm^{-1}; uv max (EtOH) 222 mμ (ε 11,200); nmr (CCl_4) δ 1.3 (s, 3), 1.35 (s, 3), 1.4–3.4 (m, 5), 3.65 (s, 6), 4.4 (m, 2), and 5.9 (m, 1).

Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 58.89; H, 7.00.

Methyl 1-Oxo-1H-2-benzopyran-4-carboxylate (7). To a solution of diol **5** (250 mg, 1 mmol) in methyl formate (10 ml, freshly distilled from P_2O_5) and tetrahydrofuran (2 ml, freshly distilled from $LiAlH_4$), kept at −10°, sodium hydride (70 mg, 3 mmol, oil free) was added in small portions during 1 hr. The solution was then warmed to room temperature and stirred for 15 hr. The reaction mixture was poured into cold 0.1 *N* aqueous hydrochloric acid and extracted with chloroform. After washing (H_2O), drying (Na_2SO_4), and evaporating the chloroform *in vacuo*, the residue was recrystallized from ether giving 195 mg of benzopyran **7** (97%): mp 93–95°, undepressed on admixture with an authentic sample of methyl 1-oxo-1H-2-benzopyran-4-carboxylate[9] (**7**), (lit.[9] mp 95–97°).

Methyl 6,7-Dihydroxy-5,6,7,8-tetrahydro-1-oxo-1H-2-benzopyran-4-carboxylate (9). A solution of diol **5** (800 mg, 3.28 mmol), dimethylformamide dimethyl acetal[19] (5 ml), and dimethylformamide (5 ml) was heated with stirring in a nitrogen atmosphere at 80° for 5 hr. Evaporation *in vacuo* produced a dark viscous oil **8** (ir ($CHCl_3$) 1710, 1670, and 1600 cm^{-1}; uv max (EtOH) 290 mμ) which was stirred at room temperature for 1 hr with 0.5 *N* aqueous HCl (50 ml). After evaporation *in vacuo* the semicrystalline residue was suspended in dioxane and the solvent was reevaporated to remove any residual water. The resulting oil was dissolved in 10% methanol–chloroform and chromatographed over silica gel (65 g). Elution with 10% methanol–chloroform and recrystallization from methanol–ethyl acetate gave 225 mg (28%) of dihydroxy α-pyrone **9**: mp 160–162°; ir ($CHCl_3$) 3600–3400, 1740–1715, 1630, 1440 cm^{-1}; uv max (EtOH) 253 (ε 7730) and 285 mμ (ε 4650), (0.01 *N* NaOH) 251 mμ (ε 8850); nmr (CD_3OD) δ 2.65 (m, 2), 3.14 (m, 2), 3.8 (s, 3), 4.0 (t, 2, J = 7 Hz), and 8.3 (s, 1).

Anal. Calcd for $C_{11}H_{12}O_6$: C, 55.00; H, 5.04. Found: C, 54.79; H, 5.09.

Methyl 3,4-Diformylmethyl-2-oxo-2H-pyran-5-carboxylate (10). Under a nitrogen atmosphere the dihydroxy-α-pyrone **9** (30 mg, 0.12 mmol) was added to an ice-cold, stirred solution of sodium periodate (60 mg, 0.281 mmol) in 50% aqueous methanol (5 ml). The solution was then warmed to room temperature and stirred in the dark under nitrogen for 3 hr. The resulting suspension was diluted with water (5 ml) and extracted three times with 25 ml of chloroform. After washing (H_2O), drying (Na_2SO_4), and evaporating *in vacuo*, the residue was dissolved in chloroform (2 ml) and the solution was filtered through Florisil (100 mg). Evaporation of the chloroform afforded 26 mg (90%) of the dialdehyde **10**: ir ($CHCl_3$) 2725, 1740–1715, 1630, 1440 cm^{-1}; uv max (EtOH) 255 and 293 mμ; nmr ($CDCl_3$) δ 3.57 (d, 2, J = 1 Hz), 3.8 (s, 3), 3.95 (d, 2, J < 1 Hz), 8.3 (s, 1), 9.63 (t, 1, J = 1 Hz), 9.71 (t, 1, J < 1 Hz).

The bis(dimethyl acetal) was prepared by allowing the dialdehyde **10** to react with trimethyl orthoformate (1 ml), methanol (0.5 ml), and Amberlite IR-120 resin (30 mg) at room temperature for 24 hr. Filtration through Florisil (300 mg) using chloroform as eluent and evaporation followed by distillation gave 31 mg (80%) of acetal: bp 168° (0.05 mm); ir ($CHCl_3$) 1740–1710, 1630, 1440 cm^{-1}; uv max (EtOH) 254 (ε 6020) and 292 mμ (ε 5730); nmr ($CDCl_3$) δ 2.95 (d, 2, J = 6 Hz), 3.3 (s, 6), 3.35 (s, 6), 3.42 (d, 2, J = 6 Hz), 3.85 (s, 3), 4.5 (t, 1, J = 6 Hz), 4.6 (t, 1, J = 6 Hz), and 8.1 (s, 1).

Anal. Calcd for $C_{15}H_{22}O_8$: C, 54.54; H, 6.71. Found: C, 54.71; H, 6.72.

Methyl 7-Hydroxymethylenecyclopenta[*c*]pyran-1(7H)-one-4-carboxylate (12). Crude dialdehyde **10** (260 mg), prepared from the dihydroxy-α-pyrone **9** (300 mg, 1.2 mmol) as described above, dissolved in 30 ml of dimethoxyethane was heated with stirring in a nitrogen atomosphere at 80° for 5 hr with 150 mg of anhydrous Amberlite IR-120 ion-exchange resin. The resin was then removed by filtration and washed thoroughly with hot dimethoxyethane. Evaporation of the solvent followed by sublimation of the crude solid gave 171 mg (61%) of yellow hydroxyfulvene **12**: mp 162–163°; ir ($CHCl_3$) 3600–3400, 1740–1715, 1660, 1630, 1440 cm^{-1}; uv max (EtOH) 357 mμ (ε 7320) and (EtOH–NaOH) 304 (ε 9270) and 378 mμ (ε 24,100); nmr ($CDCl_3$) δ 3.7 (s, 3), 6.95 (AB, 2), 7.65 (d, 1, J = 14 Hz), 8.15 (s, 1), and 14.0 (d, 1, J = 14 Hz).

Anal. Calcd for $C_{11}H_8O_5$: C, 60.00; H, 3.66. Found: C, 60.24; H, 3.87.

Methyl 7-Methoxymethylenecyclopenta[*c*]pyran-1(7H)-one-4-carboxylate (13). A suspension of hydroxyfulvene **12** (220 mg, 1 mmol) and anhydrous Amberlite IR-120 (50 mg) in 30 ml of methanol was heated at reflux for 2 hr in an atmosphere of nitrogen. The resin was removed by filtration, washed with hot methanol, and the methanol evaporated *in vacuo*. Sublimation of the residue yielded 197 mg (84%) of yellow methoxyfulvene **13**: mp 189–190°; ir ($CHCl_3$) 1740–1710, 1630, 1440 cm^{-1}; uv max (EtOH) 347 (ε 17,300) and 357 mμ (ε 17,700); nmr ($CDCl_3$) δ 3.85 (s, 3), 4.15 (s, 3), 7.2 (s, 2), 8.1 (s, 1), and 8.2 (s, 1).

Anal. Calcd for $C_{12}H_{10}O_5$: C, 61.59; H, 4.30. Found: C, 61.57; H, 4.33.

Methyl 7-Isopropoxymethylenecyclopenta[*c*]pyran-1(7H)-one-4-carboxylate (14). Treatment of hydroxyfulvene **12** with 2-pro-

(18) G. M. Whitesides, J. San Filippo, Jr., E. Stedronsky, and C. P. Casey, *J. Amer. Chem. Soc.*, in press.

(19) H. Brechbühler, H. Büchi, E. Hatz, J. Schreiber, and A. Eschenmoser, *Helv. Chim. Acta*, **48**, 1746 (1965).

panol under conditions described for the preparation of methoxyfulvene **13** gave an 89% yield of yellow isopropoxyfulvene **14**: mp 111–112°; ir ($CHCl_3$) 1740–1710, 1630, 1440 cm^{-1}; uv max (EtOH) 344 (ε 21,000) and 355 mμ (ε 21,200); nmr ($CDCl_3$) δ 1.35 (d, 6, J = 6.5 Hz), 3.9 (s, 3), 4.5 (m, 1, J = 6.5 Hz), 7.35 (AB, 2, J = 4 Hz), 8.2 (s, 1), and 8.3 (s, 1).

Anal. Calcd for $C_{14}H_{14}O_5$: C, 64.11; H, 5.38. Found: C, 64.14; H, 5.16.

Methyl 7-Chloromethylenecyclopenta[*c*]pyran-1(7H)-one-4-carboxylate (15). The hydroxyfulvene **12** (300 mg, 1.36 mmol) was stirred 12 hr at room temperature in a nitrogen atmosphere with 3 ml of oxalyl chloride. Excess oxalyl chloride was evaporated and the resulting solid was sublimed at 90° under vacuum giving 328 mg (94%) of the yellow chlorofulvene **15**: mp 126–127°; ir ($CHCl_3$) 1750–1710, 1610, 1600, 1440 cm^{-1}; uv max (pentane) 234 (ε 5010), 273 (ε 3640), 314 (ε 10,300), 327 (ε 9700) and 343 mμ (ε 5140); nmr ($CDCl_3$) δ 3.9 (s, 3), 7.3 (ABX, 2, J_{AB} = 6 Hz, J_{AX} = 2 Hz), 8.0 (d, 1, J = 2 Hz) and 8.3 (s, 1).

Anal. Calcd for $C_{11}H_7O_4Cl$: C, 55.36; H, 2.98. Found: C, 55.32; H, 3.37.

Methyl 7-Crotonylidenecyclopenta[*c*]pyran-1(7H)-one-4-carboxylate (1). To a solution of the chlorofulvene **15** (150 mg, 0.63 mmol) in dimethoxyethane (40 ml, distilled from $LiAlH_4$ in an argon atmosphere) maintained at −35°, was added an ethereal solution of lithium di(*trans*-1-propenyl)cuprate (**16**)[16] kept at −78° (0.73 mmol which was prepared from 1.47 mmol of *trans*-1-propenyllithium and 0.73 mmol of CuI). The dark red solution was stirred for 0.5 hr at −35°, then warmed to −5° and diluted with ether (150 ml). After extraction with dilute hydrochloric acid, washing with water, and drying (Na_2SO_4), the solvent was evaporated *in vacuo*. The residue was then dissolved in tetrahydrofuran (1 ml) and chromatographed over a column of zinc carbonate (7 g), supported on Celite (14 g), prepared in hexane suspension. Elution with ether gave 96 mg of product which was rechromatographed on a silicic acid (10 g)–Celite (10 g) column prepared in hexane and eluted with ether. Evaporation *in vacuo* and recrystallization from chloroform gave 40.5 mg (27%) of fulvoplumierin (**1**): mp 148–150° (lit.[3] mp 151–152°); ir ($CHCl_3$) 1730–1710, 1620, 1585, 1520, 1435 cm^{-1}; ir (Nujol) 1740, 1710, 1620, 1580, 1530 cm^{-1}; uv max (EtOH) 272 (ε 7000) and 365 mμ (ε 33,700); nmr (100 MHz) ($CDCl_3$) δ 2.05 (d, 3, J = 5.5 Hz), 3.95 (s, 3), 6.4–7.3 (ABX, 2, J_{AB} = 14, J_{AX} = 8 Hz), 7.3–7.6 (AB, 2, J_{AB} = 3 Hz), 7.9 (d, 1, J = 8 Hz), and 8.3 (s, 1); mass spectrum (70 eV) *m/e* (rel intensity) 244 (100), 212 (55), 184 (24), 156 (37), 128 (81).

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The Synthesis of (−)-Aromadendrene and Related Sesquiterpenes

G. Büchi, W. Hofheinz, and Joseph V. Paukstelis[1]

Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139.
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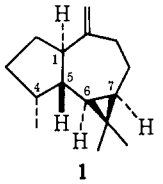
Abstract: Addition of hydrobromic acid to (−)-perillaldehyde (**3**) followed by base-induced elimination of hydrobromic acid gave the bicyclic aldehyde **4**. Wittig reaction, followed by Diels–Alder condensation with acrolein yielded the adduct **6**. Epimerization and reduction to the olefin **8**, followed by oxidation, furnished a mixture of diols containing mainly **9** and minor amounts of the diastereomer **10**. In two separate sequences of chemical operations the diols **9** and **10** were transformed to the epimeric olefins **13** and **16**. Neither proved to be the enantiomer of aromadendrene or alloaromadendrene. An analogous sequence of reactions again starting with the aldehyde **6** proceeding *via* the olefin **20**, the diol **21**, and the ketone **23** afforded (−)-aromadendrene (**24**) the enantiomer of naturally occurring (+)-aromadendrene (**1**). This finding requires revision of the previously postulated stereostructures of aromadendrene and a number of other related sesquiterpenes. Naturally occurring globulol, alloaromadendrene, ledol, and viridoflorol are now represented by structures **29**, **30**, **31**, and **32**, respectively. New evidence on the configuration of the crucial degradation product **27** shows that degradative and synthetic evidence concerning the stereochemistries of this group of sesquiterpenes is no longer in conflict.

Aromadendrene is a member of a group of naturally occurring sesquiterpenes structurally characterized by fusion of a cyclopropane ring to a hydroazulene skeleton. The currently accepted structure, exclusive of stereochemistry, was originally proposed in 1953.[2] Subsequent degradative work[3,4] eliminated an alternate structure proposed by the early workers. Studies on the stereochemistry of aromadendrene were pursued by two independent groups who both arrived at structure **2**.[3,4] The stereochemical arguments presented at that time seemed reasonable but supporting evidence was nevertheless needed. Synthetic work described in this paper provides unambiguous evidence that natural (+)-aromadendrene has in fact the relative and absolute stereochemistry indicated in structure **1**.[5]



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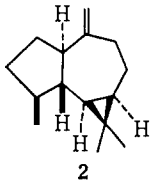

2

While considereing synthetic approaches to aromadendrene it was decided to construct the perhydroazulene portion of the molecule by skeletal rearrangement

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