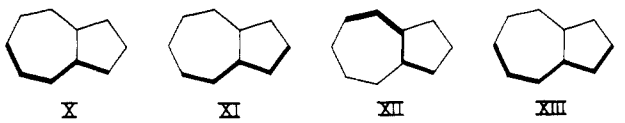
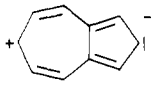
and a transoid linkage through the central bond, $^3J_{C\text{-}1\text{-}C\text{-}4}$.

Compared to the naphthalene system where the cisoid vicinal coupling constants, e.g., $^3J_{C\text{-}1\text{-}C\text{-}4}$ or $^3J_{C\text{-}7\text{-}C\text{-}10}$ are large (ca. 8 Hz) and the transoid vicinal coupling constants, e.g., $^3J_{C\text{-}2\text{-}C\text{-}8}$ or $^3J_{C\text{-}1\text{-}C\text{-}7}$ are smaller (ca. 4–5 Hz), the reversed situation holds for azulene. In this case, the transoid linkages like $^3J_{C\text{-}1\text{-}C\text{-}7}$ or $^3J_{C\text{-}2\text{-}C\text{-}4}$ show values of about 8 Hz and the cisoid linkages like $^3J_{C\text{-}4\text{-}C\text{-}7}$ and $^3H_{C\text{-}6\text{-}C\text{-}10}$ values of 3–4 Hz. For the cisoid linkages again a double pathway is possible and these values can be understood as a sum of ^3J and ^4J spin–spin coupling constants. Thus the low values for the cisoid linkages suggest that the ^4J spin–spin coupling constants are negative. Only the small transoid spin–spin coupling constant through the central bond is in accordance with the similar coupling in naphthalene. Again, a correlation with quantum mechanical data like π bond orders fails for the azulene system.

Spin–Spin Coupling Constants over Four and Five Bonds. In azulene three different $^4J_{CC}$ connections are possible. Furthermore, a $^5J_{CC}$ spin–spin coupling constant relates C-2 with C-6. In the formulas X–XIII these linkages are shown. Contrary to the naphthalene system these spin–spin coupling constants can easily be observed with 1 to 2 Hz. The rather large $^5J_{C\text{-}2\text{-}C\text{-}6}$ value of 2.6 Hz is especially remarkable. If long-range $^{13}C^{13}C$ spin–spin coupling constants are related to π-electron polarizability, this value would suggest that polar forms like XIV are of some significance.



X XI XII XIII



XIV

Conclusion

We have shown in this work that a complete $^{13}C^{13}C$ spin–spin coupling matrix can be obtained by the 2D-INADEQUATE technique. Data from earlier labeling studies were helpful in cases where the limited digital resolution of the data system used was not sufficient. Although the sign of the spin–spin coupling constants cannot be extracted from these measurements at present the qualitative interpretion of these values raises interesting questions on the electronic system of the azulene moiety. Unfortunately, a quantitative agreement between MO theory and these experimental results is not in sight.

Experimental Section

The 2D-INADEQUATE spectra of **2** and **3** have been measured on a Bruker WH-400 NMR spectrometer with a 80 k Aspect 2000 computer and a Diablo Series 30 disk drive; ca. 0.5 g of freshly chromatographed (Al_2O_3/petroleum ether) **2** or **3** was dissolved in 2 mL of $CDCl_3$ and transferred to 8-mm sample tubes. The temperature of the NMR probe was maintained at 32 °C and the solutions were not degassed. The spectral width was 2604.2 Hz, 32 FIDs on 8192 data points were taken for each 2D experiment, resulting in 256K data. The 90° pulse width was 18 μs, for each FID 256 scans were accumulated and a relaxation delay of 12 s was used which gave a total experiment time of about 35 h for one τ value. A squared sine bell was used as a weighting function in f_1 dimension; Gaussian multiplication was applied in the f_2-dimension. 2D-Fourier transformation yielded a 2D datafile of 512K computer words giving a digital resolution of 46.7 Hz in the f_1 and 0.32 Hz in the f_2 dimension after zero-filling. The pulse sequence of the 135° pulse angle method as published by Freeman was used.[4] To detect all possible spin–spin coupling constants the measurements have been performed with refocusing delays (τ values) adjusted to 3, 5, 7, and 57 Hz. Quadrature detection was used in both dimensions, with a phase cycling procedure described in ref 11 using 32 steps, thus the spectral width in f_1 dimension was the same as in f_2. The measurements were repeated with the standard 1D-INADEQUATE technique in high resolution using 64K data points which led partly to a confirmation of the 2D results.

The 1D-INADEQUATE measurements of **1** have been performed on 0.8 g of freshly chromatographed (Al_2O_3/petroleum ether) **1** dissolved in 4 mL $CDCl_3$ using a 10-mm o.d. NMR tube at 32 °C. The labeled material was measured on the same instrument with standard high-resolution techniques. The preparation of the ^{13}C-labeled azulenes is described elsewhere: 4-^{13}C-**1**,[1,12] 4,7-$^{13}C_2$-**1**,[2] 6-^{13}C-**1**,[13] 1-^{13}C-**5**,[14] 3- and 4-^{13}C-**5**,[15] and 2-^{13}C-**6**.[15] The chemical shifts of **5** and **6** will be reported in ref 15.

Acknowledgment. This work was supported by the Fonds der chemischen Industrie. We are indebted to Prof. K. Hafner, Darmstadt, for a generous gift of compounds **2** and **3**.

Registry No. **1**, 275-51-4; 1-*4*-^{13}C, 74626-95-2; 1-*6*-^{13}C, 87295-52-1; 1-*4,7*-$^{13}C_2$, 78950-01-3; **2**, 769-31-3; **3**, 1654-55-3; **4**, 17647-77-7; **5**, 7206-60-2; **6**, 19227-07-7; **7**, 90-12-0; **8**, 91-57-6.

(11) Bax, A.; Freeman, R.; Fraenkiel, T. A.; Levitt, M. H. *J. Magn. Reson.* **1981**, *43*, 478–483.
(12) Becker, J.; Wentrup, C.; Katz, E.; Zeller, K. P. *J. Am. Chem. Soc.* **1980**, *102*, 5110–5112.
(13) Gugel, H.; Zeller, K. P.; Wentrup, C. *Chem. Ber.* **1983**, *116*, 2775–2784.
(14) Zeller, K. P. *Angew. Chem.* **1982**, *94*, 448; *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 440; *Angew. Chem. Suppl.* **1982**, 1016–1020.
(15) Wetzel, A.; Zeller, K. P., to be submitted.

Total Synthesis of Curzerenone, Epicurzerenone, and Pyrocurzerenone

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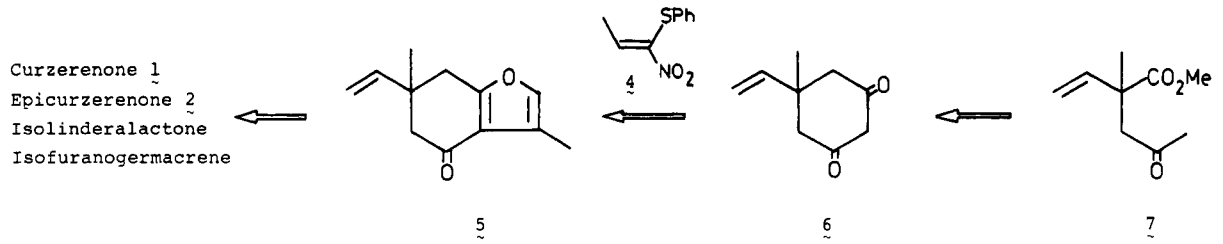
Received February 14, 1984

Curzerenone (**1**) and epicurzerenone (**2**), representative furanoelemanoids, and pyrocurzerenone (**3**) were synthesized via the 3-methylfuran annulation reaction using 1-nitro-1-(phenylthio)propene (**4**) as the crucial step. The cyclic 1,3-dione **6**, derived from γ-keto ester **7**, reacted with the nitro olefin **4** with KF catalysis to yield dihydrofuran **14** as a diastereomeric mixture, which was converted to 3-methylfuran **5** on $NaIO_4$ oxidation followed by elimination of benzenesulfenic acid from the resulting sulfoxides in good overall yield. Curzerenone (**1**) and epicurzerenone (**2**) were synthesized from **5** in three steps.

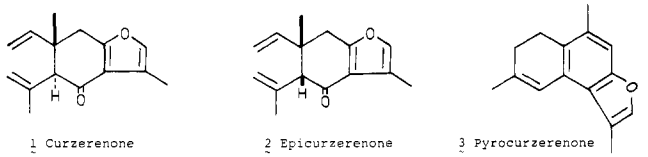
Although the elemane skeleton is quite common, only five furanoelemanoids, curzerenone (**1**),[1] epicurzerenone (**2**),[1] sericenine,[2] isofuranogermacrene,[1a] and isolinderalactone,[3] have so far been found in nature. In addition,

0022-3263/84/1949-3728$01.50/0

Scheme I



syntheses of these furanoelemane sesquiterpenes have not been described until recently.



In connection with the reaction of 1,3-dicarbonyl compounds and nitro olefins leading to 4-acyl-2-alkylfurans,[4] we have developed a novel synthesis of the 4-acyl-3-methyldihydrobenzofuran system using the KF-catalyzed reaction of 1-nitro-1-(phenylthio)propene (**4**) with cyclic 1,3-diones[5,6] and recently reported the first total synthesis of curzerenone (**1**) and epicurzerenone (**2**).[7] Curzerenone (**1**), epicurzerenone (**2**), and pyrocurzerenone (**3**) are the constituents of the drug zedoary, the rhizomes of *Curcuma zedoaria* Roscoe (Zingiberaceae), and **3** is the first sesquiterpenoid of the cadinane type containing a furan ring.[1] It is also noteworthy that both **1** and **2** exist in racemic forms and they provide a unique thermal elemane–germacrene–cadinane rearrangement.[1] In this paper we describe the synthesis of these furanoelemanoids in full detail.

Results and Discussion

At the outset of this research we considered 3,6-dimethyl-6-vinyl-6,7-dihydrobenzofuran-4(5*H*)-one (**5**) as a common key intermediate for the synthesis of furanoelemanoids (Scheme I). Furthermore, in order to construct the key compound **5** we also envisaged a synthetic route employing our 3-methylfuran annulation reaction using 1-nitro-1-(phenylthio)propene (**4**)[5] and a cyclic 1,3-dione **6** as shown in Scheme I. The transformation of **6** into the key intermediate **5** by this method was expected to proceed efficiently because this cyclic 1,3-dione **6** is a symmetrical molecule.

Hence we set about the synthesis of 5-methyl-5-vinylcyclohexane-1,3-dione (**6**) starting with γ-keto ester **7** since **7** was readily obtainable by the Lewis acid promoted reaction of 2-nitropropene and the ketene methyl trimethylsilyl acetal derived from methyl tiglate recently developed by us.[8]

The conversion of the γ-keto ester **7** to the desired 1,3-dione **6** was straightforwardly performed as follows. Boron trifluoride catalyzed thioacetalization of **7** with ethanedithiol in CH_2Cl_2 gave thioacetal **8** in high yield. Hydrolysis of **8** with aqueous ethanolic KOH followed by treatment of the resulting acid **9** with oxalyl chloride in refluxing benzene afforded acid chloride **10**, which was then converted into diazo ketone **11** by the standard procedure[9] in excellent overall yield.

The Wolff rearrangement of **11** with silver oxide in refluxing methanol resulted in formation of homologated ester **12**. Deprotection of the thioacetal group with methyl iodide in aqueous acetonitrile gave δ-keto ester **13**, which was then cyclized on treatment with sodium ethoxide in hot xylene to afford the crystalline 1,3-dione **6**.

Having constructed the desired 1,3-dione **6**, we focused our attention on its transformation into the key intermediate **5** by the 3-methylfuran annulation technology. Thus the crucial step was conducted by heating **4**, **6**, and KF in dimethoxyethane (DME) at 50 °C followed by consecutive treatment with KF in benzene at 80 °C, producing dihydrofuran **14** as a diastereomeric mixture. The initial KF-catalyzed reaction in DME gave the normal Michael adduct, a nitro compound which was then converted into the cyclization product **14** on further treatment with KF in benzene. As was the case of our synthesis of ligularone,[5] the two-step procedure provided the annulation product **14** in better yield than does one-step treatment in benzene.

Oxidation of **14** with sodium periodate in aqueous methanol to the corresponding sulfoxides and subsequent elimination of benzenesulfenic acid in refluxing benzene containing pyridine and active alumina afforded the key intermediate dihydrobenzofuran **5** in good yield.

While our work was in progress Magnus and Gopalan reported an alternative synthesis of **5** which culminated in the total synthesis of isolinderalactone and linderalactone.[10]

The remaining synthetic task for the elaboration of curzerenone (**1**) and epicurzerenone (**2**) was the introduction of an isopropenyl moiety into **5**. Contrary to our expectations, however, the straightforward introduction of the isopropenyl group via aldol condensation with acetone[11] or its equivalent such as acetone dimethyl acetal[12]

(1) (a) Hikino, H.; Agatsuma, K.; Takemoto, T. *Tetrahedron Lett.* **1968**, 2855. (b) Hikino, H.; Konno, C.; Agatsuma, K.; Takemoto, T.; Horibe, I.; Tori, K.; Ueyama, M.; Takeda, K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 478. Also curzerenone (**1**) has recently been isolated from myrrh, *Commiphora Abyssinica*, and from Chinese *Curcuma aeruginosa*. See: Brieskorn, C. H.; Noble, P. *Planta Med.* **1982**, *44*, 87. Fang, H.; Yu, J.; Chen, Y.; Hu, Q. *Yaoxue Xuebao* **1982**, *17*, 441.

(2) Hayashi, S.; Hayashi, N.; Matsuura, T. *Tetrahedron Lett.* **1968**, 1999.

(3) Takeda, K.; Horibe, I.; Teraoka, M.; Minato, H. *J. Chem. Soc. C* **1969**, 1491.

(4) Yanami, T.; Ballatore, A.; Miyashita, M.; Kato, M.; Yoshikoshi, A. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1144.

(5) Miyashita, M.; Kumazawa, T.; Yoshikoshi, A. *J. Org. Chem.* **1980**, *45*, 2945.

(6) The Stetter reaction and the Moiseenkov procedure for the synthesis of 4-acyl-3-methyldihydrobenzofurans from cyclic 1,3-diones are known. See: Stetter, H.; Lauterbach, R. *Angew. Chem.* **1959**, *71*, 673; *Chem. Ber.* **1960**, *93*, 603; *Chem. Ber.* **1962**, *95*, 43. Moiseenkov, A. M.; Lakhvich, F. A.; Akhrem, A. A. *Chem. Abstr.* **1972**, *76*, 99847.

(7) Preliminary communication: Miyashita, M.; Kumazawa, T.; Yoshikoshi, A. *Chem. Lett.* **1981**, 593.

(8) Miyashita, M.; Kumazawa, T.; Yoshikoshi, A. *Chem. Lett.* **1980**, 1043. Miyashita, M.; Yanami, T.; Kumazawa, T.; Yoshikoshi, A. *J. Am. Chem. Soc.* **1984**, *106*, 2149.

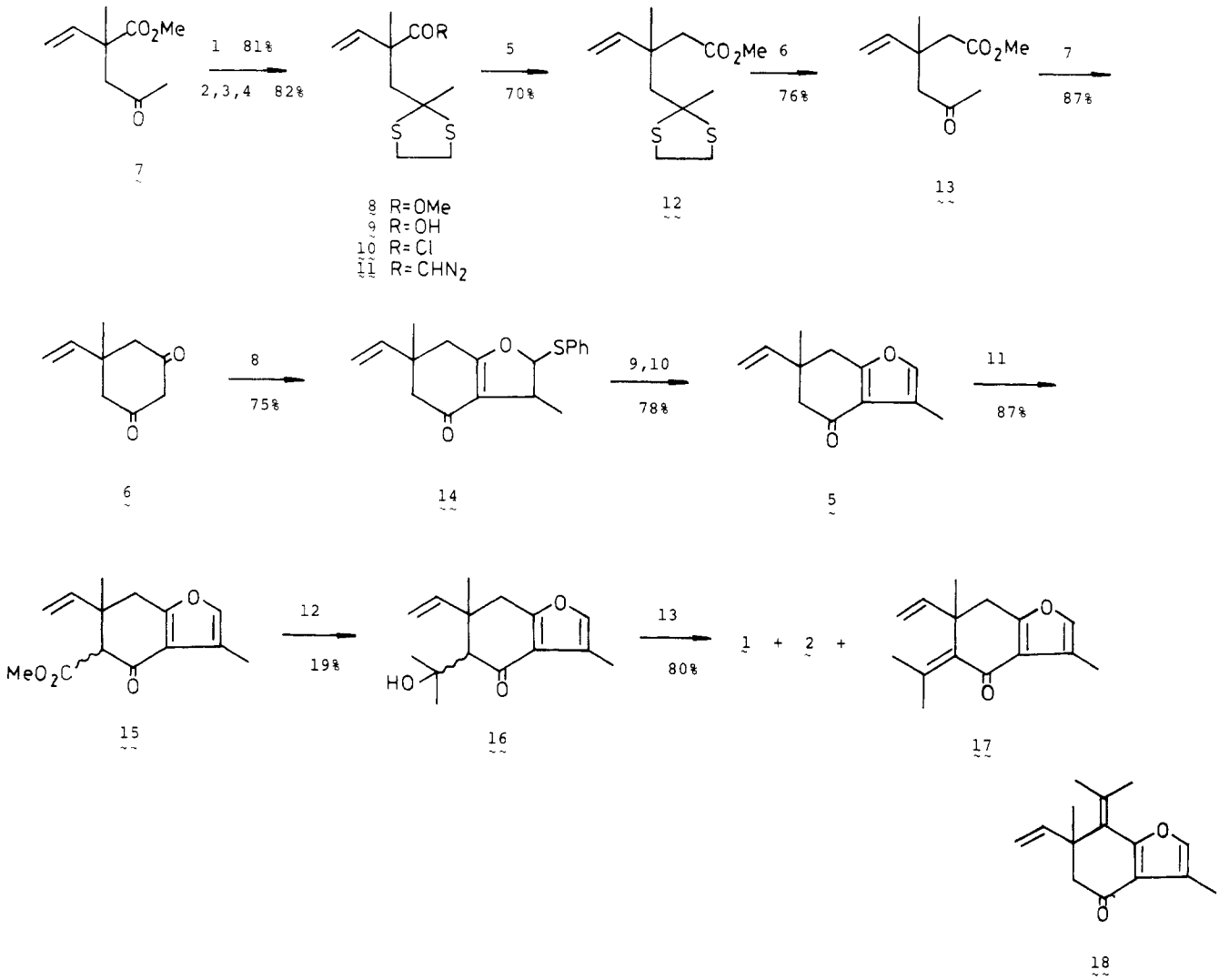
(9) Bachmann, W. E.; Struve, W. S. *Org. React.* **1942**, *1*, 38.

(10) Gopalan, A.; Magnus, P. *J. Am. Chem. Soc.* **1980**, *102*, 1756. Another synthesis of this compound has recently been reported. See: Masaki, Y.; Sakuma, K.; Hashimoto, K.; Kaji, K. *Tennen Yuki Kagobutsu Toronkai Koen Yoshishu, 24th* **1981**, 269.

(11) House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310. Hagiwara, H.; Uda, H.; Kodama, T. *J. Chem. Soc., Perkin Trans. 1* **1980**, 963.

(12) Saigo, K.; Osaki, M.; Mukaiyama, T. *Chem. Lett.* **1976**, 769.

Scheme II[a]



[a] (1) $BF_3 \cdot OEt_2$, $(CH_2SH)_2$, CH_2Cl_2; (2) KOH, EtOH, then H_2O^+; (3) $(COCl)_2$, PhH; (4) CH_2N_2, NEt_3, Et_2O; (5) Ag_2O, MeOH; (6) MeI, aqueous CH_3CN; (7) MeONa, $PhMe_2$; (8) $MeCH{=}C(PhS)NO_2$, KF, DME, then KF, PhH; (9) $NaIO_4$, aqueous MeOH; (10) Δ, C_5H_5N, Al_2O_3, PhH; (11) NaH, KH, $(CH_3O)_2CO$, PhH; (12) NaH, Et_2O, then MeMgI; (13) $POCl_3$, C_5H_5N.

was unsuccessful owing to its steric interference arising from neighboring alkyl substituents. Meanwhile it was found that **5** underwent carbomethoxylation by the procedure of Deslongchamps[13] to give β-keto ester **15** in high yield as an isomeric mixture (approximate ratio of 3:2).[14]

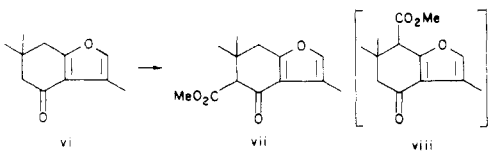
On treatment with sodium hydride followed by methylation with methyllithium[15] in ether, however, **15** did not give the desired ketol **16** but the retroaldol reaction product **5** in ca. 40% yield. Methylation of **15** with methylmagnesium iodide in place of methyllithium produced a mixture of ketol **16**, isocurzerenone (**17**),[16] and another dehydration product in 19%, 6%, and 20% yields, respectively, along with the recovered starting material **15** (51%). These compounds were cleanly separated by silica gel chromatography. Ketol **16** was an isomeric mixture with respect to the hydroxyisopropyl substituent (approximate ratio of 2:1), and the dehydration product was found, surprisingly, to be **18** from its IR (1690 cm^{-1}) and ^1H NMR spectra (1.24 (s, 3 H), 1.98 (s, 3 H), 2.13 (d, 3 H, J = 1), 2.17 (s, 3 H), 2.60 and 2.75 (ABq, 2 H, J = 16), 5.01 (d, 1 H, J = 10), 5.04 (d, 1 H, J = 17), 5.93 (dd, 1 H, J = 17, 10), 6.97 (br s, 1 H).

Despite numerous attempts to effect the methylation of **15**, the yield of **16** could not be improved, even under forced reaction conditions, and a substantial amount of starting material **15** was recovered unchanged.

These results led us to the following mechanistic rationale (Scheme III). The β-keto ester **15** which consists of two diastereomers with respect to the ester group (vide ante)[14] probably generated two enolate anions (i and ii) on treatment with NaH due to kinetic proton abstraction. The equatorial isomer presumably produced the enolate (i), while the alternative diastereomer possessing an axial

(13) Ruest, L.; Blouin, G.; Deslongchamps, P. *Synth. Commun.* **1976**, *6*, 169.

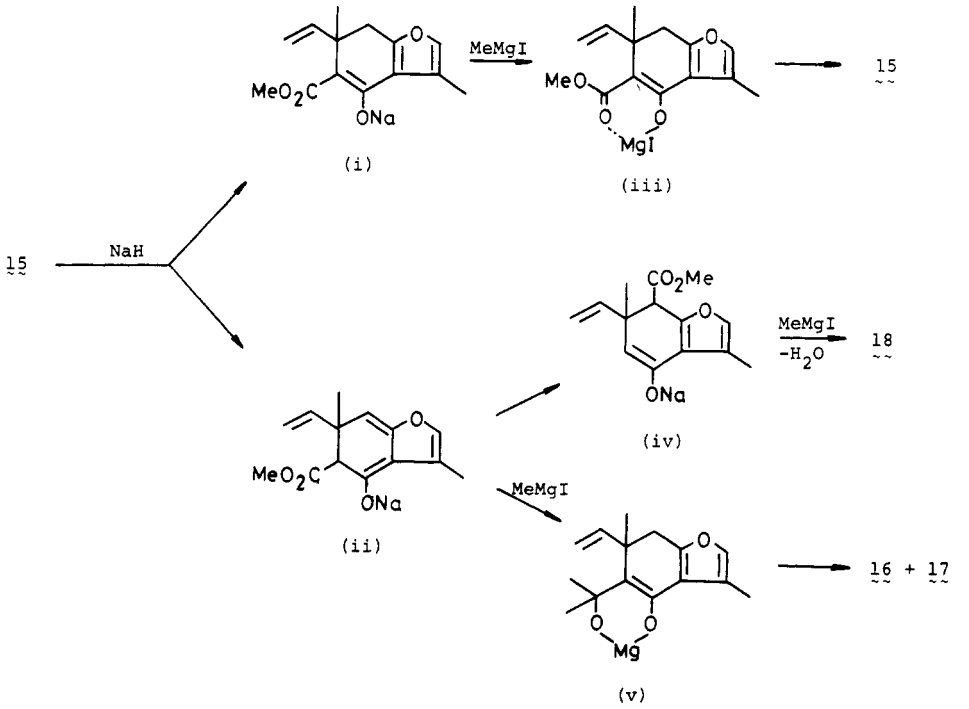
(14) The product was not regioisomers since the carbomethoxylation of vi by the same procedure gave single product vii in 76% yield and any regioisomers such as viii were not detected.



(15) A similar reaction was successfully applied to the synthesis of isoshobunone. See: Alexandre, C.; Rouessac, F. *J. Chem. Soc., Chem. Commun.* **1975**, 275.

(16) This compound has not been found in the nature as yet.

Scheme III



substituent generated another anion (ii) as shown in Scheme III.

We considered that the desired ketol **16** was produced from ii via the magnesium chelate v, while the unexpected compound **18** was derived from another intermediate (iv) in which the methoxycarbonyl group at C_5 in ii was intramolecularly rearranged to the C_7 position (Scheme III).

On the other hand, the fact that considerable amounts of starting material **15** were recovered may be better rationalized by assuming the intermediacy of the stable magnesium chelate iii which would be inert to nucleophilic attack of the Grignard reagent on the ester group due to the delocalized enolate anion iii.

Dehydration of **16** with phosphoryl chloride in pyridine gave a mixture of curzerenone (**1**), epicurzerenone (**2**), and isocurzerenone (**17**), in about a 3:2:1 ratio, in 80% yield.

Racemic curzerenone and epicurzerenone were spectroscopically identified by comparison with the natural compounds.[1] On the other hand, thermal rearrangement of **1** or **2** at 250–270 °C leading to pyrocurzerenone (**3**) has already been reported by Hikino et al.,[1] and hence the synthesis of **3** was also accomplished.[17]

Experimental Section

Melting points were determined with a Yamato melting point apparatus, Model MP-21, and are uncorrected. IR spectra were recorded on a JASCO A-3 spectrophotometer. ^1H NMR spectra were recorded on a JEOL JNM-PS-100 (100 MHz) spectrometer, except where noted, in CCl_4. Chemical shifts are expressed in δ values relative to Me_4Si as internal standard. Coupling constants (J) are given in hertz. Mass spectra were obtained on a JEOL 01-SG high-resolution mass spectrometer. High-performance liquid chromatography (HPLC) was carried out on a Waters Limited ALC/GPC-244. Solvent systems that developed the major reaction products in a moderate R_f range (0.4–0.6) are described for preparative, silica gel, thin-layer chromatography (TLC). Microanalyses were performed by the Microanalytical Laboratory in this institute.

Methyl 4,4-(Ethylenedithio)-2-methyl-2-vinylpentanoate (8). BF_3 etherate (0.638 mL, 5.1 mmol) was added dropwise to a solution of 7[8] (790 mg, 4.6 mmol) and ethanedithiol (0.482 mL, 5.1 mmol) in dry CH_2Cl_2 (15 mL) under N_2 at 0 °C. The mixture was stirred at 0 °C for an additional 2 h and then allowed to warm to room temperature overnight. The reaction mixture was poured into cold aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The extract was washed with water and saturated brine and dried over $MgSO_4$. Evaporation of the solvent gave an oil, which was purified by a silica gel column with petroleum ether–ether (10:1) to afford 915 mg (81%) of **8**: IR (neat) 1735, 1720, 920 cm^{-1}; ^1H NMR 1.38 (s, 3 H), 1.70 (s, 3 H), 2.31 and 2.62 (ABq, 2 H, J = 14), 3.23 (s, 4 H), 3.62 (s, 3 H), 5.03 (d, 1 H, J = 10), 5.05 (d, 1 H, J = 17), 5.96 (dd, 1 H, J = 17, 10). An analytical sample was prepared by distillation: bp 135–140 °C (bath temperature, 3 mmHg). Anal. Calcd for $C_{11}H_{18}O_2S_2$: C, 53.62; H, 7.36; S, 26.02. Found: C, 53.43; H, 7.46; S, 25.87.

1-Diazo-5,5-(ethylenedithio)-3-methyl-3-vinylhexan-2-one (11). A mixture of **8** (4.53 g, 18.4 mmol) and KOH (85% assay, 2.43 g, 36.8 mmol) in 95% ethanol (35 mL) was stirred at reflux for 3 h under N_2. After evaporation of two-thirds of the solvent, water (15 mL) was added, and the mixture was acidified with 10% HCl at 0 °C and extracted with ether. The ether extract was washed with saturated brine and dried over $MgSO_4$. Evaporation of the solvent left an oil which was purified by a short silica gel column with CH_2Cl_2–ether (2:1) to give 4.19 g (98%) of the acid **9** as a viscous oil.

A mixture of **9** (2.67 g, 11.5 mmol) and oxalyl chloride (3.0 mL, 34.5 mmol) in dry benzene (6 mL) was stirred at room temperature for 1 h under N_2 and then at reflux for 3.5 h. The mixture was cooled and the solvent was evaporated to give the acid chloride **10**, which was immediately submitted to the next reaction.

To a solution of excess diazomethane and triethylamine (1.16 g, 11.5 mmol) in ether (30 mL) was added dropwise at 0 °C a solution of **10** in ether (10 mL). The mixture was stirred at 0 °C for an additional 2 h and then at room temperature for 1 h and filtered. After removal of the solvent, the residual oil was purified by a silica gel column with petroleum ether–ether (10:1) to give 2.47 g (84%) of **11** as a yellow oil: IR (CCl_4) 2110, 1645, 1630, 1340, 922 cm^{-1}; ^1H NMR 1.30 (s, 3 H), 1.72 (s, 3 H), 2.36 and 2.70 (ABq, 2 H, J = 15), 3.27 (s, 4 H), 5.17 (d, 1 H, J = 17), 5.19 (d, 1 H, J = 10), 5.37 (s, 1 H), 6.12 (dd, 1 H, J = 17, 10). An analytical sample was prepared by distillation: bp 110–120 °C (bath temperature, 0.7 mmHg). Anal. Calcd for $C_{11}H_{16}N_2OS_2$: C, 51.53; H, 6.29; N, 10.93; S, 25.01. Found: C, 51.38; H, 6.49; N, 11.05; S, 24.81.

Methyl 5,5-(Ethylenedithio)-3-methyl-3-vinylhexanoate (12). To a solution of the diazo ketone (**11**) (2.47 g, 9.65 mmol)

(17) For an alternative synthesis of pyrocurzerenone (**3**), see: Viswanatha, V.; Krishna Rao, G. S. *J. Chem. Soc., Perkin Trans. 1* **1974**, 450.

in absolute methanol (34 mL) was added at reflux one-fifth of a slurry of silver oxide freshly prepared from silver nitrate (500 mg). The mixture was stirred at reflux for 30 min, and the residual silver oxide was added every 30 min for ten times. After the addition was complete, stirring was continued at reflux for an additional 3 h, then the mixture was cooled and filtered. Removal of the solvent gave an oil which was purified by silica gel column chromatography [hexane–ether (10:1) as solvent] to afford **12** (1.76 g, 70%) as an oil: IR (neat) 1735, 1717, 1640, 915 cm^{-1}; ^1H NMR 1.30 (s, 3 H), 1.76 (s, 3 H), 2.26 and 2.48 (ABq, 2 H, J = 15), 2.40 (s, 2 H), 3.28 (s, 4 H), 3.62 (s, 3 H), 4.97 (d, 1 H, J = 17), 4.99 (d, 1 H, J = 10), 6.03 (dd, 1 H, J = 17, 10). An analytical sample was prepared by distillation: bp 120–130 °C (bath temperature, 1 mmHg). Anal. Calcd for $C_{12}H_{20}O_2S_2$: C, 55.35; H, 7.74; S, 24.62. Found: C, 55.42; H, 7.80; S, 24.77.

Methyl 3-Methyl-5-oxo-3-vinylhexanoate (13). A solution of the thioacetal **12** (1.66 g, 6.38 mmol) and methyl iodide (7.9 mL, 128 mmol) in 85% aqueous acetonitrile (38 mL) was stirred at 45 °C for 18 h. The mixture was poured into cold water and extracted with ether. The ether extract was washed with 10% aqueous Na_2SO_3, water, and saturated brine and dried over $MgSO_4$. Evaporation of the solvent gave an oil which was purified by silica gel column chromatography [hexane–ether (5:1) as solvent] to afford **13** (885 mg, 76%) as an oil: IR (neat) 1735, 1717, 1688, 920 cm^{-1}; ^1H NMR 1.16 (s, 3 H), 2.06 (s, 3 H), 2.53 (s, 2 H), 2.65 (s, 2 H), 3.57 (s, 3 H), 4.91 (d, 1 H, J = 17), 4.92 (d, 1 H, J = 10), 5.91 (dd, 1 H, J = 17, 10). An analytical sample was prepared by distillation: bp 80–85 °C (bath temperature, 9 mmHg). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.31; H, 8.43.

5-Methyl-5-vinylcyclohexane-1,3-dione (6). To a stirred solution of sodium methoxide in xylene, prepared from NaH (480 mg, 20 mmol) and absolute methanol (2 mL) in xylene (30 mL) on heating at 100 °C for 30 min under N_2, was added dropwise a solution of **13** (1.84 g, 10 mmol) in xylene (5 mL) at 110 °C over 1 h with slow distillation of methanol generated. The mixture was further stirred at 115 °C for an additional 2 h. The cooled reaction mixture was acidified with 10% HCl and extracted with ethyl acetate. The extract was washed with water and saturated brine and dried over $MgSO_4$. Removal of ethyl acetate gave a xylene solution which was chromatographed on a short silica gel column. Elution with ethyl acetate afforded **6** (1.33 g, 87%) as colorless crystals: mp 100–102 °C (recrystallized from CCl_4); IR (KBr) 3600–2100 (br), 1618, 1582, 1520, 1340, 1226, 922 cm^{-1}; ^1H NMR ($CDCl_3$) 1.13 (s, 3 H), 2.3–3.0 (m, 4.2 H), 3.35 (s, 1.8 H), 5.02 (d, 1 H, J = 17), 5.07 (d, 1 H, J = 11), 5.75 (dd, 1 H, J = 17, 11). Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 70.86; H, 7.77.

3,6-Dimethyl-6-vinyl-6,7-dihydrobenzofuran-4(5*H*)-one (5).[10] A mixture of **6** (31 mg, 0.2 mmol), **4**[5] (51 mg, 0.26 mmol), KF (2 mg, 0.04 mmol), and dry DME (1 mL) was stirred at 50–55 °C for 3.5 h under N_2. The cooled reaction mixture was passed through a short silica gel column with ether. Evaporation of the eluate gave crude adduct, which was stirred with KF (2 mg) in dry benzene (1 mL) at reflux for 3.5 h under N_2. After filtration of the mixture through a neutral alumina column (Woelm, Activity III) with ether, the eluate was evaporated to leave an oil. The residue was separated by TLC [petroleum ether–ether (2:1) as solvent] to give **14** (45 mg, 75%) as a diastereomeric mixture.

A solution of **14** (45 mg, 0.15 mmol) and $NaIO_4$ (49 mg, 0.23 mmol) in 60% aqueous methanol (1.5 mL) was stirred at room temperature for 42 h. The mixture was poured into water and extracted thoroughly with CH_2Cl_2. The extract was washed with water and saturated brine and dried over $MgSO_4$. The crude product obtained on evaporation of the solvent was dissolved in dry benzene (2 mL) containing pyridine (30 μL) and active alumina (0.3 g), and the mixture was stirred at 100 °C for 3 h under N_2. After filtration, the solvent was removed in vacuo to give an oil which was purified by TLC [petroleum ether–ether (4:1) as solvent] to afford **5** (22 mg, 78%): IR (CCl_4) 1680, 1640, 1610, 1560, 1075, 920 cm^{-1}; ^1H NMR 1.22 (s, 3 H), 2.14 (d, 3 H, J = 1), 2.32 and 2.45 (ABq, 2 H, J = 15), 2.70 and 2.82 (ABq, 2 H, J = 16), 4.99 (d, 1 H, J = 11), 5.01 (d, 1 H, J = 18), 5.82 (dd, 1 H, J = 18, 11), 7.01 (br s, 1 H). An analytical sample was prepared by distillation: bp 110–120 °C (bath temperature, 20 mmHg). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.79; H, 7.69.

Methyl 3,6-Dimethyl-4-oxo-3-vinyl-4,5,6,7-tetrahydrobenzofuran-5-carboxylate (15). A mixture of NaH (26 mg, 1.11 mmol), dimethyl carbonate (0.313 mL, 3.7 mmol), and **5** (70 mg, 0.37 mmol) in dry benzene (2 mL) was refluxed for 1 h under N_2 and then a catalytic amount of KH was added. The resulting mixture was further stirred at reflux for 18 h. The cooled reaction mixture was acidified with acetic acid (0.1 mL) and partitioned with a mixture of ether and water. The organic layer was washed with water and saturated brine and dried. Evaporation of the solvent left an oil which was purified by TLC [hexane–ether (2:1) as solvent] to afford **15** (80 mg, 87%) as an oil: bp 105–115 °C (bath temperature, 8 mmHg); IR (CCl_4) 1738, 1680, 1560, 1436, 1160, 922 cm^{-1}; ^1H NMR 1.23 and 1.27 (s each, 3 H in total), 2.17 (d, 3 H, J = 1), 2.60 and 3.42 (ABq, J = 17) and 2.75 and 3.15 (ABq, J = 18) (2 H in total), 3.21 and 3.34 (s each, 1 H in total), 3.63 and 3.69 (s each, 3 H in total), 4.84–5.20 (m, 2 H), 5.60–6.15 (m, 1 H), 7.03 (br s, 1 H). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.68; H, 6.45.

Reaction of 15 with Methylmagnesium Iodide. A mixture of NaH (8 mg, 0.35 mmol) and **15** (86 mg, 0.35 mmol) in dry ether (1 mL) was stirred at room temperature for 1 h under Ar, and then an ethereal solution of MeMgI (1 M, 2.1 mL, 2.1 mmol) was added at room temperature. The resulting mixture was stirred at reflux for 3 h. The cooled mixture was poured into chilled 10% HCl and extracted with ether. The extract was washed with water and saturated brine. Evaporation of the solvent left an oil which was purified by TLC [hexane–ether (2:1) as solvent] to give unchanged **15** (44 mg, 51%), **16** (16 mg, 19%), isocurzerenone (**17**)[16] (5 mg, 6%), and **18** (16 mg, 20%). **16**: an oil; IR (CCl_4) 3470, 1672, 1562, 1422, 1382, 918 cm^{-1}; ^1H NMR 1.10–1.45 (9 H), 2.16 (br s, 3 H), 4.80–5.25 (m, 2 H), 5.75–6.40 (m, 1 H), 6.98 (br s, 1 H); M^+ 248.1368, calcd for $C_{15}H_{20}O_3$ 248.1411. **17**: an oil; IR (CCl_4) 3093, 1658, 1566, 1437, 1413, 1075, 1054, 913 cm^{-1}; ^1H NMR 1.41 (s, 3 H), 1.99 (s, 3 H), 2.05 (s, 3 H), 2.21 (s, 3 H), 2.60 and 2.94 (ABq, 2 H, J = 16), 5.03 (d, 1 H, J = 12), 5.09 (d, 1 H, J = 18), 6.24 (dd, 1 H, J = 18, 12), 6.99 (s, 1 H); M^+ 230.1331, calcd for $C_{15}H_{18}O_2$ 230.1307. **18**: an oil; IR (CCl_4) 1690, 1582, 1350, 1104, 920 cm^{-1}; ^1H NMR 1.24 (s, 3 H), 1.98 (s, 3 H), 2.13 (d, 3 H, J = 1), 2.17 (s, 3 H), 2.60 and 2.75 (ABq, 2 H, J = 16), 5.01 (d, 1 H, J = 10), 5.04 (d, 1 H, J = 17), 5.93 (dd, 1 H, J = 17, 10), 6.97 (br s, 1 H); M^+ 230.1355, calcd for $C_{15}H_{18}O_2$ 230.1307.

Curzerenone (1) and Epicurzerenone (2). $POCl_3$ (74 mg, 0.48 mmol) was added dropwise to a solution of **16** (24 mg, 0.097 mmol) in pyridine (0.48 mL) at room temperature under N_2. The mixture was gradually heated to 100 °C over 30 min and kept at this temperature for 5 min. After cooling to room temperature, the mixture was poured into a stirred mixture of hexane (20 mL) and cold water (20 mL). Stirring was continued for a further 20 min, and the organic layer was separated. The aqueous layer was successively washed with water, dilute Na_2CO_3, water, aqueous cupric sulfate, water, and brine and dried ($MgSO_4$). Removal of the solvent left an oil which was purified by TLC [hexane–ether (95:5) as solvent, with five times of development] to give **17** (3 mg, 13%) and a mixture of **1** and **2** (15 mg, 67%). The mixture of **1** and **2** in a 7:5 ratio was cleanly separated by HPLC [uPorasil ($^3/_8$ in. × 1 ft) column with hexane–$CHCl_3$ (9:1) as solvent]. The major product was curzerenone (**1**) as identified by comparison of the IR and ^1H NMR spectra with those of natural curzerenone. The minor product was epicurzerenone (**2**) as spectroscopically identified with natural epicurzerenone.[1]

Acknowledgment. We thank Professor H. Hikino for providing us with the IR and ^1H NMR spectra of natural curzerenone and epicurzerenone.

Registry No. (±)-**1**, 20493-56-5; (±)-**2**, 20085-85-2; (±)-**3**, 20013-75-6; **4**, 67808-91-7; (±)-**5**, 73696-87-4; **6**, 91445-19-1; (±)-**7**, 78924-38-6; (±)-**8**, 78924-39-7; (±)-**9**, 78924-40-0; (±)-**10**, 78924-41-1; (±)-**11**, 78924-42-2; (±)-**12**, 78924-43-3; (±)-**13**, 78924-44-4; **14**, 78924-46-6; (±)-*cis*-**15**, 78924-47-7; (±)-*trans*-**15**, 78924-50-2; (±)-*cis*-**16**, 78924-48-8; (±)-*trans*-**16**, 78924-51-3; (±)-**17**, 78924-49-9; (±)-**18**, 91445-20-4; MeI, 74-88-4.