conformational variation to diminish overlap between the filled orbitals. The contrast between stabilizing and destabilizing homoallylic interaction is emphasized.

Since this work was submitted, Haselbach[25] has published a PES study of 9-isopropylidenebenzonorbornadienes and related systems. His work lends additional support for our conclusions. It also reemphasizes the conformational idea that interaction between a lone pair in a bicyclic system and the other unsaturated bridges should have little influence on lone pair orientation. If the interaction is between a lone pair and a single unsaturated bridge, the molecule will distort so that both the unfavorable interaction and its stereochemical impact will be minimized. If the interaction is between a lone pair and two unsaturated bridges, the lone pair orientation will reflect the delicate balance of all π- and σ-type interactions.

References and Notes

(1) The term homoallylic is used as an abbreviation in this work. More precise terminology would be bishomoantiaromatic or bishomoazirinyl.
(2) (a) I. Morishima, K. Yoshikawa, M. Hashimoto, and K. Bekki, *J. Am. Chem. Soc.*, **97**, 4283 (1975); (b) I. Morishima and K. Yoshikawa, *ibid.*, **97**, 2950 (1975).
(3) G. R. Underwood and H. S. Friedman, (a) *J. Am. Chem. Soc.*, **96**, 4989 (1974); (b) paper submitted for publication. I thank Professor Underwood for a preprint.
(4) S. F. Nelson and J. M. Buschek, *J. Am. Chem. Soc.*, **96**, 6987 (1974).
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(9) K. N. Houk, Y. M. Chang, and P. S. Engel, *J. Am Chem. Soc.*, **97**, 1824 (1975).
(10) K. Tori, T. Tsushima, H. Tanida, K. Kushida, and S. Satoh, *Org. Magn. Reson.*, **6**, 324 (1974).
(11) To our knowledge, the PES spectra of the important reference compounds 7-azanorbornane and 7-azanorbornene have not been reported.
(12) The apparent anomalies of compounds **11** and **13** of ref 2a are presumably due to conformational changes since the bicyclic compound **17** shows a normal value.
(13) This value differs from the tabulated value of ref 2a and was derived from the actual spectrum of **5.** The band at 9 eV of Figure 2 is measurably broader and exhibits a shoulder at 9.4 eV which indicates that it is composed of two bands.
(14) See, for example, E. Heilbronner and H. D. Martin, *Helv. Chim. Acta*, **55,** 1490 (1972), and references therein.
(15) R. W. Hoffmann, R. Schuttler, W. Schafer, and A. Schweig, *Angew. Chem.*, **84,** 533 (1972).
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(17) Since PES is a Franck–Condon process, the nuclei in the radical cation retain their ground state configuration.
(18) P. Bischof, E. Heilbronner, H. Prinzbach, and H. D. Martin, *Helv. Chim. Acta*, **54,** 1072 (1971).
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(21) J. K. Stille and K. N. Sannes, *J. Am. Chem. Soc.*, **94**, 8489 (1972). A warning is pertinent as this result implies that carbanion inversion is faster than carbanion protonation by solvent water.
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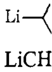
η^5-Cyclohexadienyltricarbonylchromium(0) Intermediates in the Reaction of Carbanions with η^6-Arenetricarbonylchromium(0)

Sir:

The electron withdrawing effects of a chromium tricarbonyl unit π-bonded to an aromatic ring are reflected clearly in the reactivity patterns of the arene and its substituents.[1] We[2] and others[3] have observed coupling of carbanions with π-arene ligands, in processes which promise to be valuable in organic synthesis. The reaction of a carbanion derived from a carbon acid of $pK_a = 25$ or higher converts complex **1**, η-benzenetricarbonylchromium(0), into an intermediate within minutes at 0 °C or below in tetrahydrofuran.

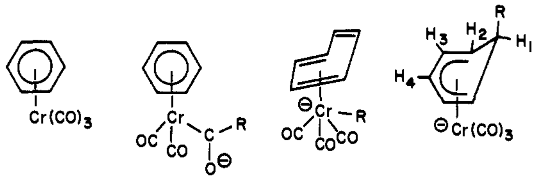
Table I.[a] ^{1}H NMR Data for Complex 4

Carbanion, R	H_4	H_3	H_2	H_1	H in R
1. $LiC(CH_3)_2CN$	4.87	4.61	2.7	2.6	1.00 (s, $-CH_3$)
2. $LiCH_2CN$	4.92	4.22	2.6	2.6	1.48 (d, $J \simeq 6$ Hz, $-CH_2$)
3. Li	4.82	4.35	[———— 3.1–1.4 (~10 H) ————]		
4. $LiCH(SPh)_2$	4.92	4.41	2.80	2.40	3.40 (d, $J \simeq 10$ Hz, $-CH$) 7.20 (m, $-C_6H_5$)

[a] All spectra were measured in THF-d_8 at −30 to −60 °C. The pattern of absorption for H_4 and H_3 was essentially the same for all four entries. Peak positions are in parts per million downfield from Me_4Si.

At least three structural types are reasonable for the intermediate: structure **2** results from attack of the carbanion, R^-, at a carbonyl ligand, as observed for **1** and phenyllithium;[4] structure **3** shows the carbanion attached to chromium with concomitant loss of one coordination site on the arene (or loss of one carbon monoxide, not shown);[5] and structure **4** results from addition of the carbanion to the arene ligand, a transition-metal analogue of the Meisenheimer complex.

Scheme I

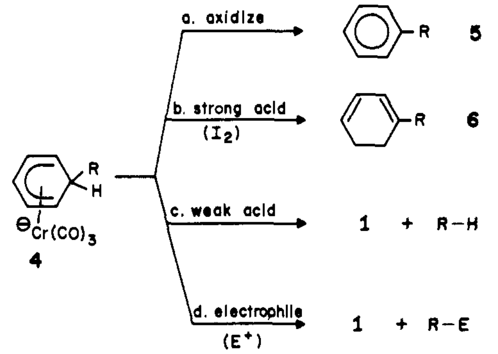


1 **2** **3** **4**

The reactivity of this intermediate has been probed by exposing it to oxidizing agents, proton sources, and organic electrophiles. We wish to report preliminary results of these studies along with ^{1}H NMR spectral data which point to the structural type represented by **4** for the key intermediates, the first examples of η^5-cyclohexadienyltricarbonylchromium(0) complexes.

Monitoring of the reaction of lithiocyanomethane[6] with **1** at −40 °C in THF-d_8 under argon shows complete conversion of **1** within minutes (absence of singlet at δ 5.45). New absorptions appear at δ 4.92 (broad, triplet, 1 H, H_4 in **4**), 4.22 (m, 2 H, H_3), 2.6 (m, 3 H, H_2 and H_1), and 1.48 (d, $J = 6$ Hz, 2 H, $-CH_2CN$ as R in **4**). The peak assignments are parallel with those for closely related manganese,[7] iron,[8] and iridium[9] η^5-cyclohexadienyl complexes, and are supported by the following double irradiation experiments. Irradiation at δ 2.6 (H_2 and H_1) provides a triplet at δ 4.92 ($J_{4,3} = 6$ Hz), a broad doublet at 4.22 ($J_{4,3} = 6$ Hz), and a singlet at 1.48. Irradiation at 4.92 converted the absorption at δ 4.22 to a broad singlet, with small unresolved couplings (apparently $J_{4,2}$ or $J_{4,1}$ is >0 but <2 Hz), and left the other absorptions essentially unchanged. Irradiation at δ 4.22 provides a broad singlet at δ 4.92 with no other significant changes. Irradiation at δ 1.48 had no significant effect on the spectrum. These decoupling experiments generally support the chemical shift assignments and provide strong evidence that the carbanion unit is attached to one carbon of the arene ring.

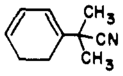
The intermediate is stable for long periods below 0 °C but decomposes rapidly in the presence of oxidizing agents (air) or electrophilic species (see below). No fluxional behavior was observed up to 37 °C. Similar data have been obtained for a series of carbanions, as displayed in Table I. Generally, H_1 and H_2 overlap significantly, but entry 4 (Table I) shows an example where they appear separately. The stereochemistry of



the addition of the carbanion is not clear from the ${}^1H$ NMR data. Exo attack is proposed (in **4**) based on analogy in other metal systems[7] and the absence of C-H stretching vibration in the region 2300-2400 cm^{-1}, where a band is observed in complexes related to **4** where R = H.[10,11]

The reactivity of the intermediates is generally consistent with the η^5-cyclohexadienyl structure but with some unanticipated properties. Three types of reactions have been observed, as summarized in Scheme I. For example, addition of a solution of excess iodine in THF or ceric ammonium nitrate in acetonitrile causes oxidation of the intermediate with eventual formation of Cr(III), carbon monoxide, and the arene (**5**); a hydrogen substituent has been replaced by the carbanion unit. With a wide variety of carbanions, the overall yields are in the range of 70-95% using iodine (path a, Scheme I).[2c] Titration with iodine demonstrates that approximately 2.5 mol of I_2 are required per mole of **4.**[12]

Addition of excess (five-eightfold) of trifluoroacetic acid to **4** at −78 °C followed by warming to 0 °C leads to new chromium complexes which have not been characterized. The organic ligand is separated from the chromium by treatment with iodine at 25 °C to afford mainly dihydroarene **6,** where the carbanion resides at the end of the diene system (path b, Scheme I). For example, 2-lithio-2-cyanopropane produced **4** [(R = $C(CH_3)_2CN$)] which was treated with trifluoroacetic acid (5 mol equiv/0 °C/3.5 h) and then excess iodine (25 °C/3.5 h). A mixture of cyclohexadienes (**7**, **8**, and **9**) was isolated in a combined yield of 90% and a ratio of 90:7:3, respectively.[13]



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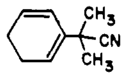

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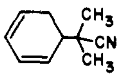

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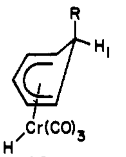
When **4** [R = $C(CH_3)_2CN$] was allowed to react with excess of a weak acid (water, 2,2,2-trifluoro-*tert*-butyl alcohol) or with 1 mol equiv of trifluoroacetic acid at −78 °C, a dramatic line broadening in the ${}^1H$ NMR spectrum and color changes in the solution are observed. Treatment with iodine at −78 °C followed by warming to 25 °C produces the alkylarene, **5** [R = $C(CH_3)_2CN$] in good yield. If the solution is warmed above −30 °C after addition of a proton source, complex **1** reappears rapidly (singlet at δ 5.4 in the ${}^1H$ NMR spectrum) along with 2-cyanopropane; greater than 80% of **1** was recovered (path c, Scheme I). Addition of D_2O to **4** [R = $C(CH_3)_2CN$] at −78 °C followed by warming to 25 °C produced **1** with no deuterium above natural abundance, while the 2-cyanopropane contained one deuterium per molecule.

Reaction of **4** [R = $C(CH_3)_2CN$] with excess methyl iodide in THF at 25 °C proceeds to completion over several hours to produce complex **1** and 2-cyano-2-methylpropane as the only products. Similarly, potential hydride acceptors such as benzophenone, triphenylcarbenium fluoroborate, and triisopropylborane react rapidly with **4** to abstract the carbanion unit. In each case, complex **1** is regenerated efficiently; adducts of $^-C(CH_3)_2CN$ with triphenylcarbenium ion and benzophenone have been isolated.[14]

Pathways for formation of **2** and **3,** and for the reversal of anion attack (paths c, d in Scheme I) are not yet well defined. Presumably the cyclohexadienyl complex (**4**) is oxidized by iodine to effect removal of H_1 (perhaps as a proton[15]) and to weaken the arene-chromium bond until the arene is released. The addition of a proton source leads to rapid protonation of **4,** even at −78 °C, to give a new intermediate, presumably a hydrido-chromium complex (e.g., **10**).[16] This species is capable of regenerating **1** under very mild conditions (ca. −30 °C); but excess acid brings about protonation at the cyclohexadienyl ligand, perhaps to give **11,** and prevents reversal to **1.** Reaction of **11** with iodine increases the oxidation state of chromium and causes release of the diene ligand.[18] Olefin isomerization occurs at some point *before* the diene is released from the metal, with the main product resulting from an intermediate such as **12.**[19]



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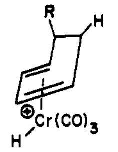

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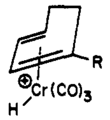

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Work is in progress to provide direct evidence for the proposed intermediates and to determine the scope of the reactions of **4** as outlined in Scheme I.[20]

Reference and Notes

(1) (a) Cf. W. E. Silverthorn, *Adv. Organomet. Chem.*, **13,** 47 (1975); (b) M. F. Semmelhack, Proceedings of a Symposium on Applications of Organometallic Reagents in Synthesis, American Chemical Society Centennial Meeting, New York, N.Y., April 1976, in press.

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(3) For examples, see (a) R. J. Card and W. S. Trahanovsky, *Tetrahedron Lett.*, 3823 (1973); (b) I. U. Khand, P. L. Pauson, and W. E. Watts, *J. Chem. Soc. C*, 2257 and 2261 (1968), and 116 (1969); (c) P. J. C. Walker and R. J. Mawby, *Inorg. Chim. Acta*, 7, 621 (1973); (d) J. F. Helling and G. G. Cash, *J. Organomet. Chem.*, **73,** C10 (1974).

(4) H. V. Beck, E. O. Fischer, and C. G. Kreiter, *J. Organomet. Chem.*, **26,** C41 (1971).

(5) Addition of the carbanion to chromium would require promotion of an electron pair to a high energy orbital unless one of the ligands is removed.

(6) Lithiocyanomethane was generated by reaction of lithium diisopropylamide with 1 mol equiv of acetonitrile in THF at −30 °C.

(7) (a) P. J. C. Walker and R. J. Mawby, *Inorg. Chim. Acta*, 7, 621 (1973); (b) P. L. Pauson and J. A. Segal, *J. Chem. Soc., Dalton Trans.*, 1677 (1975); (c) *ibid.*, 1684 (1975); (d) P. J. C. Walker and R. J. Mawby, *ibid.*, 622 (1973); D. A. Sweigart and L. A. P. Kane-Maguire, *J. Chem. Soc., Chem. Commun.*, 13 (1976).

(8) Cf. I. U. Khand, P. L. Pauson, and W. E. Watts, *J. Chem. Soc. C*, 116 (1969).

(9) Cf. C. White and P. M. Maitlis, *J. Chem. Soc. A*, 3322 (1971).

(10) (a) P. H. Bird and M. R. Churchill, *Chem. Commun.*, 777 (1967); (b) I. U. Khand, P. L. Pauson, and W. E. Watts, *J. Chem. Soc. C*, 2024 (1969).

(11) Infrared spectra of complex **4** [R = $CH(PhS)_2$] were obtained in THF-d_8 by Ms. C. Carter.

(12) We thank Mr. Joel Belasco for carrying out this experiment.

(13) Each of the isomers was isolated separately, and structures are assigned based primarily on ${}^1H$ NMR spectral data. The uv and ir spectra are consistent with the structures; GC-MS on the mixture confirmed the molecular weight of each component. Diels-Alder adducts of each isomer with *N*-phenyltriazoline-1,3-dione were prepared; each provided spectral data consistent with the proposed structures of the dienes **7**-**9.**

(14) The remarkably easy cleavage of exo-carbon-carbon bond in **4** is not unprecedented for η^5-cyclohexadienyl complexes. For example, *exo*-η^5-(RC_6H_6)-η^5-$(C_5H_5)Fe^{II}$ with R = C_2H_5, $C_6H_5CH_2$, and C_5H_5 reacts with triphenylcarbenium ion or *N*-bromosuccinimide to give η^6-(C_6H_6)-η^5-$(C_5H_5)Fe^{II}$ complexes: see A. N. Nesmeyanov, N. A. Vol'kenau, L. S. Shilovtseva, and V. S. Petrakova, *J. Organomet. Chem.*, **85,** 365 (1975). R. J. Mawby and co-workers have observed similar behavior in η^5-cyclohexadienyltricarbonylmanganese(II) complexes: see P. J. C. Walker and R. J. Mawby, *J. Chem. Soc., Chem. Commun.*, 330 (1972), and A. Mawby, P. J. C. Walker, and R. J. Mawby, *J. Organomet. Chem.*, **55,** C39 (1973).

(15) Electron transfer from **4** to iodine could lead to an η^5-cyclohexadienyltricarbonylchromium(II) complex of the type proposed as a transient intermediate in Friedel-Crafts reactions of η-arenetricarbonylchromium(0).[16] Such a species would be expected to rearomatize by expulsion of a proton in the absence of a strong acid.

(16) Cf. W. R. Jackson and W. B. Jennings, *J. Chem. Soc. B*, 1221 (1969).

(17) No Cr-H absorption was detected in the ^1H NMR spectrum between 20 ppm downfield and 10 ppm upfield; the severe line broadening may have obscured the signal. Warming to −30 °C provided a spectrum consistent with a simple mixture of **1** and 2-cyanopropane, and normal line widths. A referee pointed out that the reversal reactions (**4** → **1**) "are surprising" and suggested that a second (undetected) intermediate is responsible for the reversal. This possibility cannot be ruled out by the data in hand, but **4** is the only intermediate detected (>90% yield) and the products of reversal are obtained in >80% yield. Therefore, if a second intermediate is involved in the reversal reactions, it must be in rapid equilibrium with **4** and remain at low concentration. These points are currently under investigation.

(18) Complexes of 1,3-dienes with chromium-carbonyl units are rare, but a 1,3-butadienetetracarbonylchromium(0) has recently been characterized. Cf. I. Fischler, M. Budzwait, and E. Koerner von Gustdorf, *J. Organomet. Chem.*, **105**, 325 (1976).

(19) The isomers **7**, **8**, and **9** were shown to be stable to the acid and iodine conditions used to quench the intermediate. Presumably, rapid hydrogen shifts occur in the diene-chromium species such as **11** and **12**, with **12** being the isomer favored at equilibrium.

(20) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support of this work.

(21) Recipient of a Camille and Henry Dreyfuss Teacher-Scholar Grant, 1973-1978.

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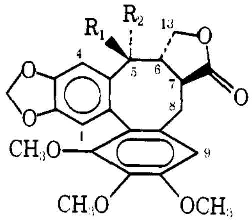
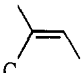
Isosteganacin

Sir:

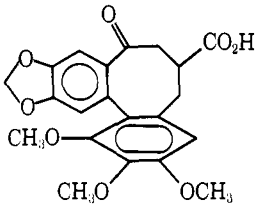
In 1974 Kupchan reported the isolation and structure elucidation of steganone (**1**) and related dibenzocyclooctadiene lignan lactones, among which steganacin (**2**) and steganangin (**3**) showed significant antileukemic activity.[1] We have recently described the first total synthesis of (±)-steganacin[2] and now report some unusual stereochemical considerations which control synthesis in this series.



1, R_1, R_2 = =O
2, R_1 = OAc; R_2 = H



3, R_1 = O_2C ; R_2 = H
4, R_1 = OH; R_2 = H
5, R_1 = H; R_2 = OH



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In our preceding communication we reported the preparation of (±)-steganone (**1**) by hydroxymethylation of the racemic keto acid **6** with HCHO in dilute base. When crude crystalline steganone (mp 223-226 °C) from this reaction was reduced with $NaBH_4$ (1:1 MeOH-CH_2Cl_2, 25 °C, 3 min) we obtained a mixture of three isomeric alcohols separable by careful preparative TLC (SiO_2, 20% cyclohexane-ether). The two major alcohols were steganol (**4**) and episteganol (**5**), as described by Kupchan, whereas the third alcohol (10-15% yield) was a new substance, mp 242-244 °C, which we named isosteganol.[3] This new isomer was not seen when the $NaBH_4$ reduction was carried out on highly purified steganone (mp 229-230 °C). Careful TLC and HPLC analyses revealed that the isosteganol *had not been produced in the* $NaBH_4$ *reduction step,* but was in fact a significant by-product from the initial hydroxymethylation of keto acid **6**.

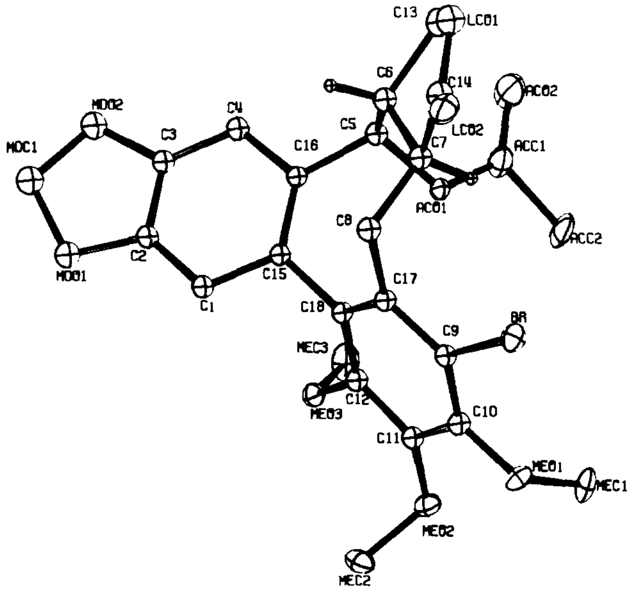
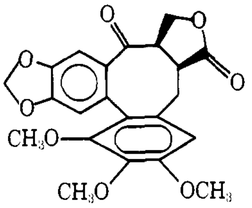


Figure 1. Computer drawing of 9-bromoisosteganacin from x-ray data. Thermal ellipsoids enclose 50% electron density, except for hydrogen positions on C-6 and C-7. These are predicted positions assuming tetrahedral geometry, C-H distances of 1.0 Å and arbitrary thermal parameters.

Oxidation of isosteganol (Jones reagent, 25 °C, 15 min) yields the $C_{22}H_{20}O_8$ ketone isosteganone, mp 209-212.5 °C.[4] Reduction of isosteganone ($NaBH_4$, CH_2Cl_2-MeOH, 0 °C, 3 min) yields exclusively isosteganol. Pure isosteganone shows striking spectroscopic differences from steganone. Whereas the latter shows the 1667 cm^{-1} $\nu_{C=O}$ stretch and δ 7.53 NMR singlet (deshielded ortho proton) characteristic of such an aryl ketone, isosteganone shows a 1707 cm^{-1} ketone carbonyl stretch and has no proton NMR signal downfield of δ 6.71. These data imply that the ketone carbonyl of isosteganone is not coplanar with the adjacent aromatic ring.

Treatment of isosteganone with either sodium acetate (EtOH, reflux, 3 h) or by heating in a soft glass tube (230 °C, 3 min) led to quantitative formation of steganone. We conclude that the difference between iso and normal series could arise (1) from cis vs. trans γ-lactone ring junctions (**7** vs. **1**), or (2) from hindered rotation about the biaryl bond (**8** vs. **1**), or (3) possibly from both sources (**9** vs. **1**). Models of ketolactones **7**, **8**, or **9** all show the ketone carbonyl out of the plane of the methylenedioxyphenyl ring.



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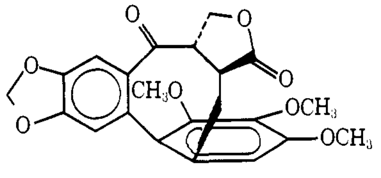

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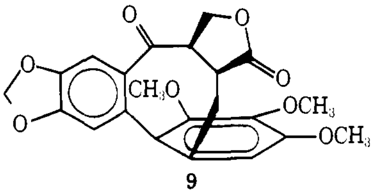

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Evidence on these alternatives was derived from esterification of keto acid **6** (3% HCl in MeOH, reflux 6 h) to yield oily keto ester **10** [ir 1728, 1653 cm^{-1}].[5] Chromatography (SiO_2, 20% hexane in ether) resolved **10** into two distinctly different crystalline $C_{22}H_{22}O_8$ keto esters (ca. 1:1), the more