Table I. Comparison of Analgesia. Morphine Sulfate *vs.* I

Method	AD_{50} (mg/kg)[a] Morphine sulfate	AD_{50} (mg/kg)[a] I
Rat tail flick[b]	5.8	No effect (0.25–8.0)[g]
	2.2	50 (0.5–50.0)
Mouse tail electroshock[c,d]	1.2	~60 (32–64)
Mouse hot plate[e]	1.7	50 (5.0–50.0)
Mouse foot clamp[f]	1.1	No effect (64.0–128.0)
Mouse tail clip[f]	8.2	Could not estimate (0.5–100.0)

[a] AD_{50} = analgesic dose in 50% of the animals (as calculated by graphical means). Morphine sulfate administered intravenously as a water solution. Compound I administered intraveneously as a propylene glycol solution. Sodium chloride (0.9%) and propylene glycol solutions were administered as negative controls. Satisfactory AD_{50} values were also obtained for codeine phosphate, *d*-propoxyphene, and sodium salicylate. [b] Tested essentially by the method of F. E. D'Amour and D. L. Smith, *J. Pharmacol.*, **72**, 74 (1941). [c] P. L. Nilsen, *Acta Pharmacol. Toxicol.*, **18**, 10 (1961). [d] Intraperitoneal administration. [e] Method of G. Woolfe and A. D. Maconald, *J. Pharmacol.*, **98**, 121 (1950), as modified by N. B. Eddy and D. Leimbach, *ibid.*, **107**, 385 (1953). [f] C. Bianchi and J. Franceschini, *Brit. J. Pharmacol.*, **9**, 280 (1954). [g] Values in parentheses represent the range of dosesa dministered in milligrams per kilogram.

propylene glycol solution) or with other members of the series in doses up to 50 mg/kg (intravenous, water solution). On the other hand, morphine sulfate in doses of from 1 to 5 mg/kg showed some degree of analgesia in all dogs tested. Crossover studies between morphine sulfate and I in some of the dogs compensated for individual variations in response to the painful stimuli employed.

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Stereospecific Transannular Cycloaddition to a 1,6-Cyclodecadiene[1]

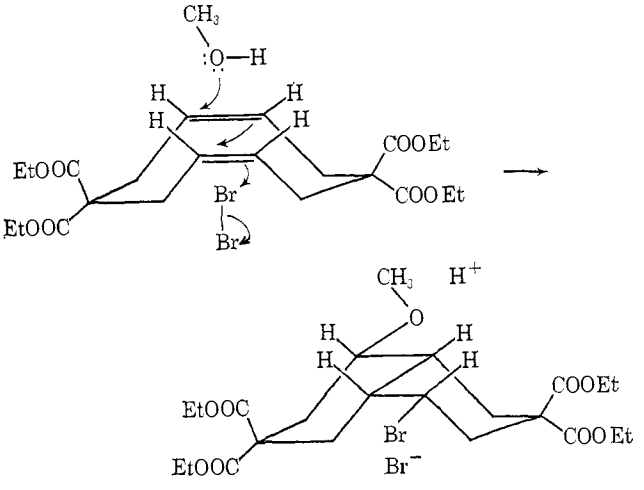
Sir:

The reaction of *cis*-1,4-dichloro-2-butene with diethyl malonate and 2 equiv of sodium ethoxide has been reported to form diethyl 3-cyclopentene-1,1-dicarboxylate, diethyl 2-vinylcyclopropane-1,1-dicarboxylate, and a small amount of a crystalline solid which was thought to be a bi- or tricyclic derivative on the basis of lack of reaction with bromine in ether or with potassium permanganate in acetone.[2]

In the present investigation, the crystalline solid, mp 161–162°, has been identified as tetraethyl *cis,cis*-3,8-cyclodecadiene-1,1,6,6-tetracarboxylate on the basis of analytical data and particularly the nuclear magnetic resonance spectrum.[3] The presence of two double bonds was confirmed by catalytic hydrogenation in acidic solution to produce the saturated cyclodecane derivative, mp 145–146°.[4]

Although the 1,6-cyclodecadiene derivative does not add bromine in carbon tetrachloride, it does react with bromine in methanol at room temperature to form a derivative, mp 129–130°, in high yields (>90%). The analyses and nmr spectrum of the product[5] indicate that it is a bicyclo-disubstituted derivative formed by a transannular cycloaddition reaction.

Since the product is formed in high yields, it was of considerable interest to determine by X-ray crystallographic studies the structure of the product, which could be a substituted bicyclo[4.4.0]- or -[5.3.0]decane formed by a stereospecific cycloaddition. The crystals of the product are monoclinic, space group $P2_1/c$, with the following unit-cell dimensions: a = 13.56, b = 16.92, c = 12.25 A, β = 97.16°, and there are 4 molecules/unit cell. Integrated intensities of 2411 independent nonzero reflections were measured using a scintillation counter, with Cu Kα radiation, and the structure was solved by Patterson and Fourier methods. Several cycles of least-squares refinement have been carried out, and the agreement index, R, is 14% at this stage. A complete report of the crystallographic investigation will be made when refinement has been completed. These crystallographic studies have demonstrated that the addition occurs with the formation of the decahydronaphthalene derivative and that the reaction is stereospecific to form tetraethyl 4-bromo-8-methoxydecahydronaphthalene-2,2,6,6-tetracarboxylate with the bromo and methoxy groups in a *cis* position relative to the *cis*-fused rings, as indicated by



Found: C, 62.12; H, 7.83; mol wt, 418. The nmr spectrum consisted of four olefinic protons, a broad singlet at τ 4.50–4.85; the protons of four carbethoxy groups, a quartet centered at τ 5.78 and a triplet centered at τ 8.70 with a mutual coupling of 7 cps; and an eight-proton multiplet at τ 6.98–7.82 which simplified into an AB pattern (J = 15 cps) when the olefinic protons were decoupled.

(4) *Anal.* Calcd for $C_{22}H_{36}O_8$: C, 61.66; H, 8.47. Found: C, 61.81; H, 8.34. The nmr spectrum taken in $CDCl_3$ consisted of the protons of four carbethoxy groups, a quartet centered at τ 5.90 and a triplet centered at τ 8.78 with a mutual coupling of 7 cps; and two broad singlets of eight protons each centered at τ 7.95 and 8.56.

(5) *Anal.* Calcd for $C_{23}H_{35}O_9Br$: C, 51.59; H, 6.59; Br, 14.9. Found: C, 51.73; H, 6.68; Br, 15.3. The nmr spectrum shows absorptions for four carbethoxy groups consisting of two overlapping quartets centered at τ 5.78 and 5.80 and a triplet centered at τ 8.74 with a mutual coupling of 7 cps; one methoxy group, a singlet at τ 6.65; one proton α to oxygen, a broad band from τ 6.35 to 6.60; one proton α to bromine, a broad band from τ 5.4 to 5.6 (partially obscured by the absorption of the ethoxy methylenes); and a broad ten-proton band at τ 7.00–8.35.

(1) Taken in part from the Ph.D. Dissertation of R. M. G., University of Texas, Aug 1965.

(2) K. C. Murdock and R. B. Angier, *J. Org. Chem.*, **27**, 2395 (1962).

(3) *Anal.* Calcd for $C_{22}H_{32}O_8$: C, 62.25; H, 7.60; mol wt, 424.

The stereospecificity of the addition appears to involve the reacting groups entering from opposite sides of the molecule in which the two double bonds exist side by side in one conformation with which a concerted reaction could occur as indicated. In contrast, free-radical transannular cycloadditions to *cis,cis*-1,5-cyclooctadiene have been reported[6] to give yields up to 63% of *exo*-substituted *cis*-tricyclo[3.3.0]octanes which have configurations of the substituent groups relative to the *cis*-fused rings opposite from that of the presently reported novel ionic transannular cycloaddition to cyclodecadiene. X-Ray crystallographic studies are currently in progress on the substituted cyclodecadiene to determine the relative position of the two olefinic groups.

Other high-yield transannular cycloaddition reactions of this type of cyclodecadiene will be reported separately. The inactivity of the tetraethyl *cis,cis*-3,8-cyclodecadiene-1,1,6,6-tetracarboxylate toward conventional tests for olefinic groups including tetranitromethane is unusual and is exhibited by other similarly substituted 1,6-cyclodecadienes synthesized in this work. However, further investigation will be required to determine whether steric factors alone or in combination with interaction of the double bonds account for the inactivity.

This stereospecific transannular cycloaddition reaction also provides an experimental analogy to a hypothetical reaction scheme for sesquiterpene biogenesis involving proposed stereospecific double bond cyclizations.[7]

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The Formation of Tetrakis(trimethylsilyl)allene by an Unusual Reaction from Hexachlorobenzene and Some Derivatives

Sir:

Incidental to a study concerned with the preparation of monomers containing a polyhalophenyl group and other substituents such as silicon, we have noted[1] that polychlorobenzenes react with trimethylchlorosilane and lithium in tetrahydrofuran to give mono- and disilylated derivatives. With a view to the synthesis of compounds having a larger number of trimethylsilyl groups, hexachlorobenzene was treated with a liberal excess of trimethylchlorosilane and lithium. One of the products isolated contained no chlorine. Some of the physical constants were: bp 69–70° (0.2 mm), $n^{20}D$ 1.4770, d^{20}_4 0.8322. The molecular weight by osmometry was 332 and 304, and by mass spectrography, 328. The compound appeared to be the highly unexpected tetrakis(trimethylsilyl)allene.

$$(Me_3Si)_2C{=}C{=}C(SiMe_3)_2$$

This was supported by other analytical data: nmr, singlet at τ 9.78 (no other protons present); infrared, strong absorption at 1880 cm^{-1}. *Anal.* Calcd for $C_{15}H_{36}Si_4$; Si, 34.3; mol wt, 328; molar refraction, 111.4. Found: Si, 34.1, 34.4; mol wt, 328 (mass spectrum); molar refraction, 111.6.

The compound, which is colorless when freshly prepared but which turns light yellow on standing, reacted vigorously with bromine to give trimethylbromosilane.

Tetrakis(trimethylsilyl)allene was prepared previously in an elegant study by West, Carney, and Mineo[2] from the tetralithium derivative of propyne. Some arylated silicon allenes have been reported recently.[3] We have shown that our tetrakis(trimethylsilyl)allene has the same refractive index and retention time as a sample of the compound prepared previously.[4]

Some additional observations are made at this time relative to studies on mechanisms for the formation of the allene. Among mechanisms being considered are those involving precursory benzyne, dibenzyne, and to a lesser extent the carbenoid types,[5] as well as anion radicals. (1) As might have been expected, pentachlorophenyltrimethylsilane as well as 1,4-di(trimethylsilyl)-tetrachlorobenzene give on treatment with an excess of trimethylchlorosilane and lithium in THF the tetrakis(trimethylsilyl)allene. (2) The yield of allene starting with 1,4-di(trimethylsilyl)tetrachlorobenzene was in *excess* of 50%. (3) The formation of the allene is rapid, as evidenced by its detection (vpc) when a first aliquot was removed at the end of 5 min from the reaction starting with pentachlorophenyltrimethylsilane and also with 1,4-di(trimethylsilyl)tetrachlorobenzene.

The allene is not formed to any significant extent from hexafluorobenzene under the corresponding conditions used with hexachlorobenzene. Studies are being extended to a variety of polyhalogenated compounds, including homocyclic and heterocyclic types, and with trapping agents in addition to the organosilicon compounds.

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