rate constant over several powers of ten, the rate for displacement on propyl in all cases exceeds that on isopropyl by at least a factor of ten.[6] In addition, for nucleophiles of high basicity, the competing E2 elimination reaction intrudes much more severely in attack on isopropyl than on propyl halides.[7] Both considerations lead to the conclusion that a carbanionic mechanism would discriminate against the formation of 2,3-dimethylbutane (IV), which could be formed only by displacement on isopropyl iodide.

Table II. Relative Yields of Isomeric Hexanes from Reaction of $Na^+C_{10}H_8\cdot^-$ with an Equimolar Mixture of 1- and 2-Iodopropanes

Temp	IV, %	III, %	II, %	[III]/([II] × [IV])$^{1/2}$
Ambient	25.4 ± 1.5	49.8 ± 0.6	26.8 ± 2.0	1.98
Ambient[a]	23.3	52.2	24.5	2.18
−78°	23.2 ± 0.3	51.8 ± 0.9	25.0 ± 0.6	2.15
(Average)	24.1	51.1	24.8	2.09

[a] Sufficient I added to react with only *ca.* one-half alkyl iodide present. Duplicate experiment was not carried out.

The relative yields of the isomeric hexanes formed in the reaction of I with an equimolar mixture of *n*-propyl iodide and isopropyl iodide are presented in Table II. Three striking features of these data are worthy of note: (1) the statistical product distribution, (2) the absence of any discrimination in the formation of 2,3-dimethylbutane, and (3) the fact that all three hexanes are formed with equal activation energy, as indicated by the insensitivity of the product distribution to a change in temperature of 100°. On all counts we are forced to the conclusion that the reaction of I with alkyl iodides results in the formation of alkyl free radicals which possess sufficient lifetime to combine by a free-radical process.

Table III. Per Cent Yield[a] of Aliphatic Hydrocarbons from Reaction of $Na^+C_{10}H_8\cdot^-$ with $CH_3(CH_2)_4X$

Products	Cl	Br	I
n-Pentene	43.9	29.2	17.3
1-Pentene	0[b]	0[b]	3.7
n-Decane	0	5.0	55.7
Total	43.9	34.2	76.7
$\pi^{1/2}$ (CH_3CH_2X)[c]	−2.7 v	−2.08 v	−1.67 v
$\Delta\pi^{1/2}$ [d]	−0.2 v	+0.42 v	+0.83 v

[a] In general the yield is reproducible to ±10% of the value reported. [b] A minute, unresolved shoulder on the trailing edge of the pentane peak in the vapor phase chromatogram admits the possibility of the presence of trace amounts of 1-pentene. [c] Polarographic half-wave potential [M. von Stackelberg and W. Stracke, *Z. Elektrochem.*, **53**, 118 (1949)]. Data for the *n*-amyl halides are unavailable. [d] For definition, see text.

This conclusion is supported further by the pronounced influence of the halide in determining the product distribution in the reaction of I with a series of *n*-amyl halides (Table III). The decane:pentane product ratio decreases dramatically in the order iodide > bromide > chloride, a trend readily explicable in terms of the radical coupling mechanism. The reaction which gives rise to the excess of pentane over pentene, whether abstraction of hydrogen atoms from solvent (5) or further reduction to the anion (6) followed by proton abstraction (9),[8] is most certainly only first order in radical concentration. Thus pentane is formed at a rate less sensitive to the concentration of alky radicals than that for decane formation, a process second order in radical concentration. The concentration of alkyl radicals is a function of their rate of formation, which in turn is a function of the activation energy for electron transfer from radical anion to alkyl halide. At least qualitatively, it would seem reasonable to expect this activation energy to parallel the difference in reduction potential between electron acceptor (alkyl halide) and reducing agent (radical anion). These differences[9] ($\Delta\pi^{1/2}$) decrease in an order which directly corresponds to the decane:pentane product ratio (Table I).

Acknowledgment. We are pleased to thank the Mobil Oil Corporation for support of this research at Princeton University and the Esso Research and Engineering Company for support at Linden, N. J. We are grateful to Professors John F. Garst and Gordon A. Hamilton for helpful discussions.

(6) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Company, Inc., New York, N. Y., 1962, pp 11–13; *Chem. Rev.*, **56**, 571 (1956).

(7) See, for example, M. L. Dahr, E. D. Hughes, C. K. Ingold, and S. Masterman, *J. Chem. Soc.*, 2055 (1948).

(8) This latter alternative is suggested by two recent investigations closely related to the work reported here: (a) J. F. Garst, W. Ayers, and R. C. Lamb, *J. Am. Chem. Soc.*, **88**, 4260 (1966); (b) S. J. Cristol and R. V. Barbour, *ibid.*, 4261 (1966).

(9) The polarographic half-wave potential for naphthalene reduction is −2.50 v [H. A. Latinen and S. Wawzonek, *J. Am. Chem. Soc.*, **64**, 1765 (1942)].

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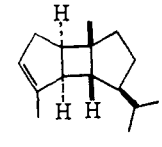
The Total Synthesis of the (±)-Bourbonenes

Sir:

The sesquiterpenoid hydrocarbons α- and β-bourbonene, isolated from *Geranium bourbon* oil, have been shown to possess the stereostructures **1** and **2**, respectively.[1,2] We wish to report a total synthesis of the bourbonenes which supports these structural assignments.



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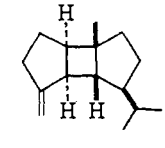


2

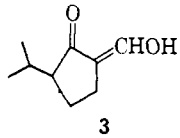
2-Isopropylcyclopentanone, prepared by treatment of the cyclohexylimine of cyclopentanone with

(1) J. Křepinský, Z. Samek, and F. Šorm, *Tetrahedron Letters*, 3209 (1966).

(2) J. Křepinský, Z. Samek, F. Šorm, and D. Lamparsky, *ibid.*, 359 (1966).

ethyl magnesium bromide followed by isopropyl bromide,[3] was condensed with ethyl formate in the presence of sodium methoxide to give a quantitative yield of the hydroxymethylene ketone **3**, bp 75° (1.5 mm), ν_{max} 3500 (broad), 1735, 1705, 1670, and 1605 cm^{-1}. Reduction of **3** with lithium aluminum hydride in ether furnished the alcohol **4**, bp 94–95° (25 mm), ν_{max} 3450, 1662, and 895 cm^{-1}, in 60% yield.[4] The presence of the exocyclic methylene grouping was substantiated by the nmr spectrum, which showed two signals (1 H each) at δ 4.95 and 5.11, while the proton α to the hydroxyl function gave rise to a multiplet centered at δ 4.2. Treatment of **4** with thionyl chloride in ether afforded a 67% yield of the chloromethyl derivative **5**, bp 36° (0.3 mm), ν_{max} 1645 and 690 cm^{-1}, the nmr spectrum of which showed a singlet at δ 4.12 (2 H, $=CCH_2Cl$) and a broad signal at δ 5.7 (1 H, $-CH=C-$).[5] Hydrogenolysis of **5** with lithium aluminum hydride in isopropyl ether yielded 1-methyl-3-isopropylcyclopent-1-ene (**6**), bp 55° (25 mm), ν_{max} 1650 and 830 cm^{-1}, in 66% yield.[6] The nmr spectrum of **6** showed a multiplet at δ 5.21 (1 H, $-CH=C-$), a singlet at δ 1.63 (3 H, $=C(CH_3)-$), and a pair of doublets centered at δ 1.77 (6 H, $(CH_3)_2CH-$).[7]

Irradiation[8] of a mixture of **6** and 2-cyclopentenone in pentane gave, in addition to the known cyclopentenone photodimers,[9] a 64% yield of two tricyclic ketones in the approximate ratio 1:1. Both ketones showed carbonyl absorption at 1735 cm^{-1} and absence of olefinic protons in their nmr spectra. On the basis of their nmr spectra and by analogy with other photochemical cycloadditions of cyclopentenone which have been shown to yield exclusively *cis,anti,cis* adducts,[9,10] the two ketones are assigned structures **7** and **8**. The angular methyl substituent in **7** appears as a well-defined singlet at δ 1.12 whereas that of **8** is



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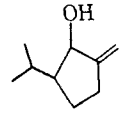

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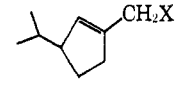
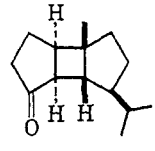


5, X = Cl
6, X = H



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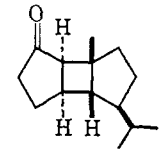

8

shifted upfield and merges with the signal due to the isopropyl group at δ ~0.9, in agreement with "head-to-tail" and "head-to-head" modes of cycloaddition.[11] Comparison of **7** with the tricyclic ketone obtained by ozonolysis of natural β-bourbonene[1] showed that they were identical, and treatment of **7** with triphenylphosphinemethylene afforded racemic β-bourbonene (**2**) which was indistinguishable from natural material on the basis of infrared and nmr spectra and vapor phase chromatography.[12] In contrast, ketone **8** failed to react with triphenylphosphinemethylene under the same conditions and was markedly less reactive toward carbonyl reagents in general. Brief treatment of synthetic β-bourbonene in ethanol with hydrochloric acid effected isomerization to α-bourbonene (**1**), which had spectral properties corresponding to those reported[1] and was identified by comparison with material obtained by similar acid-catalyzed isomerization of the authentic β isomer.

Acknowledgment. We wish to thank the National Science Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for generous support of this research.

(3) G. Stork and S. R. Dowd, *J. Am. Chem. Soc.*, **85**, 2178 (1963).
(4) A. S. Dreiding and J. A. Hartman, *ibid.*, **75**, 939 (1953).
(5) F. F. Caserio, G. E. Dennis, R. H. DeWolfe, and W. G. Young, *ibid.*, **77**, 4182 (1955).
(6) R. F. Nystrom and W. G. Brown, *ibid.*, **70**, 3738 (1948); L. F. Hatch and J. J. D'Amico, *ibid.*, **73**, 4393 (1951).
(7) The isopropyl substituent in each of the compounds **3–6**, as well as 2-isopropylcyclopentanone, shows magnetically nonequivalent methyl groups (see H. J. Jakobsen, P. Madsen, and S. O. Lawesson, *Tetrahedron*, **22**, 1851 (1966)).
(8) A Hanovia 450-w high-pressure mercury lamp was used with a Pyrex filter. The photolysis was carried out by adding successive portions of cyclopentenone until most of the olefin **6** was consumed, and then filtering off the crystalline cyclopentenone dimers.
(9) P. E. Eaton, *J. Am. Chem. Soc.*, **84**, 2344 (1962).
(10) P. E. Eaton, *ibid.*, **84**, 2454 (1962).
(11) Confirmation of the stereochemistry of 7 is being sought through X-ray analysis of its thiosemicarbazone.
(12) We are indebted to Professor F. Šorm for samples of authentic β-bourbonene and the tricyclic ketone derived from it.

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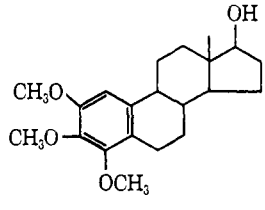
Analgesic Efficacy of Poly(alkoxy)estratrienes

Sir:

It was reported recently[1] that a new series of polyalkoxyestratrienes, as typified by *d*-2,3,4-trimethoxyestra-1,3,5(10)-trien-17β-ol (1), were potent analgesics when tested in mice, rats, cats, and dogs using morphine and meperidine as controls. In the course of subsequent laboratory work, we have been unable to reproduce the previously reported pharmacological results.



I

Our results, wherein I has been compared with morphine sulfate in several of the more commonly used analgesia screens, are given in Table I.[2] As Table I indicates, compound I was only weakly analgesic when tested in the mouse and rat. In the foot-clamp and tail-clip procedures, no satisfactory dose-response relationship could be established. In dogs, no significant differences from controls could be elicited with I in doses of 5 and 10 mg/kg (intravenous,

(1) (a) L. R. Axelrod, P. N. Rao, and D. H. Baeder, *J. Am. Chem. Soc.*, **88**, 856 (1966); (b) L. R. Axelrod and D. H. Baeder, *Proc. Soc. Exptl. Biol. Med.*, **121**, 1184 (1966).
(2) The results obtained with I are typical for all members of the series which were screened. In addition, we are aware of results comparable to ours which have been obtained independently in five other laboratories.