band at 5.92 μ indicating the presence of unreduced starting material, it was re-treated with the reducing agent as described above. The crude crystalline product obtained from the residue with ethyl acetate (162 mg., m.p. 214–222°) had to be recrystallized four times from methanol–ethyl acetate before the melting point became constant at 250–252°: $[\alpha]^{22}\text{D}$ +25.6° (*c* 0.952); ultraviolet end absorption only; $\lambda_{\max}^{\text{Nujol}}$ 3.05 (m), 6.25 (m, s.), 8.08 (l) μ. The Rosenheim and hydrochloric acid color reactions were negative.

Anal. Calcd. for $C_{29}H_{45}NO_4$ (471.7): C, 73.84; H, 9.62. Found: C, 73.51; H, 9.34.

Acetylation of XIVb with acetic anhydride and pyridine gave the **triacetate XIVa** as needles from aqueous ethanol: m.p. 202–203°; $[\alpha]\text{D}$ +26.9° (*c* 0.595); $\lambda_{\max}^{\text{Nujol}}$ 2.95 (m), 5.77 (s), 6.20 (vs), 8.05–8.11 (vs) μ.

Anal. Calcd. for $C_{33}H_{49}NO_6$ (555.7): C, 71.32; H, 8.89. Found: 71.24; H, 8.95.

Acetylation of crystalline material (m.p. 187–193°) isolated from the first two mother liquors from the purification of the N-acetyl derivative XIVb from another reduction run yielded a product, m.p. 196–198°, $[\alpha]\text{D}$ +32°. This rotation value shows that little, if any, of the abnormal 11β-ol corresponding to triacetyl-8,9-dihydroisojervin-11β-ol A (IVa) could have been formed in the lithium borohydride reduction of XIIIb, since this compound, having the 5α-configuration, should be even more dextrorotatory than IVa, $[\alpha]\text{D}$ +133°.

For the re-oxidation to triacetyl 5,6-dihydroisojervine (XIIIa), the triacetate (37.5 mg., 0.0674 mmole) was treated with the equivalent amount of the chromium trioxide–sulfuric acid reagent of Djerassi, *et al.*, as described for the reaction IIb → Ib. The residue of the chloroform extract (28.3 mg.) was recrystallized three times from aqueous ethanol, giving 13.4 mg. of needles: m.p. 212–213°, undepressed by admixture of an authentic sample of XIIIa; $[\alpha]^{21}\text{D}$ +38.5° (*c* 0.509), lit.[1b] $[\alpha]\text{D}$+37.5°; $\lambda_{\max}^{\text{alc}}$ 237 mμ (ε 8550). The infrared spectrum was identical with that of XIIIa.

Anal. Calcd. for $C_{33}H_{47}NO_6$ (553.7): C, 71.58; H, 8.56. Found: C, 71.45; H, 8.59.

A Novel Method for the Preparation of Bicyclooctane Systems[1]

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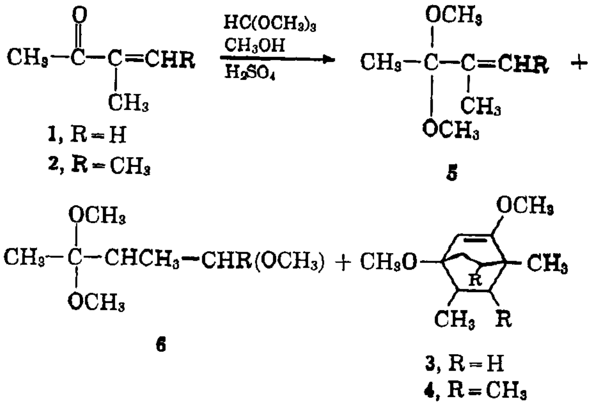
Received August 11, 1964

Reaction of 3-methyl-3-buten-2-one (**1**), *trans*-3-penten-2-one (**7**), and *trans*-3-methyl-3-penten-2-one (**2**) each with trimethyl orthoformate in the presence of orthophosphoric acid gave substituted 4-methoxybicyclo[2.2.2]-octanones (**8**, **9**, and **10**), respectively. The intermediate of the reaction was found to be a 1-methoxy-4-(1-methoxyvinyl)-1-cyclohexene derivative (**13**). An acid-catalyzed cyclization of 4-substituted 4-(1-methoxyvinyl)-1-methoxy-1-cyclohexenes gave 4-substituted 1,3-dimethoxybicyclo[2.2.2]oct-2-enes, whereas of cyclization 1,4-di-phenyl-4-vinyl-1-cyclohexene (**30**) gave 1,4-diphenylbicyclo[3.2.1]oct-3-ene (**31**).

It has previously been found[2] that the reaction of a methanol solution of 16-dehydropregnenolone acetate with trimethyl orthoformate in the presence of an acid catalyst furnished a bicyclo[2.2.2]octane system.[3] The reaction has now been extended to methyl vinyl ketone derivatives and the mechanism of the reaction was studied. In the course of this work, there was encountered an acid-catalyzed cyclization of 1,4-diphenyl-4-vinyl-1-cyclohexene (**30**) to 1,4-diphenylbicyclo[3.2.1]oct-3-ene (**31**).

When a methanol solution of *trans*-3-methyl-3-penten-2-one (**2**) was treated with trimethyl orthoformate in the presence of sulfuric acid, there was obtained 2,4-dimethoxy-1,5,6,7-tetramethylbicyclo[2.2.2]-oct-2-ene (**4**) in 50% yield (identified as 4-methoxy-1,5,6,7-tetramethylbicyclo[2.2.2]octan-2-one (**10**) after mild acid hydrolysis) and 24% yield of a mixture of 4,4-dimethoxy-3-methyl-2-pentene (**5**, R = CH_3) and 2,2,4-trimethoxy-3-methylpentane (**6**, R = CH_3) which was separated by vapor phase chromatography. An analogous reaction of 3-methyl-3-buten-2-one (**1**) also gave a similar set of the products. Methyl vinyl ketone, on the other hand, gave no bicyclooctane compound but 4-methoxy-2-butanone under the similar conditions.[4] A similar reaction of mesityl oxide gave a mixture of at least nine compounds from which no bicyclooctane derivative could be separated.



1, R = H
2, R = CH_3
5
6
3, R = H
4, R = CH_3

It was later found that methanol is not necessary for this reaction and the best yields of the bicyclooctane derivatives were obtained when orthophosphoric acid was used as a catalyst. Among other catalysts examined were boron trifluoride etherate and *p*-toluenesulfonic acid, where bicyclooctane derivatives were also obtained. Treatment of 3-methyl-3-buten-2-one (**1**), *trans*-3-penten-2-one (**7**), or *trans*-3-methyl-3-penten-2-one (**2**) each with an equivalent amount of trimethyl orthoformate in the presence of orthophosphoric acid gave the corresponding bicyclooctanes, **8** (72% yield), **9** (10%), and **10** (54%), respectively. Formation of methyl formate followed by that of methanol was observed in each case. The low yield observed

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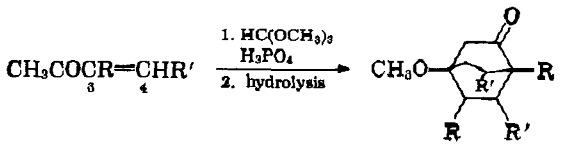
(1) (a) Bridged Ring Compounds. Part II. For part I, see ref. 2. (b) A preliminary account of part of this work has appeared: K. Morita and Z. Suzuki, *Tetrahedron Letters*, **No. 6**, 263 (1964).

(2) K. Morita, G. Slomp, and E. V. Jensen, *J. Am. Chem. Soc.*, **84**, 3779 (1962).

(3) For the syntheses of bicyclooctane systems, see "Elsevier's Encyclopaedia of Organic Chemistry," Series III, Vol. 12A, E. Josephy and F. Radt, Ed., Elsevier Publishing Co., Amsterdam, 1948, p. 1066 ff; R. A. Raphael, "Chemistry of Carbon Compounds," Vol. IIA, E. H. Rodd, Ed., Elsevier Publishing Co., Amsterdam 1953, p. 346 ff.

(4) M. F. Ansel, J. W. Lown, D. W. Turner, and D. A. Wilson, [*J. Chem. Soc.*, 3036 (1963)] reported that trimethyl orthoformate, in methanol with a trace of hydrochloric acid, and ethyl vinyl ketone gave 1,3,3-trimethoxypentane and that an analogous reaction of 2-methyl-1-penten-3-one gave 3,3-dimethoxy-2-methyl-1-pentene.

in the case of **7** presumably suggests that the main reaction proceeded to form 2-methoxy-1,3-pentadiene. The observed polymeric material could be derived from it. Only a polymeric material was obtained from methyl vinyl ketone under similar conditions, although quantitative formation of methyl formate and methanol was observed. Above experiments suggest that the presence of the substituent at C-3 favors the formation of bicyclooctane rings, whereas alkyl substituent at C-4 is unfavorable. The reason for the former will be discussed later.

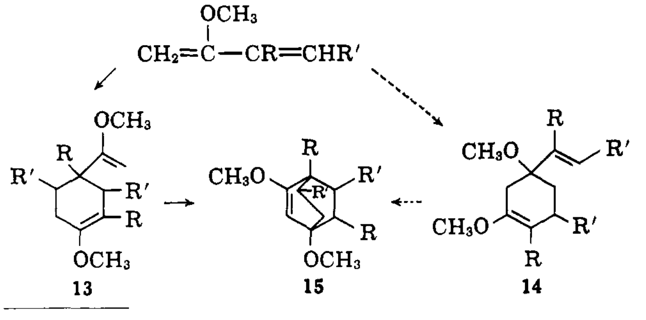


1, R = CH_3; R' = H
7, R = H; R' = CH_3
2, R = R' = CH_3

8, R = CH_3; R' = H
9, R = H; R' = CH_3
10, R = R' = CH_3
11, R, R' = $-(CH_2)_3-$
12, R, R' = $-(CH_2)_4-$

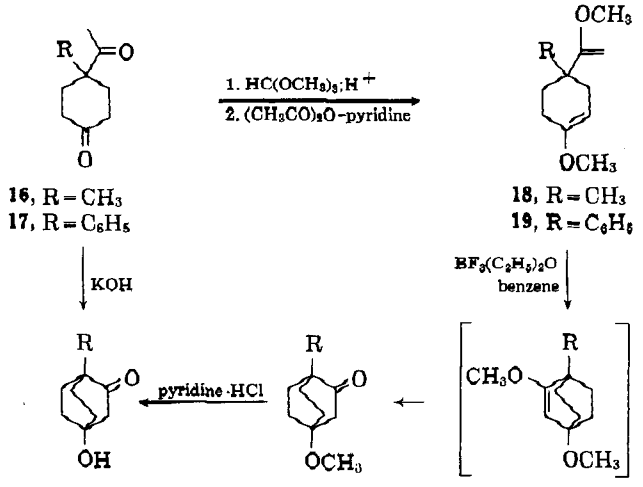
Voronkov and Rabkina[5] reported that the treatment of cyclohexanone with tetramethylsilane in the presence of orthophosphoric acid furnished 1-methoxycyclohexene. Treatment of 3-methyl-3-buten-2-one (1) and *trans*-3-methyl-3-penten-2-one (2) each with tetramethylsilane in the presence of orthophosphoric acid gave no bicyclooctane derivatives but compounds which appeared to contain a silicon atom shown by the strong infrared peak at 1095 cm.^{-1} that can be assigned for Si–O–C absorption. Reaction of 3-methyl-3-buten-2-one (1) with morpholine in the presence of orthophosphoric acid gave 3-methyl-4-morpholino-2-butanone.

The formation of 2-methoxy-1,3-butadiene derivatives at an intermediate stage is indicated by the isolation of methyl formate and methanol from the reaction mixture. Among four possible Diels–Alder-type dimers of 2-methoxy-1,3-butadiene derivatives, two (**13** and **14**) can furnish the same bicyclooctene structure (**15**). Theoretical consideration indicates that the more probable intermediate is **13** rather than **14**, as was pointed out in an earlier paper.[2] We now present the experimental evidence which supports the assumption.



13 **15** **14**

Although Nazarov and his associates[6] reported that the dimerization of a dioxane solution of 2-methoxy-1,3-butadiene at 180–190° gave 1-methoxy-4-(1-methoxyvinyl)-1-cyclohexene (**13**, R = R' = H), it might be argued that the orientation of the Diels–Alder reaction may alter in the presence of an acid catalyst.[7] This was found not to be the case, since dimerization of an ether solution of 2-methoxy-1,3-butadiene in the presence of boron trifluoride etherate at −30° led to the isolation of 1-methoxy-4-(1-methoxyvinyl)-1-cyclohexene (**13**, R = R' = H). 1-Methoxy-4-(1-methoxyvinyl)-1-cyclohexene derivatives (**13**) then would be converted into 1,3-dimethoxybicyclo[2.2.2]oct-2-ene derivatives (**15**) by an acid treatment if the suggested mechanism is really operating. Treatment of benzene solutions of **18** and **19** derived from **16** and **17**, respectively, with boron trifluoride etherate at reflux temperature afforded, after acid hydrolyses, **20** and **21** respectively, in good yields. Demethylation of **20** and **21** with pyridine hydrochloride gave known compounds[8] **22** and **23**, respectively.



16, R = CH_3
17, R = C_6H_5

18, R = CH_3
19, R = C_6H_5

22, R = CH_3
23, R = C_6H_5

20, R = CH_3
21, R = C_6H_5

The Dieckmann condensation of dimethyl ketal **24** derived from dimethyl 4-acetyl-4-methylpimelate gave a product which presumably has a structure **25**. Reaction of this material with trimethyl orthoformate in the presence of orthophosphoric acid gave, after a mild acid hydrolysis, 5-carbomethoxy-4-methoxy-1-methylbicyclo[2.2.2]octan-2-one (**26**) in 78% yield.

Compounds **8**, **9**, and **10** each appear to consist predominantly of one stereochemical modification, whereas 4-methoxy-5,6:1,7-bispropanobicyclo[2.2.2]-octan-2-one (**11**),[9] derived from 1-acetyl-1-cyclopentene, and 4-methoxy-5,6:1,7-bisbutanobicyclo[2.2.2]octan-2-one (**12**),[2] derived from 1-acetyl-1-cyclohexene, 5-carbomethoxy-4-methoxy-1-methylbicylo[2.2.2]octan-2-one (**26**) and 5-carboxy-4-methoxy-1-methylbicyclo-

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(5) M. G. Voronkov and S. M. Rabkina, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, **12**, 2240 (1960); *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 2074 (1960).

(6) I. N. Nazarov, G. P. Verkholtova, and L. D. Bergelson, *Izv. Akad. Nauk*, 511 (1948); *Chem. Abstr.*, **43**, 2576*i* (1949).

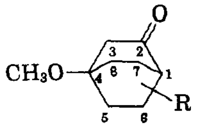
(7) *Cf.* S. Potnis, K. Shohara, R. C. Schulz, and W. Kern, *Makromol. Chem.*, **63**, 78 (1963); R. H. Hall, *Chem. Ind.* (London), 1772 (1955).

(8) J. Colonge and R. Vuillemet, *Bull. soc. chim. France*, 2235 (1961).

(9) K. Morita and E. V. Jensen, unpublished results; I. A. Favorskaya and L. V. Fedorova [*Zh. Obshch. Khim.*, **24**, 242 (1954)] apparently obtained this substance by an acid-catalyzed dimerization of 1-(1-methoxyvinyl)-1-cyclopentene, but assigned an incorrect structure. Also see I. A. Favorskaya and E. M. Auviner, *ibid.*, **33**, 2795 (1963).

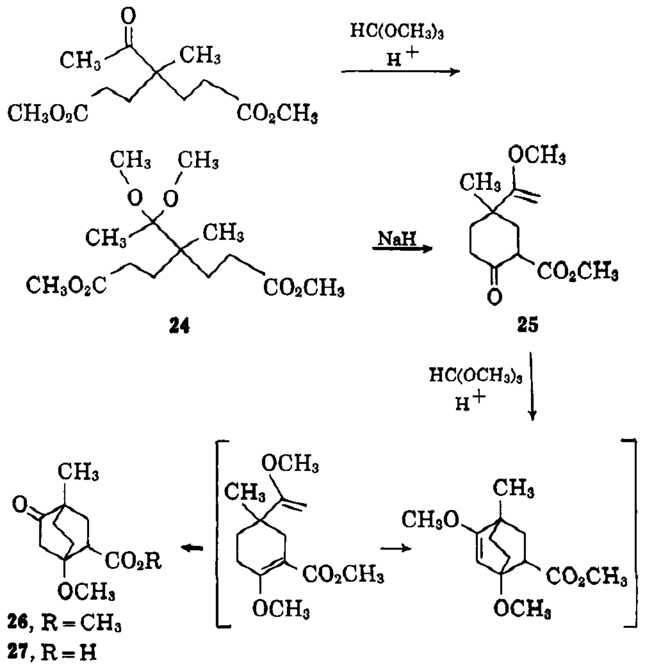
TABLE I

PHYSICAL CONSTANTS OF SUBSTITUTED 4-METHOXYBICYCLO[2.2.2]OCTAN-2-ONES



		M.p., °C, or		Infrared λ, cm.⁻¹		N.m.r., τ	Bridge-head		Calcd., %		Found, %	
Compd.	R	b.p., °C. (mm.)	$n_D{}^{\circ C.}$	C=O	OCH₃	OCH₃	methyl	Formula	C	H	C	H
20	1-Methyl	117–119 (17)	1.4802^{20}	1725	1110	6.85	9.14	$C_{10}H_{16}O_2$	71.39	9.58	71.32	9.59
8	1,5-Dimethyl	114–116 (12)	1.4799^{20}	1723	1109	6.87	9.17	$C_{11}H_{18}O_2$	72.49	9.95	72.25	9.96
9	6,7-Dimethyl	94–95 (5)	1.4792^{20}	1723	1109	6.90	. . .	$C_{11}H_{18}O_2$	72.49	9.96	72.71	9.69
10	1,5,6,7-Tetramethyl	113–116 (3)	1.4859^{20}	1723	1105 1127	6.87	9.22	$C_{13}H_{22}O_2$	74.24	10.55	74.36	10.56
26	2-Carbomethoxy-1-methyl	135–138 (2)	1.4850^{20}	Overlap	1110	6.78 6.80	9.06	$C_{12}H_{18}O_4$	63.69	8.01	63.65	8.00
27	2-Carboxy-1-methyl	98.5–99.5	. . .	Overlap	1110	6.66^a 6.69	9.07	$C_{11}H_{16}O_4$	62.24	7.59	62.44	7.62
21	1-Phenyl	82.5–83.5	. . .	1725	1107	6.81	. . .	$C_{15}H_{18}O_2$	78.22	7.88	78.47	7.86
11	5,6:1,7-Bispropano	142–143 (2.5)	1.5215^{26}	1723	1109	6.79^a 6.77	. . .	$C_{15}H_{22}O_2$	76.88	9.47	76.81	9.25
12	5,6:1,7-Bisbutano	 $79–79.5^c$	1.5290^{23b}	1723^b 1723^c	1111^b 1109^c	$6.80^{a,b}$ $6.78^{a,c}$	. . .					

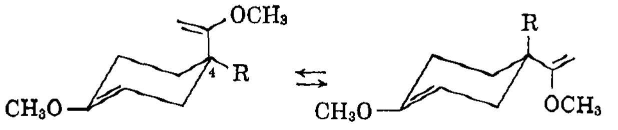
[a] In deuteriochloroform. [b] Major isomer (an oil). [c] Minor isomer (crystals).



[2.2.2]octan-2-one (**27**) were each found to consist of two stereoisomers.

The structures for **20** and **21** were established beyond doubt as already described. The assignment of the structures for **8**, **9**, **10**, and **26** is based on the n.m.r., infrared, and mass spectra (*cf.* Table I).

The 1-methoxy-4-(1-methoxyvinyl)-1-cyclohexene derivatives (**13**) may exist in two conformations, **28** and **29**; **28** is apparently a more preferable one for the ring-closure reaction. The bulkier the substituent (R) at C-4 is, the more the equilibrium should lie on the left-hand side. One could then anticipate that the presence of a substituent at C-4 would favor the formation of bicyclooctane ring. The fact mentioned previously corroborates the assumption.



28 **29**

The successful conversion of 4-substituted 1-methoxy-4-(1-methoxyvinyl)-1-cyclohexenes to 1-substituted 4-methoxybicyclo[2.2.2]octan-2-ones led us to investigate an acid-catalyzed cyclization of other vinylcyclohexene derivatives. Substituted vinylcyclohexene derivatives can easily be obtained by the dimerization of substituted butadienes.[10,11]

Reaction of a formic acid solution of 1,4-diphenyl-4-vinyl-1-cyclohexene (**30**) with sulfuric acid at a reflux temperature for 9 hr. gave 1,4-diphenylbicyclo[3.2.1]-oct-3-ene (**31**),[12] m.p. 74.0–74.5°, in a good yield.

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(10) Dimerization of (a) 2-acetoxy-1,3-butadiene and 2-formyloxy-1,3-butadiene: A. L. Klebanski and K. K. Cherychalova, *Zh. Obshch. Khim.*, **16**, 1101 (1946); *Chem. Abstr.* **41**, 2693ᵇ (1947); (b) isoprene: I. N. Nazarov, *et al.*, *Zh. Obshch. Khim.*, **25**, 307 (1955); *Chem. Abstr.*, **50**, 1627*h* (1956); C. Walling and J. Perisach, *J. Am. Chem. Soc.*, **80**, 5819 (1958); G. S. Hammond, N. J. Turro, and R. S. H. Lin, *J. Org. Chem.*, **28**, 3297 (1963); (c) chloroprene: I. N. Nazarov and K. I. Kuznetsova, *Zh. Obshch. Khim.*, **30**, 134 (1960); *J. Gen. Chem. USSR*, **30**, 143 (1960); (d) 2-carboxy-1,3-butadiene: E. A. Braude and E. A. Evans, *J. Chem. Soc.*, 3238 (1956); A. Yakubovich and E. V. Volkova, *Dokl. Akad. Nauk SSSR*, **84**, 1183 (1952); C. C. J. Culvenor and T. A. Geissman, *J. Org. Chem.*, **26**, 3045 (1961); *J. Am. Chem. Soc.*, **83**, 1647 (1961); (e) 2-formyl-1,3-butadiene: R. Pummer, F. Aldebert, F. Büttner, F. Graser, E. Pirson, H. Rick, and H. Sperber, *Ann.*, **583**, 161 (1953); (f) 2-cyano-1,3-butadiene: C. S. Marvel and N. O. Brace, *J. Am. Chem. Soc.*, **71**, 37 (1949).

(11) Dimerization of 2-phenyl-1,3-butadiene: I. N. Nazarov and A. I. Kuznetsova, *Zh. Obshch. Khim.*, **30**, 139 (1960); *J. Gen. Chem. USSR*, **30**, 148 (1960); K. Alder and J. Haydn, *Ann.*, **570**, 201 (1950).

(12) Although it has been known that an acid-catalyzed cyclization of 1,5-dienes forms six-membered rings in general, there are several examples where 1,5-dienes give five-membered ring.[13]

(13) (a) P. G. Stevens and S. C. Spalding, Jr., *J. Am. Chem. Soc.*, **71**, 1687 (1949); (b) I. N. Nazarov and L. N. Pinkina, *Bull. Acad. Sci. USSR*, 633 (1946); *Chem. Abstr.*, **42**, 7731ⁱ (1948); also see E. A. Braude and J. A. Coles, *J. Chem. Soc.*, 1430 (1952); (c) W. Kimel, *et al.*, *J. Org. Chem.*, **22**, 1161 (1957); **23**, 153 (1958); O. Isleu, *et al.*, *Helv. Chim. Acta*, **41**, 160 (1958); Y. R. Naves, *et al.*, *Bull. soc. chim. France*, 1213 (1957); (d) J. J. Beereboom, *J. Am. Chem. Soc.*, **85**, 3525 (1963).

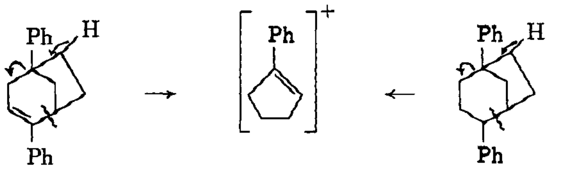
TABLE II

PHYSICAL CONSTANTS OF BICYCLOOCTANONE OXIMES

Parent ketone	Oxime m.p., °C.	Formula	Calcd., %			Found, %		
			C	H	N	C	H	N
8	128–129	$C_{11}H_{19}NO_2$	66.97	9.71	7.10	67.15	9.72	6.99
10	150–151	$C_{13}H_{23}NO_2$	69.29	10.29	6.22	69.62	10.30	6.24
20	127–128	$C_{10}H_{17}NO_2$	65.54	9.35	7.64	65.42	9.35	7.59
21	235–236	$C_{15}H_{19}NO_2$	73.44	7.81	5.71	73.30	7.85	5.66
22	208–208.5	$C_9H_{15}NO_2$	63.88	8.94	8.28	63.91	9.12	8.20

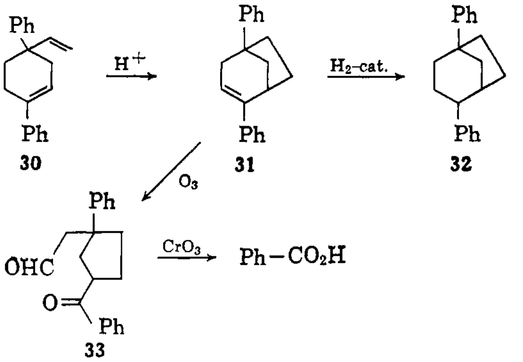
Treatment of a nitromethane solution of **30** with sulfuric acid at room temperature also gave **31**. When nitropropane was used instead of nitromethane at either −50° or at room temperature, a sulfonic acid, $C_{20}H_{20}SO_3$, m.p. 173.0–174.5°, as well as **31**, was obtained. Room temperature reaction (2 hr.) of a benzene solution of **30** with boron trifluoride etherate gave 70% of **31** and 30% of unchanged **30**.

Assignment of the structure is based on the evidence of (1) analysis and molecular weight (260, by mass spectrometry; 264 by osmometry, theory 260); (2) presence of only one ethylenic linkage of the type Ph—CR═CH—CH₂— as shown by $\lambda_{\max}^{\mathrm{EtOH}}$ 249 mμ (ε 13,600), n.m.r. (in CCl_4) having a triplet centered at τ 4.24, J = 3.5 c.p.s., and hydrogenation to the dihydro compound 1,4-diphenylbicyclo[3.2.1]octane (**32**), m.p. 158.5–160.5°; (3) absence of a methyl group (n.m.r.); (4) presence of an original type of monosubstituted phenyl groups [singlet n.m.r. peak at τ 2.83 and infrared peaks (KBr) at 693, 700, 748, 760, 770 cm.$^{-1}$]; (5) presence of a bridge-head hydrogen adjacent to a double bond (broad n.m.r. peak at τ 6.95 which corresponds to one hydrogen); (6) presence of a five-membered ring indicated by the mass spectra of **31** and **32** that show an intense peak at m/e = 143 which can be ascribed to the fragment as shown below;



31 *m/e* 143 **32**

(7) the ozonolysis of the ethylenic linkage of **31** to give a benzoyl derivative (**33**), $\lambda_{\max}^{\mathrm{EtOH}}$ 243 and 282 mμ with ε 11,800 and 820, respectively, $\lambda_{\max}^{\mathrm{C=O}}$ 1690 and 1715 cm.$^{-1}$, n.m.r. triplet centered at τ 0.70, J = .30 c.p.s. (CH_2CHO group), which forms benzoic acid on chromic acid oxidation.



30 **31** **32** **33**

The investigation of the cyclization of other vinylcyclohexene derivatives is now in progress.

Experimental

All melting points and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 125 spectrophotometer. Ultraviolet spectra were recorded on a Shimadzu Model SV-50 A automatic spectrophotometer. N.m.r. spectra were obtained with either a Varian DP 60 or an HR 100 instrument using carbon tetrachloride, except where specified otherwise, as a solvent and tetramethylsilane as internal standard. Vapor chromatography was performed with a Yanagimoto GCG 220 for the analytical and with a Beckman Megachrom GC-100 for the preparative purpose. Molecular weight was determined with Mechrolab vapor pressure osmometer, Model 301.

General Procedure for the Preparation of Substituted 4-Methoxybicyclo[2.2.2]octan-2-ones from Substituted Methyl Vinyl Ketones.—To a mechanically stirred mixture of 1 mole of substituted methyl vinyl ketones and 1.1 moles of trimethyl orthoformate was added 0.02 to 0.05 mole of orthophosphoric acid. The mixture was then heated and methyl formate was allowed to distil slowly from the reaction mixture through a 70-cm. Vigreux column. After about 5 hr., when the distillation of methyl formate had ceased, bath temperature was raised to let methanol distil out during a period of about 3 hr. The mixture was then heated at about 150° (bath temperature) for 30 min. To the cooled reaction mixture was added 35 ml. of 10% hydrochloric acid solution and the mixture was stirred for 30 min. at room temperature. Ether was added and the mixture was washed with a small amount of water and dried over anhydrous sodium sulfate. The product was separated by the distillation *in vacuo*.

Compounds **8**, **9**, and **10** were thus obtained from 3-methyl-3-buten-2-one (**1**),[14] *trans*-3-penten-2-one (**7**),[15] and *trans*-3-methyl-3-penten-2-one (**2**)[16] in yields of 72, 10, and 54%, respectively. Physical constants of the products are recorded in Table I.

When triethyl orthoformate was used instead of trimethyl orthoformate in the case of 3-methyl-3-buten-2-one (**1**) under the similar condition described above, 16% of the product distilled at 95–105° (5 mm.) was obtained. It exhibited three peaks in vapor phase chromatography on a silicone rubber column. No further study was carried out.

Oximes.—To a solution of 0.1 mole of a bicyclooctanone in 40 ml. of ethanol was added a mixture of 0.11 mole of hydroxylamine hydrochloride and 0.15 mole of sodium hydroxide in 20 ml. of water. The mixture was then heated at reflux for 1 hr. Dilution with water gave a nearly quantitative yield of the oxime. Analytical samples were recrystallized from ethanol or chloroform–ethanol. Physical constants are given in Table II.

Reactions of *trans*-3-Methyl-3-penten-2-one (2) and 3-Methyl-3-buten-2-one (1) with Trimethyl Orthoformate in the Presence of Sulfuric Acid. A. Reaction of 2.—To a stirred mixture of 19.5 g. (0.2 mole) of **2**, 31 g. (0.34 mole) of trimethyl orthoformate, and 29 ml. of methanol was added 0.13 ml. of concentrated sulfuric acid at about 10°. The ice bath was removed and the mixture was maintained at room temperature for 5 hr. by occasional cooling. Aqueous sodium hydroxide solution was added to a cooled mixture and the mixture was extracted with ether. The ethereal extract was washed with water, dried, and concentrated. Distillation of the residue gave two fractions. The first fraction, b.p. 40–43° (5 mm.), 6.1 g., was found to be a mixture of two compounds and was separated by preparative vapor chromatography. The peak with retention time of 3.3 min. (Carbowax 1000 analytical column at 128°) was **4,4-dimethoxy-3-methyl-2-pentene** (**5**, R = CH_3), $n^{20}\mathrm{D}$ 1.4400, $\lambda_{\max}^{\mathrm{film}}$

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[14] T. White, *J. Chem. Soc.*, 238 (1943).

[15] V. Grignard, M. Fluchaire, *Ann. chim.*, **9**, 5 (1928).

[16] L. E. Hinkel, E. E. Ayling, J. F. J. Dippy, T. H. Angel, *J. Chem. Soc.*, 814 (1931).

multiplet between 1040 and 1145 cm.$^{-1}$ (ketal) and no carbonyl absorption.

Anal. Calcd. for $C_8H_{16}O_2$: C, 66.63; H, 11.19. Found: C, 66.81; H, 10.69.

The peak with retention time of 8.3 min. was **2,2,4-trimethoxy-3-methylpentane** (6, R = CH_3), $n^{20}D$ 1.4222, λ_{max}^{film} multiplet between 1040 and 1145 cm.$^{-1}$ (ketal) and no carbonyl absorption.

Anal. Calcd. for $C_9H_{20}O_3$: C, 61.33; H, 11.44. Found: C, 61.58; H, 11.26.

The second fraction, b.p. 100–110° (7 mm.), 12.3 g., was a mixture of **2,4-dimethoxy-1,5,6,7-tetramethylbicyclo[2.2.2]oct-2-ene** (4) and **4-methoxy-1,5,6,7-tetramethylbicyclo[2.2.2]octan-2-one** (10). The infrared spectrum showed the presence of both a ketone (1723 cm.$^{-1}$) and an enol ether (1634 cm.$^{-1}$), and the mixture gave pure **10** on mild acid hydrolysis.

B. Reaction of 1.—A mixture of 100 g. of **1**, 144 ml. of trimethyl orthoformate, 116 ml. of methanol, and 0.6 ml. of concentrated sulfuric acid was treated as in A. Distillation of the residue gave two fractions. The first fraction, b.p. 92–101° (67 mm.), 73.3 g., was presumably a mixture of **3,3-dimethoxy-2-methyl-1-butene** (5, R = H) and **1,3,3-trimethoxy-2-methylbutane** (6, R = H) which showed the absence of ketone and the presence of ketal absorption in the infrared spectrum. No further structural study was carried out, since only decomposed material was isolated by the preparative vapor chromatography. The second fraction, b.p. 89–94° (4 mm.), 11.7 g., was a mixture of **2,4-dimethoxy-1,5-dimethylbicyclo[2.2.2]oct-2-ene** (3) and **4-methoxy-1,5-dimethylbicyclo[2.2.2]octan-2-one** (9) shown by its infrared spectrum (1723, 1634 cm.$^{-1}$) and by the conversion into 9 on acid hydrolysis.

3-Methyl-4-morpholino-2-butanone.—To a stirred and water-cooled mixture of 50 g. (0.6 mole) of *trans*-3-methyl-3-buten-2-one (1) in 50 ml. of methanol was added 62 g. (0.71 mole) of morpholine and 2 ml. of orthophosphoric acid. The mixture was then distilled slowly and 42 ml. of distillate was collected during a period of 4 hr. The cooled reaction mixture was diluted with water and the separated white gummy material (3.2 g.), presumably a crude polymer of 3-methyl-3-buten-2-one, m.p. 245–260°, η_{inh} 0.652, was removed by filtration.

Anal. Calcd. for C_5H_8O: C, 71.39; H, 9.59. Found: C, 69.18; H, 9.57; N, 0.75.

Aqueous potassium hydroxide solution was added to the filtrate to make the filtrate alkaline and the mixture was extracted with ether. The ethereal extract was washed with water, dried, and concentrated. The residue was distilled *in vacuo*. There was obtained 43.3 g. of **3-methyl-4-morpholino-2-butanone**: b.p. 84° (3.5 mm.); $n^{20}D$ 1.4600; λ_{max}^{film} 1710 cm.$^{-1}$ (saturated ketone); n.m.r. τ 6.45 (triplet, J = 4.3 c.p.s.), 7.94 (singlet), 9.0 (doublet, J = 6.1 c.p.s.).

Anal. Calcd. for $C_9H_{17}NO_2$: C, 63.12; H, 10.01; N, 8.18; mol. wt., 171. Found: C, 63.09; H, 10.06; N, 7.88; mol. wt., 176.

The hydrochloride, which was prepared in a conventional way, melted at 164–164.5°.

Anal. Calcd. for $C_9H_{18}ClNO_2$: C, 52.04; H, 8.73; Cl, 17.07; N, 6.74. Found: C, 51.91; H, 8.71; Cl, 17.18; N, 6.71.

Dimerization of 2-Methoxy-1,3-butadiene in the Presence of Boron Trifluoride Etherate.—To a stirred mixture of 1.5 g. (0.016 mole) of boron trifluoride etherate in 300 ml. of dry ether, was added dropwise 7.6 g. (0.09 mole) of 2-methoxy-1,3-butadiene[17] in 300 ml. of dry ether at −30° during a period of 4 hr. The mixture was then stirred at 0° for 3 hr., neutralized with sodium methoxide in methanol solution, and diluted with ether. The mixture was then washed with water and, after the insoluble material had been removed by filtration, was dried over anhydrous sodium sulfate and concentrated. Distillation of the residue *in vacuo* gave 0.65 g. (8.5%) of a product which was found to be predominantly **1-methoxy-4-(1-methoxyvinyl)-1-cyclohexene** (13, R = R′ = H).[18] The identity was established by the comparison of its infrared spectra and the retention time of vapor chromatography with those of the material [b.p. 78–79° (1.5 mm.), $n^{20}D$ 1.4820] prepared according to Nazarov, *et al.*[6] Other products (0.7 g.) with a higher boiling point were present in the reaction mixture and there was large amount of an undistillable material.

4-Methoxy-1-methylbicyclo[2.2.2]octan-2-one (20).—To a magnetically stirred solution of 15.4 g. (0.1 mole) of 4-acetyl-4-methyl-1-cyclohexanone[8] and 32.0 g. (0.3 mole) of trimethyl orthoformate in 30 ml. of methanol was added dropwise 0.3 ml. of concentrated sulfuric acid. The reaction was exothermic and a red color developed. Stirring was continued at room temperature for 24 hr. and then sodium methoxide in methanol was added until the red color disappeared. After the removal of methanol and methyl formate *in vacuo*, 200 ml. of ether was added and the precipitated solid was removed by filtration. The ethereal filtrate was concentrated and 50 ml. of dry pyridine was added to the residue, followed by 30 g. of acetic anhydride. The mixture was heated at reflux for 3 hr. and then slowly distilled until the boiling point reached 130° and distillation ceased. It took about 5 hr. The residue was distilled *in vacuo* to furnish 12.2 g. (67%) of a crude **18**, b.p. 105–108° (13 mm.).

To a stirred solution of 12.2 g. (0.067 mole) of the above material in 150 ml. of dry benzene was added dropwise 5.0 g. (0.035 mole) of boron trifluoride etherate in 150 ml. of dry benzene during a period of 1 hr. The mixture was stirred at room temperature for 16 hr., and then heated at reflux for 4 hr. The cooled dark red solution was washed once with 30-ml. of 1 *N* hydrochloric acid and three times with 30-ml. portions of water and dried over anhydrous sodium sulfate. After removal of benzene, the residue was distilled *in vacuo* to furnish 8.14 g. (80%) of **20**, b.p. 121–123° (20 mm.).[19]

4-Methoxy-1-phenylbicyclo[2.2.2]octan-2-one (21).—A mixture of 4.32 g. (0.02 mole) of 4-acetyl-4-phenyl-1-cyclohexanone,[8] trimethyl orthoformate (7.00 g., 0.066 mole), and 10 ml. of methanol was treated similarly as described above and 4.00 g. (82%) of a crude **19**, b.p. 128–130° (1 mm.), was obtained. Treatment of the above material with boron trifluoride etherate as described above gave 3.26 g. (96%) of **21**. The analytical sample was recrystallized from benzene–petroleum ether.[19]

Demethylation of 20.—A mixture of 6.91 g. of **20** and 30 g. of pyridine hydrochloride was vigorously stirred at 200–210° for 7 hr. in an atmosphere of nitrogen. After cooling, 30 ml. of water was added and the solution was extracted with chloroform. The chloroform extracts were combined and washed with water, dried over anhydrous sodium sulfate, and concentrated. The residue was distilled to give 3.0 g. (48%) of crude **22**, b.p. 110–120° (0.2 mm.), m.p. 55–57°. Recrystallization from petroleum ether–benzene gave crystals with m.p. 60° which was identical with **1-hydroxy-1-methylbicyclo[2.2.2]octan-2-one** (lit.[8] m.p. 60°) prepared according to Colonge and Vuillement.[8] The identity was established by the comparison of their infrared spectra and by the mixture melting point.

Demethylation of 21.—Demethylation of **21**, carried out in the same manner described above, gave crystalline product **23**, m.p. 186° (lit.[8] m.p. 183°). The identity was established by the comparison of their infrared spectra and by the mixture melting point.

5-Carbomethoxy-4-methoxy-1-methylbicyclo[2.2.2]octan-2-one (26).—A mixture of 54 g. (0.25 mole) of γ-acetyl-γ-methylpimelic acid,[20] 300 ml. of absolute methyl alcohol, and 20 ml. of concentrated sulfuric acid was heated on a steam bath for 10 hr. After the usual work-up, 50 g. (82%) of dimethyl ester, b.p. 132–135° (1 mm.), $n^{20}D$ 1.4582, was obtained.

Anal. Calcd. for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 58.92; H, 8.21.

To a magnetically stirred mixture of 24.4 g. (0.1 mole) of the dimethyl ester and 16.0 g. (0.15 moles) of trimethyl orthoformate in 30 ml. of methanol was added dropwise 0.2 ml. of concentrated sulfuric acid at room temperature. The mixture was stirred at room temperature for 24 hr. and methanolic sodium methoxide was added until the deep red color disappeared. The mixture was concentrated and diluted with ether. The ether extract was washed with water and dried over anhydrous potassium carbonate. The product (**24**) was distilled, and the fraction boiling at 120–122° (1 mm.) amounted to 20.4 g. (70%).

A solution of 14.5 g. (0.05 mole) of the ketal **24** in 20 ml. of toluene was added to a suspension of sodium hydride in toluene (obtained from 4 g. of 50% sodium hydride dispersion) and the mixture was stirred at 90° for 30 hr. To the cooled reaction mixture were added 100 ml. of ether and 20 ml. of water. The

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(17) A. A. Petrov, *Acta Univ. Voronegiensis*, **8**, 68 (1935); *Chem. Abstr.*, **32**, 6616^5 (1938); *cf.* E. A. Brande, E. R. H. Jones, F. Sondheimer, and J. B. Toogood, *J. Chem. Soc.*, 607 (1949).

(18) Vapor phase chromatography of the material on a silicon rubber column indicated the presence of up to 5% of a contaminant with a retention time close to that of the principal product. The material prepared according to Nazarov also exhibited a similar v.p.c. pattern.

(19) *Cf.* Table I.

(20) H. A. Bruson and T. W. Riener, *J. Am. Chem. Soc.*, **64**, 2850 (1942).

TABLE III

ACID-CATALYZED CYCLIZATIONS OF 1,4-DIPHENYL-4-VINYL-1-CYCLOHEXENE

Run	Wt. of **30**, g.	Catalyst, ml.	Solvent, ml.	Temp., °C.	Time, hr.	Product
1	1.3	H_2SO_4, 1.0	$C_3H_7NO_2$, 7	−50	2	Mixture of **31** and **34**
2	1.3	H_2SO_4, 1.0	$C_3H_7NO_2$, 7	30	2	Mixture of **31** and **34**
3	0.52	H_2SO_4, 0.5	CH_3NO_2, 15	30	2	**31**
4	2.6	H_2SO_4, 0.5	HCOOH, 8	115	9	**31**
5	2.6	BF_3–Et_2O, 5	Benzene, 15	30	2	7:3 mixture of **31** and **30**
6	0.52	HCl (sat.)	C_2H_5OH, 10	78	2	No reaction
7	0.52	H_3PO_4, 15	. . .	70	2	No reaction

organic layer was separated and dried over anhydrous sodium carbonate. After removal of ether and toluene the product was distilled, and the fraction boiling at 125–130° (7 mm.) amounted to 5.9 g. This product presumably has a structure **25**, evidenced by its infrared spectrum.

To a mixture of 5.4 g. of this product, 8.0 g. of trimethyl orthoformate, and 20 ml. of methanol was added dropwise 0.2 ml. of concentrated sulfuric acid with stirring at room temperature. Stirring was continued for 24 hr., and then 100 ml. of ether and 30 ml. of water were added. The ethereal extract was washed twice with 30-ml. portions of water and once with 20-ml. of 1 *N* hydrochloric acid, dried over anhydrous sodium sulfate, and concentrated. The residue was distilled *in vacuo* to furnish 4.2 g. (78%) of **26**.[19] Vapor chromatography on silicone rubber column showed two peaks.

To a solution of 3.0 g. of potassium hydroxide in a mixture of 50 ml. of water and 20 ml. of methanol was added 3.5 g. of **26** and the mixture was stirred at room temperature for 12 hr. The reaction mixture was neutralized with 12 *N* hydrochloric acid. After removal of water, the residue was extracted with acetone. Removal of acetone and recrystallization from benzene–petroleum ether gave 2.5 g. (89%) of **27**.[19] The assumption that the product consists of two stereoisomers is based on the n.m.r. spectrum which shows two methoxyl peaks at τ 6.66 and 6.69.

Diethyl γ-acetyl-γ-methylpimelate, b.p. 143–147° (0.7 mm.), n^{21}D 1.4593, was prepared in a way similar to the above method.

Anal. Calcd. for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.83; H, 8.85.

Analogous reactions starting from diethyl γ-acetyl-γ-methylpimelate gave an over-all yield of 35% of **27**, m.p. 98.5–99.5°.

An Acid-Catalyzed Cyclization of 1,4-Diphenyl-4-vinyl-1-cyclohexene (30).—To a stirred mixture of **30** in the solvent specified in Table III was added an acid catalyst, and the mixture was treated under the reaction conditions indicated in Table III. The reaction mixture was poured onto ice–water and extracted with ether. The ethereal extract was washed successively with saturated sodium bicarbonate solution and water, and dried over anhydrous sodium sulfate. After the removal of the solvent, the residue was analyzed by vapor chromatography on a silicone gum (SE 30) column at 235°.

In the cases of runs 3 and 4, the crystalline residue was recrystallized from ethanol to yield **31**, m.p. 74.0–74.5°.

Anal. Calcd. for $C_{20}H_{20}$: C, 92.24; H, 7.74; mol. wt., 260. Found: C, 91.94; H, 7.73; mol. wt., 264, 260 (mass spectrometry).

In the cases of runs 1 and 2, the residue was recrystallized twice from chloroform to give the colorless crystalline sulfonic acid **34**: m.p. 173–174.5°; $\lambda_{\max}^{\text{KBr}}$ 1329, 1156, 1150 cm.$^{-1}$. The material was soluble in aqueous alkali.

Anal. Calcd. for $C_{20}H_{20}O_3S$: C, 70.56; H, 5.92; S, 9.42; mol. wt., 340. Found: C, 70.02; H, 5.84; S, 9.09; mol. wt., 341.

From the mother liquor, **31** was isolated.

1,4-Diphenylbicyclo[3.2.1]octane (32).—To a solution of 300 mg. of **31** in 55 ml. of *n*-propyl alcohol, was added Urushibara nickel, prepared[21] from 4 g. of $NiCl_2 \cdot 6H_2O$ and 10 g. of zinc dust, and the mixture was hydrogenated at room temperature. After about 3 hr., the absorption of the theoretical amount of hydrogen was observed. The catalyst was removed by filtration and the solvent was evaporated *in vacuo*. The residual white solid was recrystallized from petroleum ether to give 220 mg. of **32**, m.p. 158.5–160.5°.

Anal. Calcd. for $C_{20}H_{22}$: C, 91.54; H, 8.46. Found: C, 91.15; H, 8.54.

Ozonolysis of 31.—Ozone was passed through a solution of 1.7 g. of **31** in 50 ml. of methylene chloride at −78° for 30 min. The ozonized mixture was added to a suspension of 5 g. of zinc dust in 50 ml. of acetic acid and the mixture was stirred at room temperature for 1 hr. Solid was removed by filtration and the combined filtrate and washings were washed with a cold saturated bicarbonate solution and water. The organic layer was dried over anhydrous sodium sulfate. Removal of the solvent gave 1.73 g. of a yellow oil: $\lambda_{\max}^{\text{EtOH}}$ 243 mμ (ϵ 11,800); $\nu_{\max}^{\text{film}}$ 1690, 1715 cm.$^{-1}$; n.m.r. peak at τ 0.70 (triplet, J = 3.0 c.p.s.). The material is presumably crude **1-(3-benzoyl-1-phenylcyclopentyl)acetaldehyde (33)**. A mixture of 1.48 g. of the oil and 1.18 g. of silver oxide in a mixture of 40 ml. of 2 *N* sodium hydroxide solution, 20 ml. of water, and 20 ml. of methanol was stirred at room temperature for 9 hr. The formation of a silver mirror was observed. After the removal of solid, the mixture was acidified with 6 *N* sulfuric acid and extracted with ether. The ethereal extract was washed with water and dried over anhydrous sodium sulfate. The removal of the solvent gave 1.19 g. of an oil. To a solution of 0.98 g. of this oil in a mixture of 2.5 ml. of acetic acid, 25 ml. of water, and 3.5 ml. of concentrated sulfuric acid was added 1.2 g. of chromic acid, and the mixture was heated at reflux for 7 hr. The reaction mixture was diluted with water and extracted with ether. The ethereal solution was extracted with 2 *N* sodium hydroxide solution. The alkaline extract was acidified and extracted with ether. Removal of the solvent gave 0.71 g. of yellowish semisolid from which 0.14 g. of benzoic acid, m.p. 120°, was obtained after extraction with petroleum ether and recrystallizations from ethyl alcohol. The identity was established by the comparison of the infrared spectra and by the mixture melting point.

Acknowledgment.—The authors wish to thank Messrs. Y. Fujiwara and T. Takahashi, and Miss T. Takazawa for their technical assistance and a member of the analytical section of this laboratory for the microanalyses, physical determinations, and preparative vapor chromatography.

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(21) S. Taira, *Bull. Chem. Soc. Japan*, **34**, 1294 (1961).