Syntheses of γ-Ionone Analogues. I–II.

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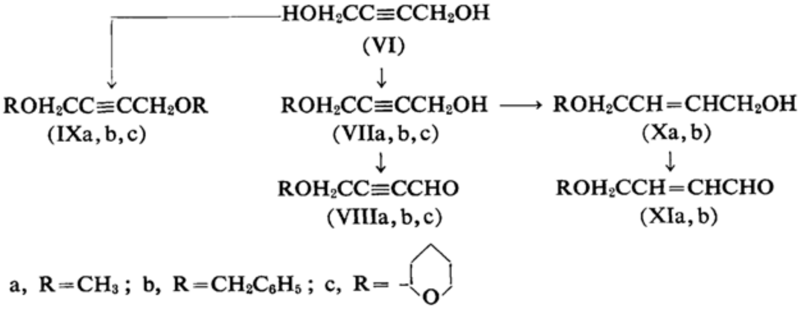
I. Several Asymmetric Bifunctional Dienophiles and their Diels-Alder Adducts with 2, 3-Dimethyl-1, 3-butadiene

Tetrolaldehydes or crotonaldehydes containing an adequate functional substituent in the γ-position seem to be suitable as the dienophiles for the preparation of the Diels-Alder adducts which can be used as the key intermediates for a certain synthetical project concerning γ-ionone analogues. In spite of their apparently simple structure, such compounds and their Diels-Alder adducts have hitherto scarcely been reported.

One of the present authors and his co-workers[1] synthesized the diethylacetals of γ-hydroxytetrolaldehyde (I), γ-dialkylaminotetrolaldehyde (II) and of γ-dialkylaminocrotonaldehyde (III), and then explained that all these acetals could neither give the free parent aldehydes nor behave as a dienophile, while they reported that γ-methoxycrotonaldehyde (XIa) was proved to be a dienophile. In this paper the authors wish to describe the preparation of several dienophiles in such series and the Diels-Alder reactions of them with a typical symmetric diene, 2, 3-dimethyl-1, 3-butadiene.

Five dienophiles — γ-methoxy-, γ-benzyloxy- and γ-tetrahydropyran-2-yloxytetrolaldehyde (VIIIa, VIIIb and VIIIc), γ-methoxy- and γ-benzyloxycrotonaldehyde (XIa and XIb) —were prepared successfully by the manganese dioxide oxidation of the corresponding carbinols (VIIa, VIIb, VIIc, Xa and Xb) as shown by the following scheme:



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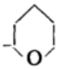
[1] I. Ichikizaki, Ching-Chung Yao, Y. Fujita and Y. Hasebe, This Bulletin, **28**, 80 (1955).

4-Methoxy-2-butyn-1-ol (VIIa) was prepared in 43% yield through a partial methylation of 2-butyn-1,4-diol (VI) with dimethyl sulfate in an aqueous alkali. A modified procedure was applied for the preparation of 4-benzyloxy-2-butyn-1-ol (VIIb) by adding benzyl chloride at 110~115°C into a xylene suspension of monosodium butyndiolate prepared beforehand from a large excess of VI with sodamide in liquid ammonia. In both cases appreciable amounts of 1,4-dialkoxy-2-butynes (IXa and IXb) were isolated.

Catalytic hydrogenation of the acetylenic carbinols, VIIa and VIIb, in the presence of a palladium-calcium carbonate catalyst in ethyl acetate gave the corresponding ethylenic carbinols, Xa and Xb, in good yields.

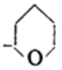
An attempted preparation of 4-tetrahydropyran-2′-yloxy-2-butyn-1-ol (VIIc) directly from VI and dihydropyran was proved to be unsatisfactory, since it was extremely difficult to separate the pure product from the reaction mixture containing 1,4-bistetrahydropyran-2′-yloxy-2-butyne (IXc), unchanged VI besides VIIc. IXc was, therefore, prepared at first by heating VI with two moles of dihydropyran in the presence of a catalytic amount of concentrated hydrochloric acid or *p*-toluenesulfonic

TABLE I. 4-ALKOXY-2-BUTYN-1-ALS AND 4-ALKOXY-2-BUTEN-1-ALS
$ROCH_2C{\equiv}CCHO$ (VIII), $ROCH_2CH{=}CHCHO$ (XI)

Compound		B. p. °C/mmHg	n_D^T	Yield, % based on the parent carbinol	Molecular formula	Analysis, % Found Calcd.	
Number	R					C	H
VIIIa	$-CH_3$	68~69/25	1.4504^{20}	41	$C_5H_6O_2$	59.99 61.21	6.58 6.16
VIIIb	$-CH_2C_6H_5$	116~117/1.0 111~112/0.7	1.5383^{21}	55	$C_{11}H_{10}O_2$	75.58 75.84	5.93 5.79
VIIIc[a]		83~84/0.8	1.4902^{16}	68	$C_9H_{12}O_3$	64.55 64.27	7.54 7.19
XIa	$-CH_3$	73~74/27		45	$C_5H_8O_2$	59.76 59.98	8.15 8.05
XIb	$-CH_2C_6H_5$	111~113/1.0	$1.5310^{18.5}$	52	$C_{11}H_{12}O_2$	74.92 74.97	6.88 6.86

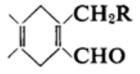
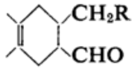
a) ν_{max}(liquid film) 2245, 2200 (C≡C); 1670 (C=O, conj.); 1185, 1125, 1083, 1060, 1031, 967, 944, 904, 874 cm^{-1} (C-O-C); no absorption band of hydroxyl group is observed.
$\lambda_{max}^{n\text{-hexane}}$ 221 mμ (ε 26400)

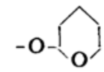
TABLE II. SOLID DERIVATIVES OF 4-ALKOXY-2-BUTYN-1-ALS AND 4-ALKOXY-2-BUTEN-1-ALS
$ROCH_2C{\equiv}CCHO$ (VIII), $ROCH_2CH{=}CHCHO$ (XI)

Parent aldehyde		Semicarbazone					2,4-Dinitrophenylhydrazone			
		Appearance	M. p. °C	λ_{max}^{EtOH} mμ (ε)	Molecular formula	Analysis, % Found Calcd. N	Appearance	M. p. °C	Molecular formula	Analysis, % Found Calcd. N
Number	R									
VIIIa	$-CH_3$						Orange-yellow needles	111 ~112.2	$C_{11}H_{10}O_5N_4$	19.90 20.14
VIIIb	$-CH_2Ph$	Slightly yellow needles	138.5 ~139[a]	236 (33700) 281 (41500)	$C_{18}H_{17}O_2N_3$	13.47 13.67	Yellow needles	121~122	$C_{17}H_{14}O_5N_4$	15.89 15.81
VIIIc							Yellow needles	120 ~120.5[b]	$C_{10}H_8O_5N_4$	21.13 21.21
XIa	$-CH_3$						Red-orange needles	140~141	$C_{11}H_{12}O_5N_4$	19.83 19.99
XIb	$-CH_2Ph$	Needles	148~149	264 (34500)	$C_{12}H_{15}O_2N_3$	18.27 18.02	Orange silk-like needles	166.5	$C_{17}H_{16}O_5N_4$	15.68 15.72

a) Phenylsemicarbazone
b) This 2,4-dinitrophenylhydrazone was identical with that of 4-hydroxy-2-butyn-1-al (I).

TABLE III. DIELS-ALDER ADDUCTS OF γ-SUBSTITUTED TETROL- AND CROTONALDEHYDES WITH 2,3-DIMETHYL-1,3-BUTADIENE


(XIV),

(XV)

Dienophiles Number	Condition of D-A reaction Temp. °C	Time hr.	Adduct Number	R	Yield %	B. p. °C/mmHg	n_D^T	Molecular formula	Analysis, % Found Calcd. C	H
VIIIa	140~150	13	XIVa	-OCH$_3$	84.3	113~117 /3	1.5161^{18}	$C_{11}H_{16}O_2$	71.68 73.30	8.93 8.95
VIIIb	145~153	14	XIVb	-OCH$_2$Ph	81.6	141~145 /0.03	1.5554^{20}	$C_{17}H_{20}O_2$	79.37 79.65	7.83 7.86
VIIIc	120~130	21	XIVc[a]		72	146~147 /0.75	1.5221^{20}	$C_{15}H_{22}O_3$	71.60 71.97	8.80 8.86
XIa	125~135	13	XVa	-OCH$_3$	73	82~84[b] /2.5		$C_{11}H_{18}O_2$	72.58 72.49	9.81 9.96
XIb	125~135	13	XVb	-OCH$_2$Ph	71.5	130~135 /0.01		$C_{17}H_{22}O_2$	79.12 79.03	8.49 8.58
Croton-aldehyde	140~150	9	XVI	-H	72.4	98/18[c]	1.4731^{20}	$C_{10}H_{16}O$	78.70 78.89	10.68 10.59

a) λ_{max}^{EtOH} 235 mμ (ε 7600); ν_{max} (liquid film) 1675 (C=O); 1198, 1181, 1118, 1078, 1057, 1028, 973, 907, 873 cm^{-1} (C-O-C-O)

b) Ref. 1, b. p.$_{2.5}$ 82~84°C.

c) O. Diels and K. Alder, *Ann.*, **470**, 62 (1929), reported b. p.$_{12}$ 89°C.

acid in tetrahydrofuran, then it was similarly treated with one equivalent of VI to afford pure VIIc in a good yield. The tetrahydropyranyl ether thus prepared was fairly soluble in water and afforded the 2,4-dinitrophenylhydrazone of 5-hydroxypentanal (XII) in quantitative yield by the Brady reagent.

So far as the authors were aware, none of the acetylenic primary carbinols had ever been reported to be oxidized into the aldehydes by the technique after Attenburrow[2], however, all of the 4-alkoxy-2-butyn-1-ols (VIIa, VIIb and VIIc) and the 4-alkoxy-2-buten-1-ols (Xa and Xb) were successfully oxidized by the usual method with active manganese dioxide to yield the corresponding aldehydes (VIIIa, VIIIb, VIIIc, XIa and XIb), which were all proved to be the dienophiles of moderate activity as descrided later. Their properties and analytical data are shown in Table I and their solid derivatives are summarized in Table II.

It is worth noticing in this connection that the same oxidation technique seems not to be applicable to γ, γ-dialkoxyacetylenic carbinol, because 4,4-diethoxy-2-butyn-1-ol (XIII)[1,3] was recovered unchanged on treatment with active manganese dioxide under more vigorous conditions than that generally adopted[2,4,5].

Treatment of 4-tetrahydropyran-2'-yloxy-2-butyn-1-al (VIIIc) with the Brady reagent afforded in an excellent yield 2,4-dinitrophenylhydrazones of 5-hydroxypentanal (XII) and that of 4-hydroxy-2-butyn-1-al (I), while the latter was also obtained in a good yield by similar treatment of 4,4-diethoxy-2-butyn-1-ol (XIII). This means that VIIIc is readily hydrolyzed and quantitatively affords the above two aldehydes, namely XII and I.

The condensation between each of the aldehydes (VIIIa, VIIIb, VIIIc, XIa and XIb) and 2,3-dimethyl-1,3-butadiene under the conditions as listed in Table III essentially afforded only a sole adduct. Some chemical evidences, which will be described in the following paper, of the adducts and the ultraviolet absorption data of their semicarbazones listed in Table IV demonstrate that they all have normal structures as expected.

On the Diels-Alder reaction involving α,β-acetylenic carbonyl compound, only a few examples which have resulted in the formation of an inhomogeneous product owing to the migration of the double bonds or the partial aromaticization have been reported[6,7]. It

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[2] J. Attenburrow, A. F. B. Cameron, I. H. Chapman R. M. Evans, B. A. Hem, A. B. A. Jansen and T. Walker, *J. Chem. Soc.*, **1952**, 1094.

[3] R. G. Jones and M. G. Main, *J. Am. Chem. Soc.*, **75**, 4048 (1953).

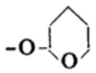
[4] M. Harfenist and A. Bavley, *J. Org. Chem.*, **19**, 1608 (1954).

[5] B. C. L. Weedon et al., *J. Chem. Soc.*, **1953**, 1578, 3286.

[6] J. C. Lunt and F. Sondheimer, ibid., **1950**, 3361.

[7] E. A. Braude, E. R. H. Jones, F. Sondheimer and J. B. Toogood, ibid., **1949**, 607.

TABLE IV. SOLID DERIVATIVES OF THE DIELS-ALDER ADDUCTS

Adduct		2,4-Dinitrophenylhydrazone				Semicarbazone				
Number	R	Appearance	M. p. °C	Molecular formula	Analysis, % Found Calcd. N	Appearance	M. p. °C	λ_{max}^{EtOH} mμ (ε)	Molecular formula	Analysis, % Found Calcd. N
XIVa	-OCH$_3$	Red-orange needles	203～204	$C_{17}H_{20}O_5N_4$	15.93 15.55	Needles	218.5～ 219.5 (decomp.)	272.5 (23400)	$C_{12}H_{19}O_2N_3$	17.89 17.71
						Prisms	175～177	273 (28100)	$C_{18}H_{23}O_2N_3$	13.55 13.41
XIVb	O-CH$_2$Ph	Red-orange needles	203	$C_{23}H_{24}O_5N_4$	12.86 12.84	Needles	179～180[b]	237 (11700) 284 (32900)	$C_{24}H_{27}O_2N_3$	11.07 10.79
XIVc		Dark-red needles	209～210[a]	$C_{21}H_{26}O_6N_4$	13.60 13.02	Needles	187～188	272 (28300)	$C_{16}H_{25}O_3N_3$	13.50 13.67
XVa	-OCH$_3$	Yellow needles	159～160	$C_{17}H_{22}O_5N_4$	15.54 15.46	Needles	152～153[c]	232.5 (12400) 269 (33700)	$C_{12}H_{21}ON_3S$	16.40 16.46
XVb	O-CH$_2$Ph	Yellow needles	134.5～135	$C_{23}H_{26}O_5N_4$	12.41 12.78	Plates	143[b]	248 (27100)	$C_{24}H_{29}O_2N_3$	10.64 10.73
XVI	-H	Bright yellow needles	193～194	$C_{16}H_{20}O_4N_4$	16.64 16.86					

a) Found: C, 58.38; H, 6.02. Calcd. C, 58.59; H, 6.09%; $\lambda_{max}^{CHCl_3}$ 234 mμ (ε 25300), 259 (15100), 378 (31400)
b) Phenylsemicarbazone
c) Thiosemicarbazone, Ref. 1, m.p. 152°C

should be noted, therefore, that when the condensation between VIIIc and 2, 3-dimethyl-1, 3-butadiene was carried out at 140°C the expected adduct (XIVc) was obtained in only 24% yield and the principal product was colorless crystals, m.p. 60°C, formulated as $C_{10}H_{12}O$, which could also be obtained in 34% yield by heating XIVc with *p*-toluenesulfonic acid in tetrahydrofuran. This crystalline product has a strong menthol-like odor and becomes gradually a dark-brown resinous matter on exposure to air and light. By considering the fact that its properties and the infrared spectrum closely resemble those of phthalane⁸⁾ the authors estimated its structure as 5, 6-dimethyl-1, 3-dihydroisobenzofuran (XVII). The nuclear magnetic resonance spectrum⁹⁾ of this compound, obtained at 56.4 mc., was in complete accord with the structure XVII. The spectrum of XVII displayed three singlet peaks at -2.53, 1.55 and 2.84 p.p.m. whose area varied in a ratio of approximately 1 : 2 : 3, respectively. The resonance of -2.53 p.p.m. can be assigned to the aromatic hydrogens, while that of 2.84 p.p.m. is definitely associated with the hydrogens of methyl groups. The methylene groups linked with oxygen atom satisfactorily were accounted for by the peak of 1.55 p.p.m.

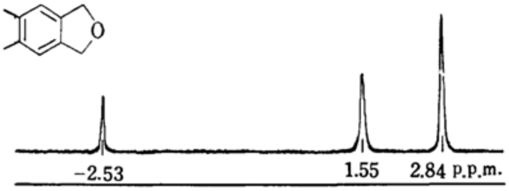


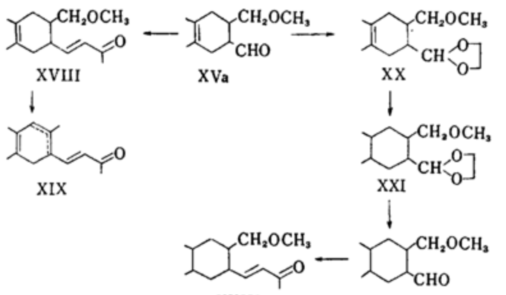
Fig. 1. NMR spectrum of 5,6-dimethyl-1,3-dihydroisobenzofuran.

II. Synthesis of 2-Methylene-4, 5-dimethylcyclohexylmethanol and Related Compounds

In this paper the authors wish to describe the preliminary work which has been carried out in the course of study for the preparation of an analogue of γ-cyclogeraniol and related compounds by employing the Diels-Alder adducts reported in the preceding paper.

An attempt was made at first to synthesize 4-(2′-methylene-4, 5-dimethyl-4′-cyclohexenyl)-but-3-en-2-one by employing 3, 4-dimethyl-6-methoxymethyl-3-cyclohexenylmethanal (XVa) as the starting substance. Condensation of XVa with acetone in the presence of barium hydroxide afforded in 69% yield 4-(3′,4′-dimethyl-6′-methoxymethyl-3′-cyclohexenyl)-but-3-en-2-one (XVIII) which on heating with hydrogen bromide at 130°C gave a crude oil, from which a considerable amount of only one orange 2, 4 dinitrophenylhydrazone was obtained. Since the infrared spectrum of the hydrazone did not exhibit a characteristic absorption band of exocyclic methylene group, its parent aldehyde was considered to be a triply unsaturated ketone as represented by XIX which resulted from XVIII after elimination of methyl alcohol. Consequently the use of such a methoxymethyl compound as XVIII for the preparation of γ-ionone analogue was regarded as being practically unsuitable.

In order to hydrogenate a double bond in the ring of XVa a carbonyl group was once protected as the acetal. By the method of Salmi¹⁰⁾ XVa was converted into the corresponding ethylendioxy compound XX in 79% yield, which was hydrogenated over a palladium-charcoal catalyst in ethanol to give the saturated acetal XXI. The XXI was readily hydrolyzed, when heated under reflux in tetrahydrofuran with 2 N aqueous sulfuric acid, to yield the free aldehyde XXII which was condensed with acetone in the usual method giving 4-(4′, 5′-dimethyl-2′-methoxymethylcyclohexyl)-but-3-en-2-one (XXIII).



Since the conversion of a side methoxymethyl group into an exocyclic methylene had failed, a formyl group that is another functional group of such an adduct as XVa was investigated for the same purpose by employing 3, 4, 6-trimethyl-3-cyclohexenylmethanal (XVI) as a simple model.

In an autoclave XVI was hydrogenated in the presence of Raney nickel catalyst and anhydrous dimethylamine to afford in 80% yield *N*, *N*-dimethyl-2, 4, 5-trimethylcyclohexylmethylamine (XXV), together with an appreciable amount of 2, 4, 5-trimethylcyclohexylmethanol (XXIV). Though it is well known¹¹⁾

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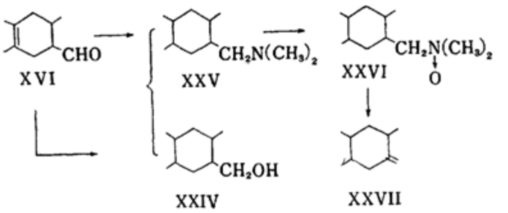
8) J. Entel, C. H. Ruof and H. C. Howard, *J. Am. Chem. Soc.*, 74, 441 (1952).

9) The NMR spectra were determined on a Varian Associates V-4300C high resolution NMR spectrometer with ca. 10% solution in CCl_4 with water as an external reference standard.

10) E. I. Salmi, *Ber.*, 71, 1803 (1938).

11) W. S. Emerson, "Organic Reactions", Vol. IV, (1948), pp. 174—255.

that primary and secondary amines are generally converted into tertiary amines by reductive condensation with various carbonyl compounds, no case with alicyclic aldehyde has been reported until the above preparation was completed[12].

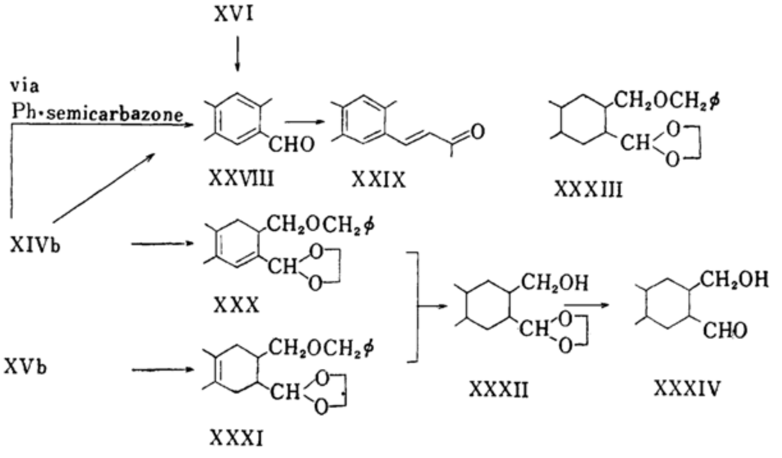


Oxidation of the tertiary amine XXV with 30% aqueous hydrogen peroxide gave in 82% yield an amine oxide XXVI as a colorless syrup which was characterized as crystalline picrate. The amine oxide XXVI was pyrolyzed in the manner described by Cope and his co-workers[13]. The decomposition proceeded smoothly at 120 ~130°/2.5 mmHg under nitrogen, and gave in yield of 61% based on XXV, a colorless mobile liquid, $C_{10}H_{18}$, which showed b.p. 59~59.2°/16.2 mmHg, n_D^{20} 1.4601 and was proved to be homogeneous by vapor phase chromatography. From the infrared absorption bands at 3077, 1648 and 885 cm^{-1} indicative of exocyclic methylene group, 1-methylene-2, 4, 5-trimethylcyclohexane (XXVII) was assigned for the hydrocarbon. The above result demonstrates that the thermal decomposition of XXVI gave exclusively the expected unsaturated hydrocarbon and also provided a further example in support of the specific formation of methylene cycloalkanes previously reported by Cope and his co-investigator[14,15].

Since three of the new Diels-Alder adducts —XIVb, XIVc and XVb—have all a functional group readily convertible to a hydroxyl group, an attempt was made to prepare from them 2-methylene-4, 5-dimethylcyclohexylmethanol (XXXVIII) which can be regarded as an analogue of γ-cyclogeraniol.

In order to isolate XIVb of high purity the phenylsemicarbazone obtainable in yield of 96% from the original adduct was hydrolyzed on steam distillation in the presence of concentrated sulfuric acid and *o*-phthalic acid, whereas 2, 4, 5-trimethylbenzaldehyde (XXVIII), m. p. 43°C (lit.[16] m. p. 42°C), was obtained in 60% yield with benzyl alcohol. The compound XXVIII was also formed in 20% yield by heating XIVb under reflux in xylene with a catalytic amount of *p*-toluenesulfonic acid, and it was characterized as the semicarbazone and 2, 4-dinitrophenylhydrazone, both of which were identical with those of an authentic sample prepared by the sulfur dehydrogenation of 3, 4, 6-trimethyl-3-cyclohexenylmethanal (XVI). On condensation with acetone, the aldehyde XXVIII afforded 4-(2′, 4′, 5′-trimethylphenyl)-but-3-en-2-one (XXIX) which showed m. p. 49.5°C (semicarbazone, m. p. 223~224°C; 2, 4-dinitrophenylhydrazone, m. p. 247~249°C).

An attempted acid-catalyzed reaction of XIVb with ethylene glycol following the method of Salmi[10] gave in only 33.5% yield an acetal which was probably XXX[17], while a considerable amount of XXVIII was yielded from



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12) The 12th Annual Meeting of the Chemical Society of Japan, Kyoto, April, 1959.

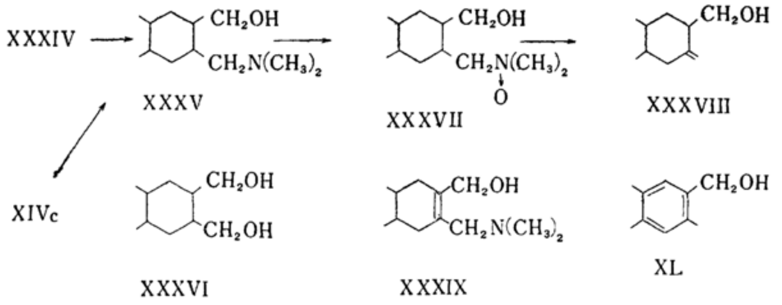
13) A. C. Cope, R. A. Pike and C. F. Spencer, *J. Am. Chem. Soc.*, **75**, 3212 (1953).

14) A. C. Cope, C. L. Bumgardner and E. E. Schweizer, ibid., **79**, 4729 (1957).

15) A. C. Cope, E. Ciganek, C. F. Howell and E. E. Schweizer, ibid., **82**, 4663 (1960).

16) L. Gattermann, *Ann.*, **347**, 347 (1906).

17) Such migration of double bonds in the presence of acid will be discussed in the following paper, Part III.



the elimination of benzyl alcohol. However, 6-benzyloxymethyl-3, 4-dimethyl-3-cyclohexenylmethanal (XVb) could be converted into the corresponding acetal XXXI in a good yield without the elimination of benzyl alcohol.

XXX as well as XXXI usually afforded XXXII on hydrogenation over a palladium-charcoal catalyst; however, they occasionally afforded an appreciable amount of 2-benzyloxymethyl-4, 5-dimethylcyclohexylmethanal ethylene acetal (XXXIII), when hydrogenated with a catalyst prepared from less active charcoal. This result suggests that the hydrogenation of double bonds proceeded more rapidly than the hydrogenolysis of the benzyloxy group. On hydrolysis with diluted aqueous sulfuric acid in tetrahydrofuran the acetal XXXII was readily converted into the hydroxy aldehyde XXXIV.

On catalytic hydrogenation with dimethylamine over Raney nickel catalyst, XXXIV afforded in 60% yield *N*, *N*-dimethyl-4, 5-dimethyl-2-hydroxymethylcyclohexylmethylamine (XXXV) and simultaneously a considerable amount of 1, 2-bishydroxymethyl-4, 5-dimethylcyclohexane (XXXVI), m. p. 113∼115°C. XXXV was successively oxidized with 30% hydrogen peroxide in the usual method to the *N*-oxide XXXVII, which was decomposed at 120∼130°C to exclusively yield 2-methylene-4, 5-dimethylcyclohexylmethanol (XXXVIII), b. p. 94∼97°C/17.5 mmHg, n_D^{27} 1.4729, as shown by its infrared absorption bands at 3058, 1642 and 884 cm^{-1}.

In another attempt to prepare the hydroxy amine XXXV directly from XIVc by similar reductive alkylation of dimethylamine with the aldehyde XXXIV as described above, XXXV was obtained in yield of 43.5% and it was usually contaminated with a base which was assumed from the methiodide to be the unsaturated aminoalcohol XXXIX. In this reduction a neutral compound, $C_{10}H_{14}O$, which shows m.p. 84.5°C; λ_{max}^{EtOH} 217 mμ (ε 175), 267 (338) and 274 (322), was also isolated in 32% yield. The infrared spectrum exhibited the presence of hydroxyl group (∼3360, 1038) as well as of 1, 2, 4, 5-tetra-substituted aromatic group (879 cm^{-1}), and clearly suggested that this compound was to be 2, 4, 5-trimethylbenzyl alcohol (XL) which had been reported elsewhere to show m. p. 168°C[18]. The NMR spectrum provided an independent confirmation of its structure. The spectrum[9] consisted of five peaks at −2.23, −2.10, 0.30, 2.25 and 2.50 p. p. m. the chemical shifts of which permit the unequivocal assignment. The two non-equivalent hydrogens on the ring are accounted for by the peaks of −2.23 and −2.10 p. p. m. The three methyl groups were found at 2.50 p. p. m. as a singlet peak, while the methylene group with hydroxyl group was found at a lower magnetic field (0.30 p. p. m.). The resonance at 2.25 p. p. m. can be assigned to the proton of hydroxyl group.

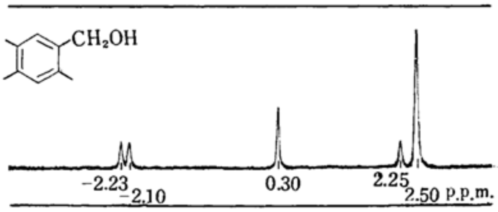


Fig. 2. NMR spectrum of 2, 4, 5-trimethylbenzyl alcohol.

Experimental[19]

4-Methoxy-2-butyn-1-ol (VIIa) and 4-Methoxy-2-buten-1-ol (Xa).—These compounds were prepared by the method of Ichikizaki et al[1]. 4-Methoxy-2-butyn-1-ol (VIIa), b. p. 105.5∼106°C/20.5 mmHg, n_D^{20} 1.4595, was obtained in 43% yield. In addition to VIIa, 1, 4-dimethoxy-2-butyne (IXa), b.p. 63∼65°C/20 mmHg, was obtained in 9% yield as a by-product. 4-Methoxy-2-buten-1-ol (Xa), b.p. 88∼89°C/20 mmHg, n_D^{12} 1.4490, was obtained by hydrogenation of VIIa with a palladium-calcium carbonate catalyst (5% Pd) in 89% yield.

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[18] W. J. Hickinbottom, "Chemistry of Carbon Compounds", Vol. III-A, Ed. by E. H. Rodd, Elsevier Pub. Co. (1954), p 499.

[19] All melting points were determined on the Kofler block and are uncorrected. The ultraviolet spectra were determined with a Hitachi EPU-2A spectrophotometer and the infrared spectra were obtained with a Perkin-Elmer model 112, a Kōken model DS-301, and a Nippon Bunkō model IR-S recording spectrophotometers with sodium chloride optics.

4-Benzyloxy-2-butyn-1-ol (VIIb). — 2-Butyne-1, 4-diol (VI) (200 g.) was added portionwise to a solution of sodamide (prepared from 35 g. of sodium) in liquid ammonia (1 l.) under vigorous stirring at −45∼−50°C over a period of 10 min. After being stirred for additional 2 hr. under cooling, the reaction mixture was diluted with xylene (800 ml.) and then set aside overnight to evaporate ammonia. The residual suspension was heated gradually to 100°C under stirring to remove the remaining ammonia as completely as possible. To it benzyl chloride (200 g.) was added dropwise over a period of 30 min. under vigorous stirring at 110∼115°C and the mixture was stirred for an additional hour. After being cooled, the reaction mixture was poured into cold water (500 ml.) and the xylene layer separated was washed with 10% sulfuric acid and water and dried over sodium sulfate. Distillation gave two fractions, 198 g. (69.2%), b. p. 142∼147°C/4 mmHg and 9 g., b. p. 170∼175°C/2 mmHg. Upon redistillation the lower boiling fraction afforded pure 4-benzyloxy-2-butyn-1-ol (VIIb), b. p. 143∼146°C/2.5 mmHg, n_D^{25} 1.5379.

Found : C, 73.76 ; H, 7.07. Calcd. for $C_{11}H_{12}O_2$: C, 74.97 ; H, 6.86%.

Upon redistillation the higher boiling fraction afforded pure 1, 4-dibenzyloxy-2-butyne (IXb), b. p. 169∼170°/1.5 mmHg, $n_D^{19.5}$ 1.5590.

Found : C, 81.20 ; H, 6.71. Calcd. for $C_{18}H_{18}O_2$: C, 81.17 ; H, 6.81%.

4-Benzyloxy-2-buten-1-ol (**Xb**).—A solution of 4-benzyloxy-2-butyn-1-ol (VIIb) (100 g.) in ethyl acetate (140 ml.) was hydrogenated with a palladium-barium carbonate catalyst (2.5% Pd, 1.5 g.) at 22°C until 14515 ml. of hydrogen (1.05 equiv.) had been absorbed. After removal of the catalyst and solvent the residue was distilled to afford 4-benzyloxy-2-buten-1-ol (Xb) (83 g., 82%), b. p. 125∼127.5°C/2 mmHg, n_D^{25} 1.5267.

Found : C, 74.08 ; H, 7.88. Calcd. for $C_{11}H_{14}O_2$: C, 74.13 ; H, 7.92%.

1, 4-Bistetrahydropyran-2′-yloxy-2-butyne (**IXc**). —A solution of dihydropyran (18.5 g., 0.22 mol.) in tetrahydrofuran (20 ml.) was added dropwise to a solution of VI (8.6 g., 0.1 mol.) in tetrahydrofuran (20 ml.) containing 2 drops of concentrated hydrochloric acid with stirring at 60°C over a period of 30 min. and the resulting mixture was gently refluxed for additional 3 hr. After being cooled, the reaction mixture was made alkaline with a cold 5% aqueuos sodium carbonate solution and extracted with three 80 ml. portions of ether. The combined extracts were washed 4 times with a saturated aqueous sodium chloride solution, dried over potassium carbonate and evaporated. Distillation of the residue under nitrogen gave the bis-ether IXc (17 g., 67%), b.p. 144∼146°C/1.0 mmHg, n_D^{16} 1.4913 ; ν_{max}^{film} 2226 (C≡C), 1186, 1120, 1081, 1056, 1022, 973, 946, 905 and 872 cm^{-1} (C-O-C-O).

Found : C, 65.66 ; H, 8.70. Calcd. for $C_{14}H_{22}O_4$: C, 66.11 ; H, 8.72%.

4-Tetrahydropyran-2′-yloxy-2-butyn-1-ol (**VIIc**). —A solution of the bis-ether IXc (25.4 g., 0.1 mol.) in tetrahydrofuran (10 ml.) was added dropwise to a solution of VI (8.6 g., 0.1 mol.) in tetrahydrofuran (30 ml.) containing 3 drops of concentrated hydrochloric acid under gentle reflux and then boiled for 3 hr. The resultant reaction mixture was worked up as described in the preceding section to leave a pale yellow oil which was distilled through a 8 cm. Vigreux column to yield VIIc (23.0 g., 68%), b. p. 122∼124°C/0.8 mmHg, n_D^{10} 1.4913 ; ν_{max}^{film} 3470∼3450 (OH) and 2220 cm^{-1} (C≡C). The characteristic absorption bands in its finger-print region were almost superimposable on those of the bis-ether IXc.

Found : C, 63.27 ; H, 8.46. Calcd. for $C_{11}H_{14}O_3$: C, 63.51 ; H, 8.29%

Upon treatment with the Brady reagent, this compound yielded 2, 4-dinitrophenylhydrazone of 5-hydroxypentanal which was crystallized from aqueous methanol and showed m. p. 115°C, undepressed on admixture with the authentic sample.

4, 4-Diethoxy-2-butyn-1-ol (**XIII**).—This compound was obtained in 57.7% by the method of Ichikizaki et al.1), and had b.p. 118∼119°C/3 mmHg and n_D^{26} 1.4335 (lit.1) b. p. 88°C/0.5 mmHg, n_D^{25} 1.4493).

The 2, 4-dinitrophenylhydrazone crystallized from 50% methanol in yellow needles, m. p. 120∼120.5°C (lit.1) m. p. 119°C).

Found : N, 21.13. Calcd. for $C_{10}H_8O_5N_4$: N, 21.21%.

General Procedure for Oxidation of Carbinols (VII and X) with Manganese Dioxide.—A solution of the carbinol (5 g.) obtained above in benzene (5 ml.) was added dropwise to a suspension of manganese dioxide (50 g.) prepared by the method of Attenburrow et al.2) in the same solvent (350 ml.) over a period of 5∼15 min. under vigorous stirring at room temperature and the resultant mixture was stirred for additional 3∼5 hr. During this period the initial temperature increased 10∼12°C. The reaction mixture was filtered and the precipitate was washed with petroleum ether. The washing was combined with the filtrate and evaporated in a nitrogen atmosphere under reduced pressure. Fractionation of the residue afforded the desired aldehydes whose properties and elemental analyses are listed in Table I. The solid derivatives prepared from these aldehydes are summarized in Table II.

Attempted Oxidation of 4, 4-Diethoxy-2-butyn-1-ol (XIII) with Manganese Dioxide. — XIII was treated with manganese dioxide according to the general procedure described above. Distillation afforded a trace of fore-run and unchanged starting material (76%). Although XIII was treated with a large excess of the oxidizing agent in boiling benzene for 10 hr., the unchanged starting material was recovered (78 %), and the desired aldehyde could not be obtained.

Reaction of 4-Tetrahydropyran-2′-yloxy-2-butyn-1-al (VIIIc) with the Brady Reagent.—VIIIc was treated with the Brady reagent in the usual manner giving a mixture of two 2,4-dinitrophenylhydrazones. Recrystallization from aqueous methanol yielded 2, 4-dinitrophenylhydrazone of 4-hydroxy-2-butyn-1-al in yellow needles, m. p. 120∼120.5°C, undepressed on admixture with a sample prepared from XIII.

On addition of water the mother liquor afforded

2, 4-dinitrophenylhydrazone of 5-hydroxypentanal in orange-yellow leaflets, m. p. 115°C, undepressed on admixture with the authentic sample prepared as described below.

5-Hydroxypentanal (**XII**).—This compound was prepared in 65 % yield by the method of Schniepp et al.[20] and showed b. p. 61∼61.5°C/5 mmHg and n_D^{17} 1.4510 (lit. b. p.5 4∼55°C/3 mmHg, n_D^{25} 1.4514[20]; b. p. 80°C/12 mmHg, n_D^{20} 1.4510[21]).

The 2, 4-dinitrophenylhydrazone crystallized from 50% methanol in orange-yellow leaflets, m. p. 115∼116°C (lit. m. p. 109°C[22]; m. p. 107∼109°C[23]).

Found: N, 20.19. Calcd. for $C_{11}H_{14}O_5N_4$: N, 19.85%.

General Procedure for Diels-Alder Addition of 2, 3-Dimethyl-1, 3-butadiene to γ-Alkoxytetrolaldehydes VIII and γ-Alkoxycrotonaldehydes XI.—A solution of freshly distilled aldehyde (1 equiv.), 2, 3-dimethyl-1, 3-butadiene (1.05 equiv.) and a trace of quinol in an appropriate solvent was taken in a 50∼100 ml. glass bomb and was heated under nitrogen in an oil bath under the conditions described in Table III. After removal of the solvent the residue was distilled under reduced pressure to afford a crude product which was purified by redistillation through a short Vigreux column to give a pure adduct.

Some physical properties and sold derivatives of the adducts thus obtained are summarized in Tables III and IV.

Phenylsemicarbazone of 2-Benzyloxymethyl-4, 5-dimethylcyclohexa-1, 4-dienylmethanal (**XIVb**).—A solution of the aldehyde XIVb (4.0 g.) in ethanol (20 ml.) and phenylsemicarbazide (3.8 g.) in the same solvent (12 ml.) were refluxed for 5 min. The cooled reaction mixture was diluted with water and allowed to stand overnight at room temperature. A white precipitate which had been separated was collected and crystallized from ethanol-ethyl acetate to afford phenylsemicarbazone of XIVb (5.8 g., 96%) in needles, m. p. 179∼180°C.

The elemental analysis and the ultraviolet absorption data are listed in Table IV.

5, 6-Dimethyl-1, 3-dihydroisobenzofuran (**XVII**).—*a*) *From 4-Tetrahydropyran-2'-yloxy-2-butyn-1-al* (*VIIIc*) *and 2, 3-Dimethyl-1, 3-butadiene.*—A solution of the aldehyde VIIIc (3.06 g.) in benzene (10 ml.) was treated with 2, 3-dimethyl-1, 3-butadiene (1. 8 g.) in the presence of a trace of quinol at 140°C for 10 hr. by the general procedure described above. Distillation afforded two fractions: b. p. 90∼110°/1.5 mmHg (1.5 g., 55.5%) and b. p. 133∼135°C/0.55 mmHg (1.1 g., 24.1%).

The lower boiling fraction of colorless oil solidified immediately after distillation and crystallized from aqueous methanol in colorless fine plates which melted at 60°C and had a characteristic menthol-like odor. The infrared spectrum (KBr disk) showed absorption bands at 1606 (w), 1543 (m), 1495 (m), 1440 (s), 1418 (m), 1389 (s), 1320 (m), 1214 (m), 1127 (m), 1086 (m), 1028 (s), 890 (s) and 768 cm^{-1} (s), and also indicated the absence of the carbonyl group.

Found: C, 80.82; H, 8.40. Calcd. for $C_{10}H_{12}O$: C, 81.04; H, 8.16%.

Upon treatment with the Brady reagent this compound yielded red 2, 4-dinitrophenylhydrazone which crystallized from ethanol-ethyl acetate in red needles, m. p. 208∼209°C.

Found: C, 55.11; H, 5.62; N, 15.74. Calcd. for $C_{16}H_{16}O_5N_4$: C, 55.48; H, 5.24; N, 16.18%.

An attempt to prepare the semicarbazone of this product in the usual manner was unsuccessful.

These evidences, therefore, strongly suggest that the lower boiling product is probably 5, 6-dimethyl-1, 3-dihydroisobenzofuran (XVII).

The higher boiling fraction of a pale yellow viscous oil was an expected adduct which was proved to be identical with XIVc (Tables III and IV) by mixed melting point determination of their 2, 4-dinitrophenylhydrazones and by infrared comparison.

b)—*From 4, 5-Dimethyl-2-tetrahydropyran-2'-yloxymethylcyclohexa-1, 4-dienylmethanal* (*XIVc*).—A solution of the aldehyde XIVc (0.5 g.) in tetrahydrofuran (20 ml.) was heated with *p*-toluenesulfonic acid (0.1 g.) under reflux for 3 hr. After removal of the solvent the residue was taken in ether and the ethereal solution was washed with a 2 % aqueous sodium carbonate solution and water, dried and evaporated. Distillation of the residue afforded an oil which boiled at 130°C (bath temperature)/15 mmHg and solidified rapidly. Recrystallization from petroleum ether yielded colorless plates which melted at 60°C and proved to be identical with XVII obtained from a) by mixed melting point determination and infrared comparison.

The compound XVII was unstable and on exposure to air or light furnished a dark-brown resinous material.

3, 4-Dimethyl-6-methoxymethyl-3-cyclohexenylmethanal Ethylene Acetal (**XX**).—A mixture of the aldehyde XVa (6.6 g.), ethylene glycol (4.0 g.), *p*-toluenesulfonic acid (20 mg.) and benzene (30 ml.) was taken in a flask provided with an azeotropic water separator and heated under reflux in an oil bath (120∼130°C) until no more aqueous phase has been separated from an azeotropic distillate (for ca. 4 hr.). The solvent was removed under reduced pressure and the residual brown oil was thoroughly extracted with ether. The combined ethereal extracts were washed with a 10 % aqueous sodium carbonate solution and with water, dried over sodium sulfate and evaporated under reduced pressure. Distillation of the residue afforded the acetal XX (6.5 g., 79.3%) as a colorless liquid, b. p. 105∼106°C/2.0 mmHg, n_D^{25} 1.4868.

Found: C, 68.90; H, 9.97. Calcd. for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80%.

This compound afforded 2, 4-dinitrophenylhydrazone, m. p. 160°C, undepessed on admixture with that of XVa.

4, 5-Dimethyl-2-methoxymethylcyclohexylmethanal Ethylene Acetal (**XXI**).—The acetal XX (6.5 g.) in absolute ethanol (40 ml.) was hydrogenated in the presence of 5% palladium-on-charcoal (0.2 g.) at 100°C and a pressure of 120 kg./cm² for 2 hr.

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[20] L. E. Schniepp and H. H. Geller, *J. Am. Chem. Soc.*, **68**, 1646 (1946).

[21] C. D. Hurd and W. H. Saunders Jr., ibid., **74**, 5326 (1952).

[22] G. F. Woods and H. Sanders, ibid., **68**, 2111 (1946).

[23] G. F. Woods and D. N. Kramer, ibid., **69**, 2246 (1947).

The catalyst was removed by filtration and the filtrate was evaporated under reduced pressure. Distillation of the residue yielded the saturated acetal XXI (5.0 g., 77%), b. p. 103∼105°C/2.5 mmHg, n_D^{29} 1.4659.

Found: C, 68.44; H, 10.48. Calcd. for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59%.

The 2, 4-dinitrophenylhydrazone crystallized from ethanol in yellow plates, m. p. 129∼130°C.

Found: N, 15.40. Calcd. for $C_{17}H_{24}O_5N_4$: N, 15.38%.

4, 5-Dimethyl-2-methoxymethylcyclohexylmethanal (XXII).—A mixture of the acetal XXI (1.8 g.), tetrahydrofuran (30 ml.) and 2 N sulfuric acid (30 ml.) was heated under reflux for 24 hr. The cooled reaction mixture was made slightly alkaline with a 10% sodium carbonate solution, concentrated under reduced pressure and then extracted with ether. The ethereal extract was washed with water, dried and evaporated. Distillation of the residue afforded the aldehyde XXII (1.0 g., 69%), b.p. 93∼95°C/1.0 mmHg, n_D^{17} 1.4710; $\nu_{\max}^{\text{liquid}}$ 1730 cm^{-1} (C=O), $\nu_{\max}^{\text{CCl}_4}$ 1725.2 cm^{-1} (C=O); $\lambda_{\max}$ 226 mμ (ε 499), 294 (59) in 75% aqueous dioxane.

Found: C, 71.58; H, 10.67. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94%.

The 2, 4-dinitrophenylhydrazone showed m. p. 130°C, undepressed on admixture with that of XXI.

4-(3′, 4′-Dimethyl-6′-methoxymethyl-3′-cyclohexenyl)-but-3-en-2-one (XVIII).—The aldehyde XVa (3.6 g.) was added dropwise to a boiling solution of barium hydroxide (0.7 g.) in 90% aqueous acetone (20 ml.) and the resultant mixture was refluxed for 7.5 hr. The cooled reaction mixture was neutralized with 1 N hydrochloric acid, concentrated under reduced pressure and then extracted with ether. The dried ethereal solution was fractionated to yield the unsaturated ketone XVIII (3.0 g., 68.5%), b. p. 122∼123°C/3 mmHg, $n_D^{22.5}$ 1.5000; $\nu_{\max}^{\text{liquid}}$ 1680 (C=O), 1624 (C=C), 1115 (C-O-C) and 983 cm^{-1} (trans-CH=CH-).

Found: C, 75.42; H, 10.10. Calcd. for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97%.

The 2, 4-dinitrophenylhydrazone crystallized from ethanol in red prisms, m. p. 155∼156°C.

Found: N, 14.05. Calcd. for $C_{20}H_{26}O_5N_4$: N, 13.92%.

4-(4′, 5′-Dimethyl-2′-methoxymethylcyclohexyl)-but-3-en-2-one (XXIII).—The aldehyde XXII (1.7g.) was added dropwise to a boiling solution of barium hydroxide (0.3 g.) in 90% aqueous acetone (10 ml.) and the resultant mixture was refluxed for 10 hr., and was then treated in the same manner as that described above to yield the ketone XXIII (1.2 g., 58%), b. p. 120∼122°C/2 mmHg, n_D^{32} 1.4781.

Found: C, 74.34; H, 10.65. Calcd. for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78%.

The 2, 4-dinitrophenylhydrazone crystallized from ethanol in red-orange plates, m. p. 127∼129°C.

Found: N, 14.06. Calcd. for $C_{20}H_{28}O_5N_4$: N, 13.85%.

Reaction of 4-(3′, 4′-Dimethyl-6′-methoxymethyl-3′-cyclohexenyl)-but-3-en-2-one (XVIII) with Hydrobromic Acid.—A mixture of the unsaturated ketone XVIII (0.3 g.) and a constant boiling hydrobromic acid (b. p. 123°C, 12 ml.) was heated in a 50 ml. glass bomb at 130°C for 4 hr. The black tarry oil formed was poured into an ice-cooled 10% aqueous sodium carbonate solution and extracted with ether. The ethereal extract was washed, dried and evaporated. Distillation of the residue afforded a colorless oil (0.11 g.), b. p. 90∼100°C/0.8 mmHg, $n_D^{24.5}$ 1.5241. This oily product gave a positive Beilstein test and a 2, 4-dinitrophenylhydrazone which contained no bromine atom and crystallized from ethanol in orange needles, m. p. 174∼175°C.

Found: C, 61.15; H, 6.13. Calcd. for $C_{19}H_{22}O_4N_4$: C, 61.61; H, 5.99%.

Although the position of the double bonds on the ring could not be confirmed, the derivative obtained above was seen clearly to be 2, 4-dinitrophenylhydrazone of 4-(2′, 4′, 5′-trimethylcyclohexadienyl)-but-3-en-2-one, since elemental analysis was very satisfactory and the infrared spectrum exhibited no absorption band attributable to the exocyclic methylene group.

2, 4, 5-Trimethylcyclohexylmethanol (XXIV).—3, 4, 6-Trimethyl-3-cyclohexenylmethanal (XVI) (3.04 g.) in ethanol (30 ml.) was hydrogenated over a Raney nickel catalyst (1.5 g.) in a 100 ml. stainless-steel autoclave at 192°C and a pressure of 192 kg./cm^2 for 1 hr. The catalyst was removed by filtration and the filtrate was evaporated. Distillation of the residue afforded XXIV (2.9 g., 93%) as a colorless oil, b. p. 110°C/16 mmHg, n_D^{17} 1.4700.

Found: C, 76.62; H, 13.02. Calcd. for $C_{10}H_{20}O$: C, 76.86; H, 12.90%.

***N*, *N*-Dimethyl-2, 4, 5-trimethylcyclohexylmethylamine (XXV).**—A mixture of XVI (7.4 g.), anhydrous dimethylamine (2.9 g.), a Raney nickel catalyst (1.2 g.) and ethanol (50 ml.) was shaken with hydrogen at 180∼220°C and a pressure of 121 kg./cm^2 for 4 hr., after which time a pressure of 58 kg./cm^2 of hydrogen was absorbed. The catalyst was removed by filtration and the filtrate was evaporated under reduced pressure. Distillation of the residue afforded a crude product (7.9 g.) b. p. 100∼105°C/16 mmHg, n_D^{21} 1.4622∼1.4658. This oil was taken up in ether and extracted with diluted hydrochloric acid. The aqueous extracts were combined, neutralized with aqueous sodium hydroxide and then extracted with ether. The dried ethereal solution was distilled under reduced pressure to yield a pure amine XXV (6.6 g., 80%), b. p. 98∼99°C/15 mmHg, $n_D^{17.5}$ 1.4607.

Found: C, 78.77; H, 13.52. Calcd. for $C_{12}H_{25}N$: C, 78.61; H, 13.75%.

The methiodide crystallized from ethanol in leaflets, m. p. 262°C (decomp.).

Found: C, 48.19; H, 8.83; N, 4.18; I, 38.5. Calcd. for $C_{13}H_{28}NI$: C, 48.0; H, 8.6; N, 4.3; I, 39.0%.

The picrate was obtained as a yellow oil which could not be induced to crystallize.

The ethereal solution which had been shaken with acid was dried and then distilled under reduced pressure to yield a neutral compound (0.8 g., 10.8%), b. p. 114∼116°C/17 mmHg, $n_D^{20.5}$ 1.4668. This compound was proved to be identical with

XXIV obtained above by comparison of their infrared spectra.

***N*, *N*-Dimethyl-2, 4, 5-trimethylcyclohexylmethylamine Oxide (XXVI).**—To a solution of the amine XXV (6.11 g., 1/30 mol.) in methanol (5 ml.) was added dropwise 30% aqueous hydrogen peroxide (13 g., 1/10 mol.) under vigorous stirring at 0°C and the resultant mixture was allowed to warm to room temperature. The mixture was stirred for 11.5 hr. and set aside overnight, after which time all of the reaction mixture was homogeneous. The excess of hydrogen peroxide was then decomposed with platinum foil (0.3 g.) under stirring for 35 hr. at room temperature. After removal of the platinum foil the solution was evaporated under reduced pressure (15∼17 mmHg) at below 35°C to leave a syrupy residue which was taken up in absolute ethanol (10 ml.). The solution was evaporated through a 25 cm. Vigreux column under reduced pressure. This work-up was repeated 4 times to remove the last traces of water and afforded the amine oxide XXVI as a very viscous colorless liquid. The product thus obtained was used in the next preparation without further purification, since its practical purity was indicated by the determination of an amine oxide prepared in another run described below.

When an excess of picric acid in aqueous ethanol was mixed with an aqueous ethanolic solution of a crude amine oxide prepared from the amine XXV (0.46 g.) in the manner described above, there was obtained a picrate which crystallized from absolute ethanol in yellow plates, m. p. 165∼166.5°C. The yield was 0.82 g. (82%).

Found: C, 50.36; H, 6.80; N, 12.69. Calcd. for $C_{18}H_{28}O_8N_4$: C, 50.46; H, 6.59; N, 13.08%.

1-Methylene-2, 4, 5-trimethylcyclohexane(XXVII).—The amine oxide XXVI obtained above was taken in a 100 ml. flask fitted with a 15 cm. Vigreux column and heated to 110°C, at this temperature decomposition of the amine oxide occurred. After 30 min. the distillation became slower and the bath was heated to 180°C. The pyrolysis products, which distilled mainly at 120∼130°C (bath temperature), were swept with nitrogen through a trap cooled with a freezing mixture and then through a liquid nitrogen cooled trap. The products were combined and taken up in ether. The ethereal solution was washed twice with 10 % hydrochloric acid and 3 times with water, dried over magnesium sulfate and then in the presence of a small amount of quinol concentrated under a 25 cm. Vigreux column at atmospheric pressure. The residue was distilled under nitrogen to yield the hydrocarbon XXVII (2.8 g., 61.0% based on XXV), b. p. 59∼59.2°C/16.2 mmHg, n_D^{20} 1.4601. This hydrocarbon decolorized rapidly a dilute solution of bromine in carbon tetrachloride and readily consumed potassium permanganate in acetone solution. ν_{max}^{liquid} 3077, 1648, 885 ($>C=CH_2$); 1464, 1384 ($-CH_2-$ and CH_3) and 1770 cm^{-1} (over-tone of δ CH).

Found: C, 87.12; H, 12.63. Calcd. for $C_{10}H_{18}$: C, 86.88; H, 13.12%.

The aqueous washings were combined and concentrated under reduced pressure to leave a crystalline residue, which was taken up in absolute ethanol. The solution was evaporated to dryness yielding a crude *N*, *N*-dimethylhydroxylamine hydrochloride (2.0 g., 61.5%), m. p. 103∼105°C. A sample recrystallized from absolute ethanol in needles, m. p. 105∼106.5°C (lit. m. p. 104.5∼106.5°C[13] and m. p. 106.5∼109°C[24]).

2-Benzyloxymethyl-4, 5-dimethylcyclohexa-4, 6-(or -1, 4-) dienylmethanal Ethylene Acetal (XXX).—A mixture of the aldehyde XIVb (47.2 g.), *p*-toluenesulfonic acid (0.05 g.), ethylene glycol (26.2 g.) and benzene (250 ml.) was taken in a flask provided with an azeotropic water separator and heated under reflux at 120°C for 4 hr. The water was drawn off from time to time. After the excess of benzene was removed under reduced pressure the residue was extracted with ether. The ethereal solution was washed with a 10% aqueous sodium carbonate solution and with water, dried over sodium sulfate and then evaporated. Distillation of the residue afforded a lower boiling fraction (5.8 g.), b. p. 52∼80°C/0.001 mmHg, and an acetal XXX (18.5 g., 33.5%) as a pale yellow viscous oil, b. p. 144∼148°C/0.001 mmHg, n_D^{26} 1.5429.

Found: C, 75.73; H, 8.21. Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05%.

The lower boiling fraction on treatment with the Brady reagent yielded a 2, 4-dinitrophenylhydrazone. Recrystallization from ethanol-ethyl acetate gave a pure sample, m. p. 226°C, undepressed on admixture with the 2, 4-dinitrophenylhydrazone of 2, 4, 5-trimethylbenzaldehyde.

6-Benzyloxymethyl-3, 4-dimethyl-3-cyclohexenylmethanal Ethylene Acetal (XXXI).—A mixture of the aldehyde XVb (8.3 g.), ethylene glycol (9.0 g,), *p*-toluenesulfonic acid (0.05 g.) and benzene (40 ml.) was refluxed at 130∼135°C for 4 hr. The reaction mixture was worked up in the manner described above to yield the acetal XXXI (7.2 g., 74.2%), b. p. 150∼155°C/0.017 mmHg.

Found: C, 73.98; H, 8.55. Calcd. for $C_{19}H_{26}O_3$: C, 75.46; 8.67%.

4, 5-Dimethyl-2-hydroxymethylcyclohexylmethanal Ethylene Acetal (XXXII).—*a) From XXX.*—The acetal XXX (16.5 g.) in ethanol (40 ml.) was hydrogenated over a 5% palladium-on-charcoal catalyst (1.0 g.) in a stainless-steel autoclave at 120°C and a pressure of 120 kg./cm² for 8 hr. The catalyst was filtered off and the filtrate was evaporated. Distillation of the residue afforded a saturated acetal XXXII (3.9 g., 33%) as a viscous oil, b. p. 112∼120°C/1.3 mmHg, $n_D^{25.5}$ 1.4786.

Found: C, 66.90; H, 10.62. Calcd. for $C_{12}H_{22}O_3$: C, 67.25; H, 10.35%.

The 2, 4-dinitrophenylhydrazone crystallized from methanol-light petroleum in orange-yellow leaflets, m. p. 194∼196°C.

Found: N, 16.19. Calcd. for $C_{16}H_{22}O_5N_4$: N, 15.99%.

Further distillation afforded a higher boiling viscous oil (6.7 g.), which boiled at 120∼125°C/0.001 mmHg and was thought probably to be 2-benzyloxymethyl-4, 5-dimethylcyclohexylmethanal ethylene acetal (XXXIII), since it afforded readily

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24) A. C. Cope, N. A. LeBel, H. H. Lee and W. R. Moore, ibid., 79, 4720 (1957).

XXXII on hydrogenolysis under the same conditions as those described above.

b) *From XXXI.*—The acetal XXXI (11.4 g.) in ethanol (50 ml.) was hydrogenated over 5% palladium-on-charcoal (1.0 g.) for 5 hr. in the manner described above to yield XXXII (6.2 g., 77.5%), b. p. 131～134°C/3.0 mmHg.

The 2, 4-dinitrophenylhydrazone prepared from this liquid showed m. p. 195～196°C, undepressed on admixture with a sample obtained in a).

The 3, 5-dinitrobenzoate crystallized from benzene-petroleum ether in plates, m. p. 110～111°C.

Found: C, 55.47; H, 5.96; N, 7.01. Calcd. for $C_{19}H_{24}O_8N_2$: C, 55.87; H, 5.92; N, 6.86%.

4,5-Dimethyl-2-hydroxymethylcyclohexylmethanal (XXXIV).—A mixture of the acetal XXXII (3.1 g.), tetrahydrofuran (16 ml.) and 2 N sulfuric acid (16 ml.) was refluxed for 2.5 hr. The cooled reaction mixture was neutralized with a 30% aqueous sodium carbonate solution and extracted with ether. The ethereal solution was washed with a saturated sodium chloride solution, dried over sodium sulfate and then evaporated. Distillation of the residue under nitrogen afforded the hydroxyaldehyde XXXIV (1.9 g., 77.3%), which boiled at 99～105°C/2.0 mmHg and solidified rapidly. Recrystallization from methanol-light petroleum yielded colorless plates, m. p. 84°C; $\nu_{\max}^{\text{KBr}}$ 3333, 1724, 1456, 1124, 1087, 1047, 971, 899 and 877 cm^{-1}; $\lambda_{\max}$ 225 mμ (ε 37.3), 294 (29.1) in 75% aqueous dioxane.

Found: C, 70.81; H, 10.62. Calcd. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66%.

The 2, 4-dinitrophenylhydrazone crystallized from methanol in orange-yellow leaflets, m. p. 194～195°C, undepressed on admixture with that of XXXII.

***N, N*-Dimethyl-4,5-dimethyl-2-hydroxymethylcyclohexylmethylamine (XXXV).**—*a*) *From XXXIV.*—A mixture of the aldehyde XXXIV (1.2 g.), anhydrous dimethylamine (0.8 g.), Raney nickel catalyst (1.2 g.) and absolute ethanol (30 ml.) was shaken with hydrogen in a 100 ml. autoclave at 180～190°C and a pressure of 118 kg./cm^2 for 1.6 hr. The catalyst was filtered off and the solution was evaporated to leave an oil, which was taken up in ether and extracted twice with 2 N hydrochloric acid. The aqueous extracts were combined, made alkaline with a 10% sodium hydroxide solution and then extracted with ether. The dried ethereal solution on distillation afforded the aminoalcohol XXXV (0.8 g., 57%), b. p. 100～105°C/2.0 mmHg, $n_D^{29.5}$ 1.4666.

Found: C, 71.73; H, 12.40. Calcd. for $C_{12}H_{25}ON$: C, 72.30; H, 12.64%.

The methiodide crystallized from ethanol-ethyl acetate in prisms, m. p. 221°C.

Found: C, 45.40; H, 8.33. Calcd. for $C_{13}H_{28}ONI$: C, 45.87; H, 8.28%.

The ethereal solution which had been shaken with hydrochloric acid was distilled to yield an oil (0.15 g., 12%), which boiled at 115～121°C/2.0 mmHg and solidified on being set aside for a short time. Recrystallization from light petroleum afforded colorless plates, m. p. 113～115°C.

Found: C, 69.01; H, 11.23. Calcd. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70%.

This compound is thought probably to be 1, 2-bishydroxymethyl-4, 5-dimethylcyclohexane(XXXVI), since the elemental analysis is very satisfactory and the infrared spectrum exhibits strong absorption bands of the hydroxyl group at 3310 and 1045 cm^{-1} but no band attributable to an aldehyde group.

b) *From XIVc.*—A mixture of the aldehyde XIVc (2.9 g.), anhydrous dimethylamine (2.0 g.), Raney nickel (2.0 g.) and ethanol (40 ml.) was shaken with hydrogen at 200～220°C and a pressure of 197 kg./cm^2 for 3 hr. When the resultant reaction mixture was worked up as in the case of XXXIV, there were obtained a crude amino compound (1.2 g., 43.5%) and a neutral one (0.8 g., 31.6%).

The amino compound boiled at 80°C/0.55 mmHg, n_D^{15} 1.4755, and the infrared spectrum exhibited strong absorption bands of hydroxyl group at 3370 and 1066 cm^{-1} and characteristic bands attributable to the *tert*-amino group at 2838, 2800 and 2742 cm^{-1}.

Found: C, 72.53; H, 12.80; N, 7.10. Calcd. for $C_{12}H_{25}ON$: C, 72.30; H, 12.64; N, 7.03%.

The methiodide crystallized from methanol-ethyl acetate in leaflets, m. p. 221°C, undepressed on admixture with that of XXXV obtained in a).

From the crude methiodide, there was obtained a small amount of crystals which were slightly soluble in methanol-ethyl acetate. Recrystallization afforded a pure sample, m. p. 271～272°C.

Found: C, 46.30; H, 7.93. Calcd. for $C_{13}H_{26}ONI$: C, 46.00; H, 7.73%.

The elemental analysis indicates that the methiodide is probably that of *N, N*-dimethyl-4, 5-dimethyl-2-hydroxymethyl-1-cyclohexenylmethylamine (XXXIX).

The neutral product of colorless liquid obtained above boiled at 95～105°C/0.6 mmHg and solidified rapidly. Recrystallization from petroleum ether yielded 2,4, 5-trimethylbenzyl alcohol(XL) in needles, m. p. 84.5°C.

The infrared spectrum (KBr disk) exhibited strong absorption bands of hydroxyl group at 3360 and 1038 cm^{-1} and other principal bands at 1621 (w), 1513 (m), 1450 (s), 1078 (s), 1009 (s), 996 (s), 899 (m), 888 (m), and 877 cm^{-1} (s). $\lambda_{\max}^{\text{EtOH}}$ 217 mμ (ε 175), 265 (338) and 274 (322).

Found: C, 80.02; H, 9.51. Calcd. for $C_{10}H_{14}O$: C, 79.95; H, 9.39%.

***N, N*-Dimethyl-4, 5-dimethyl-2-hydroxymethylcyclohexylmethylamine Oxide (XXXVII).**—To a solution of the amine XXXV (0.6 g.) in methanol (3.6 ml.) was added 30% aqueous hydrogen peroxide (1.5 g.) and the resultant mixture was stirred at 30°C for 50 hr., after which time the reaction mixture gave no color with phenolphthalein. The excess of hydrogen peroxide was then decomposed with a small amount of platinum foil and the solution was worked up as in the case of XXVI to yield the amine oxide XXXVII (0.55 g., 84.6%) as a colorless glass, which was characterized as the picrate which could not be induced to crystallize. The product thus obtained was used in the next pyrolysis without further purification.

4, 5-Dimethyl-2-methylenecyclohexylmethanol (XXXVIII).—The amine oxide XXXVII (0.4 g.) obtained above was pyrolysed as in the case of XXVII to yield a neutral XXXVIII (0.12 g., 42%),

b. p. 94~97°C/17.5 mmHg, n_D^{27} 1.4729. The infrared spectrum (liquid film) exhibited absorption bands of hydroxyl group at 3385 and 1053 cm^{-1}, the bands attributable to exocyclic double bond at 3058, 1642 and 884 cm^{-1} and other principal bands at 1765, 1459 and 1384 cm^{-1}.

Found: C, 77.79; H, 11.85. Calcd. for $C_{10}H_{18}O$: C, 77.86; H, 11.76%.

2, 4, 5-Trimethylbenzaldehyde (XXVIII).—*a) By Sulfur Dehydrogenation of 3, 4, 6-Trimethyl-3-cyclohexenylmethanal (XVI).*—The aldehyde XVI (2.3 g.) was heated under reflux with sulfur (1.2 g.) at 220~230°C in an oil bath until the evolution of hydrogen sulfide ceased (for ca. 40 min.). The resultant yellowish dark-brown mixture was distilled to yield a yellow oil (0.45 g.), b. p. 128~130°C/18 mmHg, n_D^{20} 1.5591 (lit.[25] b. p. 55~60°C/5~10 mmHg).

The 2, 4-dinitrophenylhydrazone crystallized from ethanol-ethyl acetate in red needles, m. p. 223~224.5°C.

Found: C, 58.40; H, 5.07. Calcd. for $C_{16}H_{16}O_4N_4$: C, 58.53; 4.91%.

The semicarbazone crystallized from ethanol-ethyl acetate in needles, m. p. 239°C; ν_{max}^{EtOH} 226 mμ (ε 16500), 285 (23400),

Found: C, 64.36; H, 7.35. Calcd. for $C_{11}H_{15}ON_3$: C, 64.36; H, 7.37%.

b) By the Action of p-Toluenesulfonic Acid on 2-Benzyloxymethyl-4, 5-dimethylcyclohexa-1, 4-dienylmethanal (XIVb).—A mixture of the unsaturated aldehyde XIVb (1.0 g.), *p*-toluenesulfonic acid (0.3 g.) and xylene (10 ml.) was heated under reflux for 4 hr. The cooled reaction mixture was neutralized with a 10% aqueous sodium carbonate solution and extracted with ether. The ethereal solution was washed with water, dried over sodium sulfate and then evaporated. Distillation of the residue afforded a colorless oil (0.2 g., 35%), b. p. 80~90°C/0.6~0.8 mmHg.

The 2, 4-dinitrophenylhydrazone crystallized from ethanol-ethyl acetate in bright red prisms, m. p. 225~226.5°C, undepressed on admixture with that of XXVIII obtained in a).

c) By Hydrolysis of Phenylsemicarbazone of 2-Benzyloxymethyl-4, 5-dimethylcyclohexa-1, 4-dienyl methanal (XIVb).—Steam distillation of the phenylsemicarbazone (4.5 g.) of XIVb from a mixture of *o*-phthalic acid (4.5 g.), ethylene glycol (40 ml.), concentrated sulfuric acid (14.0 g.) and water (40 ml.) afforded benzyl alcohol (0.3 g.) and the aldehyde XXVIII (1.3 g., 60%) as a colorless liquid after the usual workup. The regenerated aldehyde was distilled to yield a pure compound, which boiled at 87°C/1.0 mmHg and was crystallized upon treatment with petroleum ether. Recrystallization from methanol-petroleum ether afforded colorless plates, m. p. 43°C (lit.[16] m. p. 42°C); λ_{max}^{EtOH} 215 mμ (ε 22400), 261 (14700), 298 (2400). The infrared spectrum (KBr disk) exhibited a strong absorption band of carbonyl group at 1686 cm^{-1}, and other principal bands at 3000 (m, sh), 2934 (m), 2856 (m), 2742(m), 1608 (s), 1551 (s), 1501 (m), 1454 (s), 1386 (m), 1255 (m), 1187 (s), 1082 (m), 887 (m) and 775 cm^{-1} (s).

Found: C, 80.95; H, 8.21. Calcd. for $C_{10}H_{12}O$: C, 81.04; H, 8.16%.

The 2, 4-dinitrophenylhydrazone crystallized from ethyl acetate in bright red needles, m. p. 226~227°C.

The semicarbazone crystallized from chloroform-ethyl acetate in fine needles, m. p. 239~240°C.

The melting points of mixtures of the above derivatives with samples obtained in a) showed no depression.

4-(2′, 4′, 5′-Trimethylphenyl)-but-3-en-2-one (XXIX).—A solution of the aldehyde XXVIII (0.4 g.) obtained in c) in acetone (5 ml.) was added dropwise to a boiling mixture of barium hydroxide (0.2 g.), acetone (8 ml.) and water (2 ml.) and the resulting mixture was heated under reflux for 18.5 hr. The cooled reaction mixture was acidified with 1 N hydrochloric acid, concentrated under reduced pressure and then extracted with ether. The ethereal extracts were combined, washed and dried. Distillation of the residue afforded a colorless oil (0.2 g., 40%), which boiled at 120~140°C (bath temperature)/3.0 mmHg and solidified on standing. Recrystallization from petroleum ether yielded XXIX in colorless prisms, m. p. 49.5~50°C (lit.[26] m. p. 51°C); λ_{max}^{EtOH} 216.5 mμ (ε 12600), 233 (10700), 305 (21900); ν_{max}^{KBr} 1683 (conjugated C=O), 1660 (conjugated C=C), 978 (trans -CH=CH-) and 869 cm^{-1}.

The 2, 4-dinitrophenylhydrazone crystallized from methanol-chloroform in dark-red needles, m. p. 247~249°C.

Found: N, 15.29. Calcd. for $C_{19}H_{20}O_4N_4$: N, 15.21%.

The semicarbazone crystallized from ethanol-ethyl acetate in leaflets, m. p. 223~224°C; λ_{max}^{EtOH} 237 mμ (ε 18600), 307 (42600).

Found: N, 17.20. Calcd. for $C_{14}H_{19}ON_3$: N, 17.13%.

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