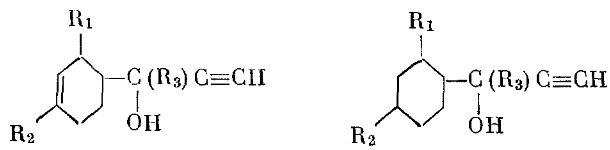
ETHYNYLATION OF CYCLOALIPHATIC KETONES*

(UDC 542.91 + 547.362)

D. A. Kazlauskas and G. P. Kugatova-Shemyakina

Institute for the Chemistry of Natural Products, Academy of Sciences, USSR,
and Institute of Chemistry and Chemical Technology, Academy of Sciences, Lithuanian SSR
Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 1,
pp. 95-103, January, 1965
Original article submitted October 14, 1963

This work was carried out with the object of synthesizing tertiary acetylenic alcohols of types A and B for use by us in the future as starting compounds for the preparation of cycloaliphatic polyenic ketones and polyenic esters.

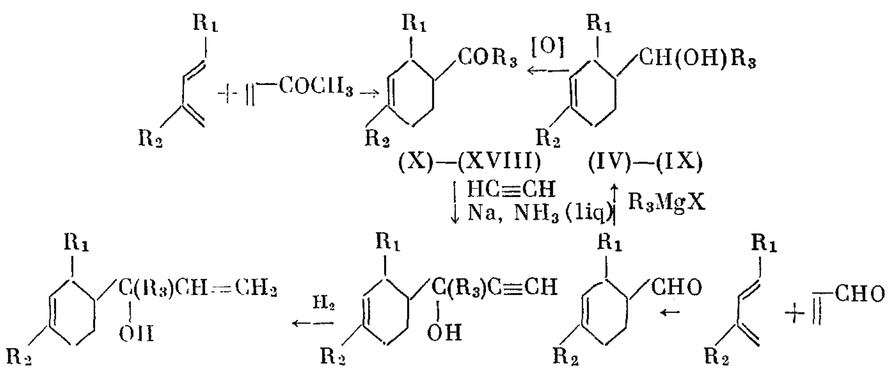


Type A Type B

R_1, R_2 = H or CH_3; R_3 = alkyl or phenyl

In spite of the fact that there is an extensive literature on tertiary acetylenic alcohols [1], alcohols of these types have scarcely been investigated at all. Only two alcohols of type B have been described, (XXXVI) and (XXXVII), in connection with the study of their soporific action [2] and their isomerization into aldehydes [3].

The ketones (X)-(XVIII), from which the alcohols (XIX)-(XXVII) of type A were synthesized, were prepared either by the diene condensation of 3-buten-2-one with butadiene, piperylene, or isoprene [4, 9] or by the chromic acid oxidation of the secondary alcohols (IV)-(IX), which were prepared in their turn by the Grignard reaction from the 3-cyclohexene-1-carboxaldehydes (I)-(III) [5].

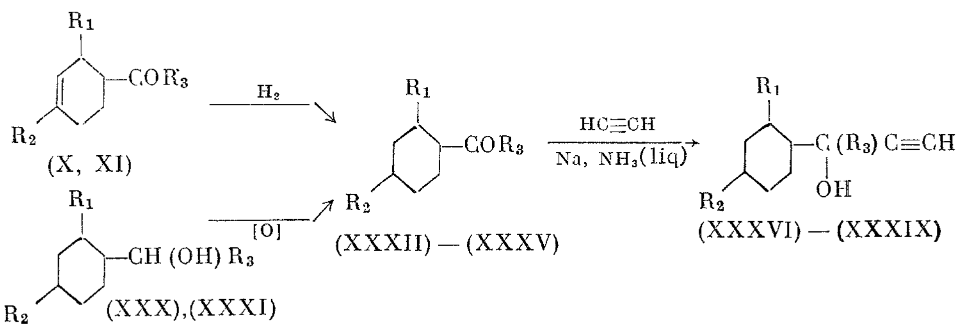


(XXVIII), (XXIX) (XIX)—(XXVII) (I)—(III)

(I)−R_1, R_2 = H; (II)−R_1 = CH_3; R_2 = H; (III)−R_1 = H; R_2 = CH_3; (X), (XIX)−R_1, R_2 = H; R_3 = CH_3; (XI), (XX)−R_2 = H; R_1, R_3 = CH_3; (XII), (XXI), (XXVIII)−R_1 = H; R_2, R_3 = CH_3; (IV), (XIII), (XXII), (XXIX)−R_2 = H; R_1 = CH_3; R_3 = C_2H_5; (V), (XIV), (XXIII)−R_1, R_2 = H; R_3 = $CH(CH_3)_2$: (VI), (XV), (XXIV)−R_2 = H; R_1 = CH_3; R_3 = $CH(CH_3)_2$; (VII), (XVI), (XXV)−R_1 = H; R_2 = CH_3; R_3 = $CH(CH_3)_2$; (VIII), (XVII), (XXVI)−R_1, R_2 = H: R_3 = phenyl; (IX), (XVIII), (XXVII) −R_1=H; R_2−CH_3; R_2 = phenyl.

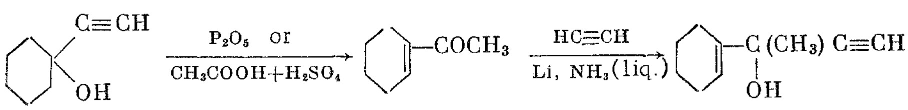
*This article is published in accordance with a resolution of the Conference of Chief Editors of Journals of the Academy of Sciences of the USSR of July 12, 1962, as a dissertation paper by D. A. Kazlauskas.

It was of interest to compare the reactivities of the ketones (X)-(XII) and the aldehydes (I)-(III) of the 3-cyclohexene series in the ethynylation reaction, for we have shown previously that the carbonyl group of 3-cyclohexene-1-carboxaldehydes is of low reactivity in a number of reactions [6]. It was found that under comparable conditions (sodium acetylide in liquid ammonia) the ketones (X)-(XII) condense somewhat more readily with acetylene than the corresponding aldehydes with formation of the acetylenic alcohols (XIX)-(XXI) in 63-76% yield, whereas acetylenic alcohols were obtained from the corresponding aldehydes in 35-55% yield [7]. However, when the condensation was with lithium acetylide in liquid ammonia the yields of the same alcohols (XIX)-(XXI) attained 76-86% and approached the yields of the alcohols (XXXVI)-(XXXIX) of type B, which were prepared from the cyclohexyl ketones (XXXII)-(XXXV).



(X), (XXXII), (XXXVI)—R_1, R_2 = H; R_3 = CH_3, (X), (XXXIII), (XXXVII)—R_2 = H; R_1, R_3 = CH_3; (XXX), (XXXIV), (XXXVIII)—R_1, R_2 = H; R_3 = phenyl; (XXXI), (XXXV), (XXXIX)—R_1 = H; R_2 = CH_3, R_3 = phenyl.

The high reactivity of lithium acetylide, as compared with sodium acetylide, is confirmed by the fact that the condensation of the α,β-unsaturated ketone (XL) [8] with lithium acetylide goes with formation of the alcohol (XLI) in 80% yield, whereas the use of calcium or sodium acetylide in the condensation reduces the yield to 62 or 34% respectively.



(XL) (XLI)

Hence, when lithium acetylide is used the reactivities of cyclohexyl, and also 1-cyclohexen-1-yl and 3-cyclohexen-1-yl, ketones are leveled out.

The yields of the acetylenic alcohols (XIX)-(XXI) depend somewhat on the position of the methyl group in the cyclohexene ring, as was observed earlier in the condensation of 3-cyclohexene-1-carboxaldehydes with acetylene [7]. A higher yield of alcohol was obtained from the ketone (XII) with the methyl group in the 4-position, and the lowest yield was obtained from the ketone (XI) with the methyl group in the 2-position.

The acetylenic alcohols (XXI) and (XXII) are selectively hydrogenated in presence of a Lindlar catalyst with formation of the dienic alcohols (XXVIII) and (XXIX).

To confirm the structures of the alcohols synthesized, their infrared absorption spectra were studied in the range 650-4000 cm^{-1} (Fig. 1). The absorption band at 1650-1656 cm^{-1} corresponds to the stretching vibrations of the C=C bond in the ring, and the absorption band at 2100 cm^{-1} corresponds to a monosubstituted acetylene. In the region of ≡C−H vibrations there is an absorption band at 3300 cm^{-1}, characterizing the presence of an acetylenic hydrogen. The fact that the acetylenic alcohols (XXI) and (XXII) are selectively hydrogenated to the dienic alcohols (XXVIII) and (XXIX) is confirmed by the disappearance of the bands due to the stretching vibrations of C≡C and ≡C−H with the simultaneous appearance of a new band at about 1625 cm^{-1}. The absorption band at 3500 cm^{-1} confirms the presence of a hydroxy group in all the compounds synthesized.

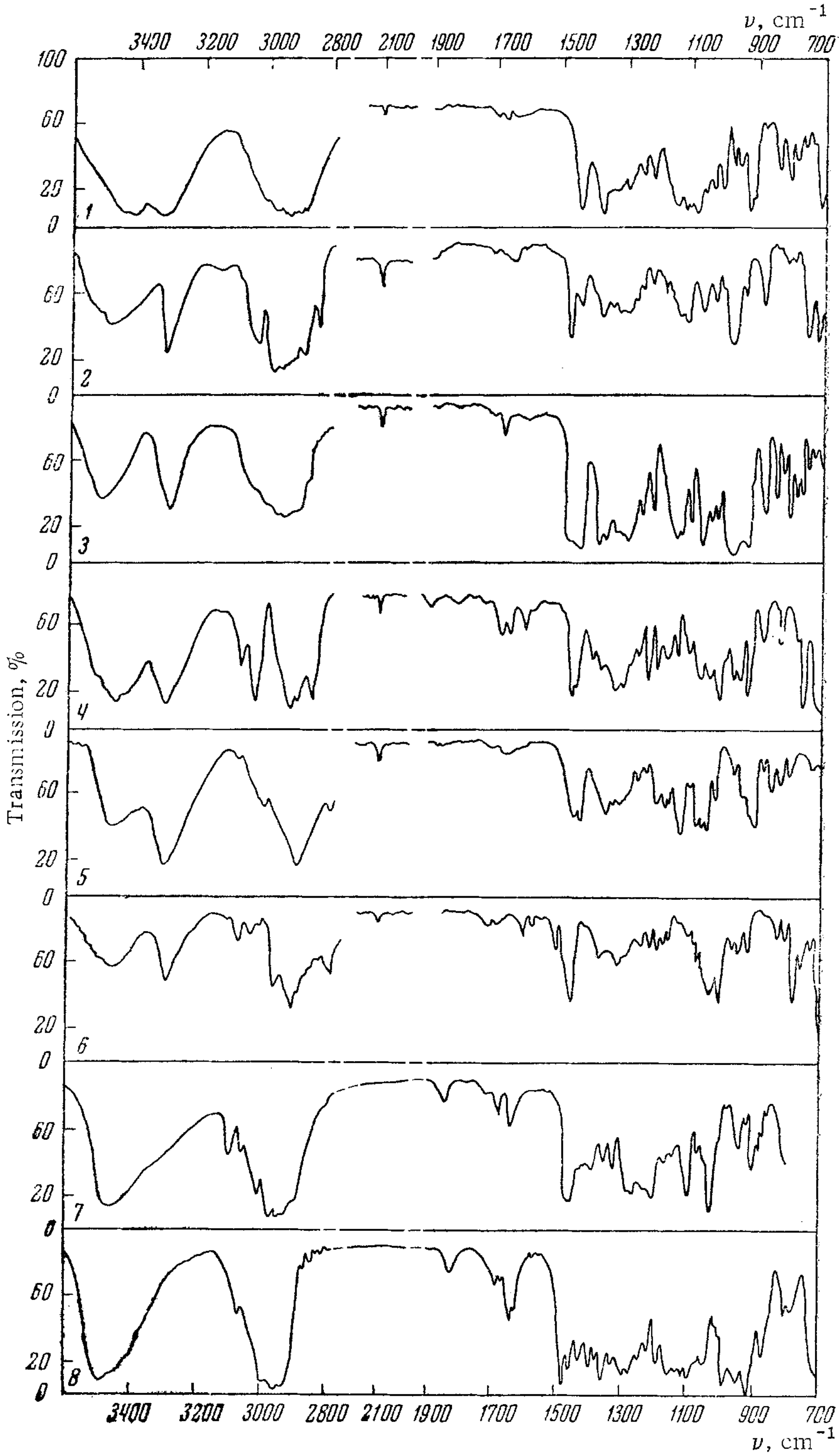


Fig. 1. Infrared absorption spectra: 1) α-ethynyl-α,4-dimethyl-3-cyclohexene-1-methanol (XXI); 2) α-ethyl-α-ethynyl-2-methyl-3-cyclohexene-1-methanol (XXII); 3) α-ethynyl-4-methyl-α-isopropyl-3-cyclohexene-1-methanol (XXV); 4) α-ethynyl-α-phenyl-3-cyclohexene-1-methanol (XXVI); 5) α-ethynyl-4-methyl-α-phenylcyclohexanemethanol (XXXIX); 6) α-ethynyl-α-methyl-1-cyclohexene-1-methanol (XLI); 7) α,4-dimethyl-α-vinyl-3-cyclohexene-1-methanol (XXVIII); 8) α-ethyl-2-methyl-α-vinyl-3-cyclohexene-1-methanol (XXIX).

TABLE 1

No.	Compound	Yield, %	B.p., °C (p, mm)	d_4^{20}	n_D^{20}	*MR* found	*MR* calcd.	Found, % C	Found, % H	Molecular formula	Calcd., % C	Calcd., % H
IV	α-Ethyl-2-methyl-3-cyclohexene-1-methanol	78	80—81 (3) *	—	1,4819	—	—	77,53	12,00	$C_{10}H_{18}O$	77,86	11,76
V	α-Isopropyl-3-cyclohexene-1-methanol	70	92—93 (8)	0,9480	1,4854	46,47	47,24	78,09	11,74	$C_{10}H_{18}O$	77,86	11,76
VI	α-Isopropyl-2-methyl-3-cyclohexene-1-methanol	68	96—97 (7)	0,9510	1,4872	50,96	51,85	78,43	12,09	$C_{11}H_{20}O$	78,51	11,98
VII	α-Isopropyl-4-methyl-3-cyclohexene-1-methanol	70	97—98 (7)	0,9502	1,4880	51,18	51,85	78,64	12,11	$C_{11}H_{20}O$	78,51	11,98
VIII	α-Phenyl-3-cyclohexene-1-methanol	86	117—118 (7) m.p. 82—83 (from petroleum ether)	—	—	—	—	83,15	8,51	$C_{13}H_{16}O$	82,93	8,57
IX	4-Methyl-α-phenyl-3-cyclohexene-1-methanol	82	125—126 (1)	—	1,5512	—	—	83,35	9,02	$C_{14}H_{18}O$	83,12	8,97
XXX	α-Phenylcyclohexanemethanol	75	m.p. 48—50 (from petroleum ether)†	—	—	—	—	—	—	$C_{13}H_{18}O$	—	—
XXXI	4-Methyl-α-phenylcyclohexanemethanol	81	123—124 (2)	—	1,5355	—	—	82,60	9,88	$C_{14}H_{20}O$	82,30	9,87

*The literature [9] gives: b.p. 111.5-112° (20 mm); n_D^{20} 1.4830.

†The literature [10] gives: b.p. 168° (20 mm); m.p. 41°.

TABLE 2

No.	Compound	Yield, %	B.p., °C (p, mm)	d_4^{20}	n_D^{20}	MR		Found, %		Molecular formula	Calcd., %		2,4-Dinitrophenylhydrazones and semicarbazones					
						found, %	calcd., %	C	H		C	H	m.p., °C	found, %		molecular formula	calcd., %	
														C	H		C	H
XIII	1-(2-Methyl-3-cyclohexen-1-yl)-1-propanone	60	58—59 (1)	0,9280	1,4662	45,41	45,72	78,78	10,48	$C_{10}H_{16}O$	78,89	10,59	100—101 144—145	57,75 58,07	5,74 6,21	$C_{16}H_{20}N_4O_4$* $C_{16}H_{20}N_4O_4$*	57,82 57,82	6,07 6,07
XIV	2-Methyl-1-(2-methyl-3-cyclohexen-1-yl)-propanone	62	64—65 (2)	0,9210	1,4693	46,08	45,72	78,69	10,38	$C_{10}H_{16}O$	78,89	10,59	158—159	63,25	9,22	$C_{11}H_{19}N_3O$	63,12	9,15
XV	1-(3-Cyclohexen-1-yl)-2-methyl-1-propanone	62	80—81 (4)	0,9298	1,4690	48,70	50,34	79,59	10,90	$C_{11}H_{18}O$	79,46	10,92	142—143	64,31	9,51	$C_{12}H_{21}N_3O$	64,54	9,48
XVI	2-Methyl-1-(4-methyl-3-cyclohexen-1-yl)-1-propanone	61	81—82 (4)	0,9328	1,4672	49,50	50,34	79,77	11,09	$C_{11}H_{18}O$	79,46	10,92	136—137 165—167	59,11 64,72	6,27 9,48	$C_{17}H_{22}N_4O_4$* $C_{12}H_{21}N_3O$	58,94 64,54	6,40 9,48
XVII	3-Cyclohexen-1-yl phenyl ketone	56	108—109 (1)	—	1,5590	—	—	—	—	$C_{13}H_{14}O$	—	—	172—173	69,16	6,95	$C_{14}H_{17}N_3O$	69,11	7,04
XVIII	4-Methyl-3-cyclohexen-1-yl phenyl ketone	58	122—123 (1)	—	1,5562	—	—	83,85	8,25	$C_{14}H_{16}O$	83,96	8,05	146—147	63,14	5,26	$C_{20}H_{20}N_4O_4$*	63,15	5,30
XXXIV	Cyclohexyl phenyl ketone	55	110—112 (1,5)**	—	—	—	—	—	—	$C_{13}H_{16}O$	—	—	166—168	—	—	$C_{14}H_{19}N_3O$	—	—
XXXV	4-Methylcyclohexyl phenyl ketone	59	115—116 (1)	—	1,5380	—	—	83,39	8,68	$C_{14}H_{18}O$	83,12	8,97	171—172	62,58	5,60	$C_{20}H_{22}N_4O_4$*	62,81	5,80

*2,4-Dinitrophenylhydrazone (from ethanol).
†Semicarbazone (from methanol).
‡The literature [11] gives: b.p. 150-152° (11 mm); d_4^{20} 1.0543; n_D^{20} 1.5591; m.p. of 2,4-DNPH 168-169°.
**The literature [10] gives: m.p. 51°; m.p. of semicarbazone 168-169°.

TABLE 3

No.	Compound	Yield, % with		B.p., °C (p, mm)	d_4^{20}	n_D^{20}	MR		Found, %		Molecular formula	Calcd., %	
		Na	Li				found, %	calcd., %	C	H		C	H
XIX	α-Ethynyl-α-methyl-3-cyclohexene-1-methanol	66	83	63—64 (2)	0,9830	1,4943	44,68	45,23	80,09	9,55	$C_{10}H_{14}O$	79,95	9,39
XX	α-Ethynyl-α,2-dimethyl-3-cyclohexene-1-methanol	63	76	74—75 (1,5)	0,9814	1,4995	49,05	49,85	80,83	9,83	$C_{11}H_{16}O$	80,44	9,83
XXI	α-Ethynyl-α,4-dimethyl-3-cyclohexene-1-methanol	76	86	68—69 (1)	0,9817	1,4993	49,12	49,85	80,43	10,09	$C_{11}H_{16}O$	80,44	9,83
XXII	α-Ethyl-α-ethynyl-2-methyl-3-cyclohexene-1-methanol	68	—	77 (1)	0,9740	1,5002	53,86	54,47	80,95	10,17	$C_{12}H_{18}O$	80,85	10,18
XXIII	α-Ethynyl-α-isopropyl-3-cyclohexene-1-methanol	59	75	75 (1)	0,9711	1,4995	53,97	54,47	80,96	10,14	$C_{12}H_{18}O$	80,85	10,18
XXIV	α-Ethynyl-2-methyl-α-isopropyl-3-cyclohexene-1-methanol	66	—	84 (1)	0,9611	1,4988	58,75	59,08	81,36	10,45	$C_{13}H_{20}O$	81,20	10,48
XXV	α-Ethynyl-4-methyl-α-isopropyl-3-cyclohexene-1-methanol	61	72	86 (1)	0,9614	1,4990	58,74	59,08	81,43	10,48	$C_{13}H_{20}O$	81,20	10,48
XXVI	α-Ethynyl-α-phenyl-3-cyclohexene-1-methanol	73	80	118—119 (1)	—	1,5639	—	—	84,70	7,73	$C_{15}H_{16}O$	84,87	7,60
XXVII	α-Ethynyl-4-methyl-α-phenyl-3-cyclohexene-1-methanol	70	—	125—126 (1)	—	1,5629	—	—	84,62	8,06	$C_{16}H_{18}O$	84,91	8,02
XXXVI	α-Ethynyl-α-methylcyclohexanemethanol	79	84	87—88 (9) *	—	1,4907	—	—	—	—	$C_{10}H_{16}O$	—	—
XXXVII	α-Ethynyl-α,2-dimethylcyclohexanemethanol	76	—	94—95 (8) **	—	1,4876	—	—	79,23	10,91	$C_{11}H_{18}O$	79,46	10,92
XXXVIII	α-Ethynyl-α-phenylcyclohexanemethanol	68	—	107—108 (1)	—	1,5530	—	—	84,33	8,66	$C_{15}H_{18}O$	84,07	8,47
XXXIX	α-Ethynyl-4-methyl-α-phenylcyclohexanemethanol	72	—	114—115 (1)	—	1,5519	—	—	84,02	8,85	$C_{16}H_{20}O$	84,16	8,83
XLI	α-Ethynyl-α-methyl-1-cyclohexene-1-methanol	34	81	67—68 (2)	0,9850	1,5007	44,92	45,23	79,99	9,56	$C_{10}H_{14}O$	79,95	9,39

* The literature [2] gives: b.p. 106-110° (23 mm); n_D^{20} 1.4792.

† The literature [2] gives: b.p. 110-113° (20 mm); n_D^{20} 1.4870.

EXPERIMENTAL

The infrared spectra of (XXI), (XXII), (XXVI), (XXVIII), and (XXXIX) were run on a UR-10 double-beam spectrophotometer (Zeiss) in a thin layer (0.05-0.02 mm) with NaCl and LiF prisms, and (XXV), (XXIX), and (XLI) were examined on an SP-100 spectrophotometer (Unicam).

Preparation of Alkyl- and Phenyl-3-cyclohexane-1-methanols (IV)-(IX). One mole of the aldehyde (I), (II), or (III) in 250 ml of dry ether was added with stirring to a solution of an organomagnesium compound prepared from 1 g-atom of magnesium turnings and 1 mole of ethyl iodide, isopropyl iodide, or bromobenzene in 500 ml of dry ether. The reaction mixture was then poured into a flask containing ammonium chloride solution and pieces of ice. The ether layer was washed with water and dried with magnesium sulfate. After the removal of solvent the residue was vacuum-distilled. The constants of the alcohols are given in Table 1.

Preparation of the α-Phenylcyclohexanemethanols (XXX) and (XXXI). The alcohol (XXX) was prepared from chlorocyclohexane and benzaldehyde [10]. The alcohol (XXXI) was prepared analogously to the alcohols (IV)-(IX) from 4-methylcyclohexanecarboxaldehyde [5] and bromobenzene. Their constants are given in Table 1.

Preparation of Alkyl 3-Cyclohexen-1-yl Ketones (XIII)-(XVI). Chromic mixture prepared from 80 g of sodium dichromate, 330 ml of water, and 60 ml of sulfuric acid was added dropwise with stirring to 0.6 mole of the alcohol (IV), (V), (VI), or (VII) mixed with 150 ml of water. The rate of addition of the chromic mixture was such that the temperature of the oxidation was kept in the range 40-60°. The reaction mixture was then diluted with water and extracted with a 5:1 mixture of diethyl ether and petroleum ether. The ether extract was washed with sodium carbonate solution and water and was dried with magnesium sulfate. Solvent was driven off, and the residue was vacuum-distilled. The constants of the ketones and their crystalline derivatives are given in Table 2.

Preparation of the Cyclohexenyl and Cyclohexyl Phenyl Ketones (XVII), (XVIII), (XXXIV), and (XXXV). Chromic mixture prepared from 100 g of sodium dichromate dissolved in 350 ml of acetic acid was added dropwise to 0.5 mole of the alcohol (VIII), (IX), (XXX), or (XXXI) dissolved in 100 ml of acetic acid. The reaction temperature was maintained in the range 40-60° by the rate of the addition of the oxidant. The reaction mixture was treated as in the previous experiment. The constants of the ketones and their crystalline derivatives are given in Table 2.

Preparation of the Acetylenic Alcohols (XIX)-(XXVII), (XXXVI)-(XXXIX), and (XLI). Acetylene was passed into a solution of 1.2 g-atom of sodium or lithium in 1500 ml of liquid ammonia with stirring at between − 65 and −70° until the blue color of the solution disappeared. At the same temperature with continuing passage of acetylene and stirring a solution of 1 mole of the ketone in 250 ml of methylal was added dropwise in the course of 30 min. Stirring and passage of acetylene were continued further for 3 h. Most of the ammonia was evaporated off, and the reaction mixture was decomposed with ammonium chloride and extracted with ether. The ether extract was washed with water and dried with magnesium sulfate, solvent was removed, and the residue was vacuum-distilled. The constants of the alcohols are given in Table 3.

Selective Hydrogenation of the Alcohols (XXI) and (XXII). 18 g of the acetylenic alcohol (XXI) was hydrogenated in absolute methanol in presence of Lindlar catalyst. 2.7 liters of hydrogen was absorbed. Catalyst was filtered off, solvent was driven off, and the hydrogenation product was vacuum-distilled. We obtained 16.7 g (94%) of the alcohol α,4-dimethyl-α-vinyl-3-cyclohexene-1-methanol (XXVIII); b.p. 70-71° (3 mm); d_4^{20} 0.9512; n_D^{20} 1.4960. Found: C 79.34; H 10.96%; MR 51.06. $C_{11}H_{18}O$. Calculated: C 79.46; H 10.92%; MR 51.39.

Similarly, from 4.4 g of the alcohol (XXII) we obtained 4 g (90%) of α-ethyl-2-methyl-α-vinyl-3-cyclohexene-1-methanol (XXIX); b.p. 75-76° (1 mm); d_4^{20} 0.9441; n_D^{20} 1.4967. Found: C 79.90, 79.76; H 11.38, 11.24%; MR 55.83. $C_{12}H_{20}O$. Calculated: C 79.96; H 11.18%; MR 56.00.

The authors thank L. B. Senyavina for determining the infrared spectra.

SUMMARY

1. The ethynylation of cycloaliphatic ketones was studied. With sodium acetylide, 3-cyclohexen-1-yl ketones condense rather worse than the corresponding cyclohexyl ketones do.

2. In their condensation with lithium acetylide cyclohexyl, 3-cyclohexen-1-yl, and 1-cyclohexen-1-yl ketones form tertiary acetylenic alcohols with equal ease in yields of 70-80%.

LITERATURE CITED

1. A. W. Johnson, The Chemistry of the Acetylenic Compounds, 1, The Acetylenic Alcohols, L. Arnold and Co. (1946); W. Oroshnik and A. D. Mebane, J. Amer. Chem. Soc., 71, 2062 (1949); J. R. Boisier, Prod. pharmac., 11, 237, 319 (1956); W. Chodkiewicz, Theses pour obtenir le titre de docteurs de L'Université, Paris (1958).
2. D. Papa, F. Vilani, and H. Ginsberg, Arch. Biochem. Biophys., 33, 482 (1951); J. Amer. Chem. Soc., 76, 4446 (1954).
3. T. Takeshima, K. Wakamatsu, and A. Furuhashi, Bull. Chem. Soc., Japan, 33, 640 (1958).
4. A. A. Petrov, Zh. obshch. khimii, 11, 309 (1941); K. Alder and W. Vogt, Ann., 564, 109 (1949).
5. I. N. Nazarov, G. P. Kugatova, and G. A. Laumyanskas, Zh. obshch. khimii, 27, 2450 (1957).
6. G. P. Kugatova-Shemyakina and Yu. A. Ovchinnikov, Tetrahedron, 18, 697 (1962).
7. G. P. Kugatova-Shemyakina, G. A. Laumyanskas, G. K. Krasil'nikova, and V. I. Vidugirene, Zh. obshch. khimii, 32, 2449 (1962).
8. Organic Syntheses [Russian translation] (1953), 4, p. 82; T. Takeshima, J. Scient. Res. Inst., 48, 103 (1954).
9. A. A. Petrov and N. P. Sopov, Zh. obshch. khimii, 22, 591 (1952).
10. P. Sabatier and A. Mailhe, Compt. rend., 139, 345 (1904).
11. N. Sharma and S. Dumt, J. Indian, Chem. Soc., 12, 774, 1935 (1953).

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. ***Some or all of this periodical literature may well be available in English translation.*** **A complete list of the cover-to-cover English translations appears at the back of this issue.**