SYNTHESIS OF ACETYLENIC γ -HYDROXYALDEHYDES AND THEIR REACTION WITH PRIMARY AMINES

A. S. Medvedeva, L. P. Safronova, G. G. Chichkareva, and M. G. Voronkov UDC 542.91:547.362:547.233.1

Investigation of acetylenic γ -hydroxy ketones [1-4] has shown that the presence of a hydroxyl-containing group in the α position to the triple bond has a substantial effect on their reactivity. In a continuation of these investigations it seemed of interest to study acetylenic γ -hydroxy aldehydes, about which there is no information.

The hydroxy aldehydes (V-VIII) were obtained with 50-72% yields by the use of neutral manganese dioxide in the γ modification [5,6]* The reaction was realized in the presence of a fivefold quantity of γ -MnO₂ in dry benzene at room temperature. The course of the reaction was monitored by TLC.

 $\begin{array}{c} \mathbf{R} & \mathbf{R} & \mathbf{O} \\ \mathbf{C} - \mathbf{C} \equiv \mathbf{C} \mathbf{C} \mathbf{H}_{2} \mathbf{O} \mathbf{H} & \overset{\gamma - \mathbf{M} \mathbf{n} \mathbf{O}_{2}}{\mathbf{R}^{1}} & \overset{\mathbf{O}}{\mathbf{H}} & \overset{\mathbf{O}}{\mathbf{H}} \\ \mathbf{R}^{1} & \overset{\mathbf{O}}{\mathbf{O} \mathbf{H}} & \overset{\mathbf{H}}{\mathbf{H}} \\ \mathbf{(I)} - (\mathbf{IV}) & (\mathbf{V}) - (\mathbf{VIII}) \\ \mathbf{R} = \mathbf{R}^{1} = \mathbf{C} \mathbf{H}_{3} & (\mathbf{I}), & (\mathbf{V}); & \mathbf{R} = \mathbf{C} \mathbf{H}_{3}, & \mathbf{R}^{1} = \mathbf{C}_{3} \mathbf{H}_{5} & (\mathbf{II}), & (\mathbf{VI}); \\ \mathbf{R}_{-}^{2} = \mathbf{C} \mathbf{H}_{3}, & \mathbf{R}^{1} = n - \mathbf{C}_{3} \mathbf{H}_{7} & (\mathbf{III}), & (\mathbf{VII}); & \mathbf{R} \mathbf{R}^{1} = \mathbf{C}_{5} \mathbf{H}_{10} & (\mathbf{IV}), & (\mathbf{VIII}) \end{array}$

The acetylenic γ -hydroxy aldehydes can be kept at room temperature for several days without change. On more prolonged storage they darken and become viscous. The IR spectra of compounds (V-VIII) are characterized by the stretching vibrations of the triple bond at 2210 cm⁻¹, by the conjugated CO group (1660 cm⁻¹), and OH (3400 cm⁻¹). The PMR spectrum of 2-hydroxy-2-methyl-3-pentyn-5-al (V) contains signals for the protons of the gem-dimethyl groups (δ 1.52 ppm). Singlets at 9.15 and 4.28 ppm correspond to the protons of the aldehyde and hydroxyl groups, respectively.

Available data on the reaction of acetylenic aldehydes with primary amines are extremely contradictory. According to data in [9], $CH \equiv CCHO$ adds tert-butylamine to form an acetylenic amine. Structures of an acetylenic amino alcohol [10] and an anil of malonaldehyde in the enolic form [11] have been proposed for the product from the reaction of aniline with $CH \equiv CCHO$. According to data in [12-14], the reaction of primary amines with $CH \equiv CCHO$ takes place exclusively at the triple bond, whereas according to [15] products from addition at both the CO group and the triple bond are formed, depending on the conditions.

We studied the reaction of n-butylamine with acetylenic γ -hydroxy aldehydes (V-VIII) in benzene at room temperature. The reaction occurred at the CO group; acetylenic hydroxyazomethines (IX-XII) were isolated with 51-62% yields. In spite of the fact that active manganese dioxide obtained by the method in [8] is unsuitable for the synthesis of acetylenic γ -hydroxy aldehydes, the corresponding hydroxyazomethines were obtained with good yields by simultaneous addition of the acetylenic γ -glycols and n-butyl-amine to a suspension of manganese dioxide in benzene:

* During oxidation of acetylenic glycols with chromic anhydride in sulfuric acid and with manganese dioxide [7], obtained by the method in [8], the corresponding aldehydes were isolated with yields of 9% because, evidently, such manganese dioxide has a weakly alkaline reaction.

Irkutsk Institute of Organic Chemistry, Siberian Branch of the Academy of Sciences of the USSR. Chita Pedagogical Institute. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No.1, pp.121-124, January, 1976. Original article submitted February 11, 1975.

©1976 Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$15.00.

TABLE 1. Physicochemical Constants and Analytical Data for the Obtained Compounds

											_		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1				
Com-		Vield*	bp,°С (т. тт		98	M.	u.	Fou	nd , %	N	folec- lar for-	Calcu	lated,	11 % tto V.	sristic	tra (cha frequer	rac- icies)
punod	Formula	- do	Hg)	44	Gu	punoj	cal- cul- ated	σ	H	u v	nu la	σ	н	U V	≡c c	=0 (C=N	но
S)	(CH₃)₂C(OH)C≘CCHO	70,6	5759	1,00891	,4688	30,90	29,44 (34,04	7, 19		26H8O2	34,28	7,14	- 2	215	1680	3390
(IVI)	CH ₈ (C ₂ H ₆)C(OH)C=CCHO	50,2	(2,5) 61-63	1,0030	,4725	35,19	34,06	36,65	7,99		27H1002	36,66	7,93	5	210	1662	3410
(VII)	CH ₃ (<i>n</i> -C ₃ H ₇)C(OH)C≡CCHO	72,1	(2) 69—71	0,9905	,4702	39,44	38,68	38,28	8,86		28H12O2	38,57	8,57	<u> </u>	225	1672	3400
(III)	C ₆ H ₁₀ (OH)C=CCHO	67,8	(1) 102—105	1,0771	,5107	42,26	41,09	71,06	7,90		29H12O2	71,05	7,89	 	215	1670	3400
(XI)	(CH ₃) ₂ C(OH)C==CCH=NC ₄ H ₅ -n	50.9	(2,5) 95—97	0,91951	.4760	51.21	50,58	71.56	0,28[8	.16	10H12ON	71,85/1	0.188	.38	225 1(17. 160	2 3360
8	CH ₃ (C ₃ H ₆)C(OH)C=CCH=NC ₄ H ₈ -n	(47) 62(70)	(1,5) 108-109	0.9157	,4794	55,95	55,20	72,62	10,40	.57[0	1.H190N	72,92	0.497	73 2	218 10	320. 160	1 3370
(XI)	$CH_3(n-C_8H_3)C(OH)C \equiv CCH = NC_8H_3-n$	57.8	(2) 122—123	0.9097	4778	60,66	59,82	74,00	10,86	.18	12HatON	73,841	0.76	$\frac{16}{2}$	22010	20. 160	2 3300
(IIX)	C ₆ H ₁₀ (0H)C=CCH=NC ₄ H ₉ -n	58(52)	(2,5) 144—146	0,9551	,5080	64,60	63,97	75,16	10,04	. 33 (13H210N	75,36	0,146	,76 2	215/1	312, 160	5 3330
			(3)														
* The	vields of the hudmyv szomethines du	ring oxi	Idative a	minatio	are r	niven i	n naret	these									

The yields of the hydroxy azomethines during oxidative amination are given in parentheses.

. .



In the IR spectra of the acetylenic hydroxyazomethines there are absorption bands for the triple bond at 2225-2215 cm⁻¹ and a broad band with a maximum at 3370-3300 cm⁻¹ for the hydroxyl. The band for the vibrations of the conjugated C = N bond is split (1620-1612, 1605-1601 cm⁻¹), and this is evidently explained by the general conjugation of the $-C \equiv C - C = N -$ system.

The PMR spectrum of 1-(1'-hydroxycyclohexyl)-3-n-butylimino-1-propyne (XII) contains singlets for the protons of the imino group at 7.45 ppm and the hydroxyl at 4.87 ppm and a multiplet at 3.52 ppm, corresponding to the protons of the N-methylene group. The protons of the other methylene group of the n-butyl radical and the six-membered ring form a multiplet centered at 1.58 ppm, and a triplet at 0.92 ppm corresponds to the methyl protons.

Thus, under comparable conditions, acetylenic γ -hydroxy aldehydes unlike CH \equiv CCHO [12] add primary amines not at the triple bond but at the CO group. This can evidently be explained by the electronic and steric effects of the RR'C(OH) group. The -I effect of this group promotes decrease in the electron density of the triple bond and increase in the positive charge at the carbonyl C atom, and this facilitates nucleophilic attack at the C = O bond of the acetylenic γ -hydroxy aldehydes. Such a reaction path is also promoted by steric hindrances from the tertiary carbon atom, which impede addition to the triple bond.

EXPERIMENTAL METHOD

The PMR spectra were recorded on a Tesla BS487B spectrometer at 80 MHz and $\sim 20^{\circ}$ C. The solvent was carbon tetrachloride, HMDS was used as internal standard, and the chemical shifts are given on the δ scale. The IR spectra were recorded on a UR-20 instrument.

<u>2-Hydroxy-2-methyl-3-pentyn-5-al (V)</u>. A mixture of 4.16 g of compound (I), 20 g of γ -MnO₂ [5,6], and 100 ml of dry benzene was stirred for 5 h. The manganese dioxide was removed and thoroughly washed with dry ether. After removal of the solvent 2.88 g (70.6%) of 2-hydroxy-2-methyl-3-pentyn-5-al (V) was obtained; bp 57-59°C (2.5 mm Hg).

The hydroxy aldehydes (VI-VIII) were obtained similarly.

<u>3-Methyl-6-n-butylimino-4-hexyn-3-ol (X)</u>. a) To 0.9 g of 3-hydroxy-3-methyl-4-hexyn-6-al (VI) in 20 ml of dry benzene we added dropwise 0.9 g of n-butylamine for 1 h. The reaction mixture was heated at 35°C for 2 h. After removal of the solvent 0.8 g (62%) of compound (X) was obtained: bp 110-111°C (2.5 mm Hg), n_D^{20} 1.4803.

b) To 13 g of active manganese dioxide in 100 ml of dry benzene we added simultaneously benzene solutions of 2 g of 3-methyl-4-hexyne-3, 6-diol (II) and 2.3 g of n-butylamine. The mixture was stirred for 4 h and left overnight. The filtrate was separated from the manganese dioxide and dried over magnesium sulfate. After removal of the solvent 2.04 g (70%) of compound (X) was isolated by vacuum distillation; bp 108-109°C (2 mm Hg); n_{20}^{20} 1.4794. The hydroxyimines (IX) and (XII) were obtained similarly.

The IR spectra and physicochemical constants of the obtained compounds are given in Table 1.

CONCLUSIONS

1. Previously unknown acetylenic γ -hydroxy aldehydes were obtained by oxidation of primarytertiary acetylenic γ -glycols with neutral manganese dioxide.

2. The addition of n-butylamine to acetylenic γ -hydroxy aldehydes takes place at the carbonyl group to form acetylenic azomethines.

LITERATURE CITED

- 1. L. P. Safronova and A. S. Medvedeva, Zh. Organ. Khim., 8, 1373 (1972).
- 2. A. S. Medvedeva, L. P. Safronova, and M. G. Voronkov, Izv. Akad. Nauk SSSR, Ser. Khim., 1669 (1973).
- 3. L. I. Vereshchagin, S. R. Gainulina, L. P. Kirillova, and T. V. Lipovich, Zh. Organ. Khim., <u>5</u>, 1577 (1969).
- 4. P. S. Mariano and M. Peters, Tetrahedron Letters, 2607 (1974).
- 5. L. I. Vereshchagin, S. R. Gainulina, S. A. Podskrebysheva, L. A. Gaivoronskii, L. L. Okhapkina, V. G. Vorob'eva, and V. P. Latyshev, Zh. Organ. Khim., 8, 1129 (1972).
- 6. O. Mancera, G. Rosenkranz, and F. Sondheimer, J. Chem. Soc., 2189 (1953).
- 7. M. F. Shostakovskii, T. A. Favorskaya, A. S. Medvedeva, L. P. Safronova, and V. K. Voronov, Zh. Organ. Khim., <u>6</u>, 2377 (1970).
- 8. J. Attenburrow, A. Cameron, J. Chapman, R. Evans, B. Hems, A. Jansen, and T. Walker, J. Chem. Soc., 1094 (1952).
- 9. F. Wille, L. Saffer, and W. Weisskopf, Liebigs Ann. Chem., 568, 34 (1950).
- 10. L. Cleisen, Ber., <u>36</u>, 3664 (1903).
- 11. I. Ya. Postovskii, R. O. Matevosyan, and Yu. N. Sheinker, Zh. Organ. Khim., 26, 1443 (1956).
- 12. S. M. Makin, A. A. Ismail, V. V. Yastrebov, and K. I. Petrov, Zh. Organ. Khim., 7, 2120 (1971).
- 13. S. M. Makin, V. V. Yastrebov, and A. A. Ismail, Reports of Fourth All-Union Conference on the Chemistry of Acetylene [in Russian], Vol.1, Alma-Ata (1972), p.401.
- 14. J. S. Walia, A. S. Walia, and L. J. Guillot, Chemistry and Industry, 23, 933 (1972).
- 15. A. P. Arendaruk, T. M. Godzhello, V. M. Mel'yantseva, T. V. Protopopova, and A. P. Skoldinov, Khim. Farm. Zh., 7, 6 (1973).