R. N. Myasnikova, M. I. Bardamova, I. L. Kotlyarevskii, and V. G. Kostrovskii UDC 547.362+547.56

As an expansion of our previously published studies on ethynylphenols [1, 2], we report in the present communication some data on the synthesis of aminophenols that are diacetylene derivatives, and specifically  $\alpha$ -p-hydroxyaryl- $\omega$ -aminopentadiynes. The literature data [3] and preliminary tests, carried out with certain acetylenic amines of the aromatic series, testify to the existence of a substantial physiological activity for these compounds. Consequently, the described compounds represent interest for studying their physiological action and ascertaining the relation between this action and the chemical structure. The synthesis was accomplished employing the Chodkiewicz-Cadiot reaction according to the scheme:



The differently substituted acetylenes (I)-(IV) were obtained in the same manner as the ethynylphenols [1, 2]. Bromides (V)-(VII) were synthesized in 65-70% yield by the reaction of the corresponding aminopropynes with sodium hypobromite, and they were obtained as white crystals that rapidly darken in the air. Due to the instability of the ethynylphenols the Chodkiewicz-Cadiot reaction cannot be run under the usual conditions, and satisfactory yields (up to 54%) of the differently substituted pentadiynes (VIII)-(XIX) can be obtained only at low temperature  $(-10 \text{ to } -20^\circ)$  and a comparatively long reaction time (from 3 to 10 h). The  $\alpha$ -p-hydroxyaryl- $\omega$ -aminopentadiynes represent white crystalline substances that rapidly darken in the air. The most stable are the morpholine derivatives, and the least stable are the diethylamine derivatives. All of the differently substituted compounds (VIII)-(XIX) give the hydrochlorides when their ether solutions are saturated with anhydrous hydrogen chloride. For some of the (VIII)-(XIX) compounds it proved possible to obtain the benzoyl derivatives (XX)-(XXIII) at the hydroxyl by reaction with benzoyl chloride in alkaline medium. It should be mentioned that an attempt to obtain the benzoyl derivatives by the condensation of p-benzoyloxyarylacetylenes with (V)-(VII) via the Chodkiewicz-Cadiot reaction led only to the formation of (VIII)-(XIX) with a free hydroxyl group. By means of a special experiment it was shown that under the conditions of this reaction the p-benzoyloxyarylacetylenes are saponified to ethynylphenols and benzoic acid.

Normal absorption, characteristic for two conjugated triple bonds, appears in the IR spectra of the aminoacetylenic phenols in the  $2100-2230 \text{ cm}^{-1}$  region. A different picture is observed in the absorption region of the OH bond of the hydroxyl group. A band at  $3570 \text{ cm}^{-1}$  appears in the spectra of (VIII)-(XIX)

Institute of Chemical Kinetics and Combustion, Siberian Branch of the Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 2, pp. 393-397, February, 1971. Original article submitted June 9, 1969.

© 1971 Consultants Bureau, a division of Plenum Publishing Corporation, 227 West 17th Street, New York, N. Y. 10011. All rights reserved. This article cannot be reproduced for any purpose whatsoever without permission of the publisher. A copy of this article is available from the publisher for \$15.00.



Fig. 1. Infrared spectra: 1) 0.024 g of pyridine and 0.002 g of p-ethynylphenol in 1 ml of  $CCl_4$ ; 2) 0.001 g of pyridine and 0.002 g of p-ethynylphenol in 1 ml of  $CCl_4$ ; 3) 0.002 g of phenol and 0.048 g of pyridine in 1 ml of  $CCl_4$ ; 4) 0.001 g of pyridine and 0.002 g of phenol in 1 ml of  $CCl_4$ ; 5) 0.002 g of p-ethynylphenol in 1 ml of  $CCl_4$ ; 6) 0.002 g of phenol in 1 ml of  $CCl_4$ ; 7) 0.012 g of pyridine in 1 ml of  $CCl_4$ ; 6) 0.002 g of phenol in 1 ml of  $CCl_4$ ; 7) 0.012 g of pyridine in 1 ml of  $CCl_4$ .

Fig. 2. Infrared spectra: 1) (VIII); 2) (XII); 3) (XVI) (0.005 g of substance per 0.400 g of KBr); 4) (XVI) (0.010 g of substance per ml of  $CCl_{4}$ ).

only on high dilution (in  $CCl_4$  and  $CHCl_3$ ). A broad absorption band in the 2400-3300 cm<sup>-1</sup> region appears at high concentrations of them in CCl<sub>4</sub>, while when the spectra are taken as KBr pellets the absorption band at  $3570 \text{ cm}^{-1}$  fails to appear. In order to ascertain the nature of this phenomenon we examined the IR spectra of mixtures of pyridine with phenol and with p-ethynylphenol. A narrow absorption band of the OH group is present in the  $3570 \text{ cm}^{-1}$  region when the concentration of phenol or p-ethynylphenol is 2 mg /ml CCl<sub>4</sub>. However, the addition of pyridine to these solutions causes a decrease in the intensity, and then also a complete disappearance of the  $3570 \text{ cm}^{-1}$  band, with the simultaneous appearance and increase in the intensity of the absorption band in the  $2900-3400 \text{ cm}^{-1}$  region, with a maximum at  $3100 \text{ cm}^{-1}$ , which must be attributed to the intermolecular hydrogen bond OH. . . N-. For phenol this disappearance is observed when 48 mg of pyridine was added to the initial solution, while for ethynylphenol the narrow band at 3570 cm<sup>-1</sup> disappears even when 24 mg of pyridine was added to a solution of the same concentration. Besides this, the absorption maximum of the hydrogen bond for ethynylphenol is shifted toward longer wavelengths, which testifies to the existence of stronger hydrogen bonds between pyridine and ethynylphenol than between pyridine and phenol. Simultaneously, a group of new bands appears in the spectra of phenol and ethynylphenol: 2590, 2650, 2730, and 2780 cm<sup>-1</sup>. Analogous bands of the hydrogen bond are characteristic for all of the (VIII)-(XIX) compounds containing the morpholine moiety (maximum at  $3200 \text{ cm}^{-1}$ ). Simultaneously with this there appears a group of bands of medium intensity in the  $2470-2660 \text{ cm}^{-1}$  region. For compounds (XII)-(XV), containing the pyridine molety (i.e., a stronger base), the hydrogen band with a maximum at 3050 cm<sup>-1</sup> practically disappears (as well as the OH band at 3570 cm<sup>-1</sup>), and the main absorption now appears at 2670-2780 cm<sup>-1</sup>, i.e., in the absorption region of "ammonium" compounds [4, 5] (Figs. 1 and 2).

Apparently, due to the manifestation of the electron-acceptor properties of the triple bond, the hydrogen of the phenolic hydroxyl in the p-ethynylphenols or their amino derivatives of the (VIII)-(XIX) type had a high lability and easily forms hydrogen bonds with the nitrogen of the amino group of another molecule. In this connection, when going from (XVI)-(XIX), containing the morpholine moiety, to (XII)-(XV), containing the piperidine moiety, a continuous transition from an intermolecular hydrogen bond in the case of the

|       |                      |                          | 10  | 1                                  | 1         | 1   | 12,24                              | 12,15             | ļ   | 12,24                              | 12,16  | l   | .11,59  | 11,52   |
|-------|----------------------|--------------------------|-----|------------------------------------|-----------|---|------------------------------------|-------------------|---|------------------------------------|--|---|---|---|
| 1     | lrochlorides         | found C1, empirical for- |     | ţ                                  | l         | I   | C17H20NOCI                         | C16H16NO2CI       | ļ   | C17H20NOCI                         | C <sub>16</sub> H <sub>18</sub> NO <sub>2</sub> CI | 1   | C17H20NO2CI                                     | C16H18NO3Cl                                     |
|       | Hyc                  |                          |     | . (                                | I         | I   | 12,51<br>12,52                     | 12,37<br>12,39    | ٢   | 12,35<br>12,45                     | 12,48<br>12,43                                     | 1   | 11,53<br>11,51                                  | 11,52<br>11,31                                  |
|       |                      | тр, °С                   |     | I                                  | 1         | ł   | 208209                             | 215216            | [   | 194-195                            | 192—193  | I   | 201,5-202                                       | 169,5   |
|       | 6 <b>,</b> N , Sies  |                          |     | 5,85                               | 5,81      | 5,80  | 5,53                               | 5,49              | 5,80  | 5,53                               | 5,49   | 5,44  | 5,20  | 5,16  |
|       | Empirical<br>formula |                          |     | C <sub>16</sub> H <sub>17</sub> NO | C15H15NO2 | C <sub>16</sub> H <sub>19</sub> NO              | C <sub>17</sub> H <sub>19</sub> NO | C16H17NO2         | C <sub>16</sub> H <sub>18</sub> NO              | C <sub>17</sub> H <sub>19</sub> NO | C <sub>16</sub> H <sub>17</sub> NO <sub>2</sub>    | C <sub>16</sub> H <sub>19</sub> NO <sub>2</sub> | C <sub>17</sub> H <sub>19</sub> NO <sub>2</sub> | C <sub>16</sub> H <sub>17</sub> NO <sub>8</sub> |
|       | % ,V bnuo3           |                          |     | 5,71                               | 6,01      | 5,60  | 5,27                               | 5,43              | 5,57  | 5,49                               | 5,67   | 5,62  | 4,86  | 4,87  |
|       | Mp, °C               |                          |     | 156-157                            | 155-156   | 121-123   | 155—156                            | 107108            | 102 - 103                                       | 140141                             | 113—115  | 104-106   | 107108  | 134—136   |
|       | ditions              | time,<br>h               |     | 4                                  | 4,5       | 4   | 3,5                                | 3,5               | 10  | ຄ                                  | 3  | 4   | 4,5   | ` <b>₽</b> '                                    |
|       | Reaction con         | ,<br>Ĉ                   |     | -15-+20                            | -15-+20   | -10 - +20                                       | -15-+20                            | -20-+20           | -10 - 30  |                                    |  | -10-+20   | -15-+25   | -15-+30   |
|       | ∛ield, %             |                          |     | 41                                 | 37        | 20  | 45                                 | 23                | 54  | 20                                 | 36   | 43  | 41  | 41  |
|       | -C≡CC≡C              | 2 VIVI-2010              | NRa | N N                                | N N       | N (C <sub>2</sub> H <sub>6</sub> ) <sub>2</sub> | Q                                  | 0<br>V            | N (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> | ↓<br>∠                             | 0<br>N   | N (C2Hs)2                                       | $\bigvee_{\mathbf{z}}$                          | o   |
|       | он                   | ъ                        | Я.  | Н                                  | Н         | 2-CH <sub>3</sub>                               | 2-CH <sub>3</sub>                  | 2-CH <sub>3</sub> | 3-CH <sub>3</sub>                               | 3-CH <sub>3</sub>                  | 3-CH <sub>3</sub>                                  | 3-0CH <sub>3</sub>                              | 3-0CH <sub>3</sub>                              | 3-OCH <sub>3</sub>                              |
| TABLE | Com-<br>pound<br>No. |                          |     | ХШ                                 | ΙΛХ       | IX  | ШХ                                 | ПЛХ               | X   | ΧIΧ                                | XVIII  | ТХ  | хν  | XIX   |

morpholine moiety to an ionic character of the -N - H bond in the case of the piperidine moiety is observed with change in the basicity of the amines.

## EXPERIMENTAL

<u>1-(4'-Hydroxyphenyl)-5-diethylamino-1,3-pentadiyne (VIII)</u>. To a mixture of 3 g of 4-ethynylphenol (I) in 30 ml of methanol, 0.26 g of  $NH_2OH \cdot HCl$ , 0.25 g of  $Cu_2Cl_2$ , and 4.5 g of  $C_2H_5NH_2$ , cooled to  $-10^{\circ}C$  and employing a steady stream of purified  $N_2$ , was added 3.6 g of 1-bromo-3-diethylamino-1-propyne [6] in drops [6]. The mixture was stirred at  $-10^{\circ}$  for 30 min, and at room temperature for 3 h, after which water was added and the mixture was extracted with ether. After depositing the ether solution on  $Al_2O_3$  (III activity) and elution with ether we isolated (VIII) as light-colored crystals with mp 107-110° (from ether), that darkened rapidly; yield 34.5%. Found: N 5.83%.  $C_{15}H_{11}NO$ . Calculated: N 6.16%.

Compounds (IX)-(XIX), given in Table 1, were synthesized in a similar manner. The hydrochlorides of the amines were obtained by the passage of a stream of anhydrous HCl into ether solutions of the amines.

<u>1-(2'-Methyl-4'-benzoyloxyphenyl)-5-morpholino-1,3-pentadiyne (XXI)</u>. To the sodium phenolate of compound (XVII), obtained by treating 5 g of (XVII) with 50 ml of 10% NaOH solution, was added 15 g of  $C_6H_5$ COCl in drops, and the mixture was stirred at room temperature until an oil deposited. The mixture was extracted with ether and washed in succession with water,  $Na_2CO_3$  solution and water, after which the ether solution of (XXI) was deposited on  $Al_2O_3$  (III activity) and eluted with ether. We isolated 5.7 g of (XXI), mp 87-88° (from ether). Found N 3.72%.  $C_{23}H_{21}NO_3$ . Calculated: N 3.90%.

The hydrochloride was obtained in quantitative yield by passing anhydrous HCl through an ether solution of (XXI); mp 172-173°. Found: Cl 8.86%.  $C_{23}H_{22}NO_{3}Cl$ . Calculated: Cl 8.96%.

Compounds (XX), (XXII), and (XXIII) were obtained in a similar manner. Compound (XX) was isolated in 50% yield as the hydrochloride, mp 198-199° (from ether). Found: Cl 9.00%.  $C_{24}H_{24}NO_2Cl$ . Calculated: Cl 9.00%. Compound (XXII) was obtained in 70% yield, mp 101-102° (from ether). Found: N 3.88%.  $C_{23}H_{21}NO_3$ . Calculated: N 3.90%. Hydrochloride of compound (XXII), mp 169-170° (from ether). Found: Cl 9.21; 9.25%.  $C_{23}H_{22}NO_3Cl$ . Calculated: Cl 8.96%. The yield of (XXIII) was 75%, mp 90.5-91° (from ether). Found: N 3.65%.  $C_{23}H_{21}NO_4$ . Calculated: N 3.73%. Hydrochloride of compound (XXIII), mp 185.5-186° (from ether). Found: Cl 9.00%.  $C_{23}H_{22}NO_4Cl$ . Calculated: Cl 8.61%.

## CONCLUSIONS

1. Conditions were found for the synthesis of phenolic derivatives of  $\omega$ -aminopentadiynes by the condensation of bromoaminopropynes with ethynylphenols.

2. An analysis of the IR spectra of the synthesized  $\omega$ -aminopentadiynes disclosed that the butadiynyl group exhibits strong electron-acceptor properties, which causes a substantial strengthening of the intermolecular hydrogen bond of OH. . . N when compared with phenol and ethynylphenol.

## LITERATURE CITED

- 1. I. L. Kotlyarevskii and M. I. Bardamova, Izv. Akad. Nauk SSSR, Ser. Khim., 2073 (1964).
- 2. M. I. Bardamova, R. N. Myasnikova, and L. L. Kotlyarevskii, Izv. Akad. Nauk SSSR, Ser. Khim., 443 (1967).
- L. R. Swett, W. B. Martin, J. D. Taylor, and G. M. Everett, Ann. New York Acad. Sci., 107, 891 (1963);
  I. P. Lapin, Zh. Vses. Khim. Obshchestva im. D. I. Mendeleeva, 9, 438 (1964); G. M. Everett, Nature, 177, 1238 (1956); G. M. Everett, L. E. Blockus, and I. M. Sheppered, Science, 124, 79 (1956).
- 4. K. Nakanishi, Infrared Spectra and Structure of Organic Compounds [Russian translation], IL (1965).
- 5. L.J.Bellamy, Infrared Spectra of Complex Molecules [Russian translation], IL (1960), Chapter 6, p. 14.
- 6. E.K. Andrievskaya, I. L. Kotlyarevskii, and S. I. Dondo, Izv. Akad. Nauk SSSR, Ser. Khim., 1639 (1968).