SYNTHESIS OF ACETYLENYL-N-METHYLPYRROLES

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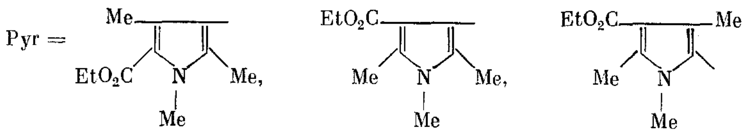
UDC 542.91:547.74

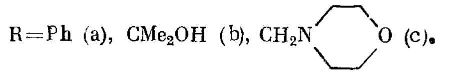
General methods for the synthesis of acetylenic derivatives of pyrrole have not been developed, although the preparation of individual acetylenylpyrroles has been described by the reaction of the α-oxides and chlorohydrins of the diacetylene series with amines [1-3], the dehydrohalogenation of substituents in the pyrrole ring [4-6], and the pyrolysis of 4-pyrrolylmethylene-3-methyl-5(4H)-isoxazolones [7].

We studied the possibility of using the acetylenic condensation of iodopyrroles as such a general method [8]. In the present paper are reported the results of condensing iodo-N-methylpyrroles with terminal acetylenes under the conditions of palladium complex [9] and copper [10] catalysis, and also with substituted copper acetylides [11]. It was established that both α- and β-iodides enter into the condensation:

$$\underset{(I)-(III)}{PyrI} \xrightarrow[(CuC\equiv CR)]{HC\equiv CR/Cat} \underset{(IVa-c)-(VIa-c)}{PyrC\equiv CR}$$

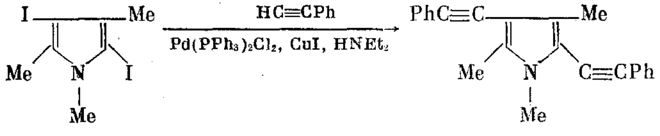


(I), (IV) (II), (V) (III), (VI)



Although all of the indicated variations of the condensation are applicable to N-methylpyrroles, the first variation is the most convenient (catalyst (Cat) = $Pd(PPh_3)_2Cl_2$–CuI). In this case the reaction proceeds at 45-50°C (in contrast to 115-155° for the other modifications) in $Et_2NH$, whose low boiling point and solubility in water greatly facilitate the isolation of the end products. The pyrrolyl iodides in their reactivity are noticeably inferior to iodobenzene [9, 11]. Ethyl 4-iodo-1,3,5-trimethylpyrrole-2-carboxylate (I) is less active than its α-iodo isomer (III). However, a shift of the electron-acceptor carbethoxyl group to the 3 position, adjacent to the iodine, increases the reactivity of the iodine, and ethyl 4-iodo-1,2,5-trimethylpyrrole-3-carboxylate (II) reacts with acetylenes more vigorously than the β- and α-iodo isomers (I) and (III). A longer condensation time does not affect the yields of acetylenylpyrroles (IV)-(VI), which, as a rule, reach 80-90%.

Polyiodopyrroles, devoid of electron-acceptor substituents, are unstable. Despite this, the 2,4-diiodide (VII), whose molecule is additionally destabilized by the presence of three methyl substituents, was successfully condensed with phenylacetylene; the yield of bis(phenylethynyl)pyrrole (VIII) was 50%



(VII) (VIII)

The condensation does not permit obtaining the ethynyl compounds directly, since acetylene is bifunctional, and a method for its monoarylation is unknown. At the same time, monosubstituted acetylenes are precursors and in many cases are the key intermediates in the synthesis of various groups of their functional derivatives. To obtain the ethynylpyrroles we

Institute of Chemical Kinetics and Combustion, Siberian Branch of the Academy of Sciences of the USSR, Novosibirsk. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 8, pp. 1871-1876, August, 1980. Original article submitted July 30, 1979.

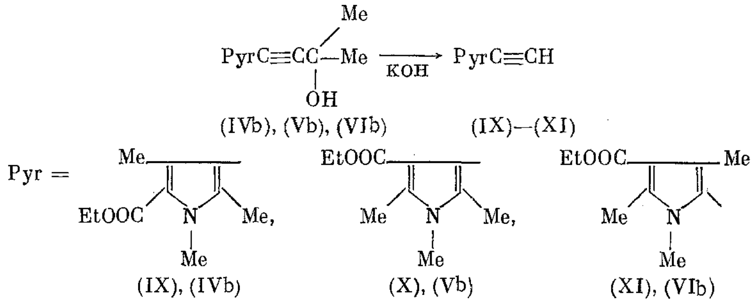
 0568-5230/80/2908-1346$07.50 

TABLE 1. Acetylenyl-N-methylpyrroles

| Compound | Yield, % | Reaction time, h | mp, °C (from hexane) | Empirical formula | Found/Calculated, % | | | PMR spectrum ($CCl_4$, δ, ppm) | Infrared spectrum ($CHCl_3$, ν, $cm^{-1}$) |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | C | H | N | | |
| (IVa) | 93,4 | 22,5 | 89–90 | $C_{18}H_{19}NO_2$ | 76,92/76,84 | 6,95/6,81 | 5,20/4,98 | ($CDCl_3$): 1,30 t ($CH_3CH_2$), 2,28, 2,37 (3- and 5-$CH_3$), 3,73 ($CH_3N$), 4,23 q ($\underline{CH_2}CH_3$), 7,25 m (Ph) | 2218 (C≡C), 1685 (C=O) |
| (IVb) | 85,6 | 50,5 | 121–122 | $C_{15}H_{21}NO_3$ | 68,44/68,42 | 7,91/8,04 | 5,35/5,32 | 1,30 t ($\underline{CH_3}CH_2$), 1,32 ($CH_3CCH_3$), 2,23 (3- and 5-$CH_3$), 3,77 ($CH_3N$), 4,29 q ($\underline{CH_2}CH_3$), 6,72 (OH) | ($CCl_4$): 2234 (C≡C), 1695 (C=O), 3625 (OH) |
| (IVc) | 70,7 | 23 * | 76–77 | $C_{17}H_{24}N_2O_3$ | 67,00/67,08 | 7,76/7,95 | 9,41/9,20 | 1,33 t ($\underline{CH_3}CH_2$), 2,25 (3- and 5-$CH_3$), 2,45 t ($CH_2NCH_2$), 3,43 ($NCH_2C≡$), 3,57 t ($CH_2OCH_2$), 3,76 ($CH_3N$), 4,18 q ($CH_3\underline{CH_2}$) | 2240 (C≡C), 1690 (C=O) |
| (Va) | 92,5 | 11 | 59–60 | $C_{18}H_{19}NO_2$ | 76,83/76,84 | 6,91/6,81 | 5,04/4,98 | ($CDCl_3$): 1,30 t ($\underline{CH_3}CH_2$), 2,33, 2,47 (2- and 5-$CH_3$), 3,53 ($CH_3N$), 4,27 q ($\underline{CH_2}CH_3$), 7,42 m (Ph) | 2210 (C≡C), 1700 (C=O) |
| (Vb) | 85,6 | 27 | 90–91 | $C_{15}H_{21}NO_3$ | 68,36/68,42 | 8,12/8,04 | 5,40/5,32 | 1,26 t ($\underline{CH_3}CH_2$), 1,49 ($CH_3CCH_3$), 2,08, 2,31 (2- and 5-$CH_3$), 3,29 ($CH_3N$), 4,15 q ($\underline{CH_2}CH_3$) | 2232 (C≡C), 1700 (C=O), 3615 (OH) |
| (Vc) | 65,0 | 20,5 | 63–64 | $C_{17}H_{24}N_2O_3$ | 67,01/67,08 | 8,04/7,95 | 9,47/9,20 | ($CDCl_3$): 1,30 t ($\underline{CH_3}CH_2$), 2,26, 2,45 (2- and 5-$CH_3$), 2,60 t ($CH_2NCH_2$), 3,50 ($CH_3N$), 3,58 ($NCH_2C≡$), 3,75 t ($CH_2OCH_2$), 4,28 q ($\underline{CH_2}CH_3$) | 2228 (C≡C), 1690 (C=O) |
| (VIa) | 89,0 | 17 | 67–68 | $C_{18}H_{19}NO_2$ | 76,85/76,84 | 6,91/6,81 | 5,05/4,98 | ($CDCl_3$): 1,27 t ($\underline{CH_3}CH_2$), 2,29, 2,40 (2- and 4-$CH_3$), 3,44 ($CH_3N$), 4,16 q ($\underline{CH_2}CH_3$), 7,19 m(Ph) | 2210 (C≡C), 1693 (C=O) |
| (VIb) | 82,0 | 30,5 | 94–95 | $C_{15}H_{21}NO_3$ | 68,63/68,42 | 8,06/8,04 | 5,33/5,32 | 1,35 t ($\underline{CH_3}CH_2$), 1,56 ($CH_3CCH_3$), 2,25, 2,52 (2- and 4-$CH_3$), 2,97 (OH), 3,61 ($CH_3N$), 4,50 q ($\underline{CH_2}CH_3$) | ($CCl_4$): 2230 (C≡C), 1700 (C=O), 3620, 3495 sh (OH) |
| (VIc) | 95,5 | 37,5 | 74–75 (petroleum ether) | $C_{17}H_{24}N_2O_3$ | 66,97/67,08 | 7,82/7,95 | 9,04/9,20 | 1,29 t ($\underline{CH_3}CH_2$), 2,23 (2- and 4-$CH_3$), 2,46 t ($CH_2NCH_2$), 3,38 ($NCH_2C≡$), 3,54 t ($CH_2OCH_2$), 3,71 ($CH_3N$), 4,18 q ($\underline{CH_2}CH_3$) | ($CCl_4$): 2235 (C≡C), 1700 (C=O) |
| (VIII) | 50,0 | 22 | 146,5–147,5 | $C_{23}H_{19}N$ | 89,20/89,28 | 6,13/6,19 | 4,51/4,53 | 1,95, 2,05 (3- and 5-$CH_3$), 3,43 ($CH_3N$), 7,45 m(Ph) | ($CCl_4$: 2212 (C≡C) |

*Compound (IVc) was obtained from (I) and N-propargylmorpholine in pyridine in the presence of $K_2CO_3$ and CuI at 115°.

employed the previously proposed scheme, which specifies the condensation of a hetaryl halide with 2-methyl-3-butyn-2-ol and cleavage of the synthesized tertiary hetarylacetylenic alcohol by the reverse Favorskii reaction [12]. Alcohols (IVb), (Vb), and (VIb) were cleaved in a high-boiling diluent using catalytic amounts of KOH, with removal of the products from the reaction sphere as they were formed [13]



The yields of (IX)-(XI) were 80-90%.

## EXPERIMENTAL

Substituted Iodopyrroles (I)-(III) and (VII). The ethyl esters of 4-iodo-1,3,5-trimethylpyrrole-2-carboxylic (I) and 5-iodo-1,2,4-trimethylpyrrole-3-carboxylic (III) acids were obtained by the substitutive iodination of the corresponding monoesters of 1,3,5-trimethylpyrrole-2,4-dicarboxylic acid (mp 196-197 and 153-154.5°) with $I_2$ in KI solution in aqueous alcohol in the presence of $NaHCO_3$ at 60-70°. The yield of (I) was 93.0%, mp 86-86.5° (from ethanol) [14], and that of (III) was 94.8%, mp 100-101° (from ethanol) [14]. The ethyl ester of 4-iodo-1,2,5-trimethylpyrrole-3-carboxylic acid (II) was obtained under the same conditions from the ester of 1,2,5-trimethylpyrrole-3-carboxylic acid in 76.0% yield, mp 102.5-103° (from ethanol). Found: C 38.98; H 4.58; I 41.23%. $C_{10}H_{14}INO_2$. Calculated: C 39.11; H 4.59; I 41.32%.

For saponification we took 9.3 g of (I) and heated it with 2.3 g of KOH in 27 ml of 96% alcohol at reflux for 4.5 h; the crude 4-iodo-1,3,5-trimethylpyrrole-2-carboxylic acid was subjected to substitutive iodination to give 4.9 g (44.8%) of 2,4-diiodo-1,3,5-trimethylpyrrole (VII), mp 54-55° (from ethanol). Found: C 23.46; H 2.64; I 70.47%. $C_7H_9I_2N$. Calculated: C 23.29; H 2.51; I 70.31%. PMR spectrum ($CCl_4$, δ, ppm): 1.97 and 2.32 (3- and 5-$CH_3$), 3.46 ($CH_3N$).

Acetylenic Condensation. a) A mixture of 6.2 g of (I), 80 mg of $Ph(PPh_3)_2Cl_2$, 40 mg of CuI, and 2.6 g of phenylacetylene in 60 ml of $Et_2NH$ was heated at 45-50° in an $N_2$ atmosphere for 22.5 h, after which it was cooled, diluted with 500 ml of ether, the precipitate was separated, the filtrate was evaporated, and the residue in benzene solution was filtered through a bed of silica gel (100/250 μ, 50 mm × 50 mm). The yield and constants of ethyl 4-phenylethynyl-1,3,5-trimethylpyrrole-2-carboxylate (IVa) are given in Table 1.

The acetylenic derivatives of pyrrole (IVb), (V), (VI), and (VII) were synthesized in a similar manner (Table 1).

b) A mixture of 3.1 g of (II) and 2.2 g of copper phenylacetylide in 40 ml of $HCONMe_2$ was refluxed in an $N_2$ stream for 8.5 h, cooled, diluted with 500 ml of ether, the precipitate was filtered, and the filtrate was washed thrice with water and dried over $K_2CO_3$. Compound (Va) was isolated as described for (IVa); yield 2.7 g (96.1%).

c) A mixture of 6.1 g of (I), 5.8 g of CuI, 5.2 g of finely ground $K_2CO_3$, and 3.7 g of N-propargylmorpholine in 30 ml of pyridine was heated at 110-115° in an $N_2$ atmosphere for 23 h, cooled, diluted with 500 ml of ether, filtered, washed in succession with 25% aqueous $NH_3$ solution and water, and dried over $K_2CO_3$. After distilling off the solvent the residue was recrystallized from petroleum ether to give 4.3 g (70.7%) of ethyl 4-(3'-N-morpholinopropyn-1'-yl)-1,3,5-trimethylpyrrole-2-carboxylate (IVc); the constants are given in Table 1.

Cleavage of Pyrrolylacetylenic Alcohols (IVb), (Vb), and (VIb). A mixture of 800 mg of (IVb) and 20 mg of powdered KOH in 1 g of m-pentaphenyl ether was heated in a sublimation apparatus at 120-140° (1 mm). The sublimed ester of 5-ethynyl-1,2,4-trimethylpyrrole-3-carboxylic acid (IX) was freed of traces of (IVb) by chromatographing on $SiO_2$ in $CHCl_3$ solution. Alcohols (Vb) and (VIb) were cleaved in a similar manner. The yields and constants of

TABLE 2. Ethynylpyrroles

| Compound | Yield, % | mp, °C (from hexane) | Found, %* | | | PMR spectrum ($CCl_4$, δ, ppm) | Infrared spectrum ($CCl_4$, ν, $cm^{-1}$) |
|---|---|---|---|---|---|---|---|
| | | | C | H | N | | |
| (IX) | 82,3 | 91–92 | 70,18 | 7,40 | 6,81 | 1,37 t ($\underline{CH_3}CH_2$), 2,28 (3- and 5-$CH_3$), 2,97 ($\overline{H}C{\equiv}C$), 3,76 ($CH_3N$), 4,25 q ($\underline{CH_2}CH_3$) | 2115, 3328 ($HC{\equiv}C$), 1700 (C=O) |
| (X) | 89,7 | 87,5–88,5 | 70,33 | 7,40 | 6,98 | 1,28 t ($\underline{CH_3}CH_2$), 2,20, 2,39 (2- and 5-$CH_3$), 3,30 ($\overline{H}C{\equiv}C$), 3,45 ($CH_3N$), 4,14 q ($\underline{CH_2}CH_3$) | 2120, 3335 ($H{-}C{\equiv}C$), 1720 (C=O) |
| (XI) | 79,5 | 88,5–90 | 70,35 | 7,27 | 6,96 | 1,30 t ($\underline{CH_3}CH_2$), 2,24, 2,46 (2- and 4-$CH_3$), 3,37 ($\overline{H}C{\equiv}C$), 3,51 ($CH_3N$), 4,20 q ($\underline{CH_2}CH_3$) | 2110, 3325 ($HC{\equiv}C$), 1700 (C=O) |

*$C_{12}H_{15}NO_2$. Calculated: C 70.22; H 7.37; N 6.82%.

(IX)-(XI) are given in Table 2.

## CONCLUSIONS

1. Iodine atoms in any position of the pyrrole ring are capable of being replaced by acetylenic groups under the conditions of palladium complex and copper catalysis. We accomplished the acetylenic condensation of a number of α- and β-iodopyrroles.

2. The alkaline cleavage of the thus-synthesized tertiary pyrrolylacetylenic alcohols leads to ethynylpyrroles.

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# ORGANOBORON COMPOUNDS.

# 378. SYNTHESIS OF CYCLIC TETRACOORDINATED BORON COMPOUNDS FROM ENAMINOBORANES, PHENYL ISOCYANATE, AND PHENYL ISOTHIOCYANATE


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UDC 542.91:547.1'127


Previously it was shown that vinylaminodialkylboranes, not completely substituted on the β-C atom of the vinyl group, add to nitriles [1-3] and isonitriles [4] to give heterocyclic tetracoordinated boron compounds.

In the present paper, in order to further study the reactivity of organoboron enamines, we studied the reaction of N-substituted cyclohexenylaminodialkylboranes (I) with phenyl isocyanate (PIC) and phenyl isothiocyanate (PITC). Although it is characteristic for compounds with a B—N bond to undergo 1,2-addition to isocyanates and isothiocyanates to give the corresponding urea and thiourea derivatives [5-8], it could be reasoned that under certain conditions the enaminoboranes (I) will behave like ordinary enamies [9-12] and enter into nucleophilic C-addition reactions. Here the formation of cyclic (chelate) compounds, containing a tetracoordinated B atom in the ring, could be expected.


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Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 8, pp. 1876-1881, August, 1980. Original article submitted July 27, 1979.




0568-5230/80/2908-1350$07.50