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REACTION OF 3-INDOLETHIOLS WITH ACETYLENES

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Indole derivatives, in particular those of 3-indolethiol, have various forms of biological activity [1-3]. In order to expand the number of potentially useful biologically active compounds and also to investigate the nucleophilic addition reaction of 3-indolethiols to acetylenes, we have studied the reaction of 3-indolethiol (I) and 2-methyl-3-indolethiol (II) with acetylene, phenylacetylene (III), 1-phenyl-2-cyanoacetylene (IV), and 3-hydroxy-3-methyl-1-cyano-1-butyne (V).

It was previously shown that mono- and divinyl monomers [4] are formed depending on the conditions of the reaction between (I) and acetylene. Introduction of a methyl group into the 2-position of the indole ring slightly reduces the reactivity of (II) in this reaction. The formation of both 2-methyl-3-vinylthioindole (VI) and 1-vinyl-2-methyl-3-vinylthioindole (VII) needs greater heating (180 and 200°C, respectively) than for the preparation of the corresponding vinyl derivatives of indole (I), which is apparently due to the electrondonating effect of the Me group, resulting in an increase in binding of the protons with the N and S heteroatoms



Introduction of an electron-withdrawing substituent into the acetylene molecule activates the triple bond in the reaction with indoles (I) and (II). Thus, with phenylacetylene (III) in the presence of alkali the reaction takes place at 90-95°C. It should be noted that the addition reaction is complicated by a competing oxidation reaction which results in the formation of bisindolyl sulfides, which considerably reduces the yield of 3-[(2-phenylvinyl)thio]indoles (VIII) and (IX) (Table 1).

The addition of indoles (I) and (II) to acetylenes (IV) and (V), which are activated by a nitrile group, occurs at ~20°C in triethylamine with a high yield of the corresponding 2-R-3-](1-R'-2-cyanoviny1)thio]indoles (X)-(XII)

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TABLE 1. Properties of Compounds Synthesized

Com- pound	Yield,	Mp or bp, °C (p, mm Hg)	Found, %				Empirical	Calculated, %			
			с	н	N	s	formula	С	н	N	s
(VI) (VII) (VIII) (IX) (X) (XI) (XII) (XIII)	65 58 57 31 86 92 77 87	$\begin{array}{c} 150(5)\\ 170(4)\\ 97-99\\ 52-53\\ 189-190\\ 192-194\\ 184-186\\ 164-166\\ \end{array}$	$\begin{array}{c} 69.8 \\ 72.3 \\ 76.4 \\ 77.4 \\ 73.8 \\ 74.4 \\ 65.5 \\ 65.9 \end{array}$	$5.8 \\ 6.1 \\ 5.2 \\ 6.1 \\ 4.4 \\ 5.2 \\ 5.5 \\ 6.0 $	7.4 6.7 5.5 5.4 9.9 9.7 10.6 10.1	16 6 14.8 12.6 11.8 11.5 10.9 12.2 11.8	$\begin{array}{c} C_{11}H_{11}NS\\ C_{13}H_{12}NS\\ C_{16}H_{13}NS\\ C_{17}H_{15}NS\\ C_{17}H_{15}NS\\ C_{17}H_{12}N_{2}S\\ C_{18}H_{14}N_{2}S\\ C_{14}H_{14}N_{2}OS\\ C_{15}H_{16}N_{2}OS\\ \end{array}$	$\begin{array}{c} 69.8 \\ 72.5 \\ 76.5 \\ 76.9 \\ 73.9 \\ 74.4 \\ 65.1 \\ 66.2 \end{array}$	5.9 6.0 5.2 5.7 4.4 4.9 5.5 5.9	$\begin{array}{c} 7.4 \\ 6.5 \\ 5.6 \\ 5.3 \\ 10.1 \\ 9.7 \\ 10.8 \\ 10.3 \end{array}$	16.9 14.9 12.8 12.1 11.6 11.0 12.4 11,8

TABLE 2. PMR Spectral Parameters of Derivatives of 3-Indolethiols

	ô, pr					
Compound	olefinic protons	aromatic protons	CH3	J. HZ		
(VI) (VII)	4.98 (A), 4.68 (B), 6.24 (X) 4.99 (A), 4.73 (B), 6.23 (X) 5,06 (A), 5,34 (B), 6.90 (X) *	6.93 - 7.43 7.00 - 7.43	2,11 2,43	${}^{3}J_{AX} = 9.6, {}^{3}J_{BX} = 16.3$ ${}^{3}J_{AX} = 9.5, {}^{3}J_{BX} = 16.4, {}^{2}J_{AB} = 0.7$ ${}^{2}J_{AY} = 9.0, {}^{3}J_{BY} = 15.8$		
(VIII) (IX) (X) (XI) (XII) (XIII)	6.16; 6.34 6.10; 6.31 5.49(25), 5,85(75) ** 5.95 5.61(45), 5.88(55) ** 5,63(45), 5,90(55) **	$\begin{array}{c} 7.00{-}7.75\\ 7.04{-}7.65\\ 7.01{-}7.60\\ 6.99{-}7.52\\ 7.15{-}7.42\\ 7.02{-}7.49\end{array}$	2,38 2,44 2,50	$J_{\rm IIII} = 10.5$ $^{3}J_{\rm IIII} = 10.8$		

*Chemical shifts of protons in vinyl group on nitrogen atoms are shown. **Relative integral intensity (%) for olefinic protons of (X), (XII), (XIII) are given in brackets.



 $\begin{array}{ll} R = H(I); & R = CH_{2}(II); & R' = H, \ R'' = Ph(III); & R' = Ph, \ R'' = CN(IV); \\ R' = (CH_{3})_{2}C(OH), & R'' = CN(V); & R = R' = H, & R'' = Ph(VIII); & R = CH_{3}, & R' = H, \\ R'' = Ph(IX); & R = H, & R' = Ph; & R'' = CN(X); & R = CH_{3}, & R' = Ph, & R'' = CN(X1); \\ R = H, & R' = (CH_{3})_{2}C(OH), & R'' = CN(XII); & R = CH_{3}, & R' = (CH_{3})_{2}C(OH), & R'' = CN(XIII). \end{array}$

The structure of the compounds obtained was confirmed by elemental analysis and spectroscopic methods (Tables 1 and 2). The PMR spectrum of (VI) contains signals from one vinyl group, and the values of the vicinal spin—spin coupling constants in it (9.6 and 16.3 Hz) are consistent with a vinylthio group [5]. In the PMR spectrum of (VII) there are signals from two vinyl groups, which are bonded to the S and N heteroatoms. The olefinic protons of (VIII) and (IX) appear as two doublets. The vicinal spin—spin coupling constants between the olefinic proton are equal to 10.5 and 10.8 Hz, respectively. In the vinyl derivatives (VI) and (VII) of 2-methyl-3-thioindole, the spin—spin coupling constants between the cis protons of the vinyl group have similar values (9.6 and 9.5 Hz). Consequently (VIII) and (IX) are cis isomers. In the PMR spectra of compounds (X), (XII), and (XIII), in addition to the signals from the aromatic protons there are two signals with different integral intensity due to olefinic protons. This suggests that the two isomeric forms Z and E of these compounds are present.



The integral intensity of the proton at lower field is always higher, which indicates that one of the isomeric forms of (X), (XII), and (XIII) predominates. An unequivocal identification of the nature of the isomeric form from a single signal from the olefinic proton is difficult. In the PMR spectrum of (XI) only one signal from an olefinic proton is detected, namely, the compound exists in a single isomeric form.

The IR spectra of the compounds obtained are characterized by an absorption in the region 1590-1580 cm⁻¹ due to stretching vibrations of the vinyl group and an absorption from the imino group at 3420-3250 cm⁻¹ [except for (VII), in which there is an absorption band at 1640 cm⁻¹ which corresponds to vibration from the NC=C bond]. In the spectra of (X)-(XIII) an absorption band due to the nitrile group occurs at 2210-2215 cm⁻¹.

It should be noted that 3-indolethiols (I) and (II) do not react with the substituted acetylenes (III)-(V) to form addition products on the nitrogen atom. The presence of nitrile and hydroxyl groups in products (XII) and (XIII) makes it favorable to study an intramolecular cyclization reaction aimed at introducing a new heterocyclic fragment - 2,5-dihydrofuran - into indoles [6]. However, despite the use of different catalysts (LiOH, KOH, HCl) and varying the temperature from 20 to 100°C, we did not achieve heterocyclization in the series of compounds studied.

EXPERIMENTAL

PMR spectra were recorded on a Tesla BS-497 spectrometer (100 MHz) in $CDCl_3$ relative to HMDS. IR spectra were recorded on a Specord IR-75 spectrophotometer as a thin film and in the form of KBr disks.

<u>2-Methyl-3-vinylthioindole (VI)</u>. To a rotating steel autoclave was added 10 g (60 mmoles) of indole (II), 7.5 g (130 mmoles) of KOH in 120 ml of water, and the mixture was saturated with acetylene at 15 atm. The mixture was heated for 1 h at 180°C, cooled, and extracted with ether. The extract was chromatographed on a column of Al_2O_3 with ether as eluent, and (VI) was isolated, n_D^{20} 1.6428.

<u>l-Vinyl-2-methyl-3-vinylthioindole (VII)</u>. To the autoclave was added 4 g (25 mmoles) of indole (II), 1.2 g (20 mmoles) of KOH, and 80 ml of dioxane; the mixture was saturated with acetylene and heated for 1 h at 200°C. After the solvent had been removed, (VII) was separated by vacuum distillation, n_D^{20} 1.6345.

<u>3-[(2-Phenylvinyl)thio]indole (VIII)</u>. To a solution of 3 g (20 mmoles) of indole (I) and 0.3 g (5 mmoles) of KOH in 25 ml of water was added 4 g (40 mmoles) of acetylene (III), and the mixture was heated for 3.5 h at 95°C. The organic layer was extracted with ether. Compound (VIII) was isolated by column chromatography (Al₂O₃, ether).

<u>2-Methyl-3-[(2-phenylvinyl)thio]indole (IX).</u> A mixture of 0.4 g (2.5 mmoles) of indole (II), 0.1 g (2 mmoles) of KOH, and 0.5 g (5 mmoles) of acetylene (III) in 18 ml of dioxane was agitated for 1 h at 90°C. After removal of the solvent, column chromatography on Al_2O_3 with chloroform as eluent separated (IX) and 0.12 g of bis(2-methylindolyl)disulfide, mp 232-233°C.

<u>3-[(1-Phenyl-2-cyanovinyl)thio]indole (X)</u>. To a solution of 0.5 g (3.3 mmoles) of indole (I) in 10 ml of Et_3N was added a solution of 0.42 g (3.3 mmoles) of acetylene (IV) in 5 ml of Et_3N with agitation. The mixture was agitated for 4 h at 20°C, and the residue was washed with ether and chloroform to give (X).

<u>2-Methyl-3-[(1-phenyl-2-cyanovinyl)thio]indole (XI)</u>. This was obtained in a similar manner from indole (II) and acetylene (IV).

<u>3-[(3-Hydroxy-3-methyl-1-cyano-1-butenyl-2)thio]indole (XII)</u>. To a solution of 0.75 g (5 mmoles) of indole (I) in 10 ml of Et_3N was added a solution of 0.55 g (5 mmoles) of acetylene (V) in Et_3N . The mixture was agitated at ~20°C for 4 h, evaporated under reduced pressure, and the residue was washed with chloroform to give (XII).

<u>2-Methyl-3-[(3-hydroxy-3-methyl-1-cyano-l-butenyl-2)thio]indole (XIII)</u>. This was obtained in a similar manner from indole (II) and acetylene (V).

CONCLUSIONS

1. The reaction of 2-methyl-3-indolethiol with acetylene gives the S-mono- and N,Sdivinyl derivatives. 2. The reaction of 3-indolethiols with activated acetylenes occurs only on the sulfur atom. The reaction of 3-indolethiols with phenylacetylene takes place stereoselectively, giving the cis isomers, while the reaction with cyanoacetylenes mainly gives a mixture of Z- and E-isomers.

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SYNTHESIS OF 1-SUBSTITUTED 1-VINYLCYCLOALKANES BY ALLYLBORATION OF CARBONYL COMPOUNDS AND ETHOXYACETYLENE WITH DIORGANYLBORYLETHYLIDENECYCLOPENTANE AND A DIORGANYLBORYLETHYLIDENECYCLOHEXANE

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 β,γ -Unsaturated (allylic) compounds of boron are useful, and in many instances the only means for the formation of new C-C bonds, and for the cyclization and functionalization of many types of compound [1, 2]. Allylboranes have been already been used with success in organic synthesis for more than two decades.

We here describe the synthesis of two representatives of hitherto unknown β , γ -unsaturated boron derivatives with an exocylic double bond, (I) and (II), and discuss some aspects of their use for the preparation of l-substituted l-vinylcyclopentanes and l-vinylcyclohexanes. The results reported here have been discussed briefly in [3].

One method for the preparation of allylic boranes is by hydroboration of allenic hydrocarbons [1, 8]. This method has, however, many limitations. The reactions are frequently ambiguous, giving mixtures of vinyl and allyl boranes, which are the products of the addition of boron to either the central (C_{sp}) or one of the terminal atoms of the allene system (C_{sp}^2) . Allylboranes are readily obtained only from 1,1-disubstituted allenes and $(R_2BH)_2$ [4, 5], the best hydroborating agent being 9-borabicyclo[3.3.1]nonane (9-BBN) [7, 8].

Hydroboration of 1,1-tetra- and 1,1-pentamethyleneallene with 9-BBN in tetrahydrofuran at -5°C has given the boron-containing ethylidenecyclopentane (I) and the ethylidenecyclohexane (II).



(I): n = 1, 76%; (II): n = 2, 83%,

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