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HOMOLYTIC ADDITION OF 1-ALKANETHIOLS TO 5-ETHYNYL-2-METHYLPYRIDINE

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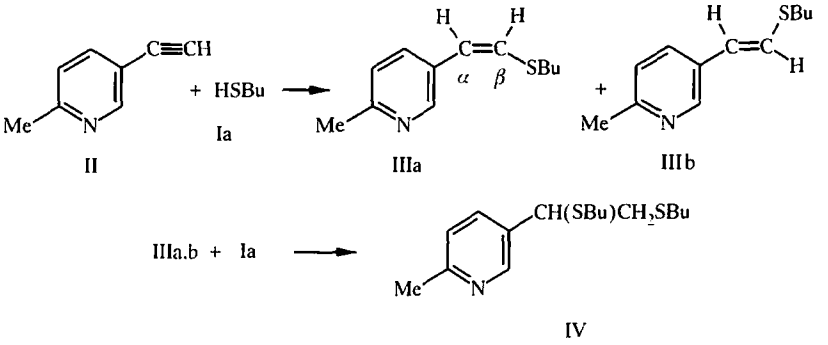
The homolytic addition of 1-butane- and 1-heptanethiol to 5-ethynyl-2-methylpyridine has been studied. Products of mono- or di-addition can be obtained by varying the reaction conditions.

Addition of alkanethiols to pyridylacetylene has been little studied [1]. It seemed interesting to study the homolytic addition of alkanethiols to the C≡C of pyridylacetylene, to examine its selectivity and to establish the factors which influence the course of the reaction. 1-Butane- (Ia) and 1-heptanethiol (Ib) were chosen as the source of the thiyl radicals. We studied in detail and in various conditions the reaction of thiol Ia with 5-ethynyl-2-methylpyridine (II) in the presence of di-*tert*-butyl peroxide or benzoyl peroxide. At 140°C with a 10-fold excess of thiol the process did not stop at the mono-addition stage but continued further as in the scheme below:



Under the above conditions the isomeric 5-(2-butylthioethenyl)-2-methylpyridines (IIIa,b) are formed in no more than 20% yield, because they readily react with second molecule of thiol to give 5-[1,2-di(butylthio)ethyl]-2-methylpyridine (IV) in a yield up to 70%. Decreasing the temperature and decreasing the excess of thiol reduces the formation of 1:2 adduct. For example at 100-110°C (5 h) and ratio of Ia:II:benzoyl peroxide 1.5 : 1 : 0.015 the vinyl derivatives IIIa,b are formed in 70% yield, while only 1.5-2% of the di-adduct IV are found in the reaction mixture.

Table 1 shows that addition is not stereospecific: in all experiments the vinyl derivatives are formed as a mixture of *cis*- (IIIa) and *trans*- (IIIb) isomers with the latter always in a greater or lesser excess. Stereoselectivity is increased at lower temperature and in the absence of initiator. The yields of products reach 90% at 30-35°C.

It should be noted that addition to the C≡C bond occurs less actively in the presence of inhibitor of radical reactions – hydroquinone – so indicating that the reaction is homolytic.

Reaction of 1-heptanethiol with 5-ethynyl-2-methylpyridine (II) under the same conditions (30-35°C) occurs similarly to give 87% yield of 1:3 mixture of two unsaturated mono-addition products – *cis,trans* isomers of 5-(2-heptylthioethenyl)-2-methylpyridine (Va,b).

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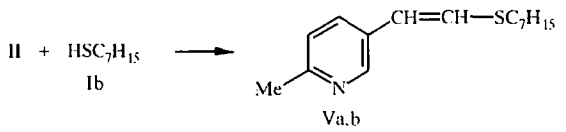
TABLE 1. Addition of Alkanethiols Ia,b to 5-Ethynyl-2-methylpyridine (II)

Alkanethiol	Initiator/inhibitor (In)	Mole ratio I:II:In	Temperature, °C	Duration, h	Yield, mol %	
					mono-adduct III (*cis*/*trans*)	di-adduct IV
1-Butanethiol	Di-*tert*-butyl peroxide	10:1:0.1	140	4	18 (1/2)	69
	—	10:1:—	140	4	20 (1/1.8)	65
	Benzoyl peroxide	1.5:1:0.15	100-110	5	76 (1/1.5)	1.5
	—	1.5:1:—	100-110	5	72 (1/3)	2.4
	—	1.5:1:—	30-35	50	90 (1/3)	—
	Hydroquinone	1.5:1:0.3	30-35	50	30 (1/1.2)	—
1-Heptanethiol	—	1.5:1:—	30-35	50	84 (1/3)	—



Va,b

V a *cis*-V, b *trans*-V

The products of thiyl radical recombination, the disulfides VIa,b, have been observed in the reaction mixture in small quantities alongside the main products.

VIa,b

a R = C_4H_9, b C_7H_{15}

The structures of the compounds synthesized have been confirmed by IR, mass, and ^1H NMR spectroscopy.

So, study of the homolytic addition of 1-alkanethiols Ia,b to pyridylacetylene II has clarified the conditions for the addition of either one or two molecules of thiol to the C≡C bond. One of the factors which affects the stereospecificity of the reaction is temperature. Mono-addition of thiols to the C≡C bond of pyridylacetylene at 30-35°C gives high yield of the unsaturated 1:1 adducts (80-90%) with preferential formation of the *trans*-isomer. In the absence of initiator (di-*tert*-butyl peroxide, benzoyl peroxide) the high yields of these products are evidently due to the presence of trace amounts of peroxy compounds which are readily formed in the presence of atmospheric oxygen [2].

EXPERIMENTAL

IR spectra of KBr disks were recorded on a UR-20 instrument. Mass spectra were recorded on MX-1310 mass spectrometer. ^1H NMR spectra of $CDCl_3$ solutions were obtained with a Tesla-567A (100 MHz) instrument. GLC analysis of reaction mixtures was carried out with a Biokhrom-1 chromatograph using a glass column (200 × 0.3 cm) filled with 5% of SKTFT-50 on Inerton AW carrier (0.100-0.125 mm).

5-Ethynyl-2-methylpyridine was synthesized by a known method from 2-methyl-5-vinylpyridine [3]. Di-*tert*-butyl peroxide [4] and dibenzoyl peroxide [5] were prepared by known methods.

Addition of 1-Alkanethiols Ia,b to 5-Ethynyl-2-methylpyridine (II). (General Method). Glass ampoule (30 or 15 ml) was 1/2 to 1/3 filled with pyridylacetylene II (20 mmol) together with the calculated amount of thiol I and the initiator. The ampoule was sealed and maintained at the required temperature for the required time (Table 1). After cooling, the excess of thiol was removed and the residue was analyzed by GLC and TLC on Silufol UV-254 plates (1:2 acetone–hexane) and then distilled in vacuum. The fractions containing a mixture of the *cis* and *trans* isomers of III (165-169°C/6 mm Hg) or V (187-190°C/2 mm Hg) were separated on a silica gel column.

***cis*-5-(2-Butylthioethenyl)-2-methylpyridine (IIIa).** Absorption band at 970 cm^{-1} was absent in the IR spectrum [6]. Mass spectrum, *m/z*: 207 (M^+). ^1H NMR spectrum: 0.85 (3H, t, CH_3); 1.15-1.75 (4H, m, $2CH_2$); 2.45 (3H, s, CH_3 in Het); 2.72 (2H, t, SCH_2); 6.30 (1H, d, J = 10.0 Hz, β-H); 6.73 (1H, d, J =10.0 Hz, α-H); 7.00 (1H, d, 3-H_{Het}); 7.42 (1H, d, 5-H_{Het}); 8.35 ppm (1H, s, 6H_{Het}) Found, %: C 69.2; H 8.1; N 6.3. $C_{12}H_{17}NS$. Calculated, %: C 69.5; H 8.3; N 6.7.

***trans*-5-(2-Butylthioethenyl)-2-methylpyridine (IIIb).** IR spectrum: 945 cm^{-1} (δ_{CH} for *trans* disubstituted double bond) [6]. Mass spectrum, *m/z*: 207 (M^+). ^1H NMR spectrum: 0.88 (3H, t, CH_3); 1.20-1.70 (4H, m, $2CH_2$); 2.46 (3H, s, CH_3 in Het); 2.71 (2H, t, SCH_2); 6.35 (1H, d, J = 16.0 Hz, β-H); 6.76 (1H, d, J = 16.0 Hz, α-H); 7.05 (1H, d, 3-H_{Het}); 7.41 (1H, d, 4-H_{Het}); 8.35 ppm (1H, s, 6-H_{Het}). Found, %: C 69.3; H 8.1; N 6.4. $C_{12}H_{17}NS$. Calculated, %: C 69.5; H 8.2; N 6.7.

***cis*-5-(2-Heptylthioethenyl)-2-methylpyridine (Va).** The absorption band at 960-970 cm^{-1} was absent in the IR spectrum [6]. Mass spectrum, *m/z*: 249 (M^+). ^1H NMR spectrum: 0.80 (3H, t, CH_3); 1.15-1.75 (10H, m, $5CH_2$); 2.43 (3H, CH_3 in Het); 2.70 (2H, t, SCH_2); 6.29 (1H, d, J = 10.0 Hz, β-H); 6.71 (1H, d, J = 10.0 Hz, α-H); 6.99 (1H, d, 3-H_{Het}); 7.37 (1H, d, 4-H_{Het}); 8.36 ppm (1H, d, 6-H_{Het}). Found, %: C 72.4; H 8.8; N 5.3. $C_{15}H_{23}NS$. Calculated, %: C 72.2; H 9.2; N 5.6.

***trans*-5-(2-Heptylthioethenyl)-2-methylpyridine (Va).** IR spectrum 947 cm^{-1} [6]. Mass spectrum, *m/z*: 249 (M^+). ^1H NMR spectrum: 0.83 (3H, t, CH_3); 1.15-1.75 (10H, m, $5CH_2$); 2.46 (3H, CH_3 in Het); 2.72 (2H, t, SCH_2); 6.32 (1H, d, J = 16.0 Hz, β-H); 6.75 (1H, d, J = 16.0 Hz, α-H); 7.05 (1H, d, 3-H_{Het}); 7.39 (1H, d, 4-H_{Het}); 8.39 ppm (1H, d, 6-H_{Het}). Found, %: C 72.1; H 9.3; N 5.4. $C_{15}H_{23}NS$. Calculated, %: C 72.2; H 9.2; N 5.6.

Synthesis of 5-[1,2-Di(butylthio)ethyl]-2-methylpyridine (IV). Fraction (2.33 g) with bp 200-212°C/6 mm Hg containing 88% IV (GLC data) was obtained from thiol Ia (0.9 g, 100 mmol); ethynylpyridine II (1.17 g, 10 mmol); and di-*tert*-butyl peroxide (0.146 g) by the method described above. Product IV, bp 205-207°C /6 mm Hg, was obtained by repeated distillation in vacuum. Mass spectrum, *m/z* 297 (M^+). ^1H NMR spectrum: 0.85 (6H, t, $2CH_3$); 1.12-1.75 (8H, m, $4CH_2$); 2.45 (3H, s, CH_3 in Het); 2.72-2.95 (6H, m, $3SCH_2$); 2.98-3.10 (1H, m, SCH); 7.07 (1H, d, 3-H_{Het}); 7.40 (1H, d, 4-H_{Het}); 8.39 ppm (1H, s, 6-H_{Het}). Found, %: C 64.9; H 8.9; N 4.8. $C_{16}H_{27}NS_2$. Calculated, %: C 64.6; H 9.1; N 4.7.

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