SELECTIVITY OF NUCLEOPHILIC ADDITION TO AND SUBSTITUTION AT ISOTHIOCYANATOCARBONYL GROUP. REACTIONS OF 4-PENTINOYL- AND 2-(2-PROPINYL)-4-PENTINOYL ISOTHIOCYANATE WITH AMINES AND METHANOL

Peter KUTSCHY, Pavol KRISTIAN, Milan DZURILLA, Dušan KOŠČÍK and Róbert NÁDASKAY

Department of Organic Chemistry and Biochemistry,
Faculty of Natural Sciences, P. J. Šafárik University, 041 67 Košice

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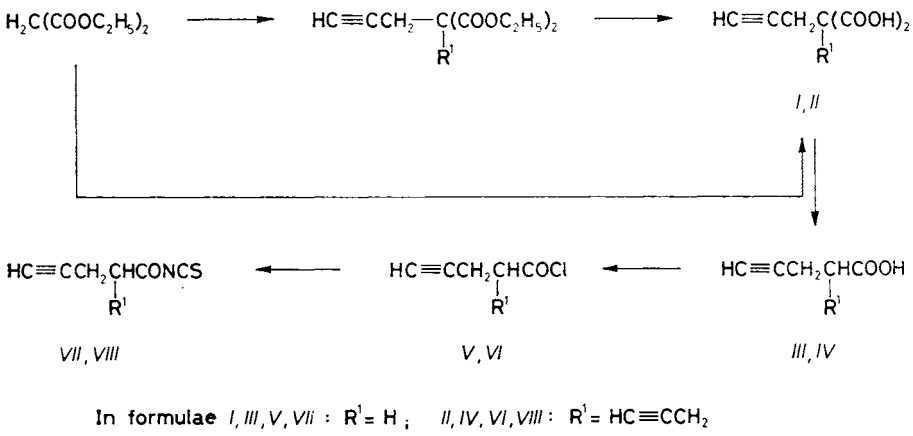
4-Pentinoyl isothiocyanate reacts with primary and secondary amines by either nucleophilic addition to N=C=S group to yield the corresponding thioureas, or a nucleophilic substitution at the carbonyl group to give 4-pentinoic acid amides. The less nucleophilic diphenylamine reacts selectively to afford the product of nucleophilic addition only. 2-(2-Propinyl)-4-pentinoyl isothiocyanate, having a sterically hindered carbonyl group, furnished with primary amines a mixture of amides and thioureas, whereas the bulkier secondary amines react selectively to form thioureas only. Both isothiocyanates afford with methanol as a nucleophile exclusively the corresponding O-methyl monothiocarbamates.

Properties of addition products of acyl isothiocyanates have recently been intensively studied, the interest being mostly focussed to N-acylthioureas, which in addition to their biological activity[1] are also suitable synthons for the synsthesis of heterocyles[2-5]. Aroyl isothiocyanates[1,4,6-8], propenoyl isothiocyanates[3,9,10] and 4-pentenoyl isothiocyanate[11] react with amines and alcohols *via* a nucleophilic addition to NCS group to afford substituted thioureas and O-alkyl monothiocarbamates. Acyl isothiocyanates react with sodium 3-methyl-1-butin-3-ol[12], thiamine[13], 3-amino-1,2,4-triazole, 5-aminotetrazole, and 2-aminobenzimidazole[14,15] by a nucleophilic substitution at carbonyl carbon of the O=C—N=C=S group to furnish the corresponding esters or amides. On the other hand, 3-chloro-3-phenylpropenoyl isothiocyanate treated with methylamine gives both the substitution and addition products[10]. Although only little attention has been paid to investigation of selectivity of nucleophilic addition and substitution, it is generally presumed that more basic amines, more polar solvents and higher temperature favour substitution[16,17].

This paper concerns the reaction of 4-pentinoyl isothiocyanate (*VII*) and 2-(2-propinyl)-4-pentinoyl isothiocyanate (*VIII*) with primary and secondary amines and methanol. The given system proved suitable for the investigation of the nucleophilic addition to the displacement rate at the CONCS grouping with respect to the pro-

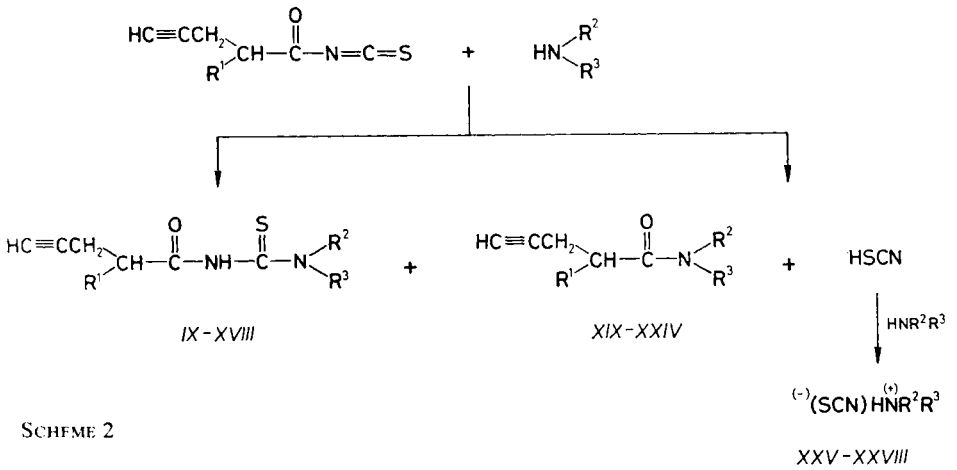
perties of the nucleophile and the structure of the isothiocyanate. Attention has also been paid to the reactivity of addition products; these results were published elsewhere[18]. Isothiocyanates *VII* and *VIII* were obtained from the corresponding carboxylic acids *III* and *IV*, the preparation of which is described in several papers[19–21] (Scheme 1). Yield of the mixture of carboxylic acids *I* and *II* with the prevailing 3-butinc-



SCHEME 1

-1,1-dicarboxylic acid is c. 50% *per* the diethyl malonate. No reliable results were obtained by reproducing the procedures described in literature and therefore, a new more effective preparation of the above-mentioned acids was elaborated involving the phase-transfer catalysis in the presence of triethylbenzylammonium chloride in aqueous sodium hydroxide, the organic phase being formed by the starting material. This method directly afforded the mixture of mono and dialkyldicarboxylic acids *I* and *II* in a 1 : 1 ratio, whereby the reaction time was reduced from 20 to 4 h and the yield was raised to 60–70%. The mixture of acids *III* and *IV* obtained by decarboxylation of acids *I* and *II* could be well separated in form of chlorides *V* and *VI* by fractional distillation. Reaction with lead thiocyanate in benzene leads to 4-pentinoyl isothiocyanate (*VII*) and 2-(2-propinyl)-4-pentinoyl isothiocyanate (*VIII*) in 70–80% yields. These compounds were identified by characteristic absorption bands ν(N=C=S) at 1 960 and 1 955 cm^{-1}, respectively. Treatment of the isothiocyanate *VII* with an equimolar amount of benzylamine in benzene for 90 min and monitoring the mixture by thin-layer chromatography showed the presence of the starting material, whilst benzylamine was not detected. A precipitate separating from the solution was identified by elemental analysis and IR spectrum (ν(S—C≡N) 2 040 cm^{-1}) as benzylammonium thiocyanate (*XXV*). The filtrate was evaporated to dryness and chromatographed over a silica gel column to give N-benzyl-N'-(4-pentinoyl)-thiourea

(*IX*) and 4-pentinoic acid N-benzylamide (*XIX*). The IR spectra of both substances disclosed characteristic $\nu(\equiv C-H)$ absorption bands at 3 310 cm^{-1}. The thiourea derivative reveals an intense $\nu(NHCS)$ band at 1 520 cm^{-1}, which is absent in the spectrum of the amide *XIX*. These findings evidence that two parallel reactions are taking place when reacting benzylamine with 4-pentinoyl isothiocyanate (*VII*): *a*) a nucleophilic addition of benzylamine to N=C bond of the N=C=S grouping to form thiourea *IX*, *b*) a nucleophilic substitution of the NCS group due to an attack of benzylamine to carbonyl carbon under formation of the amide *XIX* and hydrogen thiocyanate. The latter reacts with the so far not reacted benzylamine to yield thiocyanate *XXV*. Considering the afore-mentioned findings, reactions of isothiocyanates *VII* and *VIII* with amines were carried out with a 100%-excess of the nucleophile (Scheme 2, Table I). Reactions of isothiocyanates *VII* and *VIII* with benzylamine,



SCHEME 2

morpholine, and diphenylamine in acetone or hexane at −80°C and +50°C showed that no change in the ratio of products occured. Data listed in Table I let us presume that selectivity of this reaction, *i.e.* tendency of the nucleophile to attack the isothiocyanate or carbonyl carbon of the CONCS group first of all depends on the structure of the alkylacyl residue and properties of the amine used. With 4-pentinoyl isothiocyanate (*VII*) addition leading to thiourea *XI* is preferred when employing the less basic diphenylamine. Other amines undergo also a parallel substitution reaction leading to 4-pentinoic acid amides *XIX*–*XXII* and corresponding ammonium thiocyanates *XXV*–*XXVIII*. A more complicated is the reaction course with 2-(2-propinyl)-4-pentinoyl isothiocyanate: the substitution reaction takes place with primary amines only (benzylamine, aniline). Secondary amines, as well as more basic amines than aniline (piperidine, morpholine) selectively afford addition products to the NCS group. These findings indicate the substantial influence of a steric factor in addition to the alkylacyl substitution of isothiocyanate *VIII* and the nature of amine used.

TABLE I

Characteristic data of products *IX*—*XXVIII*

Compound	R^1	R^2	R^3	Formula (M_r)	M.p., °C (solvent[a])	Yield %	Calculated/found		
							% C	% H	% N
IX	H	H	$CH_2C_6H_5$	$C_{13}H_{14}N_2OS$ (246·3)	97·5—99 (M)	20	63·40 63·52	5·73 5·91	11·37 11·59
X	H	H	C_6H_5	$C_{12}H_{12}N_2OS$ (232·2)	134·5—135·5 (M)	26	62·04 62·30	5·21 5·39	12·06 11·81
XI	H	C_6H_5	C_6H_5	$C_{18}H_{16}N_2OS$ (308·3)	115—116 (B–H)	75	70·13 70·22	5·23 5·44	9·09 9·12
XII	H	$(CH_2)_5$		$C_{11}H_{16}N_2OS$ (224·3)	142—144 (B–H)	19	58·82 58·76	7·19 7·29	12·49 12·53
XIII	H	$(CH_2)_2O(CH_2)_2$		$C_{10}H_{14}N_2O_2S$ (226·3)	137—139 (B–H)	18	53·08 52·82	6·24 6·03	12·38 12·42
XIV	$HC\equiv CCH_2$	H	$CH_2C_6H_5$	$C_{16}H_{16}N_2OS$ (284·3)	68—70 (B–H)	38	67·60 67·42	5·67 5·73	9·85 9·66
XV	$HC\equiv CCH_2$	H	C_6H_5	$C_{14}H_{14}N_2OS$ (270·4)	135—136 (B)	34	66·64 66·42	5·22 5·42	10·36 10·63
XVI	$HC\equiv CCH_2$	C_6H_5	C_6H_5	$C_{21}H_{18}N_2OS$ (346·5)	105·5—107·5 (B–H)	80	72·80 72·59	5·24 5·52	8·08 7·84
XVII	$HC\equiv CCH_2$	$(CH_2)_5$		$C_{14}H_{18}N_2OS$ (262·4)	115—117 (B–H)	62	64·08 64·21	6·91 6·99	10·68 10·86

XVIII	$HC{\equiv}CCH_2$	$(CH_2)_2O(CH_2)_2$		$C_{13}H_{16}N_2O_2S$ (264·3)	143—145 (C–P)	93	59·08 59·32	6·10 6·03	10·65 10·66
XIX	H	H	$CH_2C_6H_5$	$C_{12}H_{13}NO$ (187·2)	67—68 (C–P)	74	76·99 77·21	7·00 6·96	7·48 7·54
XX	H	H	C_6H_5	$C_{11}H_{11}NO$ (173·2)	128—129 (B)	72	76·28 75·99	6·40 6·42	8·09 8·19
XXI	H	$(CH_2)_5$		$C_{10}H_{15}NO$ (165·2)	44—45 (C–P)	62	72·70 72·48	9·15 9·31	8·47 8·55
XXII	H	$(CH_2)_2O(CH_2)_2$		$C_9H_{13}NO_2$ (167·2)	81—82·5 (B)	62	64·64 64·73	7·48 7·92	8·38 8·23
XXIII	$HC{\equiv}CCH_2$	H	$CH_2C_6H_5$	$C_{15}H_{15}NO$ (225·3)	102·5—103·5 (B–H)	56	79·97 80·03	6·71 7·83	6·22 6·02
XXIV	$HC{\equiv}CCH_2$	H	C_6H_5	$C_{14}H_{13}NO$ (211·3)	146—148 (C)	54	79·22 79·51	6·65 6·40	6·60 6·31
XXV	—	H	$CH_2C_6H_5$	$C_8H_{10}N_2S$ (166·3)	85—87 (B)	54[b] 35[c]	57·78 57·59	6·06 6·23	16·85 16·69
XXVI	—	H	C_6H_5	$C_7H_8N_2S$ (152·2)	83—85 (B)	18[b] 14[c]	55·23 55·51	5·30 5·07	18·40 18·12
XXVII	—	$(CH_2)_5$		$C_6H_{12}N_2S$ (134·2)	92—94 (B)	48[b]	53·65 53·51	8·26 8·39	20·86 20·70
XXVIII	—	$(CH_2)_2O(CH_2)_2$		$C_5H_{10}N_2OS$ (136·2)	117—118 (B)	40[b]	44·08 44·33	7·40 7·35	20·57 20·68

[a] M methanol, B benzene, H hexane, C chloroform, P light petroleum; the yield corresponds to the reaction of [b] 4-pentinoyl isothiocyanate (*VII*) with the respective amine; [c] 2-(2-propinyl)-4-pentinoyl isothiocyanate (*VIII*) with the respective amine.

Therefore, secondary amines with a bulkier amino group react with the NSC group of the isothiocyanate *VIII* only. Different spatial conditions for the nucleophilic substitution at carbonyl group of isothiocyanates *VII* and *VIII* are accordingly involved even with primary amines, as shown by the yield ratio of amide to thiourea, which is greater with 4-pentinoyl isothiocyanate than with 2-(2-propinyl)-4-pentinoyl isothiocyanate (Table I).

Isothiocyanates *VII* and *VIII* were reacted with methanol for comparison. Methanol is a weaker nucleophile than amines and the only products from this experiment were the corresponding O-methyl monothiocarbamic acids *XXIX* and *XXX*. No nucleophilic displacement leading to methyl carboxylates was observed.

EXPERIMENTAL

The IR spectra were measured with an IR-75 (Zeiss, Jena) spectrophotometer, the ^{1}H NMR spectra were recorded on a Tesla BS 487 A spectrometer operating at 80 MHz tetramethylsilane being the internal reference; hexamethyldisiloxane was the standard for measurements in ^2H_2O. The reaction course was monitored by thin-layer chromatography on Silufol (Kavalier, Czechoslovakia) sheets.

4-Pentinoic (*III*) and 2-(2-Propinyl)-4-pentinoic (*IV*) Acids

Diethyl malonate (57·6 g, 0·36 mol) was rapidly added to a well stirred solution of 33%-sodium hydroxide (264 g, 6·6 mol) in water (528 ml) and triethylbenzylammonium chloride (29·4 g, 0·132 mol). Thereafter 1-bromo-2-propene (42·8 g, 0·36 mol) was added and the mixture was stirred at room temperature for 2·5 h. The mixture was diluted with water (750 ml), the unreacted starting material was extracted with ether (200 ml), the aqueous layer was cooled with ice and acidified with hydrochloric acid to pH ~ 1 (c. 500 ml). This solution was extracted with ether (5 × 200 ml), the organic layer was dried with magnesium sulfate, ether was evaporated and the mixture of dicarboxylic acids *I* and *II* (40—45 g, 60—70%) was heated to 160—170°C. Fractional distillation under reduced pressure afforded 4-pentinoic acid (*III*, 11 g) and 2-(2-propinyl)-4-pentinoic acid (*IV*, 13 g). Without fractionation the yield of *III* and *IV* in a 1 : 1 ratio was 25 g.

4-Pentinoic acid (III): m.p. 57°C light petroleum, −20°C, b.p. 102°C/2·3 kPa. IR spectrum ($CHCl_3$), cm^{-1}: 1 710 (C=O), 2 120 (C≡C), 2 400—3 200 (COOH), 3 312 (≡C—H), 3 515 (COOH). ^{1}H NMR spectrum (C^2HCl_3), δ, ppm: 1·98 (t, 1 H, J = 3 Hz, ≡CH), 2·56 (m, 4 H, CH_2CH_2), 11·15 (s, 1 H, OH). This compound is identical with the specimen[19—21].

2-(2-Propinyl)-4-pentinoic acid (IV): b.p. 135°C/2·3 kPa. IR spectrum ($CHCl_3$), cm^{-1}: 1 720 (C=O), 2 120 (C≡C), 2 200—3 400 (COOH), 3 312 (≡C—H), 3 500 (COOH). ^{1}H NMR spectrum (C^2HCl_3), δ, ppm: 2·04 (t, 2 H, J = 3 Hz, ≡CH), 2·69 (m, 5 H, CH_2CHCH_2), 11·38 (s, 1 H, OH). This compound is identical with the specimen[19—21].

4-Pentinoyl Chloride (*V*) and 2-(2-Propinyl)-4-pentinoyl Chloride (*VI*)

Acid *III* or acid *IV* or the 1 : 1 mixture of them (50 mmol, for the mixture the average molecular mass was considered) was dissolved in thionyl chloride (0·15 mol) and left to stand overnight at room temperature and exclusion of moisture. The mixture was fractionated under reduced pressure.

4-*Pentinoyl chloride* (V): yield 60%, b.p. 46—48°C/2·5 kPa. IR spectrum ($CHCl_3$), cm^{-1}: 1 785 (C=O), 2 125 (C≡C), 3 320 (≡C—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 2·04 (t, 1 H, J = 3 Hz, ≡CH), 2·56 (m, 2 H, ≡CCH_2), 3·12 (m, 2 H, CH_2CO). The compound is identical with the specimen[22].

2-(2-*Propinyl*)-4-*pentinoyl chloride* (VI): yield 60%, b.p. 78°C/2·5 kPa. IR spectrum ($CHCl_3$), cm^{-1}: 1 770 (C=O), 2 120 (C≡C), 3 310 (≡C—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 2·10 (t, 2 H, J = 3 Hz, ≡CH), 2·75 (m, 4 H, CH_2CHCH_2), 3·13 (m, 1 H, CH).

4-Pentinoyl Isothiocyanate (*VII*) and 2-(2-Propinyl)-4-pentinoyl Isothiocyanate (*VIII*)

A stirred mixture of acyl chloride *IV* or *VI* (20 mmol) and lead(II) thiocyanate (15 mmol) in benzene (30 ml) was heated in 1 h a oil-bath kept at 90°C, filtered with charcoal, the solvent was distilled off and the residue was fractionated under diminished pressure.

4-*Pentinoyl isothiocyanate* (VII): yield 75%, b.p. 78—81°C/2·1 kPa. For C_6H_5NOS (139·2) calculated: 51·77% C, 3·62% H, 10·66% N; found: 51·60% C, 3·75% H, 10·57% N. IR spectrum ($CHCl_3$), cm^{-1}: 1 724 (C=O), 1 960 (N=C=S), 2 120 (C≡C), 4 310 (≡C—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 2·08 (t, 1 H, J = 3 Hz (≡CH), 2·55 (m, 2 H, ≡CCH_2), 2·86 (m, 2 H, CH_2CO).

2-(2-*Propinyl*)-4-*pentinoyl isothiocyanate* (VIII): yield 80%, b.p. 84—86°C/0·8 kPa. For C_9H_7NOS (177·2) calculated: 61·00% C, 3·98% H, 7·90% N; found: 59·77% C, 3·92% H, 8·06% N. IR ($CHCl_3$), cm^{-1}: 1 720 (C=O), 1 955 (N=C=S), 2 120 (C≡C), 3 310 (≡C—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 2·08 (t, 2 H, J = 3 Hz, ≡CH), 2·69 (m, 4 H, CH_2CHCH_2), 2·88 (m, 1 H, CH).

Reaction of 4-Pentinoyl Isothiocyanate (*VII*) with Benzylamine

Benzylamine (3·64 g, 34 mmol) was dropwise added to a stirred solution of isothiocyanate *VII* (2·36 g, 17 mmol) in benzene (40 ml) at an ambient temperature during 5 min. Stirring was continued for 2 h, the separated precipitate *XXV* was allowed to stand for 1 h, filtered off, washed with benzene (5 ml) and the filtrate was evaporated. The residue was chromatographed through a silica gel column (300 g, 100—250 μm, benzene–acetone 7 : 1) to give compounds *IX* and *XIX*.

N-*Benzyl*-N'-(4-*pentinoyl*)*thiourea* (IX): IR ($CHCl_3$), cm^{-1}: 1 520 (NHCS), 1 700 (C=O), 2 120 (C≡C), 3 310 (≡C—H), 3 400 (N—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 2·03 (t, 1 H, J = 3 Hz, ≡CH), 2·53 (m, 4 H, CH_2CH_2), 4·80 (d, 2 H, J = 5 Hz, CH_2NH), 7·30 (m, 5 H, C_6H_5), 9·54 (s, 1 H), 10·75 (s, 1 H, NH).

4-*Pentinoic acid* N-*benzylamide* (XIX): IR spectrum ($CHCl_3$, cm^{-1}: 1 670 (C=O), 2 119 (C≡C), 3 310 (≡C—H), 3 440 (N—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 1·94 (t, 1 H, J = 3 Hz, ≡CH), 2·54 (m, 4 H, CH_2CH_2), 4·38 (d, 2 H, J = 5 Hz, CH_2NH), 6·19 (s, 1 H, NH), 7·25 (m, 5 H, C_6H_5).

Benzylammonium thiocyanate (XXV): IR spectrum, (KBr), cm^{-1}: 2 040 (S—C≡N), 2 570 (+) (N—H).

Reaction of 4-Pentinoyl Isothiocyanate (*VII*) with Aniline

Following compounds were obtained by an analogous procedure and reaction time 1·5 h:

N-*Phenyl*-N'-(4-*Pentinoyl*)*thiourea* (X): IR spectrum ($CHCl_3$), cm^{-1}: 1 505 (NHCS), 1 690 (C=O), 2 120 (C≡C), 3 180 (N—H), 3 310 (≡C—H), 3 405 (N—H). ^1H NMR spectrum

(C^2HCl_3), δ, ppm: 2·03 (t, 1 H, J = 3 Hz, ≡CH), 2·75 (m, 4 H, CH_2CH_2), 7·40 (m, 5 H, C_6H_5), 7·75 (s, 1 H, NH).

4-Pentinoic acid anilide (XX): IR spectrum ($CHCl_3$), cm^{-1}: 1 650 (C=O), 2 120 (C≡C), 3 315 (≡C—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 2·03 (t, 1 H, J = 3 Hz, ≡CH), 2·56 (m, 4 H, CH_2CH_2), 7·38 (m, 5 H, C_6H_5), 7·81 (s, 1 H, NH).

Anilinium thiocyanate (XXVI): IR spectrum (KBr), cm^{-1}: 2 040 (S—C≡N), 2 560 ($N^{(+)}$—H).

N,N,-Diphenyl-N'-(4-pentinoyl)thiourea (*XI*)

A solution of diphenylamine (6·2 g, 36 mmol) in benzene (10 ml) was dropwise added during 5 min to a stirred solution of 4-pentinoyl isothiocyanate (*VII*) (2·55 g, 18 mmol) in benzene (40 ml) and the mixture was left to stand for 24 h. Hexane was added till turbidity was formed, the precipitate was filtered off, washed with hexane, dried and crystallized. IR spectrum ($CHCl_3$), cm^{-1}: 1 480 (NHCS), 1 705 (C=O), 2 120 (C≡C), 3 310 (≡C—H), 3 390 (N—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 1·93 (t, 1 H, J = 3 Hz, ≡CH), 2·33 (m, 2 H, ≡CCH_2), 2·60 (m, 2 H, CH_2CO), 7·33 (m, 10 H, $N(C_6H_5)_2$), 8·70 (s, 1 H, NH).

Reaction of 4-Pentinoyl Isothiocyanate (*VII*) with Piperidine

Applying the same procedure as described with benzylamine, compounds *XII*, *XXI*, and *XXVII* were obtained employing 20 min reaction time. Compound *XXI* was also obtained by an independent synthesis: piperidine (4·3 mmol) and triethylamine (5 mmol) in benzene (5 ml) were added to a stirred and water-cooled solution of 4-pentinoyl chloride (*V*) (0·5 g, 4·3 mmol) in benzene within 5 min. The mixture was stirred for 1 h at room temperature, the separated precipitate of triethylammonium chloride was filtered off, the solvent was evaporated and the residue was crystallized to furnish amide *XXI* (75%).

1-(N-(4-Pentinoyl)thiocarbamoyl)piperidine (XII): IR spectrum ($CHCl_3$), cm^{-1}: 1 525 (NHCS), 1 708 (C=O), 2 120 (C≡C), 3 304 (≡C—H), 3 390 N—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 1·70 (m, 6 H, $(CH_2)_3$), 1·96 (t, 1 H, J = 3 Hz, ≡CH), 2·52 (m, 4 H, CH_2CH_2), 3·80 (m, 4 H, CH_2NCH_2), 8·91 (s, 1 H, NH).

1-(4-Pentinoyl)piperidine (XXI): IR spectrum ($CHCl_3$), cm^{-1}: 1 630 (C=O), 2 120 (C≡C), 3 305 (≡C—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 1·62 (m, 6 H, $(CH_2)_3$), 1·95 (t, 1 H, J = 3 Hz, ≡CH), 2·54 (m, 4 H, CH_2CH_2), 3·46 (m, 4 H, CH_2NCH_2).

Piperidinium thiocyanate (XXVII): IR spectrum (KBr), cm^{-1}: 2 035 (S—C≡N), 2 560 ($N^{(+)}$—H). ^1H NMR spectrum (^2H_2O), δ, ppm: 1·98 (m, 6 H, $(CH_2)_3$), 3·43 (m, 4 H, $CH_2N^{(+)}CH_2$).

Reaction of 4-Pentinoyl Isothiocyanate (*VII*) with Morpholine

The same procedure as with benzylamine was applied to get compounds *XIII*, *XXII*, and *XXVIII*; compound *XXII* was also synthesized by an independent procedure as *XXI* in 80% yield.

*4-(N-(4-Pentinoyl)*thiocarbamoyl)morpholine (XIII): IR spectrum ($CHCl_3$), cm^{-1}: 1 525 (NHCS), 1 690 (C=O), 2 120 (C≡C), 3 305 (≡C—H), 3 395 (N—H). ^1H NMR spectrum (C^2HCl_3–$(C^2H_3)_2SO$, 1 : 1), δ, ppm: 2·04 (t, 1 H, J = 3 Hz, ≡CH), 2·53 (m, 4 H, (CH_2CH_2), 3·60 m, 8 H, $(CH_2)_2O(CH_2)_2$).

4-(4-Pentinoyl)morpholine (XXII): IR spectrum ($CHCl_3$), cm^{-1}: 1 640 (C=O), 2 225 (C≡C), 3 312 (≡C—H). ^1H NMR spectrum ($C^2HC^1_3$), δ, ppm: 1·99 (t, 1 H, J = 3 Hz, ≡CH), 2·58 (m, 4 H, CH_2CH_2), 3·60 (m, 8 H, $(CH_2)_2O(CH_2)_2$).

Morpholinium thiocyanate (XXVIII): IR spectrum (KBr), cm^{-1}: 2 170 (S—C≡N), 2 520 ($N^{(+)}$—H). ^1H NMR spectrum (^2H_2O), δ, ppm: 3·66 (m 4 H $CH_2N^{(+)}CH_2$), 4·25 (m, 4 H, CH_2OCH_2).

Reaction of 2-(2-Propinyl)-4-pentinoyl Isothiocyanate (*VIII*) with Benzylamine

Benzylamine (3 g, 28 mmol) was added within 5 min to a stirred solution of isothiocyanate *VIII* (2·4 g, 14 mmol) in benzene at an ambient temperature. The mixture was stirred for 1 h, the precipitated *XXV* was filtered off and washed with benzene (5 ml). Addition of hexane (30 ml) to the filtrate resulted in precipitation of *XXIII*, which was filtered off and washed with hexane. The filtrate was evaporated and the residue was crystallized from hexane to give *XIV*.

N-*Benzyl*-N′-(2-(2-*propinyl*)-4-*pentinoyl*)*thiourea* (XIV): IR spectrum ($CHCl_3$), cm^{-1}: 1 520 (NHCS), 1 695 (C=O), 2 125 (C≡C), 3 312 (≡C—H), 3 408 (N—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 2·13 (t, 2 H, J = 3 Hz, ≡CH), 2·60 (m, 4 H, CH_2CHCH_2), 2·85 (m, 1 H, CH), 4·85 (d, 2 H, J = 5 Hz, CH_2NH), 7·35 (m, 5 H, C_6H_5), 9·75 (s, 1 H), 10·80 (s, 1 H, NH).

2-(2-*Propinyl*)-4-*pentinoic acid* N-*benzylamide* (XXIII): IR spectrum ($CHCl_3$), cm^{-1}: 1 670 (C=O), 2 120 (C≡C), 3 305 (≡C—H), 3 335 N—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 2·03 (t, 2 H, J = 3 Hz, ≡CH), 2·55 (m, 4 H, CH_2CHCH_2), 2·85 (m, 1 H, CH), 4·45 (d, 2 H, J = 5 Hz, CH_2NH), 6·38 (s, 1 H, NH), 7·30 (m, 5 H, C_6H_5).

Reaction of 2-(2-Propinyl)-4-pentinoyl Isothiocyanate (*VIII*) with Aniline

Reaction time 75 min and procedure as in the preceding case afforded from *VIII* and aniline a precipitate consisting of *XV* and *XXVI*. Washing with benzene removes thiourea *XV*. The filtrate was combined with that of the reaction mixture containing *XV* and *XXIV*. The solvent was evaporated and the residue was chromatographed over a silica gel (200 g, 40—100 μm, benzene–acetone 7 : 1) column affording *XV* and *XXIV*.

N-*Phenyl*-N′-(2-(2-*propinyl*)-4-*pentinoyl*)*thiourea* (XV): IR spectrum ($CHCl_3$), cm^{-1}: 1 520 (NHCS), 1 680 (C=O), 2 120 (C≡C), 3 130 (N—H), 3 302 (≡C—H), 3 395 (N—H). ^1H NMR spectrum (C^2HCl_3–$(C^2H_3)_2SO$, 1 : 1), δ, ppm: 2·13 (t, 2 H, J = 3 Hz, ≡CH), 2·60 (m, 4 H, CH_2CHCH_2), 3·00 (m, 1 H, CH), 7·45 (m, 5 H, C_6H_5), 10·95 (s, 1 H), 12·45 (s, 1 H, NH).

2-(2-*Propinyl*)-4-*pentinoic acid anilide* (XXIV): IR spectrum ($CHCl_3$), cm^{-1}: 1 690 (C=O), 2 125 (C≡C), 3 315 (≡C—H), 3 430 (N—H). ^1H NMR spectrum (C^2HCl_3–$(C^2H_3)SO$, 1 : 1), δ, ppm: 2·10 (t, 2 H, J = 3 Hz, ≡CH), 2·58 (m, 4 H, CH_2CHCH_2), 2·81 (m, 1 H, CH), 7·25 (m, 5 H, C_6H_5), 9·55 (s, 1 H, NH).

N,N-Diphenyl-N′-(2-(2-propinyl)-4-pentinoyl)thiourea (*XVI*)

Diphenylamine (4·8 g, 28 mmol) in benzene (20 ml) was added to a stirred solution of the isothiocyanate *VIII* (2·4 g, 14 mmol) in benzene (20 ml) at room temperature. The mixture was allowed to stand for 24 h, hexane was added till no more turbidity was formed, the crystalline precipitate was filtered off, washed with hexane and dried. IR spectrum ($CHCl_3$), cm^{-1}: 1 480 (NHCS), 1 720 (C=O), 2 125 (C≡C), 3 310 (≡C—H), 3 385 (N—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 2·00 (t, 2 H, J = 3 Hz, ≡CH), 2·30 (m, 4 H, CH_2CHCH_2), 2·68 (m, 1 H, CH), 7·29 (m, 10 H, $N(C_6H_5)_2$), 8·73 (s, 1 H, NH).

1-(N-(2-(2-Propinyl)-4-pentinoyl)thiocarbamoyl)piperidine (*XVII*)

The same procedure as with the preceding case and reaction time 20 min was applied for the pre-

paration of *XVII*. IR spectrum ($CHCl_3$), cm^{-1}: 1 530 (NHCS), 1 705 (C=O), 2 120 (C≡C). 3 305 (≡C—H), 2 285 (N—H). ^1H NMR spectrum, (C^2HCl_3), δ, ppm: 1·69 (m, 6 H, $(CH_2)_3$), 2·05 (t, 2 H, J = 3 Hz, ≡CH), 2·63 (m, 5 H, CH_2CHCH_2), 3·55 (m, 4 H, CH_2NCH_2).

4-(N-(2-(2-Propinyl)-4-pentinoyl)thiocarbamoyl)morpholine (*XVIII*)

The product was obtained by the same procedure from the isothiocyanate *VIII* and morpholine. IR spectrum ($CHCl_3$), cm^{-1}: 1 523 (NHCS), 1 705 (C=O), 2 120 (C≡C), 3 305 (≡C—H), 3 380 (N—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 2·08 (t, 2 H, J = 3 Hz, ≡CH), 2·58 (m, 5 H, CH_2CHCH_2), 3·80 (m, 8 H, $(CH_2)_2O(CH_2)_2$).

O-Methyl N-(4-Pentinoyl)monothiocarbamate (*XXIX*)

4-Pentinoyl isothiocyanate (1·4 g, 17 mmol) dissolved in methanol (30 ml) was left to stand at room temperature for 45 min, methanol was evaporated and the residue was crystallized from cyclohexane. Yield 78%, m.p. 81·5—83°C. For $C_7H_9NO_2S$ (171·3) calculated: 49·11% C, 5·29% H, 8·18% N; found: 48·80% C, 5·55% H, 7·94% N. IR spectrum ($CHCl_3$), cm^{-1}: 1 495 (NHCS), 1 700 (C=O), 2 120 (C≡C), 3 305 (≡C—H), 3 380 (N—H). ^1H NMR spectrum ($C^2HC^1{}_3$), δ, ppm: 2·00 (t, 1 H, J = 3 Hz, ≡CH), 2·58 (m, 2 H, ≡CCH_2), 2·85 (m, 2 H, CH_2CO), 4·13 (s, 3 H, CH_3O), 9·20 (s, 1 H, NH).

O-Methyl N-(2-(2-Propinyl)-4-pentinoyl)monothiocarbamate (*XXX*)

Treatment of isothiocyanate *VIII* with methanol yielded *XXX* by the same procedure as given for *XXIX*. Yield 85%, m.p. 108—109°C. For $C_{10}H_{11}NO_2S$ (209·3). Calculated: 57·39% C, 5·30% H, 6·70% N; found: 57·16% C, 5·47% H, 6·48% N. IR spectrum ($CHCl_3$), cm^{-1}: 1 505 (NHCS), 1 730 (C=O), 2 120 (C≡C), 3 312 (≡C—H), 3 400 (N—H). ^1H NMR spectrum (C^2HCl_3), δ, ppm: 2·20 (t, 2 H, J = 3 Hz, ≡CH), 2·56 (m, 4 H, CH_2CHCH_2), 2·90 (m, 1 H, CH), 4·13 (s, 3 H, CH_3O), 9·27 (s, 1 H, NH).

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