47. *The Inhibitory Effect of Substituents in Chemical Reactions. Part III. The Reactivity of the* iso*Thiocyano-group in Substituted Arylthiocarbimides.*

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NUCLEAR substituents exert a profound effect on the reactivity of the *iso*thiocyano-group in aryl thiocarbimides (Browne and Dyson, J., 1931, 3285). The present experiments were undertaken to find out whether or not side-chain unsaturation, or fused ring formation, can accelerate the reaction between arylthiocarbimides and ethyl alcohol. Our previous method was used (*loc. cit.*) and the results are summarised in the table below :

		Proportion converted into thiourethane at time *t* (mins.).										
Thiocarbimide.	$k \times 10^4$.	*t*.	*x*, %.	*t*.	*x*, %.	*t*.	*x*, %.	*t*.	*x*, %.	*t*.	*x*, %.	*Y*.*
1-Naphthyl	0·31	15	2·7	30	5·5	45	8·0	65	11·3	90	15·7	11·5
2-Naphthyl	0·84	10	5·7	30	14·0	45	19·7	70	28·4	95	34·5	26·5
Acenaphthyl-4	0·15	10	1·8	40	3·0	70	4·7	—	—	—	—	5·0
3-Carboxyphenyl	2·46	10	14·1	20	26·9	30	35·0	40	44·9	50	48·9	55·0
4-Carboxyphenyl	3·82	10	20·6	20	37·0	30	51·3	40	62·2	—	—	72·5
2-Carbomethoxyphenyl	1·10	10	5·9	20	11·8	40	23·1	60	32·4	80	40·4	33·0
3-Carbomethoxyphenyl	3·07	10	15·6	20	31·2	30	42·9	40	52·4	50	60·5	65·0
4-Carbomethoxyphenyl	4·53	10	25·3	20	42·8	30	56·4	40	66·2	50	73·2	79·0
2-Carbethoxyphenyl	0·91	10	4·8	20	9·0	40	18·8	70	31·9	—	—	28·5
3-Carbethoxyphenyl	3·07	10	15·7	20	30·7	30	43·3	40	50·6	50	59·6	65·0
4-Carbethoxyphenyl	4·13	10	22·0	20	40·0	30	53·1	40	63·4	50	68·9	75·0
4-Carbopropoxyphenyl	4·33	10	24·4	20	43·1	30	55·9	40	64·5	50	70·3	77·5
4-Carbobutoxyphenyl	4·13	10	22·9	20	40·5	30	54·5	40	64·1	50	70·4	75·5
4-Carbamoxyphenyl	4·53	10	24·5	20	41·8	30	57·1	40	67·6	50	72·7	79·0
Ethyl phenylacetate-4	0·74	10	5·2	25	10·0	45	17·8	75	27·1	—	—	23·5
Ethyl β-phenylpropionate-4	0·33	10	2·5	20	4·3	40	7·9	60	11·3	90	15·6	11·0
Ethyl cinnamate-4	2·26	10	11·5	20	24·7	30	24·1	50	49·3	70	57·4	55·0
4-Acetamidophenyl	0·63	10	3·9	20	7·3	40	14·4	60	19·5	90	28·0	20·5
3 : 4-Dichlorophenyl	9·45	10	47·1	20	62·9	40	77·5	—	—	—	—	86·0
3 : 4 : 5-Trimethoxyphenyl	1·11	10	7·5	20	12·1	40	23·5	65	35·2	95	47·1	33·0
4-Dimethylaminophenyl	—	No reaction										

* *Y* represents the amount (%) of thiocarbimide which has disappeared in 60 mins.

The rate of disappearance of the thiocarbimide from an *N*/13·5-solution in ethyl alcohol was measured at the boiling point of the solution, 78·5°.

These results and the earlier ones (*loc. cit.*) indicate that the general trend of addition of ethyl alcohol to arylthiocarbimides is that of a side-chain reaction favoured by "electron-recession." Supporting evidence for this contention is found in two factors : (a) in nearly all the cases examined, the meta-substituted compound is more reactive than the corresponding ortho- or para-substituted compound, and (b) the reaction is favoured by unsaturation in the substituents. As a critical test of the effect of side-chain unsaturation we examined the three para-substituted compounds

$$\underset{\text{(I.)}}{\mathrm{SCN{\cdot}C_6H_4{\cdot}CH_2{\cdot}CO_2Et}} \qquad \underset{\text{(II.)}}{\mathrm{SCN{\cdot}C_6H_4{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Et}} \qquad \underset{\text{(III.)}}{\mathrm{SCN{\cdot}C_6H_4{\cdot}CH{:}CH{\cdot}CO_2Et}}$$

The rate of addition of alcohol to (I) is about twice as rapid as to (II), again indicating that the effect of electron-recession is weakened by prolongation of the side chain. On the other hand, (III) reacts five times as rapidly as (I) and more than twice as readily as its dihydro-derivative (II), thus indicating the accelerating activity of the unsaturated side chain.

4-Dimethylaminophenylthiocarbimide is incapable of reacting with ethyl alcohol under the conditions of our experiments; in this respect the NMe_2 group offers a parallel with the $CHMe_2$ group (see 4-*iso*propylphenylthiocarbimide; *loc. cit.*, p. 3287). 3 : 4 : 5-Trimethoxyphenylthiocarbimide was unexpectedly found to react more readily than the 3 : 5-dimethoxy-compound with ethyl alcohol.

EXPERIMENTAL.

3-*Carboxyphenylthiocarbimide*.—*m*-Aminobenzoic acid (8 g.) in 2*N*-hydrochloric acid (350 ml.) was shaken with thiocarbonyl chloride (7 g.) for ½ hour. The white precipitate was washed, dried, and recrystallised from benzene, the *thiocarbimide* being obtained in colourless needles, m. p. 163° (decomp.) (Found : S, 18·1. $C_8H_5O_2NS$ requires S, 17·9%).

4-*Carboxyphenylthiocarbimide*, similarly prepared from *p*-aminobenzoic acid, formed colourless plates, decomp. 220°, from acetone (Found : S, 18·0%).

4-*Carbopropoxyphenylthiocarbimide*.—Propyl *p*-nitrobenzoate (20 g., prepared from *p*-nitrobenzoyl chloride and *n*-propyl alcohol; pale yellow plates, m. p. 36°) was reduced with iron filings (20 g.) and water (100 ml.) at 100°, hydrochloric acid (75 ml.) being added gradually until the solution became clear. The amine, liberated by sodium carbonate and extracted in ether, formed colourless needles (12 g.), m. p. 72°, from ligroin. The amine (7 g.) in chloroform (60 ml.) was added to a suspension of thiocarbonyl chloride (7 g.) in water (300 ml.). The chloroform layer was withdrawn, the solvent removed, and the residue distilled in steam. The thiocarbimide formed colourless needles, m. p. 32° (Found : S, 14·7. $C_{11}H_{11}O_2NS$ requires S, 14·5%).

In the similar preparations of the n-*butyl* ester (Found : S, 13·9. $C_{12}H_{13}O_2NS$ requires S, 13·6%) and the n-*amyl* ester (Found : S, 12·5. $C_{13}H_{15}O_2NS$ requires S, 12·8%), both pale yellow oils, b. p. 180°/5 mm. and 205°/5 mm. respectively, the following compounds were obtained : butyl *p*-nitrobenzoate, colourless plates, m. p. 36°; butyl *p*-aminobenzoate, colourless needles, m. p. 58°; amyl *p*-nitrobenzoate, pale yellow oil, b. p. 270°; amyl *p*-aminobenzoate, colourless needles, m. p. 52°.

Ethyl phenylacetate-4-*thiocarbimide*, colourless needles, m. p. 58°, from ligroin (Found: S, 14·7. $C_{11}H_{11}O_2NS$ requires S, 14·5%), *ethyl cinnamate*-4-*thiocarbimide*, short golden needles, m. p. 62° (Found : S, 13·45. $C_{12}H_{11}O_2NS$ requires S, 13·7%), and *ethyl* β-*phenylpropionate*-4-*thiocarbimide*, a pale yellow oil, b. p. 296° (Found : S, 13·45. $C_{12}H_{13}O_2NS$ requires S, 13·6%), were prepared from ethyl *p*-nitrophenylacetate, *p*-nitrocinnamate, and β-*p*-nitrophenylpropionate, respectively, by the above method.

3 : 4 : 5-*Trimethoxyphenylthiocarbimide*.—1 : 2 : 3-Trimethoxybenzene (20 g.) in glacial acetic acid (100 ml.) was slowly added to a mixture of concentrated nitric acid (250 ml.) and water (500 ml.) at 20—25°. After 1 hour, the precipitated 5-nitro-1 : 2 : 3-trimethoxybenzene was removed and recrystallised from glacial acetic acid, forming long yellow needles (16 g.), m. p. 247° (decomp.). Reduction to trimethoxyaniline was carried out with tin and hydrochloric acid, and the product extracted with warm benzene. After recrystallisation from alcohol, it formed long colourless needles (6 g.), m. p. 113°. By solution in chloroform and agitation with a suspension of thiocarbonyl chloride in water, the corresponding *thiocarbimide* was produced; colourless plates, m. p. 65° (Found : S, 14·2. $C_{10}H_{11}O_3NS$ requires S, 14·2%).

The characteristics of a number of derivatives of thiourethane (ethyl thioncarbamate), R·NH·CS·OEt, prepared during the course of this work are tabulated below.

R.	M. p.	Appearance.	R.	M. p.	Appearance.
1-Naphthyl	106°	Colourless needles	4-Carbethoxyphenyl	118°	Colourless needles
2-Naphthyl	92	Colourless plates	4-Carbopropoxyphenyl	97	Short colourless needles
Acenaphthyl-3	140	Brownish plates	4-Carbobutoxyphenyl	83	Colourless needles
3-Carboxyphenyl	210	Short colourless needles	4-Carbamoxyphenyl	67	Colourless needles
4-Carboxyphenyl	212	Colourless needles	Ethyl phenylacetate-4	69	Needles
2-Carbomethoxyphenyl	70	Colourless plates	Ethyl cinnamate-4	128	Small colourless needles
3-Carbomethoxyphenyl	104	Colourless plates	4-Acetamidophenyl	173	Colourless felted needles
4-Carbomethoxyphenyl	121	Short colourless needles	3 : 4-Dichlorophenyl	125	Colourless felted needles
2-Carbethoxyphenyl	48	Colourless plates	3 : 4 : 5-Trimethoxyphenyl	132	Colourless plates
3-Carbethoxyphenyl	76	Short colourless needles			

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[*Received, July* 18*th*, 1933.]