

## Studies in Friedel-Crafts' Reaction of Isothiocyanates. Part I. Aryl Isothiocyanates

K. K. Ginwala and J. P. Trivedi

*p*-Tolyl and *p*-anisyl isothiocyanates have been condensed with various aromatic hydrocarbons, phenols, polyhydric phenols, nitrophenols, and ethers to afford the corresponding thionamides. Effect of various catalysts, solvents, and catalyst ratio have also been investigated.

Condensation of phenyl isothiocyanate has been studied at random with different aromatic compounds in presence of acidic reagents<sup>1-3</sup>. A systematic investigation of the Friedel-Crafts reaction of aryl isothiocyanates with aromatic hydrocarbons, ethers, phenols, and polyhydroxyphenols has been undertaken and the results have been discussed in this communication.

Effect of the various condensing Lewis acids, such as, hydrogen chloride, zinc chloride, and anhydrous aluminium chloride, on the condensation has been systematically evaluated.

*p*-Anisyl and *p*-tolyl isothiocyanates in turn have been condensed with benzene, anisole, phenol, *o*- and *p*-chlorophenol, *p*-nitrophenol, quinol, resorcinol, and naphthols. In all cases, corresponding thionamides have been invariably obtained, the constitution of which has been confirmed by their alkaline hydrolysis to the corresponding acids. Yields of thionamides varied according to the catalyst and the solvent employed for the reaction. It has been observed that optimum yields of thionamides are obtained when a large excess of the Lewis acid is employed. The optimum ratio of isothiocyanate to the Lewis acid should be 1:20, whereas the optimum ratio of isothiocyanate to the compound to be condensed should be 1:5. Variations in this ratio considerably lessened the yields of thionamides.

Selectivity of the Lewis acid is another vital factor. It is observed that in absence of catalyst, there is practically no reaction; in presence of hydrogen chloride about 10 to 15% yields of thionamides are obtained; in presence of anhydrous zinc chloride, yields range from 20 to 35% and in presence of anhydrous aluminium chloride, the thionamides are obtained in 35 to 50% yield, depending on the nature of the compound condensed. Solvent seems to have an equally important role on the yield. Nitrobenzene as a solvent provided very poor yields, whereas carbon disulphide was found to be the most efficient solvent. Without solvent the yields of thionamides with aluminium chloride were 35 to 50% which were improved to 50 to 60% and in few cases up to 76%. Various thionamides prepared are described in Table I.

### EXPERIMENTAL

*p*-Tolyl and *p*-anisyl isothiocyanates were prepared according to the standard procedure<sup>4</sup> available. Following procedure illustrates the conditions providing optimum yields of thionamides.

\*All melting points are uncorrected.

1. Gattermann and Friedmann, *Ber.*, 1892, 25, 3525.
2. Karrer and Weiss, *Helv. Chim. Acta*, 1929, 12, 554.
3. River and Kunz, *ibid.*, 1932, 15, 376.
4. Vogel, "Practical Organic Chemistry", Longmans, Green and Co., London, 1951

4-Hydroxy-N-p-anisylthionbenzamide (No. 3 in Table I).—To a mixture of p-anisyl isothiocyanate (0.0149g., 0.001M), powdered anhydrous aluminium chloride (2.67g., 0.02M), and CS<sub>2</sub> (30 ml) was gradually added with shaking phenol (0.47 g., 0.005M) solution in CS<sub>2</sub> (5ml). An immediate colour change took place, indicating exothermic reaction. The mixture was protected from moisture (guard tube) and kept overnight at the room temperature. The reaction mixture was then refluxed on a water bath for 4 hours to ensure completion of the reaction. CS<sub>2</sub> was distilled and the product decomposed with ice and HCl (conc.). The crude mass obtained was washed several times with cold water and triturated for few minutes with cold alkali. It was washed with cold water and crystallised from ethylacetate in colorless needles, m.p. 218°, yield 0.15 g. (about 60%).

The above thionamide, when refluxed with 20% NaOH solution for 6 hours and the reaction product isolated by acidification of the solution, concentration to some extent, and ether extraction, afforded a product identified as p-hydroxybenzoic acid, m.p. (mixed m.p. with authentic sample) 213°. Mixed melting point of the product (absence of N and S) with thionamide was depressed to 160°.

All compounds described in the table were prepared and their constitutions (of a selected few) were confirmed by the procedures described above.

TABLE I

No.	Compound.	M.P.	Formula.	% Sulphur.	
				Found.	Reqd.
1	N-p-Anisyl-T.B.*	128°	C <sub>14</sub> H <sub>13</sub> ONS	13.0	13.2
2	N-p-Anisyl-T.A.*	157°	C <sub>13</sub> H <sub>13</sub> O <sub>2</sub> NS	11.6	11.7
3	4-Hydroxy-N-p-anisyl-T.B.	218°	C <sub>14</sub> H <sub>13</sub> O <sub>2</sub> NS	12.0	12.3
4	1-Hydroxy-2-chloro-N-p-anisyl-T.B.	215°	C <sub>14</sub> H <sub>12</sub> O <sub>2</sub> NCIS	10.7	10.9
5	2-Hydroxy-5-chloro-N-p-anisyl-T.B.	207°	"	10.8	10.9
6	2-Hydroxy-5-nitro-N-p-anisyl-T.B.	215°	C <sub>14</sub> H <sub>12</sub> O <sub>4</sub> N <sub>2</sub> S	10.3	10.5
7	N-p-Anisyl-T.G.*	215°	C <sub>14</sub> H <sub>13</sub> O <sub>3</sub> NS	11.5	11.7
8	1-Hydroxy-N-p-anisyl-2-T.N.*	210°	C <sub>10</sub> H <sub>13</sub> O <sub>2</sub> NS	10.3	10.4
9	N-p-Tolyl-T.B.	179°	C <sub>14</sub> H <sub>13</sub> NS	13.8	14.1
10	N-p-Tolyl-T.A.	172°	C <sub>13</sub> H <sub>13</sub> ONS	13.2	13.4
11	4-Hydroxy-N-p-Tolyl-T.B.	163°	C <sub>14</sub> H <sub>13</sub> ONS	13.1	13.3
12	1-Hydroxy-2-chloro-N-p-tolyl-T.B.	150°	C <sub>14</sub> H <sub>13</sub> ONCIS	11.3	11.5
13	2-Hydroxy-5-chloro-N-p-tolyl-T.B.	180°	"	11.3	11.5
14	2-Hydroxy-5-nitro-N-p-tolyl-T.B.	180°	C <sub>14</sub> H <sub>12</sub> O <sub>4</sub> N <sub>2</sub> S	10.8	11.1
15	N-p-Tolyl-thion-β-resoreylamide	180°	C <sub>14</sub> H <sub>13</sub> O <sub>2</sub> N <sub>2</sub> S	12.1	12.3
16	N-p-Tolyl-T.G.*	172°	"	12.0	12.3

\*T.B. stands for thionbenzamide; T.A. stands for thionanisamide; T.G. stands for thiongentisamide; T.N. stands for thionaphthamide.

Sincere thanks of the authors are due to the Gujarat University for awarding a research grant to one of them (J.P.T.), but for which it would have been difficult to undertake this investigation.