

From the above observations, it seems clear that Nakatsuka and Chang have found interesting complexes of praseodymium(III) and neodymium(III) which are stable in ammoniacal solutions without the precipitation of the hydroxides. However, their proposal of the existence, in solution, of oxidation states of praseodymium and neodymium greater than three does not appear tenable.

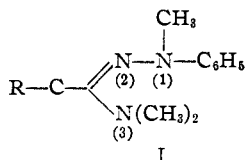
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## The Preparation of Some Tetrasubstituted Amidrazones

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We became interested in the preparation of tetrasubstituted amidrazones<sup>1</sup> of the general structure I as intermediates of possible value in another synthesis.



reaction of the corresponding hydrazine with a nitrile, imido ester or imido chloride.<sup>2</sup> However, these methods are inapplicable to the synthesis of tetrasubstituted amidrazones, and no record of any completely substituted amidrazones could be found in the literature.

The synthesis of amidrazones of the type I has now been effected easily and in good yield by the condensation of the appropriately substituted amides and hydrazines in refluxing benzene in the presence of phosphorus oxychloride. In this manner, the N<sup>1</sup>,N<sup>3</sup>,N<sup>3</sup>-trimethyl-N<sup>1</sup>-phenylamidrazones of propionic, isobutyric and phenylacetic acids have been prepared; their characterization is summarized in Tables I and II.

### Experimental

**Dimethylamides.**—The dimethylamides of propionic, isobutyric and phenylacetic acids were prepared by passing dry dimethylamine for two hours into a cooled, 50% solution of the respective acid chloride in benzene. The mixture was then filtered from dimethylamine hydrochloride, the precipitate washed with benzene, and the combined filtrate and washings distilled to give 90–95% yields of dimethylamide: N,N-dimethylpropionamide, b. p. 173–174°,  $n_D^{25}$  1.4402 (reported<sup>3</sup> b. p. 179.2–179.4° (765 mm.),  $n_D^{25}$  1.4371); N,N-dimethylisobutyramide, b. p. 178–179°,  $n_D^{25}$  1.4388; N,N-dimethylphenylacetamide, b. p. 155° (10 mm.), m. p. 43–44° (reported<sup>5</sup> b. p. 155° (10 mm.), m. p. 43.5°).

TABLE I

-R	Yield, %	B. p., °C.	Mm.	$n_D^{25}$	Formula	Analyses, % <sup>a</sup>								
						Carbon		Hydrogen		Nitrogen		Equiv. wt. <sup>b</sup>		
						Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	$pK_a$ <sup>b</sup>
CH <sub>3</sub> CH <sub>2</sub>	82	134	3	1.5618	C <sub>12</sub> H <sub>19</sub> N <sub>3</sub>	70.2	70.2	9.3	9.1	20.5	20.4	205	210	9.3
(CH <sub>3</sub> ) <sub>2</sub> CH	57	127	2	1.5538	C <sub>13</sub> H <sub>21</sub> N <sub>3</sub>	71.2	71.4	9.7	9.5	19.2	19.4	219	220	9.5
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	40			1.6008	C <sub>17</sub> H <sub>21</sub> N <sub>3</sub>	76.4	76.5	7.9	7.7	15.7	15.7	267	268	8.0

<sup>a</sup> Microanalyses by V. H. Tashinian of this Laboratory. <sup>b</sup> Apparent  $pK_a$  values and equivalent weights were obtained by potentiometric titration with 0.1 *N* hydrochloric acid of 1–1.5 millimoles of amidrazone in 15 ml. of ethanol and 10 ml. of water. <sup>c</sup> Ordinary distillation caused decomposition; consequently purification was effected through the picrate (see Table II). The free base was liberated from the picrate with lithium hydroxide, extracted into ether, and distilled in a cold-finger sublimation apparatus at 200° (1 mm.) as a viscous oil.

TABLE II

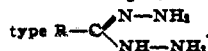
### PICRATES<sup>a</sup> OF AMIDRAZONES OF TABLE I

-R	M. p. <sup>b</sup> °C.	Formula	Analyses, %					
			Carbon		Hydrogen		Nitrogen	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
CH <sub>3</sub> CH <sub>2</sub>	173–174	C <sub>18</sub> H <sub>23</sub> N <sub>6</sub> O <sub>7</sub>	49.8	49.6	5.1	5.1	19.4	19.5
(CH <sub>3</sub> ) <sub>2</sub> CH	150–151	C <sub>19</sub> H <sub>24</sub> N <sub>6</sub> O <sub>7</sub>	50.9	51.1	5.4	5.2	18.7	19.1
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	144–145	C <sub>23</sub> H <sub>24</sub> N <sub>6</sub> O <sub>7</sub>	55.6	55.5	4.9	4.7	16.9	17.1

<sup>a</sup> The picrates were prepared by adding a saturated ethanolic solution of picric acid to the amidrazone in ethanol and were recrystallized from ethanol. <sup>b</sup> Corrected.

Both unsubstituted and monosubstituted amidrazones have been previously prepared by the

(1) This type of compound has also been referred to as a hydrazidine and as the hydrazone of an amide. Of the three possibilities, the amidrazone nomenclature appears to be the most concise and unambiguous. For example, the first compound in Table I (R = CH<sub>3</sub>CH<sub>2</sub>), in analogy with amidine nomenclature, would thus be named N<sup>1</sup>,N<sup>1</sup>,N<sup>1</sup>-trimethyl-N<sup>1</sup>-phenylpropionamidrazone. The hydrazidine designation could then be reserved for compounds of the



Amidrazones.—The tetrasubstituted amidrazones listed in Table I were prepared by the following general procedure. To a solution of 15.4 g. (0.1 mole) of phosphorus oxychloride in 50 ml. of dry benzene, heated under reflux,

(2) Wieland, "Die Hydrazine," Ferdinand Enke, Stuttgart, 1913, p. 192.

(3) Ruhoff and Reid, *THIS JOURNAL*, **59**, 401 (1937).

(4) C. A., **40**, 3725<sup>9</sup> (1946), reports this compound as boiling at 175–176° (7 mm.). This is undoubtedly a typographical error; the original article [Gavrilov, Koperina and Klyucharsava, *Bull. soc. chim. France*, [5] **12**, 773 (1945)] was unavailable.

(5) Taverna, *Res. trav. chim.*, **16**, 38 (1907).

was added with stirring during one-half hour a solution of 12.2 g. (0.1 mole) of  $\alpha$ -methyl- $\alpha$ -phenylhydrazine and 0.1 mole of the requisite dimethylamide in 25 ml. of dry benzene. Stirring and refluxing were continued for five hours after which the reaction mixture was cooled, treated with 50 g. of ice, and basified with 10 *N* sodium hydroxide. The mixture was extracted with three 100-ml. portions of ether and the combined ether extracts were dried over magnesium sulfate, filtered, and distilled to give the amidrazone.

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### Triphenylmethyl Selenocyanate

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Triphenylmethyl thiocyanate<sup>1</sup> is, in contrast to the corresponding chloride and bromide, a fairly stable compound. It is not attacked by cold water<sup>2</sup> and so slowly alcoholized by methanol and ethanol that it can be recrystallized without alteration from these solvents<sup>3,4</sup>; it melts without decomposition and can be sublimed<sup>2</sup> and even distilled under reduced pressure.<sup>2</sup> It seemed thus of interest to prepare the hitherto unknown corresponding selenocyanate and to study its behavior.

Triphenylmethyl selenocyanate,  $(C_6H_5)_3C-SeCN$ , may be prepared by mechanically shaking a solution of freshly prepared triphenylmethyl chloride (8 g.) in pure dry benzene (80 cc.) with a great excess of dry, finely-powdered potassium selenocyanate (8 g.) for five hours at room temperature in a closed brown bottle. Soon after the addition of the potassium selenocyanate, the solution turns slightly yellow and gradually a red pitchy matter separates out together with potassium chloride. After evaporation of the solvent from the filtered benzene solution under reduced pressure in a dry nitrogen atmosphere and protected from daylight, the remaining solid residue appeared as very lustrous yellowish crystals mixed with a few particles of red selenium. This material, after solution in boiling petroleum ether, filtration while hot from the small quantity of gray selenium, and cooling to 0°, yielded colorless and odorless prismatic needles of adamantane luster. The average yield of several preparations was 58%.

Anal. Calcd. for  $C_{20}H_{15}NSe$ : N, 4.02; Se, 22.67. Found: N, 3.98; Se, 22.70.

The substance, freshly crystallized from petroleum ether, shows the "instantaneous melting point"<sup>5</sup> of 129.5–130.5° and soon after melting decomposes with separation of red selenium. When slowly heated in sealed capillaries it melts at lower and irregular temperatures. Heating to 100° under 3 mm. for many hours does not alter the substance. It decomposes under the action of the sunlight with gradual separation of red selenium, but it stays unaltered for several months when kept in a desiccator carefully protected against the daylight.

The selenocyanate is insoluble in cold and hot water, very slightly soluble in cold petroleum ether, ether, glacial acetic acid, methanol, ethanol and other alcohols; soluble, without decomposition and coloration, in cold dry chloroform, carbon tetrachloride, carbon disulfide, acetone, benzene, aniline, dimethylaniline, pyridine and quinoline

(the solutions in the hot basic solvents become yellow without separation of selenium). When kept under a layer of pure alcohols it decomposes slowly at room temperature with gradual separation of selenium and formation of hydrogen cyanide. Heated for a few instants in a water-bath to 60–70° with pure alcohols (methanol, ethanol, propanols, *n*-butanol, isoamyl, benzyl,  $\beta$ -phenylethanol) the selenocyanate dissolves with rapid decomposition which, once initiated, continues, out of the bath, with evolution of hydrogen cyanide and quantitative separation of the selenium. From such solutions the methyl, ethyl and benzyl triphenylmethyl ethers were isolated and identified by their melting points (85, 83 and 105.5°) and mixed melting points with authentic samples of these substances. The alcoholysis of the selenocyanate is therefore much more pronounced than that of the corresponding thiocyanate.<sup>4</sup> In warm aqueous alcohols (for example in 60% methanol or ethanol) hydrolysis takes place instead of alcoholysis with formation of triphenylcarbinol, hydrogen cyanide and selenium. The same happens in aqueous acetone (for example, with 10% water); in a quantitative experiment 99.6% of the selenium content of the selenocyanate was recovered in the elementary state. In this solvent mixture the thiocyanate also is completely hydrolyzed, though in a slower way; thus, from 0.3 g. of the substance, after boiling in a mixture of 25 cc. of 80% acetone for four hours, 96.4% of the theoretical amount of thiocyanic acid formed was found in the solvent. Cold water does not alter appreciably the crystallized selenocyanate, probably because of the insolubility. However, by shaking the finely powdered substance mechanically for twenty-four hours at 20–22° in a closed dark-brown bottle with a great amount of water and some glass beads—a procedure which does not alter the thiocyanate<sup>2</sup>—a slight decomposition of the compound (light reddish color) is observed and the presence of hydrogen cyanide could be proved in the water as well as in the atmosphere inside the bottle. Heated with boiling water, the substance (0.3 g.) presents after one minute a weak reddish color which becomes after half an hour pronouncedly red (m. p. 104–130°) and, nine hours later an examination showed that it had changed into the carbinol (m. p. unsharply at 162°). Aqueous solutions of inorganic bases (6 *N* sodium, potassium or ammonium hydroxide) or mineral acids (3 *N* hydrochloric or sulfuric acid) do not attack the selenocyanate. Concentrated sulfuric acid dissolves them giving initially a yellow color, identical to the halochromic color with the chloride or thiocyanate,<sup>2</sup> which passes slowly to red with turbidity of the liquid. Glacial acetic acid attacks the rather insoluble substance in the cold only very slowly, but at 85–90° dissolves it with a slow separation of selenium; with 80% acetic acid this reaction is much more pronounced, either cold or hot. The action of 98% butyric acid and 85% lactic acid is analogous, but 100% formic acid, which also alters the practically insoluble selenocyanate only very slowly in the cold, brings about at 90° a rapid separation of selenium with an intense yellow color.

Triphenylmethyl thiocyanate and selenocyanate are isomorphous giving a continuous series of mixed crystals.

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### The Precipitation of Insulin by Thiocyanate<sup>1</sup>

BY MARGARET H. SCHWERT AND HANS NEURATH

Preliminary to an electrophoretic investigation of the interaction of insulin with sodium thiocyanate, Volkin<sup>2</sup> found that, whereas thiocyanate in-

(1) Part of a thesis submitted by Margaret H. Schwert to the Faculty of the Graduate School of the University of Minnesota, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Volkin, *J. Biol. Chem.*, **175**, 875 (1948).

(1) K. Elbs, *Ber.*, **17**, 700 (1884).

(2) H. Lecher and K. Simon, *ibid.*, **54**, 635 (1921).

(3) I. Lifschitz, *ibid.*, **58**, 2439 (1925).

(4) A. Hantzsch and A. Burawoy, *ibid.*, **63**, 1181 (1930).

(5) J. Timmermans, "Chemical Species," Chemical Publishing Co., New York, N. Y., 1940, p. 26.