Oxidation of Chloroacetic Acid in Refluxing Xylene.—A solution of 4.73 g (50.0 mmoles) of chloroacetic acid and 19.0 g (200 mmoles) of pyridine N-oxide in 150 ml of xylene was heated at reflux for 3.5 hr. The procedure and work-up of the reaction mixture were the same as those for the α-bromobutyric acid reaction.

The yield of carbon dioxide was 100% and that of formaldehyde as its 2,4-dinitrophenylhydrazone was 65.0%. After three recrystallizations from ethanol, the derivative had mp 160–163° (lit.[7] mp 166°). The weight of black, hard, water-soluble solid (salt) that separated from the reaction mixture was 11.8 g.

Reactions of Phenyl Isothiocyanate with Metal Derivatives of Pyrrole[1]

E. P. PAPADOPOULOS[2]

The Chemical Laboratory of Harvard University, Cambridge, Massachusetts

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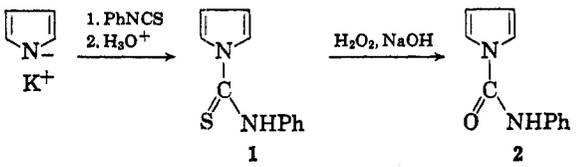
Phenyl isothiocyanate is known to react with aromatic compounds (in the presence of Lewis acids),[3,4] Grignard reagents,[5,6] and alkali metal derivatives of active methylene compounds,[3,6,7] acetylenes,[6] amides,[8] and sulfonamides[6] to form the corresponding thioanilides. With pyrrole and its homologs,[9] 2-pyrrolethiocarbanilides are formed, unless both α positions are occupied. Then reaction occurs at a β position, and when all carbon atoms are occupied, there is no reaction.

In view of the results of reactions of phenyl isocyanate with metal derivatives of pyrrole,[10] a brief investigation was undertaken of similar reactions of phenyl isothiocyanate. Pyrrolylpotassium reacts with phenyl isothiocyanate in tetrahydrofuran to give 1-pyrrolethiocarbanilide (**1**). Whereas the potassium salt of 1-pyrrolecarboxanilide (**2**) is hydrolyzed readily,[10] that

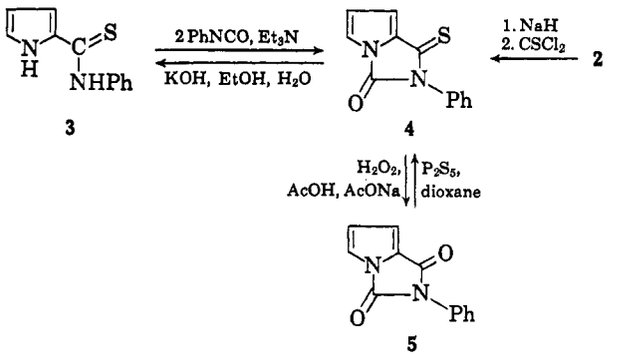


1 2

of **1** is apparently stable in aqueous solution, and precipitation of **1** occurs only after acidification. The structure formulated for **1** is supported by its oxidation to **2** with alkaline hydrogen peroxide.

The reaction of pyrrolylmagnesium bromide with phenyl isothiocyanate in ethyl ether yields a mixture of 1- (75%) and 2-pyrrolethiocarbanilide (**3**) (25%). When tetrahydrofuran is used as the solvent, the results are very similar. A 70:30 mixture of 1- and 2-pyrrolethiocarbanilide is obtained both at room and at reflux temperature.

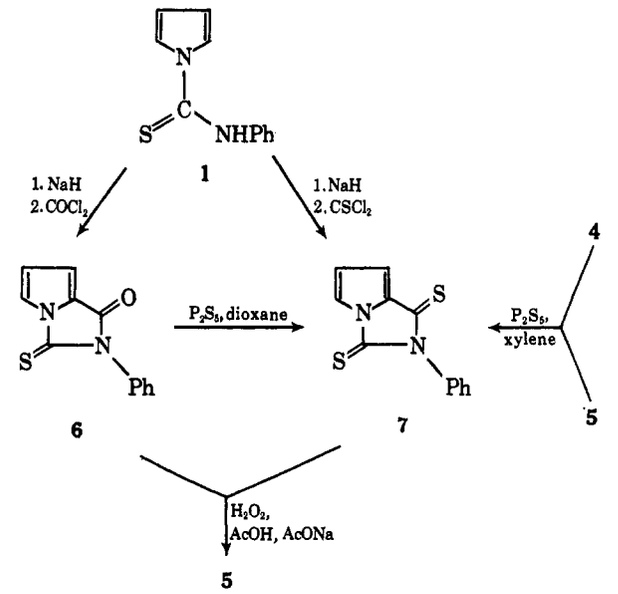
In the presence of triethylamine, 2-pyrrolethiocarbanilide (**3**)[9] reacts spontaneously with 2 equiv of phenyl isocyanate to produce 2-phenylpyrrolo-[1,2-*c*]-1-thiohydantoin (**4**) and N,N′-diphenylurea. This reaction takes place much more easily than the corresponding reaction of 2-pyrrolecarboxanilide,[10]



3 4 5

and resembles the conversion of enamine thioanilides into thiouracils by the action of phenyl isocyanate.[11] The structure assigned to **4** is confirmed by its oxidation to 2-phenylpyrrolo[1,2-*c*]hydantoin (**5**)[10] with hydrogen peroxide, and by its formation from **5** by the action of phosphorus pentasulfide. Further, **4** was obtained from the sodium salt of 1-pyrrolecarboxanilide (**2**) and thiophosgene, and, in small amounts, from the products of the reaction of the potassium and sodium salts of 2-pyrrolethiocarbanilide (**3**) with phosgene. Finally, alkaline hydrolysis of **4** afforded the expected **3**.

Probably because of the lower reactivity of phenyl isothiocyanate toward nucleophiles, as compared with phenyl isocyanate,[3] attempts to cause the former reagent to react with 2-pyrrolecarboxanilide[12] and 2-pyrrolethiocarbanilide, in the presence of triethylamine, did not yield the desired products **6** and **7**. Also unsuccessful were attempts to prepare these compounds from thiophosgene and the potassium or sodium salts



(1) This study was supported by the National Institutes of Health Grant CA 01696-14.

(2) On leave (1965–1966) from the Department of Chemistry of the American University of Beirut, Beirut, Lebanon.

(3) P. A. S. Smith, "The Chemistry of Open-Chain Organic Nitrogen Compounds," Vol. I, W. A. Benjamin, Inc., New York, N. Y., 1965, pp 241–243.

(4) K. K. Ginwala and J. P. Trivedi, *J. Indian Chem. Soc.*, **40**, 897 (1963).

(5) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall Co., Inc., New York, N. Y., 1954, p 1200.

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(11) G. Bianchetti, P. Dalla Croce, and D. Pocar, *Gazz. Chim. Ital.*, **94**, 606 (1964).

(12) A. Treibs and W. Ott, *Ann.*, **577**, 119 (1952).

of 2-pyrrolecarboxanilide and 2-pyrrolethiocarbanilide, respectively. Eventually, 2-phenylpyrrolo[1,2-*c*]-3-thiohydantoin (**6**) was obtained from the sodium salt of **1** by the action of phosgene. Similarly, the reaction of the sodium salt of **1** with thiophosgene led to 2-phenylpyrrolo[1,2-*c*]dithiohydantoin (**7**). Both **6** and **7** are oxidized to 2-phenylpyrrolo[1,2-*c*]hydantoin (**5**) with hydrogen peroxide, in the presence of acetic acid and sodium acetate. Phosphorus pentasulfide converts **6** to **7**, which is also obtained by the action of the same reagent on **4** and **5**. It is noteworthy that in this respect the reactivity of the 3-carbonyl is much lower than that of the 1-carbonyl. Thus, whereas refluxing with phosphorus pentasulfide in dioxane for 6 hr converted **5** into **4**, and **6** into **7**, the same treatment left **4** unchanged, and the conversion of **4** or **5** into **7** required prolonged refluxing with the reagent in xylene.

Experimental Section[13]

1-Pyrrolethiocarbanilide (1).—A solution of 18.4 g (0.275 mole) of pyrrole in 100 ml of tetrahydrofuran was stirred at reflux, under a nitrogen atmosphere, with 9.7 g (0.250 g-atom) of potassium until all the metal had reacted. To the resulting slurry of pyrrolylpotassium 250 ml of tetrahydrofuran was added and, after the temperature had been adjusted to 25°, a solution of 30.4 g (0.225 mole) of phenyl isothiocyanate in 100 ml of tetrahydrofuran was introduced dropwise over a period of 1 hr. The reaction mixture was stirred at room temperature for an additional 18 hr, the solvent was removed by distillation under reduced pressure, and the residual thick liquid was dissolved in 150 ml of water. Acidification of this solution with cold, dilute hydrochloric acid caused the precipitation of a heavy oil, which solidified by cooling within a few minutes to 43.0 g of crude product, mp 80–82°. One recrystallization from petroleum ether (bp 66–75°) gave 39.5 g (87%) of 1-pyrrolethiocarbanilide, mp 83.5–84.5°.

Anal.[14] Calcd for $C_{11}H_{10}N_2S$: C, 65.33; H, 4.98; N, 13.86; S, 15.83. Found: C, 65.50; H, 5.10; N, 13.88; S, 15.67.

Oxidation of 1-Pyrrolethiocarbanilide (1) to 1-Pyrrolecarboxanilide (2).—To a solution of 1 pellet of sodium hydroxide in a mixture of 9 ml of ethyl alcohol and 1 ml of water 0.2 g of **1** was added and the resulting solution was cooled in an ice–water bath.[9] With shaking, 1 ml of hydrogen peroxide (30%) was introduced dropwise, and the mixture was left to stand in the cooling bath for 0.5 hr. Dilution with 100 ml of water and filtration yielded 0.13 g of a solid, mp 150–151°, the infrared spectrum of which was identical with that of 1-pyrrolecarboxanilide (**2**).[10] After one recrystallization from methanol the melting point was 152–153°, undepressed on admixture with an authentic sample of **2**.

Reaction of Pyrrolylmagnesium Bromide with Phenyl Isothiocyanate. A. In Ethyl Ether.—Pyrrolylmagnesium bromide was prepared under a nitrogen atmosphere by the dropwise addition over a period of 0.5 hr of 15.1 g (0.225 mole) of pyrrole dissolved in 100 ml of ether to a solution of ethylmagnesium bromide made from 32.7 g (0.300 mole) of ethyl bromide and 6.1 g (0.250 g-atom) of magnesium in 200 ml of ether. Into the stirred reaction mixture, diluted with 100 ml of ether and cooled to room temperature, a solution of 28.4 g (0.210 mole) of phenyl isothiocyanate in 100 ml of ether was introduced dropwise, over a period of 1 hr. The resulting solution was stirred at room temperature for 25 hr, and it was hydrolyzed with a solution of 27 g of ammonium chloride in 200 ml of water. The combined organic layer and an ether extract of the aqueous layer were treated with decolorizing charcoal and dried over anhydrous magnesium sulfate. Removal of the solvent by distillation under reduced pressure yielded a thick, yellow liquid, which solidified by trituration with petroleum ether (bp 20–40°) and cooling in an ice bath. The infrared spectrum of the crude product (31.0 g, 73%), by comparison with the spectrum of each of a series of mixtures of **1** and **3** of known composition, showed that it was a mixture of 1- (75%) and 2-pyrrolethiocarbanilide (25%).

B. In Tetrahydrofuran.—Pyrrolylmagnesium bromide was prepared as previously from 6.1 g (0.25 g-atom) of magnesium, 30.5 g (0.28 mole) of ethyl bromide, and 15.4 g (0.23 mole) of pyrrole in a total of 250 ml of tetrahydrofuran. After cooling to room temperature, a solution of 28.4 g (0.21 mole) of phenyl isothiocyanate in 100 ml of tetrahydrofuran was added over 1 hr to the reaction mixture, which was then stirred for 20 hr. Hydrolysis with 200 ml of water containing 27 g of ammonium chloride (as in the previous treatment) yielded 34.5 g (81%) of a mixture of 1- (70%) and 2-pyrrolethiocarbanilide (30%).

This reaction was repeated in exactly the same manner except that the mixture was brought to boiling prior to the addition of phenyl isothiocyanate and was kept refluxing throughout the duration of the reaction. The product was 33.0 g (78%) of the same mixture as before.

2-Pyrrolethiocarbanilide (3).[9]—A mixture of 16.7 g (0.25 mole) of pyrrole and 33.8 g (0.25 mole) of phenyl isothiocyanate was heated in an oil bath at 110–115° (bath temperature) for 72 hr. The black, tarry product was transferred to a 1-l., round-bottomed flask and was refluxed repeatedly with petroleum ether (bp 66–75°). Filtration and cooling of the successive solutions yielded a total of 25.0 g of crude product, which was recrystallized twice from the same solvent to give 20.5 g (40%) of **3**, mp 92–94° (lit.[9] mp 96–97°), pure enough for most purposes.

2-Phenylpyrrolo[1,2-*c*]-1-thiohydantoin (4).—Addition of 5 ml of triethylamine to a mixture of 4.0 g (0.02 mole) of 2-pyrrolethiocarbanilide (**3**) and 4.8 g (0.04 mole) of phenyl isocyanate caused a vigorous, exothermic reaction. The orange-red, solid product was left to stand for 15 min, washed with 40 ml of petroleum ether (bp 20–40°), and mixed thoroughly with 100 ml of chloroform. The insoluble part (4.0 g), collected by filtration and washed with two 30-ml portions of chloroform, was identified as N,N′-diphenylurea by its infrared spectrum, melting point (241–242°), and undepressed mixture melting point with an authentic sample. Evaporation to dryness under reduced pressure of the combined chloroform filtrate and washings yielded 4.2 g of crude product, which, upon recrystallization from 95% ethyl alcohol, gave 3.3 g (72%) of **4**, orange-red needles, mp 139–140°. An analytical sample melted at 139.5–140.5°.

Anal. Calcd for $C_{12}H_8N_2OS$: C, 63.16; H, 3.53; N, 12.28; S, 14.02. Found: C, 63.00; H, 3.70; N, 12.34; S, 13.62.

Compound **4** was also obtained as follows.

A. From 1-Pyrrolecarboxanilide (2).—A mixture of 9.3 g (0.05 mole) of **2**,[10] 4.3 g of a 56% sodium hydride dispersion in mineral oil (0.10 mole of NaH), and 30 ml of tetrahydrofuran was stirred until evolution of hydrogen had stopped. After dilution with 200 ml of cyclohexane and dropwise introduction of a solution of 5.7 g (0.05 mole) of thiophosgene in 50 ml of cyclohexane, the mixture was stirred at room temperature for 3 hr and at reflux for a further 3 hr. It was then cooled and filtered, and the filtrate was combined with ether washings of the precipitate. This solution was evaporated to dryness under reduced pressure, and the residue was crystallized from 95% ethyl alcohol to yield 6.2 g of dark brown crystals. Three recrystallizations, with use of decolorizing charcoal, yielded 3.1 g of orange-red crystals, mp 131–133°, the infrared spectrum of which showed that they were **4** contaminated with starting material (**2**). Further recrystallization yielded pure **4**, mp 138–140°.

B. From 2-Phenylpyrrolo[1,2-*c*]hydantoin (5).—A mixture of 1 g of **5**,[10] 2 g of phosphorus pentasulfide, and 30 ml of dioxane[15] was refluxed for 3 hr. A further 2 g of phosphorus pentasulfide was then added, and refluxing was continued for another 3 hr after which the mixture was filtered. Evaporation of the filtrate to dryness under reduced pressure yielded a residue which was refluxed with 80 ml of petroleum ether (bp 66–75°) for 10 min. Filtration and cooling of the solution yielded 0.8 g of red crystals, mp 135–137°, the infrared spectrum of which was identical with that of **4**. Recrystallization from 95% ethyl alcohol raised the melting point to 138–140°. There was no melting point depression on mixing with authentic **4**.

Hydrolysis of 2-Phenylpyrrolo[1,2-*c*]-1-thiohydantoin (4).—A mixture of 0.5 g of **4**, 0.5 g of potassium hydroxide, 5 ml of

(13) Melting points were determined in a Thomas–Hoover capillary melting point apparatus with use of a calibrated thermometer.

(14) The last traces of hydrocarbon solvents were extremely difficult to remove.

(15) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley and Sons, Inc., New York, N. Y., in press.

95% ethyl alcohol, and 5 ml of water was refluxed for 0.5 hr. The solution was cooled, diluted with water, and acidified with dilute hydrochloric acid. The resulting yellow precipitate, upon recrystallization from petroleum ether (bp 66–75°), yielded 0.4 g of 2-pyrrolethiocarbanilide (**3**), mp 94.5–95.5°, identified by its infrared spectrum and by mixture melting point with an authentic sample of **3**.

Oxidation of 2-phenylpyrrolo[1,2-*c*]-1-thiohydantoin (4) to 2-phenylpyrrolo[1,2-*c*]hydantoin (5).—To 1 g of **4** and 1 g of sodium acetate trihydrate in 10 ml of acetic acid,[11] 2 ml of hydrogen peroxide (30%) was added, and the mixture was stirred for 24 hr. After addition of another 2 ml of hydrogen peroxide (30%), stirring was continued for a further 42 hr. The mixture was then diluted with 100 ml of water and filtered. The precipitate, washed with water and dried (0.7 g), had an infrared spectrum identical with that of **5** and, after recrystallization from 95% ethyl alcohol, melted at 225–226°. The melting point was not depressed by mixing with an authentic sample of **5**.

2-Phenylpyrrolo[1,2-*c*]-3-thiohydantoin (6).—To a solution of 6.1 g (0.03 mole) of 1-pyrrolethiocarbanilide (**1**) in 20 ml of tetrahydrofuran 2.5 g of a 56% sodium hydride dispersion in mineral oil (0.06 mole NaH) was added, and the mixture was stirred until evolution of hydrogen had stopped. After dilution with 150 ml of cyclohexane, a solution of 4 g of phosgene in 50 ml of cyclohexane was added dropwise, and the resulting mixture was stirred at room temperature for 21 hr, and at reflux for a further 2 hr. Filtration of the product yielded a yellow solution to which were added ether washings of the precipitate. When this solution was cooled and filtered, 2 g of **6**, yellow crystals, mp 144–144.5°, was obtained. Evaporation of the filtrate to dryness under reduced pressure and recrystallization of the residue from 95% ethyl alcohol gave a further 2.4 g of **6**, mp 143–144° (total yield 65%). An analytical sample melted at 144–144.5°.

Anal. Calcd for $C_{12}H_8N_2OS$: C, 63.16; H, 3.53; N, 12.28; S, 14.02. Found: C, 62.99; H, 3.57; N, 12.37; S, 13.90.

Oxidation of 2-Phenylpyrrolo[1,2-*c*]-3-thiohydantoin (6) to 2-Phenylpyrrolo[1,2-*c*]hydantoin (5).—The reaction was carried out exactly as previously described for the conversion of **4** to **5**. The product was 0.8 g of crude **5**, identified by its infrared spectrum. After recrystallization from 95% ethyl alcohol the melting point was 225–227°, undepressed on admixture with authentic **5**.

2-Phenylpyrrolo[1,2-*c*]dithiohydantoin (7).—A mixture of 4.0 g (0.02 mole) of **1**, 1.7 g of a 56% sodium hydride dispersion in mineral oil (0.04 mole NaH), and 20 ml of tetrahydrofuran was stirred until evolution of hydrogen had stopped. After addition of 130 ml of cyclohexane, followed by dropwise introduction of a solution of 2.3 g (0.02 mole) of thiophosgene in 50 ml of cyclohexane, the reaction mixture was stirred at room temperature for 3 hr, and at reflux for a further 3 hr. It was then cooled and filtered, and the residue was washed with ethyl ether. Removal of the solvents under reduced pressure from the combined filtrate and ether washings and crystallization of the residue from petroleum ether (bp 66–75°) produced 2.0 g of dark purple crystals, mp 127–131°. Recrystallization from methyl alcohol raised the melting point to 133.5–134.5° (1.2 g, 24%). An analytical sample melted at 134–134.5°.

Anal. Calcd for $C_{12}H_8N_2S_2$: C, 59.02; H, 3.30; N, 11.47; S, 26.21. Found: C, 58.73; H, 3.42; N, 11.81; S, 26.10.

Compound **7** was also obtained as follows.

A. From 2-Phenylpyrrolo[1,2-*c*]hydantoin (5).—A mixture of 1 g of **5**, 4 g of phosphorus pentasulfide, and 30 ml of xylene[16] was refluxed for 36 hr. Filtration and evaporation of the filtrate to dryness under reduced pressure produced a residue which was refluxed with 100 ml of petroleum ether (bp 66–75°) for 10 min. A new filtration, followed by cooling of the solution, yielded 0.5 g of dark purple crystals, mp 132.5–133.5°, the infrared spectrum of which was identical with that of the product of the immediately preceding reaction. After recrystallization from methanol, the melting point was 133.5–134.5°, undepressed on admixture with **7** prepared by the previous reaction.

B. From 2-Phenylpyrrolo[1,2-*c*]-1-thiohydantoin (4).—The reaction was run as described immediately before, except that 2 g of phosphorus pentasulfide, and a 22-hr refluxing period were used. The product was 0.4 g of **7**, mp 133–134°.

C. From 2-Phenylpyrrolo[1,2-*c*]-3-thiohydantoin (6).—A mixture of 1 g of **6**, 1 g of phosphorus pentasulfide, and 30 ml of dioxane[15] was refluxed for 5 hr. The same treatment as before led to 0.6 g of **7**, mp 133–134°.

Oxidation of 2-Phenylpyrrolo[1,2-*c*]dithiohydantoin (7) to 2-Phenylpyrrolo[1,2-*c*]hydantoin (5).—The reaction was run exactly as described for the conversion of **4** to **5**. The product was 0.5 g of crude **5** identified by its infrared spectrum. Upon recrystallization from 95% ethyl alcohol, the melting point became 225–227°, and was not depressed on admixture with authentic **5**.

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On the Mechanism of the Synthesis of Phenylcyclopropanes from Allylic Chlorides and Phenyllithium

DOUGLAS E. APPLEQUIST AND MICHAEL A. LINTNER

W. A. Noyes Laboratory, University of Illinois, Urbana, Illinois 61801

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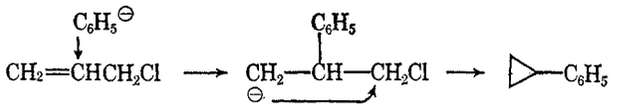
Wawzonek, Studnicka, Bluhm, and Kallio[1] have recently reported that allyl chloride reacts with phenyllithium in ether to give some phenylcyclopropane, and that some γ-substituted allyl chlorides give substituted phenylcyclopropanes. They suggested a mechanism involving β attack by a phenyl anion as shown below.



While the mechanism provides an economical interpretation of the available facts, it is sufficiently novel that critical tests of it seem in order.

A mechanism with a cyclopropene intermediate is suggested by the known formation of cyclopropenes from allylic chlorides and strong bases.[2] In this mecha-

nism, addition of phenyllithium would have to compete with the known proton abstraction reaction of cyclopropenes,[2a] but the particularly large strain of a cyclopropene with no substituents on the double bond[3] might provide sufficient driving force to enable the addition to compete.

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