

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Lithium Cleavages of Some Heterocycles in Tetrahydrofuran. II<sup>1</sup>

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A number of heterocycles have been cleaved by lithium in tetrahydrofuran. Phenothiazine, phenoxathiin and dibenzo-*p*-dioxin cleave at 25° to give the organolithium cleavage compounds, whereas at reflux phenoxathiin and dibenzo-*p*-dioxin undergo double cleavage. There was no cleavage of 2-aminodibenzo-*p*-dioxin or anisole at reflux, but 2-nitrodibenzo-*p*-dioxin yielded an unidentified acidic mixture upon hydrolysis. Triphenylamine and *N*-benzylcarbazole were cleaved at reflux to yield upon carbonation diphenylamine and carbazole, respectively; but diphenylamine could not be cleaved under reflux. It was possible to cleave *N*-phenylcarbazole at 25° to produce benzoic acid and carbazole upon carbonation of the reaction mixture. Only unidentified acidic oils were obtained from the cleavage and carbonation of phenoxathiin-10-dioxide and *N*-ethylphenothiazine-5-oxide. Both 2-chlorophenothiazine and *N*-lithio-2-chlorophenothiazine yielded phenothiazine upon carbonation after cleavage, while *N*-ethyl-3-chlorophenothiazine produced an acidic oil which was not identified. Normal cleavage of *N*-ethylphenothiazine took place at 25°, whereas at 50° ring closure occurred eliminating lithium sulfide and forming *N*-ethylcarbazole. *N*-Phenylphenothiazine cleaved normally at 25°, but did not form *N*-phenylcarbazole at 50° or at reflux. The relative ease of bond cleavage by lithium in tetrahydrofuran appears to be C-S > C-O > C-N.

Encouraging results obtained in earlier cleavage studies of heterocycles with lithium in tetrahydrofuran<sup>1</sup> led to the present extension. An attempt was made to study the effects of various groups on the cleavage reaction and to gain an insight into its applicability and scope through the cleavage of substituted and unsubstituted heterocycles. Unless otherwise stated, the cleavages were all run in tetrahydrofuran using lithium as the cleaving agent. Table I contains the compounds cleaved earlier<sup>1</sup> in addition to those reported in this study.

Phenothiazine was cleaved at 25° to produce 2-mercaptodiphenylamine. Color Test I<sup>2</sup> was never positive since the intermediate organometallic compound was destroyed by the secondary amine present.

No attempt was made to cleave phenoxathiin at 25° since this reaction proceeds smoothly in diethyl ether to yield, upon carbonation, 2-mercapto-2'-carboxydiphenyl ether and the disulfide of this same compound.<sup>3</sup> However, this reaction, when run at 50° and terminated by carbonation produced 2-mercaptophenol and phenoxathiin-4,6-dicarboxylic acid. The first of these two products resulted from the double cleavage of the parent heterocycle, while the second product presumably resulted from the dimetalation of phenoxathiin by the organometallic compound produced in the reaction.

It was necessary to reflux dibenzo-*p*-dioxin for 7 hr. in order to obtain pyrocatechol as a cleavage product. The other product, upon carbonation, was 2-carboxy-2'-hydroxydiphenyl ether.<sup>1</sup>

Although not a heterocycle, anisole was refluxed with lithium in tetrahydrofuran for 5 hr. There was a total recovery of starting material.

Noting that 3,7-dimethyldibenzo-*p*-dioxin could not be cleaved by sodium in liquid ammonia, whereas dibenzo-*p*-dioxin could be cleaved,<sup>4</sup> both 2-nitro- and 2-aminodibenzo-*p*-dioxin were subjected to the present cleavage conditions. After 17 hr. at reflux, none of the original 2-nitrodibenzo-*p*-dioxin was recovered, but there was a quantity of phenolic material, indicating cleavage had taken

place. The 2-aminodibenzo-*p*-dioxin was recovered unchanged after 2.75 hr. of reflux.

Definite proof of the cleavage of the nitrogen-carbon bond by lithium has not been reported<sup>1,5</sup> up to this time. However, after 3 hr. of reflux with lithium in tetrahydrofuran, triphenylamine yielded small quantities of diphenylamine. This reaction did not proceed at lower temperatures, but *N*-phenylcarbazole was cleaved at 30° over a period of 3 hr. to yield, upon carbonation, benzoic acid and carbazole. In diethyl ether, *N*-phenylcarbazole produced only carbazole upon carbonation after 24 hr. under reflux. *N*-Benzylcarbazole reacted after 3 hr. at reflux to produce, upon carbonation, only carbazole as a product. The benzyl lithium presumably was destroyed in the refluxing tetrahydrofuran. After 24 hr. at reflux, diphenylamine was recovered unchanged.

A rapid reaction occurred between lithium and phenoxathiin-10-dioxide or *N*-ethylphenothiazine-5-oxide. However, both compounds yielded complex reaction mixtures from which neither starting material nor identifiable product was isolated.

When lithium reacted with 2-chlorophenothiazine at 25°, there existed the possibilities of directly forming the 2-lithiophenothiazine compound with subsequent reaction with the amine, cleavage with destruction of the organolithium compound by the amine, or a combination of both reactions. The first of these reactions was the one actually realized at 25° giving rise to phenothiazine with no evidence of acidic material upon carbonation. There is only one apparent reason why the phenothiazine formed should not be cleaved since an excess of lithium was used and phenothiazine had already been cleaved at 25° in good yield. If an *N*-lithio compound were formed during the removal of the chlorine from the ring, this might hinder cleavage of the ring. Accordingly, an equivalent of phenyllithium was added to the 2-chlorophenothiazine and the resulting solution allowed to react with an excess of lithium. Phenothiazine was formed with no trace of acidic material upon carbonation. Also supporting the initial attack on the chlorine atom, rather than cleavage, is the reaction of lithium in dioxane with 2-chlorodibenzofuran. Both dibenzofuran and *o*-hydroxybiphenyl are iso-

(1) Paper I, H. Gilman and J. J. Dietrich, *J. Org. Chem.*, **22**, 851 (1957).

(2) H. Gilman and F. Schulze, *This Journal*, **47**, 2002 (1925).

(3) S. H. Eidt, Ph.D. Dissertation, Iowa State College, 1955.

(4) M. Tomita, Y. Inubushi and H. Niwa, *J. Pharm. Soc., Japan*, **72**, 206 (1952) [*C. A.*, **47**, 6428 (1953)].

(5) H. Gilman, J. B. Honeycutt, Jr., and R. K. Ingham, *J. Org. Chem.*, **22**, 338 (1957).

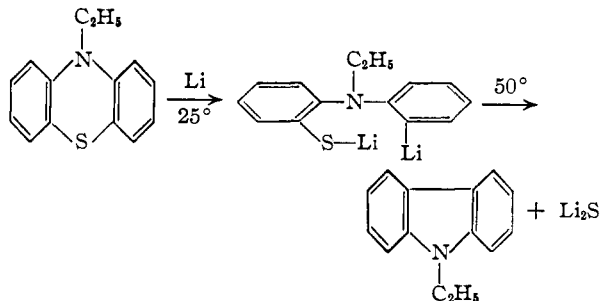
TABLE I  
 COMPOUNDS CLEAVED BY LITHIUM IN TETRAHYDROFURAN

| Compound                         | Time     | Temp., °C.      | Products on carbonation                              | %           |
|----------------------------------|----------|-----------------|--|-------------|
| Phenothiazine                    | 45 min.  | 25              | 2-Mercaptodiphenylamine                              | 36          |
| Phenoxathiin                     | 1 hr.    | 50              | 2-Mercaptophenol; phenoxathiin-4,6-dicarboxylic acid | 16<br>Trace |
| Dibenzo- <i>p</i> -dioxin        | 45 min.  | 25 <sup>a</sup> | 2-Hydroxy-2'-carboxydiphenyl ether                   | 56          |
|                                  | 7 hr.    | Reflux          | Pyrocatechol   | 13          |
| Anisole                          | 5 hr.    | Reflux          | .....  | ..          |
| 2-Aminodibenzo- <i>p</i> -dioxin | 2.75 hr. | Reflux          | .....  | ..          |
| 2-Nitrodibenzo- <i>p</i> -dioxin | 17 hr.   | Reflux          | Neutral material                                     | ..          |
|                                  |          |                 | Acidic material                                      | ..          |
| Triphenylamine                   | 3 hr.    | Reflux          | Diphenylamine  | 9           |
| Diphenylamine                    | 24 hr.   | Reflux          | .....  | ..          |
| N-Phenylcarbazole                | 3 hr.    | 30              | Benzoic acid   | 50          |
|                                  |          |                 | Carbazole  | 35          |
| N-Benzylcarbazole                | 3 hr.    | Reflux          | Carbazole  | 28          |
| Phenoxathiin-10-dioxide          | 45 min.  | 25              | Acidic material                                      | ..          |
| N-Ethylphenothiazine-5-oxide     | 45 min.  | 25              | Neutral material                                     | ..          |
|                                  |          |                 | Acidic material                                      | ..          |
| 2-Chlorophenothiazine            | 45 min.  | 25              | Phenothiazine  | 30          |
| N-Lithio-2-chlorophenothiazine   | 45 min.  | 25              | Phenothiazine  | 11          |
| N-Ethyl-3-chlorophenothiazine    | 1 hr.    | 50              | Acidic material                                      | ..          |
| N-Phenylphenothiazine            | 1 hr.    | 25              | 2-Carboxy-2'-mercaptotriphenylamine                  | 19          |
| N-Ethylphenothiazine             | 45 min.  | 25              | 2-Carboxy-2'-mercaptoethyldiphenylamine              | 51          |
|                                  | 40 min.  | 50              | N-Ethylcarbazole                                     | 27          |
| N-Benzylphenothiazine            | 45 min.  | 25              | Neutral and acidic material                          | ..          |
|                                  | 8 hr.    | Reflux          | Neutral and acidic material                          | ..          |
| Dibenzothiophene <sup>a</sup>    | 45 min.  | 50              | Biphenyl   | Trace       |
|                                  |          | 25              | Disulfide of 2-mercapto-2'-carboxybiphenyl           | Trace       |
|                                  |          |                 | 3,4-Benzothiocoumarin                                | 48          |
| Dibenzofuran <sup>a</sup>        | 45 min.  | Uncontrol.      | 3,4-Benzocoumarin                                    | 20          |
| Thianthrene <sup>a</sup>         | 45 min.  | 25°             | Acidic material                                      | ..          |
| N-Ethylcarbazole <sup>a</sup>    | 1 hr.    | Reflux          | Acidic material                                      | ..          |
| Carbazole <sup>a</sup>           | 1 hr.    | Reflux          | .....  | ..          |
| Diphenyl ether <sup>a</sup>      | 30 min.  | Uncontrol.      | Phenol   | ..          |
|                                  |          |                 | Benzoic acid   | ..          |
|                                  |          |                 | 2-Carboxydiphenyl ether                              | ..          |

<sup>a</sup> See reference 1.

lated after hydrolysis indicating that direct attack on the chlorine group is more facile than the cleavage reaction.<sup>6</sup> When N-ethyl-3-chlorophenothiazine was used, there was obtained, upon carbonation, only an acidic solid. Efforts to purify this acidic material failed, indicating that both direct attack on the chloro group and cleavage may have taken place to give a mixture of acids.

At 25°, N-ethylphenothiazine underwent a normal cleavage with lithium to yield, upon carbonation, 2-mercapto-2'-carboxyethyldiphenylamine. However, when the temperature was raised to 50°, a second step took place producing N-ethylcarbazole. This type of reaction has been reported for



(6) K. Oita, R. G. Johnson and H. Gilman, *J. Org. Chem.*, **20**, 657 (1955).

the reaction of copper on phenothiazine<sup>7,8</sup> and *n*-butyllithium on thianthrene-5-oxide.<sup>9</sup> In hopes of obtaining N-phenylcarbazole, N-phenylphenothiazine was cleaved at 25° and then refluxed for 12 hr. after removal of the excess lithium. This was done since there was also the possibility of cleavage at the N-phenyl linkage. Termination of the reaction by carbonation produced only 2-mercapto-2'-carboxytriphenylamine. In order to test an intermediate between N-ethyl- and N-phenylphenothiazine, N-benzylphenothiazine was cleaved. No N-benzylcarbazole was isolated and efforts to purify the acid fraction were unsuccessful.

#### Experimental<sup>10</sup>

The tetrahydrofuran used in all of the experiments was purified by shaking with sodium hydroxide pellets, drying over sodium metal, and finally distilling from lithium aluminum hydride prior to every reaction. An oxygen-free, dry nitrogen atmosphere was used in all reactions.

**Phenothiazine.**—A mixture of 10 g. (0.05 mole) of phenothiazine, 2 g. (0.3 g. atom) of lithium and 50 ml. of tetrahydrofuran was stirred at 25° for 45 min. Color Test I<sup>8</sup> was negative, so the reaction was terminated by hydrolysis. Extraction of the solution with aqueous potassium hydroxide afforded 2 g. of starting material in the neutral layer and 7

(7) A. Goske, *Ber.*, **20**, 232 (1887).

(8) P. Charpentier, *Compt. rend.*, **225**, 306 (1947).

(9) H. Gilman and D. R. Swayampati, *THIS JOURNAL*, **77**, 3387 (1955).

(10) All melting points are uncorrected.

g. of oil in the basic extract. This oil was distilled under reduced pressure to yield 3.6 g. (36%) of 2-mercaptodiphenylamine, b.p. 118° (0.1 mm.) (lit.<sup>11</sup> value 174–175° (8 mm.)). The infrared spectrum had absorption maxima characteristic of the S-H and the N-H functions.

**Phenoxathiin.**—A mixture of 10 g. (0.05 mole) of phenoxathiin, 2 g. (0.3 g. atom) of lithium and 50 ml. of tetrahydrofuran was stirred at 50° for 1 hr. The reaction mixture was carbonated by pouring onto a Dry Ice-ether slurry. Extraction of the carbonation mixture with aqueous potassium hydroxide was used to separate the acidic materials from the neutral material. Acidification of the basic extract with dilute hydrochloric acid followed by extraction with ether produced a soluble and an insoluble fraction. Three recrystallizations of the ether-insoluble fraction from ethanol produced a small quantity of phenoxathiin-4,6-dicarboxylic acid, melting point and mixture melting point 265–267°. Infrared spectra also were used as an aid in identification. After evaporation of the solvent, the ether-soluble portion was distilled under reduced pressure to yield 1 g. (16%) of 2-mercaptophenol, b.p. 40–44° (0.1 mm.), m.p. 5–6° (lit.<sup>12</sup> value 7.5°). Bands characteristic of the O-H and the S-H groups were present in the infrared spectrum of this compound.

**Dibenzo-*p*-dioxin.**—After 7 hr. of refluxing, a stirred mixture of 9.2 g. (0.05 mole) of dibenzo-*p*-dioxin, 2 g. (0.3 g. atom) of lithium and 50 ml. of tetrahydrofuran was carbonated in the usual manner. The carbonation mixture was extracted with dilute potassium hydroxide solution and then acidified. The acidic material was dissolved in ether and the ethereal solution washed with a dilute sodium carbonate solution to separate carboxylic acids from any phenolic material formed during the reaction. Evaporation of the ether followed by vacuum distillation of the residue yielded 1.7 g. of crude phenolic material melting 93–105°. One recrystallization of this material from petroleum ether (b.p. 60–70°)-benzene yielded 0.7 g. (13%) of catechol. The melting and mixture melting points were 105–107°. Infrared spectra also were used to verify the identity of this compound.

**Anisole.**—Refluxing a stirred mixture of 5.5 g. (0.05 mole) of anisole, 1 g. (0.15 g. atom) of lithium and 50 ml. of tetrahydrofuran for 5 hr. failed to produce any evidence of reaction or to give a positive Color Test I.<sup>2</sup> Nevertheless, the reaction mixture was carbonated in the usual manner. Evaporation of the neutral tetrahydrofuran layer afforded a near quantitative recovery of starting material.

**2-Aminodibenzo-*p*-dioxin.**—A mixture of 4 g. (0.02 mole) of 2-aminodibenzo-*p*-dioxin, 0.5 g. (0.075 g. atom) of lithium and 60 ml. of tetrahydrofuran was stirred for 2.75 hr. at reflux temperature. The reaction was terminated by hydrolysis with dilute hydrochloric acid. Since only the degree of cleavage was of interest with this particular compound, the reaction mixture was extracted with dilute potassium hydroxide solution and the basic extract acidified. Extraction of the basic extract with ether produced no acidic material. No attempt was made to purify the material in the neutral layer.

**2-Nitrodibenzo-*p*-dioxin.**—A mixture of 8.5 g. (0.037 mole) of 2-nitrodibenzo-*p*-dioxin, 2 g. (0.3 g. atom) of lithium and 60 ml. of tetrahydrofuran was stirred at reflux for 17 hr. to produce a dark black-brown paste. The reaction was terminated by hydrolysis. Extraction of the reaction mixture with aqueous potassium hydroxide afforded 1.5 g. of phenolic material which standard methods, *i.e.*, recrystallization, chromatography, etc., failed to purify. Likewise, no success was encountered when the 1.2 g. of neutral material was subjected to purification processes.

**Triphenylamine.**—A mixture of 12.2 g. (0.05 mole) of triphenylamine, 1 g. (0.15 g. atom) of lithium and 50 ml. of tetrahydrofuran was stirred under reflux for 3 hr. Color Test I<sup>2</sup> was negative, but the reaction mixture nevertheless was carbonated. Extraction of the carbonated mixture with dilute potassium hydroxide solution followed by acidification caused the evolution of carbon dioxide and the liberation of diphenylamine. One recrystallization of this material from petroleum ether (b.p. 60–70°) resulted in the isolation of 0.8 g. (9%) of product, melting and mixture melting points 53–55°. From the neutral layer was ob-

tained 7 g. (59%) of pure triphenylamine. A second run using the previous conditions gave similar results.

**Diphenylamine.**—Refluxing a stirred mixture of 17 g. (0.1 mole) of diphenylamine, 2 g. (0.3 g. atom) of lithium and 50 ml. of tetrahydrofuran for 24 hr. failed to give any evidence of reaction. There was a total recovery of starting material upon work-up.

**N-Phenylcarbazole.** Run I.—A mixture of 6 g. (0.025 mole) of N-phenylcarbazole, 1 g. (0.15 g. atom) of lithium and 60 ml. of tetrahydrofuran was stirred at 30°. Color Test I<sup>2</sup> was negative after 10 min., but it was positive at the end of 3 hr. After the reaction was terminated by carbonation, the carbonation mixture was extracted with dilute potassium hydroxide solution and acidified. The crude acidic material was vacuum sublimed and then recrystallized from water to yield 1.5 g. (50%) of benzoic acid identified by melting and mixture melting points. A small amount of carbazole also was obtained from the basic extract after acidification. Recrystallization from benzene of the crude material obtained by distillation of the solvent from the neutral layer afforded 1.5 g. (35%) of carbazole, melting and mixture melting points 246–248°.

Run II.—A mixture of 6 g. (0.025 mole) of N-phenylcarbazole, 1 g. (0.15 g. atom) of lithium and 50 ml. of diethyl ether was stirred at reflux for 24 hr. and then carbonated, Color Test I<sup>2</sup> being positive. No benzoic acid was isolated from the basic extract of the reaction mixture, but 0.3 g. of carbazole and 2.8 g. of N-phenylcarbazole were obtained from the neutral layer indicating that some cleavage had taken place.

**N-Benzylcarbazole.**—A mixture of 12.8 g. (0.05 mole) of N-benzylcarbazole, 1 g. (0.15 g. atom) of lithium and 50 ml. of tetrahydrofuran was stirred under reflux for 3 hr. and then terminated by carbonation even though Color Test I<sup>2</sup> was negative. The reaction mixture was extracted with dilute potassium hydroxide. Acidification of this extract produced 3 g. of acidic material and 0.3 g. of neutral material which proved to be carbazole. The acidic material decomposed on vacuum sublimation to yield 1.5 g. of carbazole identified by melting and mixture melting points. An additional 0.6 g. of carbazole was obtained from the neutral layer along with 6 g. of N-benzylcarbazole. Total yield of carbazole was 2.3 g. (28%). A second run which was refluxed for 2 hr. produced only 0.8 g. (10%) of carbazole.

**Phenoxathiin-10-dioxide.**—A mixture of 11.6 g. (0.05 mole) of phenoxathiin-10-dioxide, 3 g. (0.45 g. atom) of lithium and 50 ml. of tetrahydrofuran was stirred at 25° for 45 min. The reaction was terminated by carbonation. Extraction of the reaction mixture with dilute potassium hydroxide yielded a viscous oil upon acidification. This material could not be crystallized and it decomposed to a black tar when an attempt was made to vacuum sublime it. There was no material remaining in the neutral layer indicating that all the starting material was converted to acidic material during the reaction.

**N-Ethylphenothiazine-5-oxide.**—A mixture of 12.1 g. (0.05 mole) of N-ethylphenothiazine-5-oxide, 2 g. (0.3 g. atom) of lithium and 50 ml. of tetrahydrofuran was stirred at 25°. At the end of 45 min., all of the insoluble starting material had reacted to form a brown solution which gave a weak Color Test I.<sup>2</sup> The reaction mixture was carbonated, and dilute base was used to extract any acidic material from the carbonation mixture. The neutral ether layer was dried over anhydrous sodium sulfate before being distilled. Three recrystallizations of the undistilled residue, from glacial acetic acid, yielded 1.4 g. of an unidentified sulfur-containing compound, m.p. 124–126°. The basic extract was acidified and extracted with ether. By extracting the ether layer with dilute sodium carbonate solution, it was possible to isolate a thiophenolic and a more acidic material. Distillation of the thiophenolic material under reduced pressure produced 0.8 g. of material, b.p. 100–101° (0.1 mm.). This material had infrared spectrum bands characteristic of the S-H and the N-H functions, but it has not been identified. The more acidic material was a solid, but efforts to purify and identify it failed.

**2-Chlorophenothiazine.**—A mixture of 11.7 g. (0.05 mole) of 2-chlorophenothiazine, 2 g. (0.3 g. atom) of lithium and 50 ml. of tetrahydrofuran was stirred at 25° for 45 min. and then carbonated. Extraction with dilute potassium hydroxide failed to yield any acidic material. From the neutral layer was obtained 11 g. of material melting 170–

(11) A. I. Kiprianov and I. K. Ushenko, *J. Gen. Chem. (U.S.S.R.)*, **17**, 2201 (1947) [*C. A.*, **42**, 5016 (1948)].

(12) L. Hattinger, *Monatsh.*, **4**, 165 (1883).

177°. Three recrystallizations of this material from benzene-petroleum ether (b.p. 60–70°) yielded 3.5 g. (30%) of phenothiazine, melting and mixture melting points 184–186°.

**N-Lithio-2-chlorophenothiazine.**—To 11.7 g. (0.05 mole) of 2-chlorophenothiazine in 50 ml. of tetrahydrofuran was added slowly 0.054 mole of phenyllithium in 40 ml. of diethyl ether. The 40 ml. of diethyl ether was then distilled and an additional 50 ml. of tetrahydrofuran added to the reaction flask along with 1 g. (0.15 g. atom) of lithium. Stirring was then continued for 45 min. at 25°. Termination of the reaction was by carbonation. Basic extraction of the carbonation mixture failed to yield any acidic material. The neutral layer was evaporated and the residue recrystallized once from ethanol and twice from benzene-petroleum ether (b.p. 60–70°) to produce 1.3 g. (11%) of phenothiazine, identified as in the preceding experiment.

**N-Ethyl-3-chlorophenothiazine.**—A mixture of 13.1 g. (0.05 mole) of N-ethyl-3-chlorophenothiazine, 2 g. (0.3 g. atom) of lithium and 50 ml. of tetrahydrofuran was stirred for 1 hr. at 50°. Color Test I<sup>2</sup> was positive; therefore the reaction was terminated by carbonation. Extraction of the reaction mixture with dilute potassium hydroxide resulted in the isolation of 10 g. of acidic material which contained no thiophenolic compounds. This acidic material was a brown semi-solid which decomposed to a black oil when heated in ethanol or benzene. It was not purified. No neutral compounds were found when the solvent was evaporated from the neutral layer.

**N-Ethylphenothiazine. Run I.**—A mixture of 11.3 g. (0.05 mole) of N-ethylphenothiazine, 1 g. (0.15 g. atom) of lithium and 50 ml. of tetrahydrofuran was stirred at 25° for 45 min. Carbonation was accomplished in the usual manner. From the basic extract was isolated 9.5 g. of crude material melting 104–113°. Two recrystallizations of this material from petroleum ether (b.p. 60–70°)-benzene produced 7 g. (51%) of 2-carboxy-2'-mercaptoethylidiphenylamine, m.p. 114–116°. Its infrared spectrum has bands characteristic of the S-H and the carboxyl functions. The neutral layer contained 1 g. (9%) of starting material.

*Anal.* Calcd. for C<sub>18</sub>H<sub>15</sub>O<sub>2</sub>NS: S, 11.76. Found: S, 11.73, 11.54.

**Run II.**—A mixture of 11.3 g. (0.05 mole) of N-ethylphenothiazine, 2 g. (0.3 g. atom) of lithium and 50 ml. of tetrahydrofuran was stirred at 50° for 40 min. At that time

the reaction became exothermic and the color changed from brown to green. An ice-bath was used to keep the reaction temperature at 50°. Stirring was continued for an additional 10 min. before carbonation was effected. Only a trace of acidic material was found in the basic extract. The residue after evaporation of the solvent from the neutral layer was dissolved in benzene and chromatographed on alumina. Evaporation of the eluate followed by two recrystallizations of the residue from methanol-water produced 2.6 g. (27%) of pure N-ethylcarbazole identified by the method of mixture melting point and by its infrared spectrum.

**N-Phenylphenothiazine.**—A mixture of 6.3 g. (0.025 mole) of N-phenylphenothiazine, 0.5 g. (0.075 g. atom) of lithium and 60 ml. of tetrahydrofuran was stirred at 25° for 1 hr. and then carbonated in the usual manner. The basic extract contained 3.1 g. of material which was purified by vacuum sublimation and two recrystallizations from methanol-water to yield 1.5 g. (19%) of 2-carboxy-2'-mercaptotriphenylamine. The infrared spectrum contained the bands characteristic of S-H and carboxyl. The neutral layer contained a small amount of unidentified oil. Three other runs with reaction periods of up to 12 hr. at reflux failed to produce any identifiable material other than the aforementioned acid.

*Anal.* Calcd. for C<sub>19</sub>H<sub>16</sub>O<sub>2</sub>NS: S, 9.96. Found: S, 9.89, 10.06.

**N-Benzylphenothiazine.**—A mixture of 7.2 g. (0.025 mole) of N-benzylphenothiazine, 0.5 g. (0.075 g. atom) of lithium and 50 ml. of tetrahydrofuran was stirred at 25° for 45 min. and then carbonated. An unresolvable mixture resulted and no compounds could be identified from either the neutral layer or the basic extract which contained 1.4 g. of acidic material.

A second run was refluxed for 8 hr. and then carbonated. This time there was obtained a neutral and a thiophenolic material, but neither could be purified or identified.

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AMES, IOWA

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE KON. NED. GIST.-EN SPIRITUSFABRIEK]

## The Chemistry and Partial Structure of Bottromycin. IV.

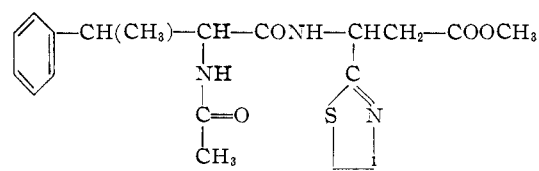
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The antibiotic bottromycin (C<sub>38</sub>H<sub>57-61</sub>N<sub>7</sub>O<sub>7-8</sub>S) yields upon mild alkaline hydrolysis a crystalline compound (C<sub>27</sub>H<sub>37</sub>N<sub>7</sub>O<sub>7</sub>S) which is biologically inactive. Upon esterification of this compound with methanolic hydrochloric acid a biologically active compound is produced which is identical with the original bottromycin. Also other biologically active esters of above-mentioned crystalline compound could be prepared.

Recently, Waisvisz and co-workers in a series of publications<sup>1-3</sup> reported on the isolation, purification and partial structure-elucidation of the antibiotic bottromycin, produced by a new species *Streptomyces bottropensis*. Upon acetylation of bottromycin, e.g., with acetic anhydride two crystalline decomposition products were obtained. One of these compounds was identified as the

methyl ester of a N-acetyl dipeptide of the structure



These results suggested that it might be worthwhile to study whether the molecule of bottromy-

(1) J. M. Waisvisz, *et al.*, *THIS JOURNAL*, **79**, 4520 (1957).

(2) J. M. Waisvisz, *et al.*, *ibid.*, **79**, 4522 (1957).

(3) J. M. Waisvisz, *et al.*, *ibid.*, **79**, 4524 (1957).