the thioctic-S^{35}_2 acid should be approximately 30. A decomposition rate of 0.3% per day would then be expected for the high specific activity product, which produces 3 × 10^{16} e.v./day/mg. This rate is obviously too low to explain the difficulties encountered in crystallizing the product from the 100 mc. preparation, since visible amounts of hexane-insoluble oil were formed from a clear hexane solution during one day's standing. It is possible that some impurity, formed in the synthesis, and originally hexane soluble, is highly sensitive to radiation. Polymerization of this impurity during the periods of standing in hexane would inhibit crystallization of the thioctic acid and would explain the appearance of the insoluble oil.

BERKELEY, CALIFORNIA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

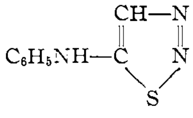
On Acylhydrazones and 1,2,3-Thiadiazoles

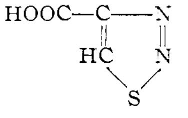
BY CHARLES D. HURD AND RAYMOND I. MORI

RECEIVED MAY 19, 1955

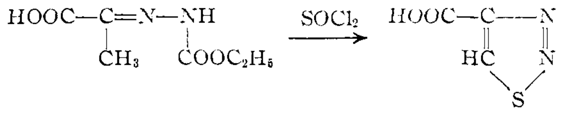
The preparation of carbethoxyhydrazones, acetylhydrazones and phenylsulfonylhydrazones of ketones and α-keto acids proceeds with good yields. The behavior of these hydrazones toward thionyl chloride was such that when there was a methylene group next to the hydrazono group then light-sensitive 1,2,3-thiadiazoles were formed in good yields. A mechanism is presented which explains their formation and also the formation of the intermediates which were isolated.

Two methods are known at present for the synthesis of monocyclic 1,2,3-thiadiazoles. One involves reaction of diazomethane and an isothiocyanate such as phenyl isothiocyanate, which yields 5-anilino-1,2,3-thiadiazole[1] (I). The other involves reaction of 1,2,3-oxadiazoles with ammonium hydrosulfide. The oxadiazoles are known also as diazoanhydrides[2] or α-keto diazo compounds[3] and are prepared by diazotization of α-amino ketones. Using this method, Wolff was able to synthesize 1,2,3-thiadiazole-4-carboxylic acid[4] (II). It is obvious that neither of these methods is well suited for synthetical purposes.

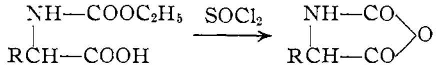

I


II

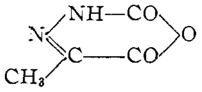
In the work to be described it will be shown that good yields of 1,2,3-thiadiazoles are obtainable in an unexpected way by interaction of thionyl chloride and acylhydrazones of the general structure $RCH_2CR'{=}N{-}NX$, wherein R' = COOH, C_6H_5, etc., and X = $COOC_2H_5$, $COCH_3$, $SO_2C_6H_5$, etc. The following synthesis of II is illustrative, the yield being 53%.

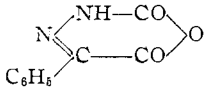

III II

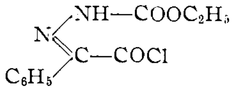
The half ester III may be compared with the half ester of an azasuccinic acid (IV) which is known[5] to yield the acid anhydride on reaction with thionyl chloride


IV

Anhydride V would be the expected product if III had behaved analogously. Some of it was indeed formed but its quantity was small. The comparable phenyl compound VI was produced in about 90% yield, however, and the acyl chloride VII was shown to be isolable as an intermediate.


V


VI


VII

No thiadiazole could result in the phenyl series because no methylene group was present in the original half ester. Evidently the presence of a methylene group adjacent to a hydrazono group favors thiadiazole formation in the reaction with thionyl chloride, rather than production of the cyclic acid anhydride.

III was prepared from pyruvic acid in quantitative yield by reaction with carbethoxyhydrazine: $CH_3COCOOH + NH_2NHCOOC_2H_5 \rightarrow III + H_2O$. The phenyl analog was prepared similarly from phenylglyoxylic acid.

A sample of 1,2,3-thiadiazole-4-carboxylic acid (II), prepared in powdered potassium bromide, was placed in a Baird double beam spectrophotometer, and these major bands were found in the infrared spectrum (medium intensity unless noted as weak (w) or strong (s)): 2.95 w, 3.25–4.00, 5.21 w, 5.98 s, 6.78 s, 7.14 s, 7.56, 8.20 s, 9.15, 10.25 s, 10.75, 11.20, 11.45, 12.55, 12.84, 13.80 μ. The assignments for carboxylic acid are 3.25–4.00, 5.98, 7.14, 8.20. Hence, the carboxylic acid structure for II is supported rather than a dipolar structure with a carboxylate ion.

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(1) H. Pechmann and A. Nold, *Ber.*, **29**, 2588 (1896).

(2) L. Wolff, H. Kopitzsch and A. Hall, *Ann.*, **333**, 1 (1904).

(3) H. Staudinger and J. Seigwart, *Ber.*, **49**, 1918 (1916).

(4) L. Wolff and co-workers, *Ann.*, **325**, 129 (1902).

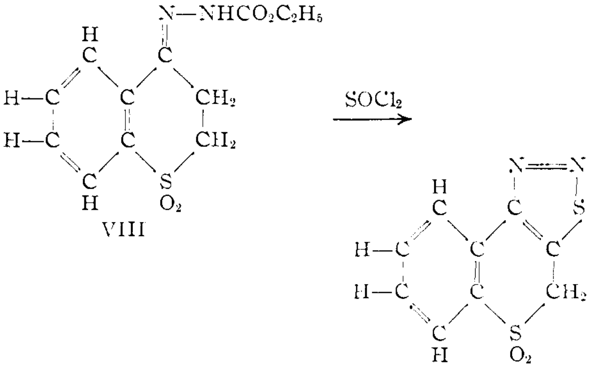
(5) H. Leuchs, *Ber.*, **39**, 857 (1906); C. Hurd and C. Buess, THIS JOURNAL, **73**, 2409 (1951).

The fate of the ethyl group in the change from III into II was not determined, but probably it escaped as ethyl chloride. It was established that benzyl chloride was formed when the benzyl ester was employed instead of the ethyl ester. An interesting aspect of the benzyl reaction was its endothermicity, whereas all of the other reactions using thionyl chloride were exothermic.

To gain evidence for a better understanding of the mechanism of this reaction several ketone acylhydrazones were included in the study.

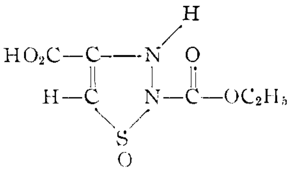
Acetophenone carbethoxyhydrazone[6] was treated with thionyl chloride to yield 4-phenyl-1,2,3-thiadiazole. Its isomer, 5-phenyl-1,2,3-thiadiazole, was prepared previously by Wolff.[2]

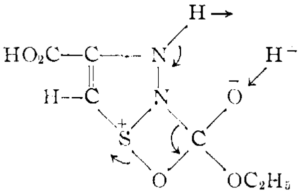
With equimolar quantities of 4-thiochromanone 1-dioxide[7] and carbethoxyhydrazine reacting in refluxing abs. ethanol for 3 hours 69% of the dioxide was recovered. On the other hand when the alcoholic mixture was refluxed for 12 hours in the presence of glacial acetic acid a 70% yield of 4-carbethoxyhydrazonothiochroman 1-dioxide (VIII) was obtained. The latter substance, on reacting with thionyl chloride, changed into 4H-thiadiazolo[5,4-c]-benzothiopyran 5-dioxide (IX).

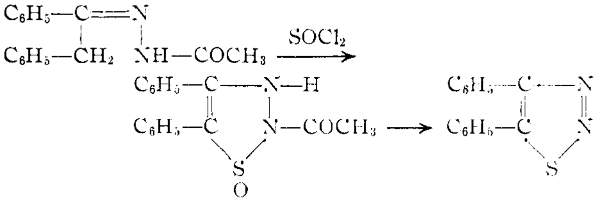

VIII

IX

If the mechanism of reaction of III and thionyl chloride involved first the formation of intermediate X followed by a cyclic step XI to yield II, then one would expect α-N-acetylhydrazonopropionic acid to behave similarly when treated with thionyl chloride. Indeed, II was obtained. Desoxybenzoin acetylhydrazone, prepared similarly, reacted with thionyl chloride to yield 2-acetyl-4,5-diphenyl-2,3-dihydro-1,2,3-thiadiazole 1-oxide (XII) and diphenyl-1,2,3-thiadiazole (XIII). XIII has been prepared by Staudinger[3] from phenylbenzoyldiazomethane and hydrogen sulfide. The probability that XII is an intermediate in the formation of XIII was confirmed when a 90% yield of the latter was obtained after refluxing XII in methanol for 24 hours.

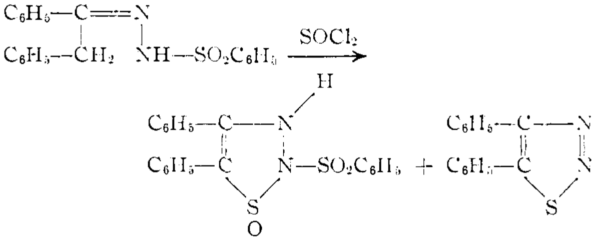

X


XI


XII

XIII

If the cyclic mechanism proposed above is correct then one would not expect any XIII on treating desoxybenzoin benzenesulfonylhydrazone, obtained from desoxybenzoin and benzenesulfonohydrazide, with thionyl chloride. Instead, however, a 12% yield of 2-phenylsulfonyl-4,5-diphenyl-2,3-dihydro-1,2,3-thiadiazole (XIV) and 63% yield of XIII were obtained in practice. This, therefore appears to rule out the possibility of the cyclic step proposed previously.


XIV

XIII

The infrared spectrum of XIV did not show the characteristic shift of sulfoxide absorption peak at 9.7 μ toward a longer wave length when the solvent was changed from carbon tetrachloride to chloroform,[8] because the sulfoxide is already hydrogen-bonded to a limited extent by the hydrogen atom attached to nitrogen. The sulfoxide peak was shifted to 9.9 μ when the spectrum was obtained in a solid potassium bromide pellet. This suggests that the sulfoxide is hydrogen-bonded to a greater extent by the presence of water in the solid potassium bromide used. The presence of water was indicated by the absorption peaks[9] at 2.95 and 6.2 μ.

The following observations help to elucidate part of the mechanism of 1,2,3-thiadiazole formation. (1) On refluxing XIV in methanol for 24 hours there was obtained 55% of XIII; but in carbon tetrachloride, 83% of starting material was recovered after 22 hours. (2) By refluxing XIV for 10 hours in carbon tetrachloride containing more than an equivalent amount of pyridine, an 89% yield of XIII was isolated. (3) On refluxing 2-acetyl-4,5-diphenyl-2,3-dihydro-1,2,3-thiadiazole 1-oxide (XII) in methanol for 24 hours XIII was obtained. From the reaction of desoxybenzoin acetylhydrazone and thionyl chloride, acetic acid was isolated as the *p*-chlorobenzylthiuronium acetate, m.p. 149–150°. Although Dewey and Sperry[10] reported the melting point at 140°, a

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(6) W. Borsche, *Ber.*, **38**, 833 (1905).

(7) C. Hurd and S. Hayao, THIS JOURNAL, **76**, 5065 (1954).

(8) D. Barnard, J. M. Fabian and H. P. Koch, *J. Chem. Soc.*, 2442 (1949).

(9) H. Gilman, "Organic Chemistry, An Advanced Treatise," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1953, p. 150.

(10) B. T. Dewey and R. B. Sperry, THIS JOURNAL, **61**, 3251 (1939).

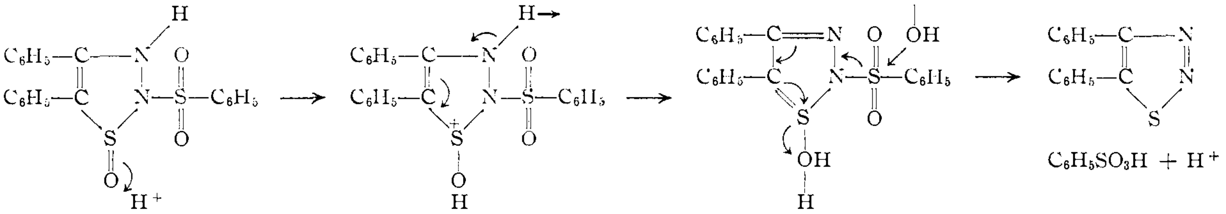
sample of it prepared as described by them was found to melt at 149–150°. (4) When XIV was refluxed in ethanol for 35 minutes two-thirds of it was recovered and 19% of XIII was obtained. By refluxing for 35 minutes in ethanol saturated with hydrogen chloride 92% of XIII was obtained. From this filtrate benzenesulfonic acid was isolated as *p*-chlorobenzylthiuronium benzenesulfonate. (5) Both dilute hydrochloric acid and pyridine catalyzed the decomposition of XIV in the presence of *p*-toluenesulfinate ion to yield only *p*-chlorobenzylthiuronium benzenesulfonate as was shown by identity of its infrared spectrum with that of the known compound[10] and by the difference of its spectrum from that of *p*-chlorobenzylthiuronium *p*-toluenesulfonate. Positions of the major bands in the infrared spectra of these two sulfonates were located, as listed below. The bands (μ) were of medium intensity unless marked w (weak) or s (strong). Samples were prepared in powdered potassium bromide. ***p*-Chlorobenzylthiuronium benzenesulfonate:** 3.10s, 3.26s, 3.65w, 6.00s, 6.27w, 6.40w, 6.73, 6.93, 7.02, 7.15, 7.30s, 8.60s, 8.88s, 9.05, 9.15, 9.67s, 9.83s, 10.03, 10.45w, 10.95w, 11.42w, 11.90, 12.10w, 12.40, 13.10, 13.20, 13.40, 13.75, 14.25, 14.63. ***p*-Chlorobenzylthiuronium *p*-toluenesulfonate:** 3.05s, 3.20s, 3.32s, 3.64, 5.95s, 6.02s, 6.27w, 6.40w, 6.73, 7.00, 7.15, 8.30s, 8.60s, 8.90s, 9.10s, 9.65s, 9.90s, 10.60w, 11.20w, 11.90w, 12.37s, 13.17, 13.70, 14.12, 14.74s. (6) On heating XIV at 60° in aniline for one-half hour XIII and benzenesulfonanilide were obtained. The infrared spectrum of the benzenesulfonanilide was identical to that of the known compound.

From these observations it seems evident that the reaction is an ionic one catalyzed by acid as well as base. Also, the oxidation–reduction is an intramolecular reaction and does not appear to proceed by prior formation of benzenesulfinate ion as was observed by Escales[11] with benzenesulfonohydrazide and with the McFadyen-Stevens[12] aldehyde synthesis.

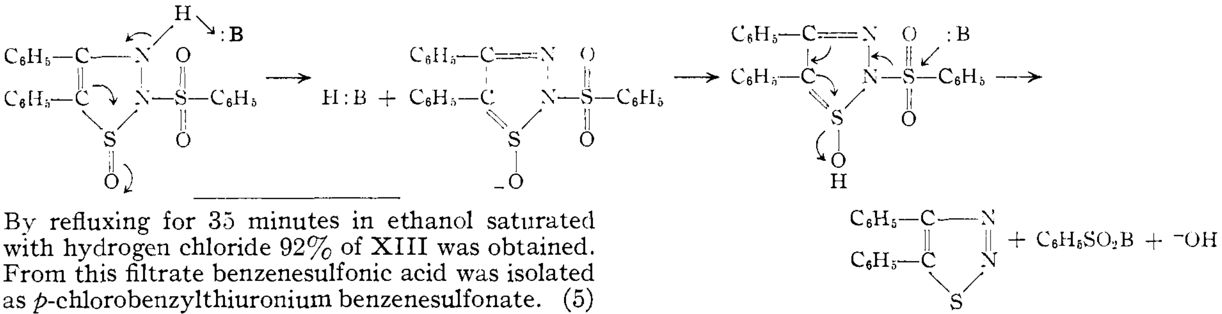
$$C_6H_5SO_2NHNHC_6H_5 + NaOH \longrightarrow C_6H_6 + C_6H_5SO_2Na + H_2O + N_2$$

The last observation indicates solvent participation in the reaction making the decomposition of XIV an intermolecular reaction with intramolecular oxidation–reduction. The reaction may be visualized as

Acid catalyzed



Base catalyzed (B: represents base)



The thiadiazoles are sensitive to light. Diphenyl-1,2,3-thiadiazole[3] becomes red when wet and blue-green when dry on exposure to light and 1,2,3-thiadiazole-4-carboxylic acid[4] becomes pink when exposed to light while still wet. 1,2,3-Thiadiazoles can now be synthesized conveniently in this novel way in good yield.

Experimental

Materials.—The following compounds were prepared by methods described in the literature: carbethoxyhydrazine,[13] m.p. 43–44°; carbobenzoxyhydrazine,[14] m.p. 69–70°; acetohydrazide,[15] m.p. 53–63° on crude material; benzenesulfonohydrazide,[16] m.p. 104–106°; acetophenone carbethoxyhydrazone,[6] m.p. 119–120°; benzenesulfonanilide,[17] m.p. 107–108°; benzaldehyde carbethoxyhydrazone,[18] m.p. 137–137.5°; desoxybenzoin carbethoxyhydrazone,[19] m.p. 101–101.5°; *p*-chlorobenzylthiuronium benzenesulfonate,[10] m.p. 184–185°; *p*-chlorobenzylthiuronium *p*-toluenesulfonate,[10] m.p. 191–192°.

***sym*-Biscarbobenzoxyhydrazine.**—To a solution of 2.64 g. (0.0528 mole) of hydrazine hydrate in 15 ml. of ethanol a solution of 10.0 g. (0.0586 mole) of carbobenzoxy chloride in 15 ml. of ethanol was added. After filtration and washing of the precipitate with dilute sodium hydroxide solution and with water, there was obtained 7.2 g. (46% yield) of *sym*-biscarbobenzoxyhydrazine, m.p. 104–105°. It was recrystallized from a mixture of ethyl acetate and hexane to a melting point of 105.5–106°.

Anal. Calcd. for $C_{16}H_{16}N_2O_4$: N, 9.34. Found: N, 9.69.

Carbethoxyhydrazonophenylacetic Acid.—To a solution of 30 g. of phenylglyoxylic acid,[20] m.p. 65–66°, in 40 ml. of methanol, 21 g. of carbethoxyhydrazine in 30 ml. of methanol was added gradually with cooling. Norit was

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(11) R. Escales, *Ber.*, **18**, 893 (1885).

(12) J. McFadyen and T. Stevens, *J. Chem. Soc.*, 584 (1936).

(13) O. Diels, *Ber.*, **47**, 2186 (1914).

(14) N. Rabjohn, THIS JOURNAL, **70**, 1181 (1948).

(15) Th. Curtius and T. S. Hofman, *J. prakt. Chem.*, [2] **53**, 524 (1896).

(16) Th. Curtius and T. Lorenzen, *ibid.*, [2] **58**, 166 (1898).

(17) A. Ginzberg, *Ber.*, **36**, 2706 (1903).

(18) H. de Graaf, *Diss. Leiden*, 138 (1930); *C. A.*, **24**, 5723 (1930).

(19) N. Rabjohn and H. D. Barnstorff, THIS JOURNAL, **75**, 2259 (1953).

(20) C. Hurd and R. McNamee, *Org. Syntheses*, **16**, 89 (1936).

used and the solution was refluxed for 10 minutes. After removing the carbon 56 ml. of water was added and 20 g. of white crystals appeared. On addition of 125 ml. of water to the filtrate 25 g. more of white product, m.p. 157–157.5° dec., was obtained, which was nearly a quantitative yield.

Anal. Calcd. for $C_{11}H_{12}N_2O_4$: C, 55.93; H, 5.12. Found: C, 55.83; H, 5.08.

Benzaldehyde Carbethoxyhydrazone. (**a**).—A 20-mmole mixture of phenylglyoxylic acid and carbethoxyhydrazine was refluxed in 10 ml. of toluene for 15 minutes and set aside at room temperature. On filtering and recrystallizing the gummy product a 47% yield of crude product, m.p. 122–124°, was obtained. Recrystallization from aqueous ethanol gave 26% of benzaldehyde carbethoxyhydrazone, m.p. 137–137.5°. The m.p. was not depressed when the sample was mixed with synthetic benzaldehyde carbethoxyhydrazone.

(**b**).—A mixture of 0.90 g. (0.0038 mole) of carbethoxyhydrazonophenylacetic acid and 10 ml. of toluene was refluxed for 2 hours. Gas was evolved. On cooling to room temperature, filtering and recrystallizing from aqueous methanol 0.36 g. (49% yield) of benzaldehyde carbethoxyhydrazone, m.p. 137.5–138°, was obtained. Mixed melting point with compound produced under (a) was 137–137.5°.

α-N-Carbethoxyhydrazonopropionic Acid (III).—To a solution of 7.4 g. of carbethoxyhydrazine in 25 ml. of warm toluene was added 6.3 g. of pyruvic acid, redistilled at 60–65° (12–15 mm.), in 25 ml. of warm toluene. The addition was carried out slowly because of the exothermic nature of the reaction. The mixture was shaken and an oil separated which solidified on standing overnight at room temperature. The white solid was collected on a filter, ground in a mortar with toluene, recollected and dried in an oven at 60°. The yield of product, m.p. 147–151°, was 12.4 g. (100%). The solid was refluxed with 200 ml. of toluene for 3 hours and set aside at room temperature. After two days 12.2 g. (99%) of product, m.p. 154–157°, was obtained. In another recrystallization of 2.15 g. of the product from 100 ml. of hot benzene by chilling the solution in an ice-bath, there was recovered 1.9 g. (88%) of α-N-carbethoxyhydrazonopropionic acid, m.p. 157–158°.

Anal. Calcd. for $C_6H_{10}N_2O_4$: C, 41.38; H, 5.79. Found: C, 40.99; H, 5.57.

Ethyl α-N-Carbethoxyhydrazonopropionate.—Ethyl pyruvate, b.p. 30° (10 mm.), $n^{25}D$ 1.4032, was prepared from ethyl lactate as described by Cornforth.[21] To a solution of 1.0 g. of ethyl pyruvate in 3 ml. of water and enough ethanol to form a solution 1.2 g. of carbethoxyhydrazine in 5 ml. of water was added. The mixture was heated gently on a steam-bath for about 5 minutes and cooled to yield 1.4 g. (80%) of ethyl α-N-carbethoxyhydrazonopropionate, m.p. 110–111°. Its melting point was unchanged after recrystallization from aqueous ethanol.

Anal. Calcd. for $C_8H_{14}N_2O_4$: N, 13.9. Found: N, 14.03.

4-Carbethoxyhydrazonothiochroman 1-Dioxide (VIII). (**a**).—A solution of 1.4 g. of 4-thiochromanone 1-dioxide,[7] 0.77 g. of carbethoxyhydrazine and 25 ml. of abs. ethanol was refluxed for 3 hours. On cooling and filtering 69% of the original 4-thiochromanone 1-dioxide, m.p. 130–131°, was recovered.

(**b**).—Experiment (a) was repeated except for the addition of 6 drops of gl. acetic acid and a refluxing period of 24 hours. It was then set aside at 20° for 12 hours and evaporated to dryness. To the residue 25 ml. of ethanol was added and warmed to dissolve it. On cooling, filtering and washing with a little ethanol there was obtained 1.26 g. (60.3% yield) of 4-carbethoxyhydrazonothiochroman 1-dioxide, m.p. 159–160°. It was recrystallized from ethanol; m.p. 159--160°.

Anal. Calcd. for $C_{12}H_{14}N_2O_4S$: N, 9.93. Found: N, 10.16.

4-Phenyl-2,3-diaza-3-pentenedioic Anhydride (VI).—A mixture of 8.6 g. of carbethoxyhydrazonophenylacetic acid and 30 ml. of thionyl chloride was heated for one-half hour at 47°. Gas was evolved as the solid dissolved. The reaction mixture was then refluxed on a steam-bath for 1.5 hours. A light yellow precipitate formed. It was then set aside at room temperature for a few hours, cooled, filtered and washed with dry carbon tetrachloride to yield 6.5 g. (98%) of product, m.p. 169–172°. The precipitate was boiled in carbon tetrachloride, cooled, filtered and recrystallized from dry toluene to yield 6.0 g. (90% yield) of product, m.p. 170–173°. Recrystallization from dry toluene yielded 5.3 g. (80%) of 4-phenyl-2,3-diaza-3-pentenedioic anhydride, m.p. 178–179°.

Anal. Calcd. for $C_9H_6N_2O_3$: C, 56.84; H, 3.18. Found: C, 56.93; H, 3.28.

Hydrazonophenylacetanilide.—To 0.08 g. of VI was added 0.10 g. of aniline. A yellow colored solution was formed and carbon dioxide was liberated. To it 1 ml. of ethanol was added, followed by water until turbid. On cooling in an ice-bath 0.1 g. (100% yield) of product, m.p. 123–124°, was obtained. After recrystallization from aqueous ethanol the m.p. was 125–125.5°.

Anal. Calcd. for $C_{14}H_{13}N_3O$: C, 70.27; H, 5.48. Found: C, 69.66; H, 5.23.

Carbethoxyhydrazonophenylacetyl Chloride (VII).—A mixture of 5.8 g. (0.025 mole) of carbethoxyhydrazonophenylacetic acid and 20 ml. of thionyl chloride was heated at 47° for 45 minutes. After cooling to room temperature 20 ml. of carbon tetrachloride was added and the mixture was maintained at −5° for 7 hours. The precipitate was collected and washed with carbon tetrachloride to yield 1.0 g. (21%) of VI, m.p. 178.5–179.5°. The mother liquor was concentrated under reduced pressure at 10°. On filtering (filtrate A) and washing with carbon tetrachloride 1 g. of product, m.p. 90° dec., was obtained. On standing for 6 hours at room temperature it became gummy and on washing with toluene there was obtained 0.7 g. of carbethoxyhydrazonophenylacetic acid, m.p. 152–154°. Recrystallization from aqueous methanol gave a melting point of 157–158°.

To filtrate A was added enough dry pentane to promote turbidity. After 6 hours at −5° it was filtered and the solid was washed with dry pentane and dried at once at 28° (0.5 mm.) for 2 hours over phosphorus pentoxide. There was obtained 2.0 g. (33% yield) of VII. It decomposed at 90–95° with liberation of gas at 95–100° and resolidified at 105–110°. It was recrystallized from carbon tetrachloride and pentane mixture.

Anal. Calcd. for $C_{11}H_{11}ClN_2O_3$: Cl, 13.9. Found: Cl, 13.4.

Pyrolysis of VII.—On heating 0.18 g. of VII at 110°, gas was evolved (presumably ethyl chloride) and a yellow precipitate was formed. The precipitate was washed with 2 ml. of hot carbon tetrachloride and 1 ml. of toluene. There was obtained 0.050 g. (36% yield) of VI, m.p. 177.5–178.5°; mixed melting point with analyzed anhydride, 178–179°.

Hydrazonophenylacetanilide was prepared as a derivative by treating the anhydride with aniline. The anilide melted at 124–125°.

1,2,3-Thiadiazole-4-carboxylic Acid (II) **and 4-Methyl-2,3-diaza-3-pentenedioic Anhydride** (V). (**a**).—A mixture of 6.0 g. of α-N-carbethoxyhydrazonopropionic acid and 10 ml. of thionyl chloride was heated for 1 hour at 60°. The mixture was then cooled to 0° and filtered. After washing the residue with 10 ml. of ethyl acetate, 2.4 g. (53% yield) of 1,2,3-thiadiazole-4-carboxylic acid, m.p. 200–205° dec., was obtained. It was dissolved in hot ethyl acetate, heated with Norit and filtered. After cooling for several hours there was obtained 1.5 g. (33% yield) of white product, m.p. 227–228° dec. in bath preheated to 185°. It started to sublime around 190° at atmospheric pressure. It decomposed around 220° if the melting point bath was not preheated. The acid became pink in color when exposed to light while still in contact with water.

Anal. Calcd. for $C_3H_2N_2O_2S$: C, 27.69; H, 1.54; N, 21.53; S, 24.6; neut. equiv., 130.1. Found: C, 27.98; H, 1.61; N, 22.00; S, 24.6; neut. equiv., 129.8.

The filtrate and washings obtained above were evaporated under reduced pressure below 60° leaving a gum which was extracted with hot ligroin (b.p. 86–100°). On cooling the extract 0.58 g. of product, m.p. 109–120°, was obtained. On recrystallizing half of the above product from ligroin 0.13 g. of needle-like precipitate, m.p. 124–128°, was obtained. It was recrystallized from carbon tetrachloride. The precipitate was boiled with Norit in carbon tetrachloride, filtered and cooled. It was recrystallized from hot benzene and ligroin. There was obtained 4-methyl-2,3-diaza-3-pentenedioic anhydride, m.p. 133–134°.

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[21] J. W. Cornforth, *Org. Syntheses*, **31**, 59 (1951).

Anal. Calcd. for $C_4H_4N_2O_3$: C, 37.50; H, 3.15; N, 21.87. Found: C, 37.90; H, 3.23; N, 22.47.

(**b**).—By carrying out the reaction with thionyl chloride at room temperature for 10 hours an 80% yield of crystalline II, m.p. 220–222° dec., was obtained.

Pyrolysis of II.—The II was immersed into an oil-bath heated to 260°. Gas was liberated and oil was formed. It was cooled to room temperature and ether was added. Dry hydrogen chloride was passed into the solution. White 1,2,3-thiadiazole hydrochloride, m.p. 68–70° (lit.[2] about 70°), was formed. It was very hygroscopic, as noted in the literature.

Ethyl 1,2,3-Thiadiazole-4-carboxylate.—A mixture of 1.2 g. (0.0059 mole) of ethyl α-N-carbethoxyhydrazonopropionate and 3 ml. of thionyl chloride was boiled on a steam-bath gently and set aside at room temperature for one-half hour. There was obtained 1.1 g. of crude product, m.p. 75–84°. It was heated with 0.5 g. of silica gel in 20 ml. of ligroin (b.p. 86–100°), filtered and cooled. There was obtained 0.2 g. (20% yield) of ethyl 1,2,3-thiadiazole-4-carboxylate, m.p. 86–86.5°.

Anal. Calcd. for $C_5H_6N_2O_2S$: C, 37.96; H, 3.83; N, 17.71. Found: C, 37.95; H, 3.76; N, 17.83.

4-Phenyl-1,2,3-thiadiazole.—4-Phenyl-1,2,3-thiadiazole, m.p. 77–78°, was prepared from acetophenone carbethoxyhydrazone and thionyl chloride in the usual manner in 64% yield.

Anal. Calcd. for $C_8H_6N_2S$: N, 17.2. Found: N, 17.68.

4*H*-Thiadiazolo[5,4-c]benzothiopyran 5-Dioxide (IX).—Ten ml. of thionyl chloride was added all at once into 0.50 g. of VIII. The red solution was warmed on a steam-bath for 10 minutes and evaporated. It was boiled for 10 minutes with 10 ml. of ethanol, filtered, concentrated and cooled. There was obtained 0.3 g. (72%) of crude orange product, m.p. 168–174°. Recrystallization of 0.2 g. of crude product from ethanol gave 90% recovery with melting point of 173–174°. Further recrystallizations yielded IX of m.p. 175.5–176.5°.

Anal. Calcd. for $C_9H_6N_2O_2S$: N, 11.8. Found: N, 11.96.

α-N-Carbobenzoxyhydrazonopropionic Acid.—To 7.50 g. of carbobenzoxyhydrazine in 20 ml. of abs. ethanol a solution of 3.98 g. of pyruvic acid in 20 ml. of abs. ethanol was added. Reaction was mildly exothermic. The alcohol was evaporated and 30 ml. of benzene was added. To the boiling solution ligroin was added until turbid. Then, after remaining at 25° for two hours the solid was collected; yield 9.30 g. (87%) of α-N-carbobenzoxyhydrazonopropionic acid, m.p. 144–148°. On boiling 0.52 g. of the product with silica gel in benzene and filtering 0.30 g. of solid, m.p. 148–149°, was obtained and recrystallization from benzene brought the m.p. to 150–151°.

Anal. Calcd. for $C_{11}H_{12}N_2O_4$: N, 11.9. Found: N, 12.02.

Reaction of α-N-Carbobenzoxyhydrazonopropionic Acid with Thionyl Chloride.—Ten ml. of thionyl chloride was added to 3.08 g. of carbobenzoxyhydrazonopropionic acid. Unlike the usual exothermic reaction, this was endothermic. The cold mixture was warmed on a steam-bath for 10 minutes and set aside overnight at room temperature. There was obtained 0.56 g. (33% yield) of II, m.p. 220–222°. The filtrate was distilled and 0.85 g. (68% yield) of benzyl chloride, b.p. 69–70° (30 mm.), was obtained. It was redistilled at 72–74° (30 mm.) to yield 0.57 g. of benzyl chloride. It was then distilled twice at 175–176° (at atmospheric pressure); lit.[22] b.p. 179°; lit.[23] b.p. 175.0–175.2° (769.3 mm.). Its infrared spectrum was identical to that obtained from commercial benzyl chloride.

α-N-Acetylhydrazonopropionic Acid.—α-N-Acetylhydrazonopropionic acid, m.p. 186–187° dec., was prepared in 100% yield from equivalent amounts of acetohydrazide and pyruvic acid in benzene. It was recrystallized from ethanol.

Anal. Calcd. for $C_5H_8N_2O_3$: N, 19.5. Found: N, 19.84.

Desoxybenzoin Acetylhydrazone.—A mixture of 3.70 g. of acetohydrazide, 9.91 g. of desoxybenzoin and 30 ml. of abs. ethanol was refluxed for 3 hours. It was then set aside at room temperature. After cooling it, 8.4 g. (67% yield) of desoxybenzoin acetylhydrazone, m.p. 151–156°, was obtained. It was dissolved in 150 ml. of hot dry benzene and passed through a column of activated alumina containing hexane. Some of the product started to crystallize out at the top of the column; but it was eluted from the column, and 500 ml. of clear white fraction was obtained. The solvent was evaporated off and about 3 g. (20% yield) of white desoxybenzoin acetylhydrazone, m.p. 151–152°, was obtained. It was recrystallized from benzene.

Anal. Calcd. for $C_{16}H_{16}N_2O$: N, 19.5. Found: N, 19.84.

Reaction of α-N-Acetylhydrazonopropionic Acid with Thionyl Chloride.—There was obtained 38% yield of crude 1,2,3-thiadiazole-4-carboxylic acid, m.p. 208–209° dec., from α-N-acetylhydrazonopropionic acid and thionyl chloride. On treatment with Norit in ethyl acetate 20% yield of product, m.p. 226–228° (dec. in bath preheated to 185°), was obtained. Its infrared spectrum was identical to that of analyzed II.

Diphenyl-1,2,3-thiadiazole (XIII) and 2-Acetyl-4,5-diphenyl-2,3-dihydro-1,2,3-thiadiazole 1-Oxide (XII).—To 1.64 g. of desoxybenzoin acetylhydrazone about 5 ml. of thionyl chloride was added. When reaction ceased, the mixture was evaporated and few drops of water were added together with 4 ml. of ethanol. There was obtained 0.32 g. (17% yield) of XII, m.p. 169–170°. It was recrystallized from ethanol.

Anal. Calcd. for $C_{16}H_{14}N_2O_2S$: C, 64.41; H, 4.74. Found: C, 64.35; H, 4.72.

The filtrate was concentrated, cooled in a Dry-Ice bath and filtered to yield 1.07 g. (69.2%) of product, m.p. 84–87°. Recrystallization from methanol gave 0.90 g. of diphenyl-1,2,3-thiadiazole (XIII), m.p. 92–93°. On recrystallizing from methanol it melted at 93–94° (lit.[3] m.p. 93–94°).

Anal. Calcd. for $C_{14}H_{10}N_2S$: N, 11.7. Found: N, 12.11.

***p*-Chlorobenzylthiuronium Acetate.** (**a**).—The preparation of *p*-chlorobenzylthiuronium acetate was carried out as described by Dewey and Sperry.[10] There was obtained 88% yield of product, m.p. 147–148°. After recrystallization from dioxane it melted also at 147–148°, but on recrystallizing from alcohol it melted at 149–150° (lit. m.p. 140°).

Anal. Calcd. for $C_{10}H_{13}ClN_2O_2S$: N, 10.68. Found: N, 10.81.

(**b**).—To 1.0 g. of desoxybenzoin acetylhydrazone about 5 ml. of cold thionyl chloride was added. After warming on a steam-bath for a few minutes the excess of thionyl chloride was distilled off. Water was added and the mixture was steam distilled. About 0.6 ml. of distillate was collected. To the cooled distillate 0.1 g. of *p*-chlorobenzylthiuronium chloride in aqueous ethanol was added. There was obtained 0.003 g. of *p*-chlorobenzylthiuronium acetate, m.p. 147–148°. On recrystallizing from aqueous ethanol it melted at 149–150°.

Behavior of XII in Refluxing Methanol.—A solution of 0.18 g. of XII in 5 ml. of methanol was refluxed for 24 hours. On cooling in a Dry-Ice bath, filtering, further concentrating and filtering there was obtained 0.13 g. (90% yield) of XIII, m.p. 92–93°. The infrared spectrum was identical to that of known XIII.

Desoxybenzoin Phenylsulfonylhydrazone.—A mixture of 4.91 g. of desoxybenzoin, 4.31 g. of benzenesulfonohydrazide and 30 ml. of abs. ethanol was refluxed for 3 hours. The mixture was cooled in an ice-bath, filtered and washed with ethanol to yield 5.2 g. (60%) of faintly yellow desoxybenzoin phenylsulfonylhydrazone, m.p. 160–162°. It was recrystallized from ethanol.

Anal. Calcd. for $C_{20}H_{18}N_2O_2S$: N, 8.00. Found: N, 8.09.

2-Phenylsulfonyl-4,5-diphenyl-2,3-dihydro-1,2,3-thiadiazole 1-Oxide (XIV) and Diphenyl-1,2,3-thiadiazole.—To 1.5 g. of desoxybenzoin phenylsulfonylhydrazone 5 ml. of thionyl chloride was added at room temperature. Gas was evolved and the mixture was heated on a steam-bath for 10 minutes. It was extracted twice with 10-ml. portions of hot ligroin (b.p. 86–100°). The extract was concentrated to 10 ml., heated with silica gel, filtered and washed with hot

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[22] W. H. Perkin, *J. Chem. Soc.*, **69**, 1203 (1896).

[23] R. S. Schiff, *Ann.*, **220**, 99 (1883).

ligroin. There was obtained 0.20 g. (12% yield) of XIV, m.p. 154–155°, from the cooled filtrate. On recrystallizing from a mixture of benzene and ligroin it melted at 156–157°.

Anal. Calcd. for $C_{20}H_{16}N_2O_3S_2$: N, 7.07. Found: N, 7.36.

On recrystallizing it from ethanol it melted at 164.5–165.5°.

Anal. Calcd. for $C_{20}H_{16}N_2O_3S_2$: N, 7.07. Found: N, 7.28.

The filtrate was evaporated and the residue was dissolved in 6 ml. of ether. It was cooled and filtered to yield 0.64 g. (63%) of diphenyl-1,2,3-thiadiazole, m.p. 90–93°. Recrystallization from ether gave 0.52 g. (51% yield) of product, m.p. 92–93°. On further recrystallization it melted at 93–94°. The infrared spectrum obtained in solid potassium bromide was found to be identical to that of known XIII.

Behavior of XIV in Refluxing Methanol.—A mixture of 0.0400 g. of XIV and 2 ml. of methanol was refluxed for 24 hours. The solution was concentrated, cooled in Dry Ice, and filtered to yield 0.0131 g. (54.5%) of XIII, m.p. 93–94°, with an infrared spectrum identical to that of known XIII.

Reaction of XIV in Refluxing Ethanol.—A mixture of 0.1136 g. of XIV and 4 ml. of ethanol was refluxed for 35 minutes, a much shorter time than the previous experiment. The mixture was cooled to 0° and filtered to collect 0.754 g. (66.4%) of starting material, m.p. 163–164°. By concentrating the filtrate, cooling to −78° and filtering there was obtained 0.0128 g. (18.8% yield) of XIII, m.p. 88–92°. Its infrared spectrum in potassium bromide was identical to that of known XIII.

Reaction of XIV in Refluxing Carbon Tetrachloride.—A mixture of 0.0956 g. of XIV and 3 ml. of dry carbon tetrachloride was refluxed for 22 hours. The solution was then concentrated to 0.5 ml. and 0.0794 g. (83.0%) of the starting material, m.p. 156–157°, was recovered. The infrared spectrum was identical to XIV.

Acid Catalysis of XIV.—To 4 ml. of ethanol saturated with hydrogen chloride was added 0.3421 g. of XIV and the whole was refluxed for 35 minutes. The solution was concentrated, cooled to −78°, and filtered to yield 0.1888 g. (91.6%) of XIII, m.p. 88–89°. Recrystallization from ether brought the m.p. to 93–94°.

The filtrate was evaporated and 3 ml. of water was added. It was filtered and to the filtrate 0.250 g. of *p*-chlorobenzylthiuronium chloride in 3 ml. of ethanol was added. The mixture was cooled and filtered to yield 0.2858 g. (92.1%) of *p*-chlorobenzylthiuronium benzenesulfonate, m.p. 184–185° (lit.[10] m.p. 184°).

Base Catalysis of XIV.—A mixture of 0.2835 g. of XIV and 0.0635 g. of dry pyridine in 3 ml. of dry carbon tetrachloride was refluxed for 10 hours. The solution was filtered and the filtrate was concentrated, cooled, and filtered to yield 0.1511 g. (88.7%) of XIII, m.p. 93–94°.

Acid Catalysis of XIV in the Presence of *p*-Toluenesulfinic Acid.—A mixture of 0.129 g. of XIV, 0.580 g. of sodium *p*-toluenesulfinate and 3 ml. of methanol was acidified with methanolic hydrogen chloride and refluxed for one-half hour. It was then evaporated to dryness by a stream of dry nitrogen and the residue was extracted with two 1-ml. portions of water. To the aqueous extract an alcoholic solution of 0.0773 g. of *p*-chlorobenzylthiuronium chloride was added. The mixture was cooled in an ice-bath, then was filtered to obtain 0.0476 g. (40.6% yield) of *p*-chlorobenzylthiuronium benzenesulfonate, m.p. 184–185° (lit.[10] m.p. 184°). Its infrared spectrum showed that it contained no *p*-chlorobenzylthiuronium *p*-toluenesulfonate.

Anal. Calcd. for $C_{14}H_{15}ClN_2O_3S_2$: N, 7.80. Found: N, 7.78.

The residue after extraction with water was washed with water and 0.0737 g. (95% yield) of XIII, m.p. 86–88°, was obtained.

Base Catalysis of XIV in the Presence of *p*-Toluenesulfinate Ion.—A mixture of 0.1936 g. of XIV, 0.0890 g. of sodium *p*-toluenesulfinate, 1 drop of very dilute methanolic hydrogen chloride and 3 ml. of pyridine was warmed at 60° for half hour. The solvent was removed under a stream of dry nitrogen and the residue was extracted twice with 1 ml. of water. To the extract there was added 2 ml. of cold ethanol which contained 0.116 g. of *p*-chlorobenzylthiuronium chloride This resulted in the formation of 0.1449 g. (79.6% yield) of *p*-chlorobenzylthiuronium benzenesulfonate, m.p. 184–185°. The infrared spectrum obtained in solid potassium bromide indicated absence of *p*-toluenesulfonate. The residue after extraction was washed with water to yield 0.1082 g. (92.99%) of XIII, m.p. 85–87°.

Reaction of XIV with Aniline.—A mixture of 0.2526 g. of XIV and 3 ml. of redistilled aniline (b.p. 90°, 31 mm.) was warmed for one-half hour at 60°. The solvent was then evaporated and 2 ml. of methanol was added. It was cooled, filtered and washed with methanol. There was obtained 0.1353 g. (89.1%) of XIII, m.p. 87–88°.

The filtrate was evaporated to dryness, extracted twice with 1.5 ml. of aqueous sodium hydroxide, filtered, cooled and acidified with concd. hydrochloric acid. There was obtained 0.972 g. (65.4% yield) of benzenesulfonanilide, m.p. 105–106° (lit.[24] 110°; 105°[25]; 102°[26]; 108.5–109°[17]). The infrared spectrum obtained was identical to that of benzenesulfonanilide, m.p. 107–108°, prepared from benzenesulfonyl chloride.

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