monosubstituted benzene ring. The nmr spectrum showed three singlets at 159, 207, and 241 cps, in addition to aromatic protons in the region between 375 and 453 cps. These were in the area ratio of 3:1:2:9, respectively. The aromatic protons were further resolved into three sets of multiplets, which enable the elucidation of the structure unequivocally, a doublet with suggestions of secondary splittings centered at 483 cps, J = 9 cps, for the *ortho* (to the amino group) protons of the *para*-disubstituted aniline ring; a complex multiplet between 412 and 435 cps for the *meta* protons of the same ring and the *meta* and *para* protons of the selenobenzene ring; and, finally, a multiplet centered at 444 cps for the *ortho* protons of the selenobenzene ring. These aromatic protons were in the ratio of 2:5:2, respectively, in agreement with the formula of *p*-(N-methylamino)-benzyl phenyl selenide. *Anal.* Calcd for $C_{14}H_{15}NSe$: C, 60.87; H, 5.48; N, 5.08. Found: C, 60.68; H, 5.41; N, 5.18.

p-Aminobenzyl Phenyl Selenide.—To a cooled solution of 7.85 g (0.05 mole) of selenophenol in 25 ml of alcohol was added 4.65 ml (0.05 mole) of aniline, 3.82 ml (0.05 mole) of 37% formaldehyde, and 4.50 ml (0.05 mole) of concentrated hydrochloric acid (sp gr 1.19). After refluxing for 30 min, the reaction mixture was made strongly basic with 10% NaOH. The crystalline solid was filtered and washed with water. The yield of crude crystals exceeded 95% of the theory. Recrystallization from 150 ml of alcohol gave 5 g of crystals that melted at 53–55°. The infrared spectrum showed two NH stretching bands for a primary amine, and strong bands indicating a *para* disubstituted, as well as a monosubstituted benzene ring. The nmr spectrum showed two types of protons, a broad band, centered at *ca.* 200 cps and a sharp singlet at 242 cps, in addition to the aromatic protons in the region between 385 and 355 cps. The area ratio of these protons were 2:2:9, repectively. The aromatic protons had the characteristic pattern described above for its N-methyl derivative. Thus, the nmr and the infrared spectra are in agreement with the structure of *p*-aminobenzyl phenyl selenide. *Anal.* Calcd for $C_{13}H_{13}NSe$: C, 59.55; H, 5.00; N, 5.35. Found: C, 59.43; H, 4.93; N, 5.17.

p-(N,N-Dimethylamino)benzyl Phenyl Selenide. Method A. *Via* **"Model Intermediate."**—To a chilled suspension of 12 g (0.05 mole) of N-*p*-(N′,N′-dimethylamino)benzyl-N-methylaniline in 25 ml of 95% alcohol was added 7.85 g (0.05 mole) of selenophenol, followed by 4.5 ml (0.05 mole) of concentrated hydrochloric acid (sp gr 1.19). After refluxing for 10 min the reaction mixture was made strongly basic with 10% sodium hydroxide. The crystalline solid was collected and washed with water (yield of crude product exceeded 95% of theory, mp 93–97°). Recrystallization from 200 ml of 95% alcohol gave 11 g (76% of theory) of colorless, columnar crystals, mp 99–101°. Its infrared spectrum showed no NH stretching bands but showed strong bands at 12.1 μ for a *para*-disubstituted benzene ring and strong bands at 13.5 and 14.5 μ for a monosubstituted benzene ring. The nmr spectra showed two sharp singlets at 169 and 242 cps, in addition to the characteristic aromatic bands indicated for the two previously described compounds. The area ratios were 6:2:9 in agreement with the formula for *p*-(N,N-dimethylamino)benzyl phenyl selenide. *Anal.* Calcd for $C_{15}H_{17}NSe$: C, 62.08; H, 5.91; N, 4.83. Found: C, 62.36; H, 5.83; N, 5.09.

Method B. Direct Condensation.—To a chilled solution of 7.85 g (0.05 mole) of selenophenol in 25 ml of 95% alcohol, was added in sequence 6.1 g (0.05 mole) of dimethylaniline, 3.85 ml (0.05 mole) of 37% formaldehyde, and 4.5 ml (0.05 mole) of concentrated hydrochloric acid (sp g 1.19). After refluxing for 60 min this reaction mixture was made basic. The oily layer was separated and when it did not crystallize on chilling the oil was washed with 95% alcohol to remove any unreacted dimethylaniline. The residue was acidified with hydrochloric acid and extracted with ether to remove any diphenyl diselenide and diphenyl selenide. The remaining residue was then made basic with 10% NaOH, extracted with ether, and the ether extract was dried over KOH pellets. Removal of the solvent gave about 1 g (7% of thoery) of a crystalline solid of mp 99–100°. Its infrared and nmr spectra were identical with those of the compound obtained by method A above.

Products from the Base-Catalyzed Chlorination of Phenol. A New Synthesis of (±)-Caldariomycin[1]

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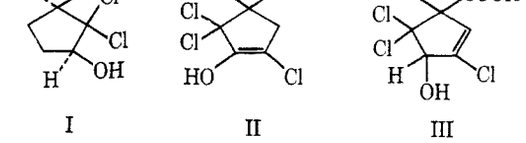
Chlorination of phenol or 2,4,6-trichlorophenol in cold, alkaline solution—a reaction first described by Hantzsch in 1887—is shown to yield 1,4-dihydroxy-3,5,5-trichloro-2-cyclopentene-1-carboxylic acid (III). Catalytic hydrogenation of this product, followed by treatment with lead tetraacetate and then with lithium borohydride, afforded a 5:1 mixture of the *cis* and *trans* isomers of 2,2-dichloro-1,3-cyclopentanediol, the latter being the racemic form of the mold metabolite caldariomycin (I). Structures of other transformation products of the acid III were also determined or confirmed.

Caldariomycin, one of the simplest known chlorine-containing mold metabolites, was first isolated in 1940 from *Caldariomyces fumago.*[3] Its properties and chemical behavior indicated it to be (+)-2,2-dichloro-*trans*-1,3-cyclopentanediol (I, or its mirror image). More recently, studies on its biosynthesis with labeled chlorine and carbon have been described,[4] along with a confirmatory total synthesis of racemic caldariomycin[5] based on the dichlorination of 1,3-cyclopentanedione and subsequent reduction to a mixture of the corresponding 2,2-dichloro-*cis*- and -*trans*-1,3-diols.



I II III

In our approach[1] to the synthesis of caldariomycin, introduction of the geminal chlorine atoms was planned for an earlier stage than in the route just cited. A search of the literature for an intermediate suitable for this purpose led to consideration of a compound formed by the base-catalyzed chlorination of phenol in a reac-

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(2) (a) Alfred P. Sloan Research Fellow, 1961–1964; (b) M.S. Thesis, The University of Kansas, June 1961.

(3) P. W. Clutterbuck, S. L. Mukhopadhyay, A. E. Oxford, and H. Raistrick, *Biochem. J.*, **34**, 664 (1940).

(4) P. D. Shaw and L. P. Hager, *J. Am. Chem. Soc.*, **81**, 1011, 6527 (1959); *J. Biol. Chem.*, **234**, 2565 (1959); **236**, 1626 (1961); P. D. Shaw, J. R. Beckwith, and L. P. Hager, *ibid.*, **234**, 2560 (1959); J. R. Beckwith, R. Clark, and L. P. Hager, *ibid.*, **238**, 3086 (1963); J. R. Beckwith and L. P. Hager, *ibid.*, **238**, 3091 (1963).

(5) J. R. Beckwith and L. P. Hager, *J. Org. Chem.*, **26**, 5206 (1961).

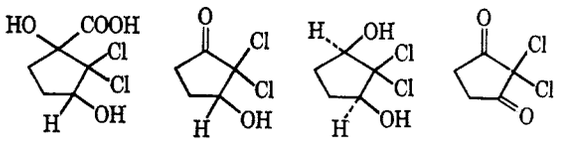
tion originally described by Hantzsch in 1887.[6] This product, a carboxylic acid of the composition $C_6H_5Cl_3O_4$, was reported to have properties consistent with its formulation as a trichlorodihydroxycyclopentenecarboxylic acid. Curiously, it was assigned the enolic structure II by Hantzsch, even though it did not give any reactions of an enolized ketone. Hantzsch also considered, but rejected, the alternative structure III. In that same period, Zincke and co-workers reported the formation of similar products from the chlorination and subsequent base treatment of other aromatic hydroxy compounds, such as catechol and *o*-aminophenol.[7] Although various aspects of these reports have since been reexamined or confirmed,[8] no detailed reinvestigation of Hantzsch's original findings appears to have been undertaken prior to initiation of the present study.[9] Recently, however, a preliminary account of a new study has appeared,[10] which, in part, parallels our own investigations and also supports our earlier assignment[1] of structure III to the Hantzsch acid.

The conditions which we found most satisfactory for the preparation of this acid were not only extremely critical but also differed to some extent from those described by Hantzsch[6a] and by Hoffmann.[6b] However, by carefully controlling the quantity of chlorine and by keeping the temperature below 5° during the alternate addition of chlorine and alkali, we were able to obtain the acid in reasonably satisfactory and reproducible yields (50–60%). For best results in the isolation of the product as its ammonium salt, we also found it necessary to regulate closely the amount and rate of addition of ammonia to the ether solution of III. The regenerated acid was found to have the properties described by Hantzsch, and its spectral features, as well as those of its methyl ester, agreed with the spectral data recorded by Moye and Sternhell.[10]

Both the free acid and its methyl ester were readily acetylated, and the nmr spectra of the resulting diacetates confirmed the presence of one olefinic proton and only one other nonexchangeable nuclear hydrogen. Apart from stereochemical considerations (see below), these results fully support the assignment of structure III to the Hantzsch acid.

On hydrogenation over palladium on carbon in ethanol, the Hantzsch acid and its esters absorbed 2 moles of hydrogen with loss of one chlorine atom. The nmr spectra of the products no longer exhibited a signal for an olefinic proton but instead contained a complex pattern corresponding to two methylene groups and a well-defined triplet associated with an adjacent lone proton (at C-3). Taken in conjunction with other data presented below, these findings point to structure IV for the reduced acid.

In accord with their formulations as α-hydroxy acids, both the Hantzsch acid (III) and its reduction



IV V VI VII

product (IV) were found to yield 1 mole of carbon dioxide on reaction with lead tetraacetate. Moreover, palladium-catalyzed hydrogenation of the resulting cleavage products afforded substantial amounts of cyclopentanone, which was isolated as the 2,4-dinitrophenylhydrazone, thereby confirming the presence of a five-membered ring (*cf.* original structure proof[3] of caldariomycin).

The lead tetraacetate cleavage product V, derived from acid IV, gave on treatment with lithium aluminum hydride or sodium borohydride essentially only 2,2-dichloro-*cis*-1,3-cyclopentanediol (IV), mp 134–135°.[5] Reduction of V by lithium borohydride, however, produced a 5:1 mixture of the *cis*- and *trans*-diols VI and I, respectively, from which the *trans* isomer, (±)-caldariomycin (I), mp 89–90°,[5] could be isolated by fractional crystallization from chloroform in about 5% over-all yield from acid IV.

In contrast to the report of Beckwith and Hager[5] that reduction of 2,2-dichloro-1,3-cyclopentanedione (VII) with lithium aluminum hydride at low temperature affords a 5:2 mixture of the *cis*- and *trans*-diols, we found that this reaction gave almost exclusively the *cis*-diol VI. However, we did obtain the *trans*-diol I, along with a considerable amount of the *cis* isomer VI, by reduction of the dione VII with lithium borohydride. The reason for this discrepancy between our results with lithium aluminum hydride and those of Beckwith and Hager is not clear, since we attempted, as far as possible, to employ the same reaction conditions and procedure they described. Conceivably, the explanation may lie in the quality or purity of the hydride used. In any event, even lithium tri-*t*-butoxyaluminum hydride gave mainly the *cis*-diol VI.

The conversion of the Hantzsch acid into (±)-caldariomycin clearly confirms the structure of the former as 1,4-dihydroxy-3,5,5-trichloro-2-cyclopentene-1-carboxylic acid (III), but it does not establish the stereochemistry. Efforts to obtain a γ-lactone from the acid, or from its conformationally more flexible reduction product IV, by treatment with N,N′-diisopropylcarbodiimide or with acetyl chloride in pyridine[11] were ineffective. Attempts to homologate the diacetate of IV in order to facilitate formation of a less strained δ-lactone were also unsuccessful. Likewise, we were unable to convert the methyl ester of IV into a 1,3-*O*-*p*-nitrobenzylidene derivative.[12] Finally, in an effort to prepare a more readily characterized halogen-free derivative, we carried out further reduction of IV and its methyl ester over palladium in methanol in the presence of potassium carbonate. Rapid uptake of hydrogen occurred, but the dechlorinated products were mixtures containing appreciable amounts of ketonic material.

Although these chemical experiments did not yield any information concerning the stereochemistry of the

(6) (a) A. Hantzsch, *Ber.*, **20**, 2780 (1887); **22**, 1238, 2827 (1889); **23**, 1483 (1890); (b) C. Hoffmann, *ibid.*, **22**, 1263 (1889).

(7) T. Zincke and F. Küster, *ibid.*, **21**, 2719 (1888); **22**, 486 (1889); **23**, 812, 2200 (1890); **26**, 2104 (1893); T. Zincke, *Ann.*, **296**, 135 (1897).

(8) *Cf.* H. van Brederode, H. Gering, and H. J. Prins, *Rec. Trav. Chim.*, **65**, 174, 190 (1946); H. J. Prins, *ibid.*, **65**, 455 (1946); **68**, 384 (1949); J. S. Newcomer and E. T. McBee, *J. Am. Chem. Soc.*, **71**, 946 (1949); E. D. Weil and J. Linder, *J. Org. Chem.*, **28**, 2218 (1963).

(9) Toward the close of his career, Hantzsch cited his original work on this subject, but he did not comment on it [see A. Hantzsch and E. Strasser, *Ann.*, **488**, 203 (1931)].

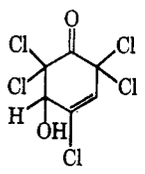
(10) C. J. Moye and S. Sternhell, *Tetrahedron Letters*, 2411 (1964).

(11) A. W. Burgstahler and D. E. Wetmore, *J. Org. Chem.*, **26**, 3516 (1961). *Cf.* the reported difficulty in lactonizing *cis*-3-hydroxycyclopentanecarboxylic acid [D. S. Noyce and J. S. Fessenden, *ibid.*, **24**, 715 (1959)].

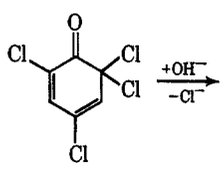
(12) *Cf.* H. Z. Sable and T. Pasternak, *Helv. Chim. Acta*, **45**, 370 (1962).

Hantzsch acid, the characteristics of the O–H stretching patterns in the infrared spectra of the methyl esters of acids III and IV, compared with those of the *trans*- and *cis*-diols I and VI, suggest a *trans*-diol configuration in III and IV. Moreover, as would be expected for an intramolecular carbonyl–hydroxyl interaction in the *trans*-diol arrangement, the position of the carbonyl band in the methyl esters of III and IV was found to occur at slightly longer wavelengths than in the corresponding ester diacetates. The presence of splitting (J = 1.5 cps) of the C-4 proton signal in the nmr spectra of both the Hantzsch acid and its methyl ester, but not in the spectra of the diacetates, likewise tends to indicate an intramolecular carbonyl–hydroxyl interaction in III and its methyl ester, as would be expected with a *trans*-diol configuration. However, in the absence of more explicit evidence, the configuration of III and IV and their derivatives must be regarded as uncertain.

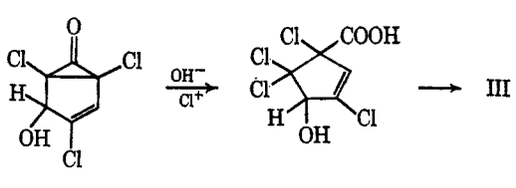
With respect to the mechanism of formation of the Hantzsch acid, a pathway involving ring contraction of an intermediate of type VIII has been proposed by Moye and Sternhell.[10] An alternative, but not necessarily more likely, mechanism would be a Favorskii-type rearrangement of the dienone IX with chlorination of the intermediate cyclopropanone X, leading to the allylic α-chloro acid XI and thence to III.



VIII

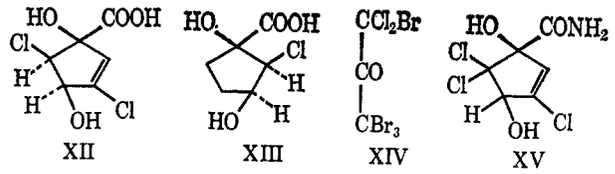


IX



X XI

Among other aspects of the chemistry of the Hantzsch acid that we have reinvestigated are reduction with sodium amalgam, degradation by bromine, ammonolysis of the methyl ester, and dehydrochlorination by sulfuric acid. In accordance with Hantzsch's observations,[6a] we found that reduction of the acid III by sodium amalgam furnished an unsaturated dichloro acid, the nmr spectrum of which confirmed his proposal that the vinyl chlorine atom had been retained and that one of the geminal chlorine atoms had been replaced. This product is therefore formulated as XII. The 4,5-*cis* stereochemistry of XII is suggested by the magnitude (6.5 cps) of the C-4 and C-5 proton coupling constants. Furthermore, the stability of this product toward aqueous alkali can also be interpreted as supporting a *cis* relationship between the hydroxyl group at C-4 and the chlorine atom at C-5.



XII XIII XIV XV

On hydrogenation over palladium on carbon, XII furnished the saturated monochloro acid XIII, which, under neutral or acidic conditions, was resistant to further hydrogenolysis. Hydrogenation of the methyl ester of XIII over palladium under basic conditions failed to completely remove the remaining chlorine atom.

The action of bromine on the Hantzsch acid in a sealed tube at 120° led, as reported,[6a] to a mixture of carbon dioxide, oxalic acid, and a polyhalogenated ketone, mp 80–81°, which was correctly identified by Hantzsch as *unsym*-dichlorotetrabromoacetone (XIV). Similar results have been observed in the bromination of other oxygenated cyclopentane derivatives.[13] In agreement with Hantzsch's additional suggestion, it was confirmed that XIV on reaction with ammonia furnishes a 2:1 mixture of bromodichloroacetamide and tribromoacetamide (plus the corresponding haloforms).

Reaction of the methyl ester of the Hantzsch acid with ammonia in methanol at 80° in the manner described by Hantzsch's co-worker, Hoffman,[6b] gave the expected diol amide XV and not a dihydroxypyridine derivative, as proposed by Hoffmann. The analytical and spectral properties of this product, as well as its behavior on acetylation, are in complete accord with its formulation as XV. The same sequence of reactions was also carried out by Hoffmann on acid XII to give a product which was identical with that obtained by sodium amalgam reduction of XV.

Hoffmann also reported that the ammonia product XV was converted by phosphorus pentachloride in a sealed tube at 350° into a perchloro derivative, mp 32°, of the composition C_4Cl_6. We have attempted to repeat this experiment but have not been able to isolate this substance. Hoffmann's designation of this product as hexachloro-1,3-butadiene is not in accord with the known[14] properties of this compound (mp −21°). The analysis and melting point recorded by Hoffmann suggest that the compound he obtained might be octachlorocyclopentene, which is reported[15] to melt at 41° and can be prepared from chlorinated cyclopentenones by reaction with phosphorus pentachloride under similar conditions.[15a,c]

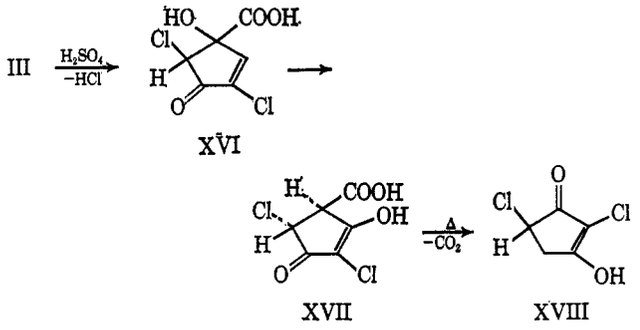
Finally, we have reexamined Hantzsch's interesting dehydrochlorination of acid III brought about by concentrated sulfuric acid at room temperature. This transformation has also been reinvestigated by Moye and Sternhell.[10] From the nmr spectrum, the initial product appears to be the nonenolic keto acid XVI, which, on prolonged contact with sulfuric acid, is slowly isomerized to the enolic β-keto acid XVII.

(13) (a) A. Hantzsch, *Ber.*, **21**, 2421 (1888); **22**, 2841 (1889); (b) H. Landolt, *ibid.*, **25**, 842 (1892); (c) F. J. Moore and R. M. Thomas, *J. Am. Chem. Soc.*, **39**, 974 (1917); (d) *cf.* ref 9.

(14) O. Fruhwirth, *Ber.*, **74**, 1700 (1941).

(15) (a) T. Zincke and F. Küster, *ibid.*, **23**, 2215 (1890); (b) F. Henle, *Ann.*, **352**, 52 (1907); (c) T. Zincke and K. H. Meyer, *ibid.*, **367**, 9 (1909).

Moye and Sternhell have suggested a plausible pathway involving a protonated α,β epoxide for this isomerization. Alternatively, it is conceivable that the oxygen transfer occurs by an intermolecular rather than an intramolecular process, but at present there is no definitive evidence to decide this point.



The *trans* stereochemistry shown in XVII has been assigned on the basis of the nmr spectrum (J_{15} = 2.7 cps).[10] Thermal decarboxylation of XVII yields an enolic β diketone, mp 119–120°,[6a] whose chemical and spectral properties are in accord with structure XVIII proposed recently by Moye and Sternhell[10] and earlier by one of us.[1] Hantzsch had formulated this compound as VII, but apparently he had overlooked the fact that such a structure would not be enolic.

Experimental Section[16]

Preparation of the Hantzsch Acid (III).—Since erratic results were obtained with the original procedures described by Hantzsch[6a] and Hoffmann,[6b] the following modification of the method that they employed was developed. In a typical run, 36.6 g (0.19 mole) of 2,4,6-trichlorophenol was dissolved in 500 ml of 2.5 *M* aqueous sodium hydroxide in a 3-l., three-necked, round-bottomed flask fitted with a gas dispersion tube, thermometer, and a Teflon stirrer. The mixture was cooled to −2° with an acetone–Dry Ice bath, and chlorine was slowly bubbled into the stirred solution while the temperature was maintained at 0–4° by alternate cooling and chlorination. After about 10 min the temperature suddenly rose to 10–15°. The flow of chlorine was stopped, and 100 ml of cold, 5 *M* sodium hydroxide was added. The stirred solution was cooled to −2°, and the flow of chlorine was again resumed. This procedure was repeated two or three times until no further spontaneous change in temperature occurred. Excess hypochlorite was decomposed by slow addition of 12 *M* hydrochloric acid. The solution was then swept with nitrogen to remove residual chlorine, filtered through Celite, and extracted with seven 150-ml portions of ether. The combined ether extracts were dried, filtered, and cooled to 0°. A slow stream of anhydrous ammonia was passed into the cooled, stirred ether solution until the resulting precipitate turned slightly yellow. Decantation and filtration afforded 43 g (88% yield) of the crude ammonium salt of the Hantzsch acid (III). Recrystallization of this material from water gave 25.5 g (52% yield) of product melting at 121–122° dec (lit.[6a] mp 122–123° dec).

For regeneration of the free acid, 132 g (0.50 mole) of the recrystallized salt was dissolved with warming in 250 ml of 35% sulfuric acid and the resulting mixture was extracted eight times with 100-ml portions of ether. The combined ether extracts were washed three times with 50-ml portions of saturated sodium chloride solution and stirred for 2 hr with 10 g of finely divided barium chloride hydrate to remove residual sulfuric acid. After filtration, the ether solution was evaporated to yield 110 g (89% recovery) of the free acid III. Recrystallization from ether–petroleum ether furnished 92 g (74% yield from the salt) of the pure Hantzsch acid (1,4-dihydroxy-3,5,5-trichloro-2-cyclopentene-1-carboxylic acid, III), mp 178–179° (lit.[6a] mp 177–178°). The acid gave a negative (qualitative and quantitative) test with periodic acid. It was transparent in the ultraviolet above 220 mμ. Its nmr spectrum (D_2O, with external tetramethylsilane as reference) showed doublets ($J \sim 1.5$ cps) at τ 4.28 and 3.42, assigned, respectively, to the nonexchangeable protons at C-4 and C-2.

Anal.[17] Calcd for $C_6H_5Cl_3O_4$: C, 29.12; H, 2.04; mol wt, 247.5. Found: C, 29.22; H, 2.02; mol wt, 248, 250 (Rast); equiv wt, 249 (titration).

The methyl ester of III, mp 125.5–126° (lit.[6a] mp 125–126°), was prepared from the acid in 90% yield in the manner described by Hantzsch[6a] or quantitatively by the action of diazomethane. It had $\lambda_{max}^{CCl_4}$ 5.73 μ. The nmr spectrum (in $CDCl_3$) had signals at τ 6.12 (ester methyl group, singlet, three protons), 5.04 (C-4 proton, doublet, J = 1.2 cps), and 4.07 (C-2 vinyl proton, doublet, J = 1.2 cps).

Anal.[17] Calcd for $C_7H_7Cl_3O_4$ (261.5): C, 32.14; H, 2.70. Found: C, 32.20; H, 2.56.

The diacetate of III, mp 191–192° (lit.[6a] mp 191–192°), was obtained from III in 75% yield in the manner described by Hantzsch.[6a] It had $\lambda_{max}^{CHCl_3}$ 5.74 μ. The nmr spectrum ($CDCl_3$) exhibited signals at τ 7.83 and 7.75 (acetate methyls, singlets, six protons), 3.85 (C-2 vinyl proton, singlet), and 3.40 (C-4 proton, singlet), corresponding to the expected downfield shift on acetylation.

The methyl ester diacetate of III was prepared by the action of diazomethane on the preceding compound or by acetylation of the methyl ester of III in refluxing acetic anhydride. It deposited from 50% aqueous acetic acid as fine prisms: mp 93–95°; $\lambda_{max}^{CCl_4}$ 5.72 μ; nmr ($CDCl_3$), τ 7.83 and 7.77 (acetate methyls, singlets, six protons), 6.15 (ester methyl, singlet, three protons), 3.95 (C-2 vinyl proton, singlet), and 3.40 (C-4 proton, singlet).

Anal. Calcd for $C_{11}H_{11}Cl_3O_6$ (345.6): C, 38.23; H, 3.21. Found: C, 38.32; H, 3.02.

Hydrogenation of the Hantzsch Acid (III).—A solution of 5.0 g (0.02 mole) of the acid III in 30 ml of 95% ethanol was stirred under 1 atm of hydrogen with 0.5 g of 30% palladium–charcoal catalyst. After 1 hr hydrogen uptake ceased (1040 ml at 25° and 740 mm), and the catalyst was removed by filtration. Evaporation of the filtrate under reduced pressure and crystallization of the product from ethyl acetate–petroleum ether afforded 3.9 g (90% yield) of 2,2-dichloro-1,3-dihydroxycyclopentane-1-carboxylic acid (IV): mp 177.5–178.5° (with III, mmp 145–158°); λ_{max}^{Nujol} 5.80 μ; nmr (pyridine-d_5), τ 7.23–8.00 (multiplet, four methylene protons) and 4.38 (C-3 proton, triplet, J = 6 cps).

Anal. Calcd for $C_6H_8Cl_2O_4$ (215.0): C, 33.51; H, 3.75; Cl, 32.98. Found: C, 33.69; H, 3.92; Cl, 32.80.

Hydrogenation of acid IV under basic conditions as described below for the methyl ester yielded a halogen-free oil that gave a mixture of orange and yellow 2,4-dinitrophenylhydrazones which were not investigated further.

The methyl ester of IV (diazomethane) crystallized from ether–petroleum ether as a fine powder: mp 62–63°; $\lambda_{max}^{CCl_4}$ 5.74 μ; nmr (CF_3CO_2H), τ 7.15–8.08 (multiplet, four methylene protons), 6.02 (ester methyl, singlet, three protons), and 5.14 (C-3 proton, triplet, J = 6.0 cps).

Anal. Calcd for $C_7H_{10}Cl_2O_4$ (229.1): C, 36.70; H, 4.40; Cl, 30.96. Found: C, 36.58; H, 4.31; Cl, 30.83.

Hydrogenation of 810 mg (3.5 mmoles) of the methyl ester of IV in 20 ml of absolute methanol with 600 mg of 5% palladium–charcoal catalyst and 1.65 g (12 mmoles) of potassium carbonate was complete after 10 min with absorption of 121 ml of hydrogen (70% of theory) at 26° and 738 mm. The mixture was filtered and the filtrate was acidified with a few drops of hydrochloric acid. Distillation of the solvent at atmospheric pressure and extraction of the residue with ethyl acetate afforded a halogen-free oil (negative Beilstein test) whose infrared and nmr spectra indicated the presence of hydroxy ester. However, the oil also deposited a considerable amount (370 mg) of an orange 2,4-dinitrophenylhydrazone (λ_{max}^{EtOH} 378 mμ) from which, by chromatography on silica gel and crystallization from ethyl acetate–etha-

(16) Melting points were determined in open capillaries with a Hershberg melting point apparatus calibrated against standard substances. Infrared spectra were taken on a Beckman IR-8 infrared spectrophotometer. Ultraviolet spectra were recorded on a Cary Model 14 spectrophotometer. The nmr spectra were determined on a Varian A-60 spectrometer with tetramethylsilane as reference, used internally, except where noted otherwise. Microanalyses were performed by the Weiler and Strauss Microanalytical Laboratory, Oxford, England. Unless otherwise stated, anhydrous magnesium sulfate was employed as a drying agent. The petroleum ether used boiled in the range 35–60°.

(17) Hantzsch[6a] also reported a correct analysis for this compound.

nol, an orange 2,4-dinitrophenylhydrazone, mp 167–168°, was isolated as the principal component. The nmr spectrum (CF_3CO_2H) of this derivative exhibited peaks at τ 7.62, 7.06, 6.05, 5.93, and 2.25–0.75, with approximate relative areas of 2:2:1:1:3, respectively. A strongly depressed mixture melting point (139–144°) and marked spectral differences showed that this derivative was not 2-cyclopenten-1-one 2,4-dinitrophenylhydrazone (orange-red, mp 167–169°).

The diacetate of IV was prepared by acetylation of the acid with refluxing acetic anhydride. It crystallized from ether–cyclohexane as a fine powder: mp 125–127°; $\lambda_{max}^{CHCl_3}$ 5.71 μ; nmr (pyridine-d_5), τ 7.85 and 7.79 (acetate methyls, singlets, six protons), 6.63–8.07 (multiplet, four methylene protons), and 3.53 (C-3 proton, triplet, J = 7.8 cps).

The methyl ester diacetate of IV was prepared quantitatively by the action of diazomethane on the preceding compound or in 85% yield by hydrogenation of the methyl ester diacetate of the Hantzsch acid (III) over 30% palladium–charcoal catalyst in absolute ethanol. It crystallized from acetic acid as needles: mp 108–109°; $\lambda_{max}^{CCl_4}$ 5.70 μ; nmr ($CDCl_3$), τ 7.85 and 7.83 (acetate methyls, singlets, six protons), 6.80–8.08 (four methylene protons, multiplet), 6.18 (ester methyl, singlet, three protons), and 4.33 (C-3 proton, triplet, J = 7.0 cps).

Anal. Calcd for $C_{11}H_{14}Cl_2O_6$ (313.1): C, 42.19; H, 4.51. Found: C, 42.05; H, 4.43.

Hydrogenation of the methyl ester diacetate of IV under the conditions described above for the methyl ester of IV was accompanied by considerable loss of acetate and the formation of ketonic products. In the presence of triethylamine the hydrogenation gave a complex mixture of products in which halogen was still present.

Conversion of Acid IV into Cyclopentanone.—In a typical experiment, 0.85 g (4.0 mmoles) of the dichlorodihydroxy acid IV was treated with 1.80 g (4.1 mmoles) of lead tetraacetate in 10 ml of glacial acetic acid containing 2 drops of water. After 40 min, evolution of carbon dioxide ceased (76 ml at 728 mm and 24°; 73% of theory). The mixture was diluted with 25 ml of water and extracted with four 25-ml portions of ether. The combined extracts were washed twice with saturated sodium chloride solution and dried, and the ether was evaporated under reduced pressure. The residue (V) was taken up in 10 ml of 95% ethanol containing 2 drops of 70% perchloric acid, and the solution was stirred under hydrogen with 0.3 g of 30% palladium–charcoal catalyst. After 4 hr hydrogen absorption was complete, the mixture was filtered, and the filtrate was treated with 2,4-dinitrophenylhydrazine reagent. The resulting yellow solid was identified as the 2,4-dinitrophenylhydrazone of cyclopentanone (0.53 g, 50% yield) by its nmr spectrum (multiplets at τ 7.0 and 8.0) and undepressed mixture melting point (146–148°) with an authentic sample after recrystallization.

2,2-Dichloro-*cis*-1,3-cyclopentanediol (VI). A. From the Dichlorodihydroxy Acid IV.—The oily product V from the action of 1.8 g (4.0 mmoles) of lead tetraacetate on 0.85 g (4.1 mmoles) of acid IV (for procedure, see above) was dissolved in 10 ml of 50% isopropyl alcohol and the resulting solution cooled to −10°. Sodium borohydride (0.2 g, 5.3 mmoles) was added to the stirred solution. After 1 hr, 50 ml of cold 2 N hydrochloric acid was added slowly, and the resulting solution was extracted with five 25-ml portions of ether. The combined extracts were washed twice with saturated sodium chloride solution and dried. Evaporation of the ether under reduced pressure, followed by sublimation (12 mm, bath temp 105°), yielded 0.23 g (34%) of 2,2-dichloro-*cis*-1,3-cyclopentanediol (VI): mp 132–134° (lit.[5] mp 135.5°); $\lambda_{max}^{CCl_4}$ (1-cm quartz cell) 2.71 (vw) and 2.77 (s) μ; λ_{max}^{KBr} 3.05 (b), 6.8 (m), 7.5 (s), 7.9 (w), 8.0 (w), 8.9 (s), 9.4 (m), 10.7 (w), 10.9 (m), 11.4 (s), 13.1 (m), 13.5 (s) μ; nmr (CF_3CO_2H), τ 7.50–8.23 (four methylene protons, multiplet) and 5.30 (C-1 and C-3 protons, unresolved peak).

Anal. Calcd for $C_5H_8Cl_2O_2$ (171.0): C, 35.11; H, 4.72; Cl, 41.46. Found: C, 35.13; H, 4.96; Cl, 41.60.

B. From 2,2-Dichloro-1,3-cyclopentanedione (VII).—The preparation of 2,2-dichloro-1,3-cyclopentanedione (VII) was conducted in the manner described by Hager and Beckwith.[5] Reduction of 500 mg (3 mmoles) of this dione, mp 82–83° (lit.[5] mp 83.5°), with 270 mg (7.1 mmoles) of lithium aluminum hydride in ether at −2° according to the procedure of these authors, and isolation of the product as was described by them, afforded 195 mg (38% yield) of 2,2-dichloro-*cis*-1,3-cyclopentanediol (VI), mp 133–134° (lit.[5] mp 135.5°). Concentration and cooling of the filtrate to −22° for 3 hr furnished an additional 25 mg (5%) of this same product (mp and mmp 132–134°). Further concentration of the filtrate, followed by sublimation (14 mm, bath temp 95°), yielded an oil from which no *trans*-diol I deposited on being cooled and seeded in carbon tetrachloride.

Reduction of VII with sodium borohydride or lithium tri-*t*-butoxyaluminum hydride also afforded only the *cis*-diol VI (20–35% yield).

2,2-Dichloro-*trans*-1,3-cyclopentanediol (I). A. From the Dichlorodihydroxy Acid IV.—The crude hydroxy ketone V, derived from the oxidation (for procedure, see above) of 1.0 g (4.7 mmoles) of the acid IV with 2.1 g (4.7 mmoles) of lead tetraacetate, was dissolved in 15 ml of dry ether. Over a period of 30 min the resulting solution was added to a stirred solution of a large excess (0.60 g, 28 mmoles) of lithium borohydride in 30 ml of anhydrous ether cooled to the temperature of Dry Ice–acetone (−75°). The reaction was maintained at this temperature for 5 hr, and the mixture was then poured onto 80 g of ice, to which 15 ml of 12 M hydrochloric acid had been added. The product was recovered by extraction with five 100-ml portions of ether. The combined extacts were washed twice with saturated sodium chloride solution and dried. After evaporation of the solvent, the residue was dissolved in chloroform, and, after repeated concentration, crystallization afforded 190 mg (24% yield) of the *cis*-diol VI, mp 133.5–134.5°. Evaporation of the mother liquors and sublimation of the residue (25 mm, bath temp 95°) yielded 41 mg (5% yield) of the *trans*-diol I: mp 88.5–89.5° (lit.[5] mp 89–90°); $\lambda_{max}^{CCl_4}$ (1-cm quartz cell) 2.69 (w) and 2.75 (s) μ; $\lambda_{max}^{CHCl_3}$ as reported by Hager and Beckwith;[5] nmr (CF_3CO_2H), τ 8.32 (four methylene protons, multiplet) and 5.17 (C-1 and C-3 protons, poorly resolved triplet).

Anal. Calcd for $C_5H_8Cl_2O_2$ (171.0): C, 35.17; H, 4.72; Cl, 41.46. Found: C, 34.95; H, 4.54; Cl, 41.10.

B. From 2,2-Dichloro-1,3-cyclopentanedione (VII).—A solution of 500 mg (3 mmoles) of the dione VII in 10 ml of anhydrous ether was added over 30 min to a stirred solution of 130 mg (6 mmoles) of lithium borohydride in 10 ml of anhydrous ether at −10°. After 3 hr the mixture was added to 30 ml of cold, 2 N hydrochloric acid and extracted with five 25-ml portions of ether. The combined extracts were washed twice with 20-ml portions of saturated sodium chloride solution and dried. Evaporation of the solvent and crystallization of the residue from chloroform gave 190 mg of solid, mp 120–125°. When sublimed (15 mm, bath temp 100°), this afforded 129 mg (25% yield) of the *cis*-diol VI, mp 134–135° (lit.[5] mp 135°). Evaporation of the mother liquors and sublimation of the residue (20 mm, bath temp 95°) furnished 66 mg (13% yield) of the *trans*-diol I, mp 89.0–90.5° (lit.[5] mp 89–90°).

3,5-Dichloro-1,4-dihydroxy-2-cyclopentene-1-carboxylic Acid (XII).—A solution of 2.47 g (0.01 mole) of the acid III in 15 ml of water was stirred with 50 g of 2% sodium amalgam. After 30 min, the aqueous layer was separated from the mercury, acidified with cold, concentrated hydrochloric acid, and extracted with five 25-ml portions of ether. The combined extracts were washed twice with saturated sodium chloride solution and dried, and the ether was evaporated. Crystallization of the residue from water afforded 1.85 g (87% yield) of the unsaturated dichloro acid XII as fine needles: mp 176–177° (lit.[6a] mp 176–177°); nmr (D_2O, external tetramethylsilane), τ 5.90 (C-5 proton, doublet, J = 6.5 cps), 5.28 (C-4 proton, doublet, J = 6.5 cps with additional fine splitting, J = 1.2 cps), and 3.95 (C-2 vinyl proton, doublet, J = 1.2 cps).

Anal.[17] Calcd for $C_6H_6Cl_2O_4$ (213.0): C, 33.83; H, 2.84. Found: C, 34.00; H, 2.80.

2-Chloro-1,3-dihydroxycyclopentane-1-carboxylic Acid (XIII).—A solution of 150 mg (0.70 mmole) of the unsaturated dichloro acid XIV in 20 ml of 95% ethanol was stirred under hydrogen with 50 mg of 30% palladium–charcoal catalyst. After completion of hydrogen uptake (32 ml at 735 mm and 24°), the mixture was filtered, and the filtrate was evaporated under reduced pressure. Crystallization of the resulting solid from ether–cyclohexane yielded 120 mg (94%) of the powdery monochloro acid XIII: mp 167.5–168.5°; nmr (CF_3CO_2H), τ 7.53 (four methylene protons, multiplet) and 5.2–5.65 (overlapping doublet and triplet, two protons).

Anal. Calcd for $C_6H_9ClO_4$ (180.6): C, 39.90; H, 5.02; Cl, 19.63. Found: C, 40.14; H, 5.14; Cl, 19.52.

Attempts to remove the remaining chlorine atom in XIII by further hydrogenolysis over platinum or palladium in ethanol or acetic acid at temperatures up to 65° gave only starting material. Hydrogenation over palladium–charcoal in methanol in the pres-

ence of potassium carbonate also failed to complete the removal of halogen. On one occasion, as an alternative procedure, treatment of 180 mg (1 mmole) of XIII with a large excess of 2% sodium amalgam in 10 ml of water for 4 hr furnished, after crystallization from ethyl acetate, 88 mg of an acidic product, mp 122–123° dec, which gave a negative Beilstein test. The nmr spectrum (CF_3CO_2H) had a complex multiplet at τ 7.3–8.3 and signals at 5.7 (singlet or close doublet) and 5.2 (triplet). Efforts to repeat the preparation of this product, however, were unsuccessful.

1,1-Dichloro-1,3,3,3-tetrabromo-2-propanone (XIV).—A solution containing 2.0 g (8.1 mmoles) of the Hantzsch acid (III) in 10 ml of water was heated in a sealed tube with 10 ml of reagent grade bromine at 120° for 1 hr. When cool, the tube was opened, and the compressed gas was identified as carbon dioxide by precipitation of barium carbonate from a solution of barium hydroxide. After evaporation of the residual bromine, the suspended solid was collected by filtration and crystallized from nitric acid to yield 0.64 g (18%) of the perhalo ketone XIV, as colorless needles: mp 80–81° (lit.[6a] mp 80–81°); $\lambda_{max}^{CHCl_3}$ 5.7 (s), 9.2 (s), 11.4 (s) μ; nmr (CCl_4), no protons.

Anal.[17] Calcd for $C_3Br_4Cl_2O$ (442.6): C, 8.14; H, 0.00; Br, 72.22; Cl, 16.02. Found: C, 8.10; H, 0.00; Br, 72.00; Cl, 16.20; mol wt, 435 (Rast, average of three determinations).

For the cleavage with ammonia, 400 mg (1.8 mmoles) of the above ketone XIV was dissolved in 20 ml of dry ether which had been saturated with anhydrous ammonia. After 2 hr at 25°, the mixture was concentrated under reduced pressure and the residue was crystallized from carbon tetrachloride to yield 170 mg of a 2:1 mixture of bromodichloroacetamide and tribromoacetamide, mp and mmp 129–130° with an authentic sample (see below) (lit.[6a] mp 131°). Thin layer chromatography with various solvent systems failed to resolve this mixture.

Authentic Bromodichloroacetamide and Tribromoacetamide.—A mixture of 10 g (0.78 mole) of dichloroacetic acid,[18] 15 ml (0.18 mole) of oxalyl chloride, and 1 drop of pyridine was allowed to stand until no more gas evolution occurred (4 hr). After evaporation of the excess oxalyl chloride under reduced pressure, 20 g of bromine and 1 g of phosphorus tribromide were added to the residue. The mixture was refluxed for 72 hr and concentrated under reduced pressure, and the brownish residue was cooled to −10°. Cold, concentrated ammonium hydroxide was added with stirring, and the resulting precipitate was collected and dried *in vacuo*. Recrystallization of this solid from chloroform afforded 1.15 g (7% yield) of bromodichloroacetamide, mp 138–139° (lit.[13b] mp 139°).

The preparation of tribromoacetamide from tribromoacetic acid[19] was conducted in a similar manner. This derivative, mp 120–121° (lit.[20] mp 120–121°) was obtained in a 57% yield after recrystallization from carbon tetrachloride.

Melting points of crystallized mixtures of bromodichloroacetamide and tribromoacetamide were determined as shown in Table I.

TABLE I

Molar ratio, $CCl_2BrCONH_2/CBr_3CONH_2$	Mp, °C
3.5	126.5–128
2.5	133.5–135.5
2.0[a]	129–130
1.0	124.5–126
0.5	125–126.5

[a] Used in mixture melting point determination with the product from XIV and ammonia.

1,4-Dihydroxy-3,3,5-trichloro-2-cyclopentene-1-carboxamide (XV).—A solution of 2.0 g (7.6 mmoles) of the methyl ester of acid III in 50 ml of absolute methanol saturated with anhydrous ammonia was heated at 80° for 25 min in a sealed tube. Concentration of the brown solution and repeated evaporation of the residue from methylene chloride afforded a dark tan solid, from which 0.34 g (17% recovery) of the starting material was isolated by extraction with methylene chloride. Recrystallization of the remaining solid from acetone–petroleum ether yielded 1.37 g (73%) of the amide XV as a fine powder: mp 192.5–194° (lit.[6b] mp 193–194°); λ_{max}^{Nujol} 2.87 (w), 3.1–3.2 (m), 3.41–3.51 (s), 5.97 (s), 6.17 (w) μ; nmr (CF_3CO_2H), τ 4.55 (C-4 proton, singlet), 4.04 (C-2 vinyl proton, singlet), and 2.35 (amide protons, broad peak, two protons).

Anal. Calcd for $C_6H_6Cl_3NO_3$ (246.5): C, 29.23; H, 2.45; Cl, 43.15; N 5.68. Found: C, 29.39; H, 2.42; Cl, 43.20; N, 5.73.

Treatment of 250 mg (1.0 mmole) of the preceding product with 25 ml of acetic anhydride at reflux, followed by concentration at reduced pressure, afforded a brown oil which was dissolved in methylene chloride and decolorized with Norit. After removal of the solvent, the residue was recrystallized from water–acetic acid to give 80 mg (37%) of the 4-monoacetate of XV: mp 161–162°; λ_{max}^{Nujol} 5.7 and 5.95 μ; nmr (CF_3CO_2H), τ 7.61 (acetate methyl, singlet, three protons), 3.95 (C-2 vinyl proton, singlet), 3.46 (C-4 proton, singlet), and 2.32 (amide protons, broad peak, two protons).

Anal. Calcd for $C_8H_8Cl_3NO_4$ (288.5): C, 33.30; H, 2.79; Cl, 36.87; N, 4.86. Found: C, 33.04; H, 2.70; Cl, 38.00; N, 4.85.

As one of the methods for the preparation of the diacetate of the amide XV, 0.5 g (1.7 mmoles) of the preceding monoacetate was heated at reflux for 24 hr in acetic anhydride. After evaporation of the mixture under reduced pressure, followed by treatment of the residue with Norit in ethyl acetate, the desired product was crystallized by the addition of petroleum ether to the hot ethyl acetate solution. This procedure afforded 0.11 g (20% yield) of the diacetate of XV as a fine powder: mp 183–184° (lit.[6b] mp 184–185°); λ_{max}^{Nujol} 5.69 and 5.89 μ; nmr (CF_3CO_2H), τ 7.65 and 7.60 (acetate methyls, singlets, six protons), 3.83 (C-2 vinyl proton, singlet), 3.13 (C-4 proton, singlet), and 2.55 (amide protons, broad singlet, two protons).

Anal. Calcd for $C_{10}H_{10}Cl_3NO_5$ (330.6): C, 36.33; H, 3.05; Cl, 32.17; N, 4.24. Found: C, 36.16; H, 3.14; Cl, 32.08; N, 4.12.

A second method for the preparation of the diacetate of the amide XVII consisted of converting the diacetate of the Hantzsch acid (III) into its acid chloride by the action of oxalyl chloride, followed by treatment with cold, concentrated ammonium hydroxide and crystallization of the product from ethyl acetate–petroleum ether (mp and mmp 183–184°; infrared and nmr spectra identical).

Action of Sulfuric Acid on the Hantzsch Acid (III).—A solution of 2.47 g (0.01 mole) of the acid III in 20 ml of concentrated sulfuric acid at 0° was allowed to warm slowly to 23° while hydrogen chloride gradually evolved. The nmr spectrum (sulfuric acid, external tetramethylsilane), after 20 min, had signals at τ 2.68 (singlet) and 4.72 (singlet), corresponding to protons in the unstable acid XVI plus some starting material. New signals at τ 5.70 (doublet, J = 2.4 cps) and 4.95 (doublet, J = 2.4 cps), owing to XVII, gradually appeared, and after 5.5 hr the spectrum no longer indicated the presence of either III or XVI. After standing overnight, the mixture was poured onto 200 g of crushed ice, and the product XVII was recovered by repeated extraction with ether. This material was obtained as an oil which, after being cooled and triturated with petroleum ether, yielded 1.75 g (83%) of the acid XVII as a pale, tan solid, mp 145–149° (lit.[6a] mp 150–151°). Efforts to recrystallize this substance from water, as described by Hantzsch,[6a] led to extensive decomposition, and therefore no further purification was attempted. In contrast to negative tests with the Hantzsch acid (III), XVII was found to give a deep red solution with ferric chloride, decolorize bromine-water rapidly, and give an orange precipitate with phenylhydrazine. The infrared, ultraviolet, and nmr spectra agreed with those recorded by Moye and Sternhell.[10] The elemental analysis reported by Hantzsch is also in accord with structure XIX. On dehydrogenation in ethanol over 30% palladium–charcoal, this substance absorbed 3 moles of hydrogen, but no solid product could be isolated.

2,4-Dichloro-1,3-cyclopentanedionenol (XVIII).—Thermal decarboxylation of the acid XVII was conducted on 200-mg batches under reduced pressure (0.5 mm) in a microsublimator. During the first stages (bath temp 120–130°) the process was interrupted several times to wipe off aqueous condensate from the condenser. After gas evolution had ceased, the residue began to turn dark brown at a bath temperature of 145–155°. Rapid sublimation of the dichlorodione XVIII then occurred. The average yield was *ca.* 50 mg (32%) of colorless, feathery crystals of

(18) A. I. Vogel, "A Textbook of Practical Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1962, p 431.
(19) L. Schaffer, *Ber.*, **4**, 370 (1871).
(20) B. M. Gupta and J. F. Thorpe, *J. Chem. Soc.*, 1896 (1922).

XVIII: mp 119–120° (lit.[6a] mp 121°); $\lambda_{max}^{CHCl_3}$ 2.90 (m), 3.1–3.4 (w), 5.80 (vs), 6.02 (s), 7.3 (s), 7.7 (w), 7.9 (m), 8.9 (s), 9.3 (w), and 10.3 (m) μ. The ultraviolet and nmr spectra were identical with those recorded by Moye and Sternhell.[10] A deep red solution was produced with aqueous ferric chloride. The correct elemental analysis (for a dichlorocyclopentanedione) was reported by Hantzsch.[6a]

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1,2,4-Triazoles. XV. Proton Magnetic Resonance Spectra of *s*-Triazolo[4,3-*a*]pyridine and *s*-Triazolo[1,5-*a*]pyridine Derivatives[1]

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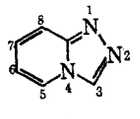
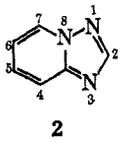
Proton magnetic resonance (pmr) spectral data at 60-Mc for 42 derivatives of the title ring systems are reported. Complete analyses of the spectra have been made and the mode and values of the various coupling constants have been determined. Long-range coupling involving protons separated by five and six bonds was observed. Data obtained for related 1-amino-2-imino-1,2-dihydropyridines are contrasted to those obtained for the bicyclic nuclei.

Interest in the chemistry of *s*-triazole and its various ring-fused derivatives has included a study[2,3] of the *s*-triazolo[4,3-*a*]pyridine nucleus (**1**) and the isomeric *s*-triazolo[1,5-*a*]pyridine nucleus (**2**), and in this communication we describe the proton magnetic resonance data for members of these systems. There has been considerable interest in relating proton magnetic resonance data to the various electronic properties associated with heteroaromatic molecules,[4] a logical extension of the extensive studies of the relationship between chemical shifts and π-electron densities in various benzenoid systems.[5] Pmr data for several bridgehead nitrogen systems of the indolizine type have been described in the recent literature[4] and the data for the two *s*-triazolopyridines are of considerable interest in relation to these studies. Closely related to the present system was an investigation[4b] of the *s*-triazolo[1,5-*a*]pyrimidine ring system (**3**).



1



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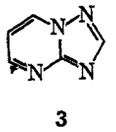

3

Interpretation and Analysis of Spectra.—The spectrum of *s*-triazolo[4,3-*a*]pyridine is shown in Figure 1 and the spectral parameters of the members of this ring system studied are listed in Table I. Those of the *s*-triazolo[1,5-*a*]pyridine system are shown in Table II. A first-order analysis of the spectra based on a five-spin model gave a satisfactory explanation for the splitting patterns obtained in all cases and verification of the multiplet assignments was possible by C-methyl substitution around the periphery of the nucleus. The similarity between the spectra of the two isomeric systems[6] is clearly shown by the data in the tables. All *s*-triazolo[4,3-*a*]pyridines unsubstituted in the 3 position exhibited a low-field, concentration-dependent peak at τ 1.34–1.14, clearly attributable to the 3 proton as this peak was removed by substitution in the 3 position. In the *s*-triazolo[1,5-*a*]pyridines, the corresponding proton in the 2 position occurred at higher field (τ 1.65). The other assignments are in good agreement with those reported[4,7,8,15,16] for similar heterocyclic systems. Inter-ring coupling between the 3 and 8 proton was found to be present, as evidenced by the following considerations. Very slow passage through the 3-proton singlet revealed a reproducible, doublet splitting of the order of 1 cps. The τ 1.79 doublet of the 5 proton, which always absorbed at lower field relative to the other pyridine ring protons, had superimposed

(1) (a) Support of this work by Public Health Service Research Grant CA 05973-03,04 National Cancer Institute, is gratefully acknowledged; (b) present address, Department of Chemistry, Rensselaer Polytechnic Institute, Troy, N. Y. 12181; (c) taken in part from the Ph.D. thesis of S. W. Thomas, University of Louisville, 1964.

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