and phosphite (30 g.) gave 2.2 g. of octachlorobiphthalyl (XIV) (40%, m.p. 375° after hot benzene washings) after 5 minutes at reflux temperature.

Reaction of Tetrachlorophthalic Anhydride with Triethyl Phosphite in the Presence of Diethyl Phosphite.—The anhydride (5.72 g.), triethyl phosphite (20 g.) and diethyl phosphite (5.5 g.) (1:6:2 mole ratio) were heated to reflux and kept there for 5 minutes. On cooling, 1.65 g. (30%) of octachlorobiphthalyl (XIV), m.p. 375–377°, separated.

In the absence of diethyl phosphite, the yield of octachlorobiphthalyl was 40%.

Attempted Reaction of Phthalic Anhydride with Triphenyl Phosphite, $(C_6H_5O)_3P$.—A mixture of anhydride and ester was kept 48 hours at about 200°. From the brown mixture 87% of unreacted phthalic anhydride could be recovered. No biphthalyl was detected.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FORDHAM UNIVERSITY, NEW YORK 58, N. Y.]

Sydnones. III. Preparation and Interconversion of Mercurated Derivatives of N-(3-Pyridyl)-sydnone[1–3a]

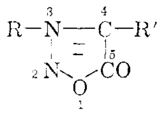
BY JACK M. TIEN AND I. MOYER HUNSBERGER[3b]

RECEIVED JUNE 6, 1960

Mercuration of N-(3-pyridyl)-sydnone (II) has produced either the sydnone–mercuric chloride "adduct" (V), C-chloromercuri-N-(3-pyridyl)-sydnone (VI) or C,C′-mercuri-bis-[N-(3-pyridyl)-sydnone] (VII), depending on the reaction conditions. The adduct V has been converted to VI and to VII. Transformation of VI to VII was accomplished in pyridine solution at room temperature, while VII was converted to VI with excess mercuric chloride. All reactions proceeded in high yield. Sydnones undergo electrophilic substitution virtually as easily as thiophene. Objections to the tropone-like formulation (XI) of sydnones are presented. Preparation of N-(3-pyridyl)-glycine hydrochloride *via* a Strecker-type reaction between 3-aminopyridine and glycolonitrile is more convenient than the earlier process and permits the preparation of large quantities of sydnone II.

Introduction

Considerable effort has been expended on the preparation of a large variety of sydnones (I) and on attempts to elucidate the unusual bond structure of the sydnone ring.[4] The quasi-aromatic nature of this ring was recognized as early as 1946,[5] and N-phenylsydnone (I, R = C_6H_5, R′ = H) was reported to undergo halogenation[5b,6a–c] and nitration[6d] under very mild conditions. Recent work in Japan,[7] in the Soviet Union[8] and in England[9] has concentrated on exploring the chemical reactions of sydnones and has provided additional evidence for the aromatic nature of the sydnone ring. Thus, sydnones unsubstituted in the 4-position (I, R′ = H) have been sulfonated with dioxane–sulfur trioxide,[8a] acetylated in the presence of boron trifluoride etherate[8b] and deuterated with deuterium sulfate.[8b]



I

The successful mercuration of N-phenylsydnone[7b,8a] suggested to us that the sydnone ring undergoes electrophilic substitution as easily as thiophene. Accordingly, we have found that sydnones can be formylated at the 4-position by reaction with N-methylformanilide and phosphorus oxychloride.[10] The present work on the mercuration of N-(3-pyridyl)-sydnone (II) was initiated in order to extend the analogy between sydnones and thiophene and to investigate the effect mercuration would have on the unusual phototropism exhibited by II.[2,11] The known phototropism of certain compounds containing mercury[12] and the antiseptic and fungicidal activity of 3-pyridylmercuric chloride[13] provided added incentive for this study.

Nakahara and Ohta[7b] obtained C-chloromercuri-N-phenylsydnone (III) by mercuration of N-

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(1) Presented, in part, at the Meeting-in-Miniature of the New York A.C.S. Section on March 11, 1960, and at the 138th Meeting of the A.C.S., New York, N. Y., September, 1960.

(2) Paper II, J. M. Tien and I. M. Hunsberger, THIS JOURNAL, **77**, 6604 (1955).

(3) (a) Supported, in part, by a research grant (CY-2962) from the National Cancer Institute of the Public Health Service and by the U. S. Air Force through the Air Force Office of Scientific Research of the Air Research and Development Command, under Contract No. AF18 (603)-127. Reproduction in whole or in part is permitted for any purpose of the United States Government. (b) To whom all inquiries should be sent: Department of Chemistry, University of Massachusetts, Amherst, Mass.

(4) For a recent review on sydnones and other "mesoionic" compounds see W. Baker and W. D. Ollis, *Quart. Revs.* (*London*), **11**, 15 (1957). Also consult: H. U. Daeniker and J. Druey, *Helv. Chim. Acta*, **40**, 918 (1957); P. Zuman, *Z. physik. Chem.* (*Leipzig*), Sonderheft July, 243 (1958); W. Pütter and G. Wolfrum (to Farbenfabriken Bayer Akt. Ges.), German Patent 1,069,633 (Nov. 26, 1959); Farbenfabriken Bayer Akt.-Ges., British Patent 823,001 (Nov. 4, 1959); W. H. Edgerton (to Smith, Kline and French), U. S. Patent 2,916,495 (Dec. 8, 1959).

(5) (a) W. Baker and W. D. Ollis, *Nature*, **158**, 703 (1946); (b) W. Baker, W. D. Ollis and V. D. Poole, *J. Chem. Soc.*, 307 (1949).

(6) (a) J. Kenner and K. Mackay, *Nature*, **158**, 909 (1946); (b) J. C. Earl, E. M. W. Leake and R. J. W. LeFevre, *J. Chem. Soc.*, 2269 (1948); (c) R. A. Eade and J. C. Earl, *ibid.*, 2307 (1948); (d) W. Baker, W. D. Ollis and V. D. Poole, *ibid.*, 1542 (1950).

(7) (a) H. Kato and M. Ohta, *Nippon Kagaku Zasshi*, **77**, 1304 (1956); *C. A.*, **53**, 5250 (1959); (b) K. Nakahara and M. Ohta, *ibid.*, **77**, 1306 (1956); *C. A.*, **53**, 5251 (1959); (c) H. Kato and M. Ohta, *Bull. Chem. Soc. Japan*, **30**, 210 (1957); (d) M. Hashimoto and M. Ohta, *Nippon Kagaku Zasshi*, **78**, 181 (1957); *C. A.*, **54**, 511 (1960); (e) M. Ohta and H. Kato, *ibid.*, **78**, 1653 (1957); (f) M. Hashimoto and M. Ohta, *Bull. Chem. Soc. Japan*, **31**, 1048 (1958); (g) H. Kato and M. Ohta *ibid.*, **32**, 282 (1959).

(8) (a) V. G. Yashunskii, V. F. Vasil'eva and Yu. N. Sheinker, *Zhur Obshch. Khim.*, **29**, 2712 (1959); (b) V. G. Yashunskii and V. F. Vasil'eva, *Doklady Akad. Nauk S.S.S.R.*, **130**, 350 (1960).

(9) F. Stansfield, *J. Chem. Soc.*, 4781 (1958).

(10) C. J. Thoman and D. J. Voaden, unpublished work performed in this Laboratory.

(11) H. S. Gutowsky, R. L. Rutledge and I. M. Hunsberger, *J. Chem. Phys.*, **29**, 1183 (1958).

(12) S. V. Raghava Rao and H. E. Watson, *J. Phys. Chem.*, **32**, 1354 (1928).

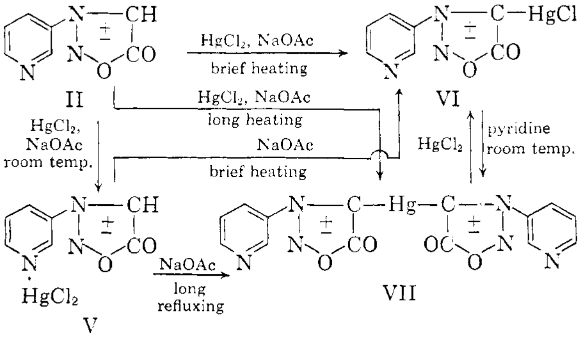
(13) (a) M. W. Swaney, M. J. Skeeters and R. N. Shreve, *Ind. Eng. Chem.*, **32**, 360 (1940); (b) R. N. Shreve and M. W. Swaney (to Mallinckrodt Chemical Works), U. S. Patent 2,297,636 (Sept. 29, 1942); *C. A.*, **37**, 1566 (1943).

phenylsydnone with mercuric chloride and sodium acetate in 50% methanol at room temperature. The conversion of III to C,C'-mercuri-bis-(N-phenylsydnone) (IV) was accomplished with potassium iodide, and mercuric chloride reconverted IV to III.[7b] The Russian workers[8a] obtained IV along with smaller amounts of III by heating N-phenylsydnone for 5 hr. in aqueous ethanol containing mercuric chloride and sodium acetate and also by treating a boiling aqueous solution of the C-acetoxymercuri-N-phenylsydnone with sodium chloride.

The mercuration of N-(3-pyridyl)-sydnone (II) might be expected to be more complex, since pyridine itself is known to react with mercuric acetate at room temperature to give an "adduct" (presumably containing a nitrogen to mercury bond) which is transformed to 3-pyridylmercuric acetate at elevated temperatures.[13a,14] Recent work[15] has shown that iodine and N-phenylsydnone form a 1:1 complex in which the iodine is attached to the carbonyl oxygen atom. Sydnones might be expected to form an "adduct" or "complex" with either iodine or a mercuric salt attached to a sydnone nitrogen atom, but such products have not yet been reported.

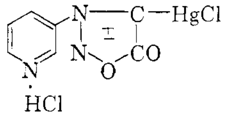
Discussion of Results

Using mercuric chloride in the presence of sodium acetate as the mercurating agent, we have found that either of three products (V, VI or VII) can be obtained in good yield from N-(3-pyridyl)-sydnone (II), depending on the temperature and the duration of the reaction. Thus, mercuration at room temperature produced the sydnone–mercuric chloride "adduct" (V), m.p. 178–179°, regardless of the nature of the solvent or the proportion of reagents used. Brief heating of the same reagents in either absolute or 40% aqueous ethanol afforded the more insoluble C-chloromercuri-N-(3-pyridyl)-sydnone (VI), m.p. 250–260° dec. The extremely insoluble and unusually high-melting mercuri-bis-sydnone (VII) was obtained by heating appropriate quantities of sydnone (II), mercuric chloride and sodium acetate for 4–5 hr. in refluxing 50% aqueous ethanol. In each case conditions were discovered which allowed the indicated product to separate in high yield from the reaction mixture in a crystalline, analytically pure condition.

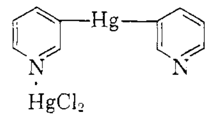


The structures of the three mercurated pyridylsydnones (V, VI and VII) were assigned on the basis of elemental analyses, infrared and ultraviolet spectra, methods of preparation and interconversion reactions. Elemental analyses of the sydnone–mercuric chloride "adduct," m.p. 178–179°, were consistent with two structures (V and VIII), but two kinds of evidence eliminated VIII. Thus, it is unlikely that a hydrochloride (VIII) could be formed in the presence of an excess of sodium acetate. Furthermore, the infrared spectrum showed a sharp band at about 3.2μ[8a,16] and a fairly strong band at about 13.8μ,[16b] both of which are characteristic of the unique CH of the sydnone ring. Hence, the sydnone ring must be unsubstituted at the 4-position. Whether structure V should be represented as the ionic N-chloromercuri chloride was not established.

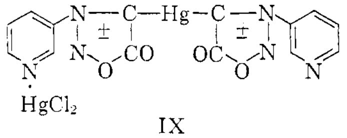
Elemental analyses of the mercurated sydnone, m.p. 250–260° dec., were consistent with either of two structures (VI or IX)[17]; the same is true



VIII



X



IX

of the infrared spectrum, which showed no absorption at 3.2μ and only a weak band at 13.7μ. The relatively great insolubility of the compound precluded a molecular weight determination. Structure IX is considered to be highly unlikely since the compound is formed from the sydnone II and also from V under milder conditions than are required to form VII. Conversion of this compound to an N-alkylpyridinium salt and elemental analysis of the latter would permit a rigorous assignment of structure, but up to the present we have been unable to accomplish such a reaction. Previous workers[13,18] apparently have not considered the possibility that compounds such as 3-pyridylmercuric chloride may have structure X.

That the high-melting mercurated sydnone has structure VII is indicated by elemental analyses and by the lack of CH absorption at both 3.2 and 13.7μ. In passing, it may be noted that the carbonyl absorption of both VI and VII was centered at 5.9 μ whereas that of V and II[2] was centered at 5.8μ.

The sydnone-mercuric chloride adduct V was transformed in high yield to either VI or VII by heating for short or long periods, respectively, in refluxing absolute ethanol containing excess sodium acetate. The conversion of V to VI is somewhat reminiscent of the earlier-mentioned conversion of the pyridine–mercuric acetate adduct to 3-pyridyl-

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(14) C. K. Kanvinde, R. S. Borkar, A. N. Kothare, and V. V. Nadkarny, *J. Univ. Bombay*, **11**, Pt. 3, 101 (1942); *C. A.*, **37**, 2008 (1943).

(15) H. Yamada and K. Kozima, THIS JOURNAL, **82**, 1543 (1960).

(16) (a) D. J. Voaden, D.Phil. Thesis, Oxford University, 1957; (b) C. V. Greco, Ph.D. Thesis, Fordham University, 1959.

(17) We are indebted to Dr. D. J. Hennessy for calling this to our attention.

(18) C. D. Hurd and C. J. Morrissey, THIS JOURNAL, **77**, 4658 (1955).

mercuric acetate.[13a,14] The much milder conditions and the preferential mercuration of the sydnone ring reflect the much greater susceptibility of the sydnone ring to substitution reactions.

The conversion of the mercuri-bis-sydnone (VII) to the C-chloromercurisydnone (VI) was accomplished in high yield by brief heating with excess mercuric chloride in 75% ethanol. The conversion of VI to VII was effected in equally high yield *at room temperature in pyridine solution.* The same procedure was used to convert other C-chloromercurisydnones to mercuri-bis-sydnones but failed to convert other chloromercuri compounds, *e.g.*, chloromercurithiophene, to mercury diaryls.[19] Hence, this very interesting reaction appears to be limited to mercurated sydnones.

TABLE I

ULTRAVIOLET SPECTRA OF N-(3-PYRIDYL)-SYDNONE AND ITS MERCURATED DERIVATIVES

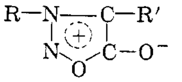
Compd.	λmax, mμ	ϵmax
II	312	8,100
	265	9,400
	236	10,000
V	312	5,354
	260[a]	6,108[a]
	229	12,577
VI	312	4,843
VII	310	7,820
	266.5	11,610
	222.3	10,180

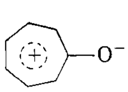
[a] Inflection point.

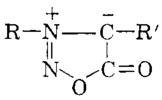
The ultraviolet spectra of the parent sydnone (II) and the three mercurated sydnones (V, VI and VII) all showed (see Table I) a maximum near 312 mμ (characteristic of pyridylsydnone), but the corresponding ϵ-values of V and VI were much lower than those of II and VII. If the compound to which we have assigned structure VI had the alternate structure IX, one might expect the spectra of this compound and of VII to bear somewhat the same relationship as the spectra of V and II. Since this is not the case, the ultraviolet spectra appear to be consistent with the structures assigned, even though it is not clear why VI was the only compound devoid of maxima below 300 mμ.

None of the mercurated pyridylsydnones was phototropic at room temperature, but exposure to daylight caused V, VI and VII to change irreversibly from colorless to yellow at a rate which decreased in the order given.

Both general considerations and the ease with which sydnones undergo electrophilic substitution reactions constitute objections to the recent formulation (XI) of sydnones.[20] The analogy between structure XI for sydnones and structure XII for tropone is faulty because only in the case of tropone is it *impossible* to write any canonical structure (dipolar or otherwise) in which a negative charge resides on a ring carbon atom; in fact, all carbon atoms of tropone possess at least small positive charges. On the other hand, it is possible to write dipolar canonical structures (such as XIII) for sydnones in which a negative charge resides on a ring atom. Since sydnones and thiophenes undergo electrophilic substitution with comparable ease, a formula such as XI (in which ring atoms bear at least a small positive charge) is unsatisfactory at least for illustrating the transition state of such reactions.[8b] The analogy between sydnones and pyrones or pyridones[20] is similarly deficient. It seems more desirable to retain Baker's ± symbolism (see formula I) which satisfactorily represents the hybrid of canonical structures some of which bear a negative charge on the exocyclic oxygen and some of which bear a negative charge on ring atoms. This does not mean that all possible dipolar structures contribute equally to the hybrid but only that structures like XIII must be important.


XI


XII


XIII

The infrared carbonyl absorption of a large variety of sydnones falls in the 5.66–5.82μ (1767–1718 cm.$^{-1}$) region,[16a] which brackets the normal carbonyl absorption of saturated γ-lactones at 1740 cm.$^{-1}$.[21] On the other hand, tropone absorbs at 1638 cm.$^{-1}$ [22] as compared to 1699 cm.$^{-1}$ [23] for cycloheptanone. These facts would seem to be more consistent with Baker's ± formulation (I) than with the tropone-like formulation (XI) for sydnones.[8a]

Although 3-aminopyridine can be converted in high yield to N-(3-pyridyl)-glycine by catalytic hydrogenation in the presence of ethyl glyoxylate,[2,24] this procedure is limited to rather small-scale runs with the usual Parr hydrogenation apparatus. However, we have found that the use of commercially available glycolonitrile in a Strecker-type reaction[25] offers a convenient method for converting any desired quantity of 3-aminopyridine to N-(3-pyridyl)-glycine. The intermediate N-(3-pyridyl)-glycinonitrile need not be isolated. A later paper will demonstrate that this procedure, like that using ethyl glyoxylate,[26] is general for converting a variety of primary amines to the corresponding N-substituted glycines.[27] The aminonitriles used in preparing

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[19] Unpublished work by J. M.T. in this Laboratory.

[20] See W. Baker and W. D. Ollis (ref. 4) and W. Baker, *Proc. Chem. Soc.*, 75 (1959).

[21] L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 186.

[22] W. von E. Doering and F. L. Detert, THIS JOURNAL, **73**, 876 (1951).

[23] G. P. Scott and D. S. Tarbell, *ibid.*, **72**, 240 (1950).

[24] I. M. Hunsberger and J. M. Tien, *Chemistry & Industry*, 88 (1959).

[25] K. Pfister, A. P. Sullivan, J. Weijlard and M. Tishler, THIS JOURNAL, **73**, 4955 (1951).

[26] J. M. Tien and I. M. Hunsberger, *ibid.*, **77**, 6696 (1955).

[27] (a) Unpublished work performed in this Laboratory by J. M. T., D. J. Voaden and G. Sugerman. (b) After this paper was submitted for publication we became aware that Japanese workers [M. Ohta and M. Masaki, *Bull. Chem. Soc. Japan*, **33**, 649 (1960)] have prepared N-(3-pyridyl)-glycinonitrile from the reaction of 3-aminopyridine with formaldehyde, sodium bisulfite and alkali cyanide. This nitrile was converted to the amide and thence to either N-(3-pyridyl)-glycine hydrochloride or the corresponding nitrosoglycine. However, our one-step process for converting 3-aminopyridine to the glycine hydrochloride is much less tedious and gives higher yields. Ohta and Masaki

"sydnone imines" were obtained by analogous methods.[28]

N-(3-pyridyl)-sydnone (II) has been subjected to a variety of tests for physiological activity. However, it showed no activity against tuberculosis and cancer and gave negative results in the antibiotic and chemotherapy tests.[29] The sydnone also was inactive as a reactivator for alkyl phosphate inhibited cholinesterase.[30] The three mercurated pyridylsydnones (V, VI and VII) presently are being screened for anticancer activity by the Cancer Chemotherapy National Service Center.

Acknowledgments.—The ultraviolet spectra were determined in this Laboratory by Rev. C. J. Thoman, S.J., and by Dr. D. J. Voaden. In addition, the authors take pleasure in thanking Dr. Voaden for many helpful discussions and for having translated all the Russian literature cited.

Experimental

All elemental analyses, unless designated otherwise, were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. Melting points were determined in a Thiele apparatus except that for compound VII the Köfler hot-stage was used. Infrared spectra were determined with a Beckman IR-5 double-beam spectrophotometer by use of the potassium bromide pellet technique. Ultraviolet spectra were obtained with a Perkin–Elmer Spectracord model 4000 spectrophotometer, the samples being dissolved in alcohol. Although only small-scale mercuration reactions are detailed below, these reactions have also been performed successfully on a much larger scale. Whenever the same product was prepared in more than one way, the identity of the samples was demonstrated by mixture m.p. and comparison of infrared spectra.

N-(3-Pyridyl)-glycine Hydrochloride.—A solution of 28.2 g. (0.30 mole) of 3-aminopyridine (Reilly Tar and Chemical Corp.) and 30 g. of 70% aqueous glycolonitrile[31] (about 0.37 mole) in 80 ml. of water was refluxed for 0.5 hr. Concentrated hydrochloric acid (100 ml.) was added to the cooled (40–60°) solution, after which refluxing was continued for another hour. The mixture was allowed to cool to room temperature and the product filtered, washed with a small amount of concentrated hydrochloric acid, and dried in air to yield 42.5 g. of the glycine hydrochloride as tan crystal rosettes, m.p. 222–225°. This material was shown to be identical with an authentic sample[2] by mixture m.p. and comparison of infrared spectra. Refrigeration of the filtrate afforded another 1.0 g. of white powdery solid, m.p. 220–224°; total yield 43.5 g. (77%).

Numerous repetitions of this preparation produced yields of glycine hydrochloride ranging from 73–90%.

N-(3-Pyridyl)-sydnone (II).—Recent work has afforded an improved procedure over that originally used[2] to isolate this sydnone. Thus, the acetic anhydride solution of the crude sydnone is treated with at least half its volume of ethanol or methanol, and this solution is evaporated (hot water-bath) in a rotary evaporator. If acetic anhydride still remains, more alcohol is added and the evaporation is repeated.[32] The crude sydnone is obtained as a light tan semi-crystalline material. Aqueous ethanol or benzene, instead of water,[2] can be used for recrystallization, but considerable care is needed to obtain perfectly colorless crystals. Thus, a solution of 1.0 g. of crude sydnone in 28 ml. of 75% ethanol is heated almost to boiling, treated with about 0.4 g. of Norit A, briefly boiled, and the process repeated until a total of 1 g. of Norit has been used. On cooling, the colorless filtrate deposits 0.3 g. of pure sydnone as colorless prisms, an additional 0.2 g. of slightly off-white prisms being obtained by concentration of the filtrate. Boiling benzene also may be used in the same manner, but a much larger volume is required and the filter funnel must be heated to prevent crystallization during filtration. A final crystallization may be accomplished by dissolving about 0.5 g. of the sydnone in 10 ml. of nitromethane at room temperature and cooling in the refrigerator. In this way, long colorless needles of very pure sydnone are obtained. It is worth noting that nitromethane is the best solvent yet found for dissolving this sydnone at room temperature.

N-(3-Pyridyl)-sydnone–Mercuric Chloride "Adduct" (V).—At room temperature a solution of 49 mg. (0.30 mmole) of sydnone II in 5 ml. of absolute ethanol was poured into a solution of 90 mg. (0.33 mmole) of mercuric chloride in 5 ml. of water. The mixture was shaken thoroughly and let to stand at room temperature. In about 5 minutes, long, thin needles started to separate. After 1 hr., filtration afforded 100 mg. of colorless fiber-like crystals, m.p. 178–179°. Refrigeration of the filtrate yielded another 17 mg.; total yield of V, 117 mg. (90%). The first fraction was analyzed without further purification.

Anal. Calcd. for $C_7H_5N_3O_2HgCl_2$: C, 19.34; H, 1.15; N, 9.80; Cl, 16.31. Found: C, 19.44; H, 1.84; N, 9.48; Cl, 16.00.

The adduct V was soluble at room temperature in methyl Cellosolve, dimethylformamide and dimethyl sulfoxide, as well as in warm dibromomethane. It was insoluble in benzene, ether, petroleum ether, dioxane and toluene. Recrystallization could be effected from hot alcohol, hot water or hot aqueous alcohol, but hot water gave pink, rather than colorless, plates. In ordinary daylight the long colorless needles (or rods) turned yellow after several days; the same change occurred more slowly in the dark.

Closely similar yields of "adduct" were obtained from the same proportions of reactants in water and in 95% ethanol and from the use of an excess of sodium acetate and mercuric chloride in 95% ethanol.

C-Chloromercuri-N-(3-pyridyl)-sydnone (VI). (a) **From N-(3-Pyridyl)-sydnone (II).**—A solution of 330 mg. (1.22 mmoles) of mercuric chloride and 100 mg. (1.22 mmoles) of anhydrous sodium acetate in 12 ml. of absolute ethanol was heated to 70–75° and mixed with a solution of 100 mg. (0.61 mmole) of sydnone II in 6 ml. of absolute ethanol also at 70-75°. The turbid solution was filtered immediately. The clear filtrate was heated to boiling and set aside. After 3–5 minutes colorless mica-like plates began to separate. After 2 hr., filtration yielded 127 mg. of product, m.p. 250–260° dec. Refrigeration of the filtrate afforded another 25 mg., m.p. 245–260° dec., total yield 152 mg. (62%). The first fraction was analyzed without further purification.

Anal. Calcd. for $C_7H_4N_3O_2HgCl$: C, 21.09; H, 1.01; N, 10.55; Cl, 8.91. Found: C, 21.32; H, 1.30; N, 10.80; Cl, 8.63.

Use of a larger excess of sodium acetate in 40% ethanol as solvent produced a higher yield, but the product melted over a wider range.

Compound VI was soluble in dimethyl sulfoxide and dimethylformamide at room temperature and in hot methyl Cellosolve and carbon disulfide; it was insoluble in chloroform, benzene, carbon tetrachloride, ether, petroleum ether and dioxane. Recrystallization from boiling nitrobenzene afforded colorless mica-like flakes which did not change to yellow unless exposed to light.

(b) **From the N-(3-Pyridyl)-sydnone–Mercuric Chloride "Adduct" (V).**—To a solution of 120 mg. (0.28 mmole) of V in 4 ml. of boiling absolute alcohol about 100 mg. (1.22 mmoles) of anhydrous sodium acetate was added. The mixture was heated until a clear solution formed and immediately allowed to cool to room temperature to yield 100 mg. (90%) of the C-chloromercuri compound VI, m.p. 250–260° dec.

(c) **From C,C′-Mercuri-bis-[N-(3-pyridyl)-sydnone] (VII).**—A mixture of 262 mg. (0.5 mmole) of VII and 1.5 g. (5.5 mmoles) of mercuric chloride in 380 ml. of 75% ethanol

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used the same method to prepare the glycines needed as intermediates for the preparation of the C-methyl and C-phenyl derivatives of N-(3-pyridyl)-sydnone. It is noteworthy that neither of these sydnones was phototropic.

[28] (a) P. Brookes and J. Walker, *J. Chem. Soc.*, 4409 (1957); (b) H. Kato, M. Hashimoto and M. Ohta, *Nippon Kagaku Zasshi*, **78**, 707 (1957); *C. A.*, **54**, 511 (1960); (c) V. F. Vasil'eva and V. G. Yashunskii, *Khim. Nauka i Prom.*, **4**, 678 (1959).

[29] Testing performed at Eli Lilly Co. through the courtesy of Dr. Nelson Easton.

[30] Testing performed by Dr. I. B. Wilson, College of Physicians and Surgeons, Columbia University.

[31] We are grateful to the American Cyanamid Co. for generous samples of this compound.

[32] The use of alcohol facilitates the removal of acetic anhydride, and this process probably has general merit in cases in which the alcohol does not react with the compound being isolated.

was refluxed for 10–15 minutes until a clear solution was obtained. The solution was cooled to room temperature to yield, after filtering and washing with 50% ethanol, 290 mg. of colorless mica-like crystals, m.p. 255–258° dec. The filtrate was diluted with water and cooled to give an additional 66 mg. of white flakes, m.p. 262–268° dec., the total yield of VI being 356 mg. (89%).

Five repetitions of this preparation gave essentially the same results. Larger amounts of ethanol produced a product of even better quality. Larger amounts of mercuric chloride accelerated the dissolution of the mercuri-bis-sydnone (VII).

C,C′-Mercuri-bis-[N-(3-pyridyl)-sydnone] (VII). (a) **From N-(3-Pyridyl)-sydnone (II).**—A solution of 489 mg. (3 mmoles) of sydnone II and 1.2 g. (14 mmoles) of anhydrous sodium acetate in 40 ml. of hot 50% ethanol was mixed with a solution of 407 mg. (1.5 mmoles) of mercuric chloride in 10 ml. of 50% ethanol and the whole refluxed for 4–5 hr. After about 15 minutes the clear solution became turbid, and tiny colorless flakes began to separate. The hot mixture was filtered and the product washed with hot ethanol to give 530 mg. (67%) of VII as colorless flakes, which were analyzed without further purification. This compound remained unchanged on heating to about 280°; above this temperature the crystals became light brown but did not melt up to 380°.

Anal. Calcd. for $C_{14}H_8N_6O_4Hg$: C, 32.03; H, 1.54; N, 16.01; Hg, 38.22. Found: C, 32.39; H, 1.63; N, 16.42; Hg, 38.5.[33]

On cooling to room temperature the filtrate deposited 73 mg. of the C-chloromercurisydnone (VI) as colorless flakes, m.p. 240–250° dec. The filtrate contained 95 mg. of chloride ion (theoretical 106 mg., based on 100% conversion of II to VII). If desired, the above filtrate can be reheated with additional sodium acetate to complete the conversion of VI to VII.

The mercuri-bis-sydnone VII was insoluble in all solvents except hot dimethylformamide and hot dimethyl sulfoxide. Impure samples of VII could be purified by washing thoroughly with a large variety of organic solvents used in succession. This compound did not change from colorless to yellow unless exposed to light.

(b) **From the N-(3-Pyridyl)-sydnone–Mercuric Chloride "Adduct" (V).**—A mixture of 200 mg. (0.46 mmole) of V and 80 mg. (0.98 mmole) of anhydrous sodium acetate was heated in 10 ml. of refluxing absolute ethanol for 3 hr. Hot filtration and washing with hot ethanol yielded 77 mg. (63 %) of VII as tiny colorless flakes, m.p. >380°.

(c) **From C-Chloromercuri-N-(3-pyridyl)-sydnone (VI).**—A suspension of 1.99 g. (5 mmoles) of VI in 8–10 ml. of reagent-grade pyridine was swirled at room temperature for 1–2 minutes until all of the solid dissolved and then set aside. The solid granules which deposited in about 5 minutes were crushed to a powder while the mixture was stirred. The mixture was set aside for another 5 minutes and the granules were crushed again to a powder, this process being repeated several times. The product was filtered, washed with 3–4 ml. of pyridine, and dried at 110° to give 1.10 g. of a nearly white powder. An additional 0.112 g. was obtained by diluting the filtrate with ether, filtering, and washing the solid with 50% ethanol. Both fractions did not melt up to 380° and gave a negative Beilstein test for halogen. The total yield of VII was 1.21 g. (92%).

Anal. Calcd. for $C_{14}H_8N_6O_4Hg$: Hg, 38.2. Found: Hg, 37.8.[33]

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[33] Determined gravimetrically in this Laboratory as mercuric sulfide.

[CONTRIBUTION FROM FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY, PRINCETON, N. J.]

The Preparation and Reactivity of 2-Substituted Derivatives of Adamantane[1,2]

BY PAUL VON R. SCHLEYER AND ROBERT D. NICHOLAS[3]

RECEIVED AUGUST 1, 1960

A method of preparation of secondary monosubstituted derivatives of adamantane is described. Free radical hydroxylation of the readily available parent hydrocarbon gave both the secondary and the tertiary alcohols. These compounds were converted to other derivatives by standard methods. The consequences of molecular rigidity and constrained geometry upon solvolytic reactivity were noteworthy. Acetolysis of the secondary tosylate proceeded at a rate 15 times slower than cyclohexyl tosylate, but almost six powers of ten faster than the analogously constituted 7-norbornyl tosylate. The determining factor for the reactivity of these compounds would appear to be the restraint to rehybridization afforded by angles more acute than the normal tetrahedral value. The implications of this conclusion for the interpretation of the reactivities of other monocyclic and bicyclic systems are discussed.

The discovery of a convenient method of preparation of adamantane (I)[4] prompted interest in the reactions of this rigid but strain-free ring system. Although many polysubstituted adamantane derivatives had been prepared during the course of synthesis of the hydrocarbon,[5] monofunctional compounds were unknown until recently. The key reaction was the finding by Landa, Kriebel and Knobloch[6] that simple heating of bromine with adamantane, obtained by these workers from petroleum sources, gave quite satisfactory yields of a homogeneous monobromide. Preparative solvolysis in aqueous solvents easily gave an alcohol, believed to be tertiary. Very recently, these reactions have been improved and extended by Stetter and co-workers,[7,8] who have confirmed the bridgehead nature of the bromide and alcohol. A large number of 1-substituted compounds have been prepared from these materials,[6,7] but simple 2-substituted adamantane derivatives have not been described in the literature.

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[1] Paper IV of a series on Bridged Ring Systems. Paper III, also concerning adamantane, P. von R. Schleyer and M. M. Donaldson, THIS JOURNAL, **82**, 4645 (1960). This paper is taken, in part, from the Ph.D. Thesis of R.D.N., Princeton University, 1960.

[2] A preliminary account of this work was presented at the Third Delaware Valley Regional Meeting, Am. Chem. Soc., Feb., 1960, Abstracts, p. 49.

[3] Gulf Research and Development Fellow, 1959–1960; National Science Foundation Summer Fellow, 1960.

[4] P. von P. Schleyer, THIS JOURNAL, **79**, 3292 (1957), and ref. 1.

[5] For work prior to 1954, an excellent review is available, H. Stetter, *Angew. Chem.*, **66**, 217 (1954). Subsequent refs. are: S. Landa and Z. Kamýček, *Coll. Czech. Chem. Comm.*, **21**, 772 (1956); **24**, 1320, 4004 (1959); H. Stetter, *et al.*, *Ber.*, **88**, 1535 (1955); **89**, 1922 (1956); **92**, 2664 (1959).

[6] S. Landa, S. Kriebel and E. Knobloch, *Chem. Listy*, **48**, 61 (1954); also see S. Landa and S. Hála, *Coll. Czech. Chem. Comm.*, **24**, 93 (1959).

[7] H. Stetter, M. Schwarz and A. Hirschhorn, *Ber.*, **92**, 1629 (1959).

[8] H. Stetter, J. Mayer, M. Schwarz and K. Wulff, *ibid.*, **93**, 226 (1960); H. Stetter and C. Wulff, *ibid.*, **93**, 1366 (1960).