

directly within the microwave cavity by reduction of millimolar solutions of the neutral parent molecule using acetonitrile as solvent.<sup>1</sup> Detailed e.s.r. and polarographic data for compounds in the table as well as several related compounds currently being studied will be presented in detail elsewhere.

Financial support of the U. S. Army Research Office (Durham) and the U. S. Air Force Directorate of Solid State Sciences is gratefully acknowledged.

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RECEIVED JULY 11, 1961

#### BIRADICALS IN THE KETYL SERIES<sup>1</sup>

Sir:

We have reported previously that the paramagnetic molecules formed on reduction of hexamethylacetone and pentamethylacetone by sodium or lithium are characterized by hyperfine splittings in which each unpaired electron spin is coupled to the nuclei in one ketone molecule and two equivalent alkali metal nuclei.<sup>2</sup> Dimeric molecules in which the two organic radicals are joined through two equivalent alkali metal ions could account for the observations. Such molecules are biradicals with each electron spin belonging predominantly to one-half of the dimer but sharing the two alkali metal nuclei with the other electron spin. The sharing refers to a time average and does not imply simultaneous presence of the electron spins at a particular site.

We have carried out new experiments with ketyls of the alkaline earths which suggest the formation of biradicals in which the two radicals are joined by a single divalent alkaline earth ion. Reduction of xanthone or benzophenone by magnesium, calcium, or barium in ethereal solvents leads in each case to a single paramagnetic species with hyperfine couplings to the protons in one molecule of the original ketone. The proton coupling constants are slightly dependent on the positive ion, varying monotonically with size of the positive ion. No trace of the dissociated ions is observed. The electron transfer reactions between the dimeric ketyls, both aliphatic and aromatic, and their parent ketones are too slow ( $k < 10^5 M^{-1} \text{ sec}^{-1}$ ) to be measured by e.s.r. spectroscopy, while the reaction of the monomeric aromatic ketyls of the alkali metals are very rapid ( $k > 10^8 M^{-1} \text{ sec}^{-1}$ )<sup>3</sup>

Use of magnesium enriched to 93% of <sup>25</sup>Mg yields further evidence bearing on the constitution of the ketyls. In the case of benzophenone magnesium ketyl the expected splitting by one <sup>25</sup>Mg nucleus ( $I = 5/2$ ) is observed. The interval between adjacent components is 0.3 gauss. The other ketyls with <sup>25</sup>Mg exhibit a broadening of all lines, but no well-resolved <sup>25</sup>Mg splitting.

(1) This work has been supported in part by the U. S. Air Force under Contract and in part by an Equipment Loan Contract with O. N. R. Grateful acknowledgment is also made to the donors of the Petroleum Research Fund administered by the American Chemical Society for partial support of this research.

(2) N. Hirota and S. I. Weissman, *J. Am. Chem. Soc.*, **82**, 4424 (1960).

(3) F. Adam and S. Weissman, *ibid.*, **80**, 1518 (1958).

The lack of observable coupling between the electronic spin in the biradicals here reported as well as in others previously described is a matter of some theoretical interest.<sup>4</sup> We are continuing experimental studies of radicals bound together by various metal ions, including tripositive ones, in order to gather further information concerning spin couplings in many electron systems.

(4) H. M. McConnell, *J. Chem. Phys.*, **33**, 115 (1960); *ibid.*, **33**, 1868 (1960).

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RECEIVED JULY 1, 1961

#### THE STEREOCHEMISTRY OF AN ETHYLENEDIAMINETETRAACETATO COMPLEX OF MANGANESE(II)<sup>1</sup>

Sir:

In further elucidation of the frequently unorthodox stereochemistry<sup>2,3</sup> of ethylenediaminetetraacetato (EDTA, Y<sup>-4</sup>) chelates, we have utilized spectrometrically measured X-ray diffraction data from the acid salt, Mn[Mn(OH<sub>2</sub>)HY]<sub>2</sub>·8H<sub>2</sub>O, to give the remarkable structural features noted below. The monoclinic cell containing 2Mn[Mn(OH<sub>2</sub>)HY]<sub>2</sub>·8H<sub>2</sub>O has  $a = 9.21$ ,  $b = 16.10$ ,  $c = 11.88 \text{ \AA}$ ,  $\beta = 90.60^\circ$ ; the space group is P2<sub>1</sub>/n. Intensity counts were taken with MoK $\alpha$  radiation for all forms  $\{hkl\}$  in the range,  $0 < (\sin \theta)/\lambda < 0.96$ . Results given herein are based upon the data for  $(\sin \theta)/\lambda < 0.67$ , comprising 4440 forms of which 90% are recordable above background. Objective analysis by Patterson and Fourier methods, with subsequent partial refinement by difference syntheses, yield structural configurations with rather accurate bond parameters. Thermal parameters range from 1.50  $\text{\AA}^2$  for manganese in the anion to above 3  $\text{\AA}^2$  for oxygen in some water molecules. The discrepancy index for all 4440 forms is 0.10.

Manganous ions in fourfold positions of P2<sub>1</sub>/n are centered in sexadentate seven-coördinate aquo complexes, [Mn(OH<sub>2</sub>)HY]<sup>-</sup>. The geometry of the inner coördination group is not that reported<sup>3</sup> for [Fe(OH<sub>2</sub>)Y]<sup>-</sup>, but is roughly that of the sterically superior NbF<sub>7</sub><sup>=</sup> configuration<sup>2,4</sup> (*cf.* ref. 4 for diagram). Bond lengths, to the nearest 0.005  $\text{\AA}$ , are Mn-O, 2.210-2.260  $\text{\AA}$ , average of five, 2.235  $\text{\AA}$ ; Mn-N, 2.350, 2.395  $\text{\AA}$ . Apart from those angles and bonds which involve the central atoms, the geometry of ring systems is very like that expected from earlier studies<sup>5,6</sup> of CoY<sup>-</sup> and Ni(OH<sub>2</sub>)H<sub>2</sub>Y. Manganous ions in twofold ( $\bar{1}$ ) positions of P2<sub>1</sub>/n display octahedral coördination; each such ion is bonded to four water molecules and two not otherwise complexed oxygen

(1) Part of a program supported by the National Science Foundation. We thank also the U. S. Army Research Office (Durham) and the Advanced Research Projects Agency for support of the work reported herein.

(2) *Cf.* J. I. Hoard, G. S. Smith and M. Lind in "Advances in the Chemistry of Coördination Compounds," C. Stanley Kirschner, The Macmillan Company, New York, N. Y., July, 1961.

(3) J. L. Hoard, M. Lind and J. V. Silverton, *J. Am. Chem. Soc.*, **83**, 2770 (1961).

(4) J. L. Hoard, *ibid.*, **61**, 1252 (1939).

(5) H. A. Weakliem and J. I. Hoard, *ibid.*, **81**, 549 (1959).

(6) Gordon S. Smith and J. L. Hoard, *ibid.*, **81**, 556 (1959).

atoms from glycinate rings of neighboring anions: Mn-O = 2.140–2.175, average, 2.165 Å. The acid hydrogens are used in extraordinarily strong hydrogen bonds, 2.460 Å. (with an estimated probable error of 0.015 Å.), which tie the complex anions into infinite strings parallel to *b*. The remaining eight water molecules of the cell are involved in the general pattern of hydrogen bonding which characterizes the crystal.

The over-all structural pattern of moderately strong bonding in three-dimensions leads to relatively subdued thermal motions as compared with  $\text{NH}_4\text{CoY}\cdot 2\text{H}_2\text{O}^5$  or  $\text{RbFe}(\text{OH}_2)\text{Y}\cdot \text{H}_2\text{O}^5$ . Indeed, we anticipate that extension of the Fourier synthesis to include all experimental amplitudes out to  $(\sin \theta)/\lambda = 0.96$  will give atomic positions requiring little or no "back-shift" corrections.

The machine computations of this paper were carried out at the Cornell Computing Center through the courtesy of Mr. Richard C. Lesser, Director. Preparation and preliminary X-ray examination of the crystals were carried out by Dr. Gordon S. Smith.

(7) Fellow of the John Simon Guggenheim Memorial Foundation, 1960.

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RECEIVED JULY 6, 1961

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#### REACTION OF 6-AMINOPENICILLANIC ACID WITH CARBON DIOXIDE

Sir:

6-Aminopenicillanic acid has been prepared by fermentation of precursor-free penicillin broth,<sup>1</sup> by enzymatic cleavage of natural penicillins,<sup>2–5</sup> and by total synthesis.<sup>6</sup> Its availability has made possible the synthesis of many new, improved penicillins which are not amenable to preparation via fermentation.  $\alpha$ -Phenoxyethylpenicillin<sup>7,8</sup> and 2,6-dimethoxyphenylpenicillin<sup>9,10</sup> are clinically important examples.

6-Aminopenicillanic acid (I) has now been found to react rapidly with carbon dioxide in neutral aqueous solution at room temperature to form 3,3-dimethyl-8-hydroxy-2-oxo-4-thia-1,7-diazabicyclo-[3.3.0]octane-2,6-dicarboxylic acid (IV). Solutions of 0.01 to 1 *M* 6-APA dissolved in 2 equivalents of sodium bicarbonate and placed under 1 atmosphere of carbon dioxide will react completely in 4 to 6 hours at room temperature. Increasing

(1) F. R. Batchelor, F. P. Doyle, J. H. C. Naylor and G. N. Rolinson, *Nature*, **183**, 257 (1959).

(2) G. N. Rolinson, *et al.*, *Nature*, **187**, 236 (1960).

(3) C. A. Claridge, A. Gourevitch and J. Lein, *ibid.*, **187**, 237 (1960).

(4) H. T. Huang, A. R. English, T. A. Seto, G. M. Shull and B. A. Sobin, *J. Am. Chem. Soc.*, **82**, 3790 (1960).

(5) W. Kaufmann and K. Bauer, *Naturwissenschaften*, **47**, 474 (1960).

(6) J. C. Sheehan and K. R. Henery-Logan, *J. Am. Chem. Soc.*, **81**, 5838 (1959).

(7) Y. G. Perron, *et al.*, *ibid.*, **82**, 3934 (1960).

(8) The trade name of Bristol Laboratories for potassium  $\alpha$ -phenoxyethylpenicillin is Syncillin.

(9) E. T. Knudsen and G. N. Rolinson, *Brit. Med. J.*, *ii*, 700 (1960).

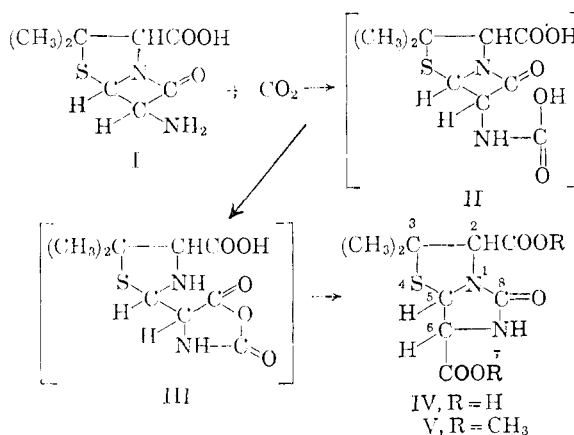
(10) The trade name of Bristol Laboratories for sodium 2,6-dimethoxyphenylpenicillin is Staphicillin.

the carbon dioxide pressure increases the rate. The reaction rate is fastest in the pH range 5–7, which suggests that unprotonated amino groups and molecular carbon dioxide are the primary reactants.

When the reaction is completed, as indicated by a negative hydroxylamine assay for  $\beta$ -lactams, Compound IV can be isolated in 80–90% yields as the crystalline disodium salt, m.p. 250–251° (dec.),  $[\alpha]^{25\text{D}} + 277^\circ$  (*c* 1,  $\text{H}_2\text{O}$ ) (calcd. for  $\text{C}_9\text{H}_{10}\text{N}_2\text{O}_5\text{SNa}_2$ : C, 35.53; H, 3.31; N, 9.21. Found: C, 35.56; H, 3.76; N, 9.02). The microcrystalline free acid, m.p. 136–138°, decarboxylates readily.

Analytical and spectral data were consistent with Structure IV, which then was confirmed by conversion with methanolic HCl to the known<sup>11</sup> dimethyl ester (V), m.p. 170–171°,  $[\alpha]^{25\text{D}} + 238^\circ$  (*c* 1,  $\text{CH}_3\text{OH}$ ) (Calcd. for  $\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_6\text{S}$ : C, 45.82; H, 5.59; N, 9.72. Found: C, 46.01; H, 5.67; N, 9.85). Identity with an authentic sample, prepared by reaction of methyl D- $\alpha$ -4-carbomethoxy-5,5-dimethyl- $\alpha$ -amino-2-thiazolidineacetate hydrochloride<sup>12</sup> with phosgene, was established by comparison of optical rotations, melting points, mixed melting point, infrared spectra, and elemental analyses.

The ease with which this transformation occurs is surprising, but it is more easily understood if the course of the reaction is considered to involve intermediates II and III.



The sequence is analogous to that advanced for the penicillic acid rearrangement of the natural penicillins.<sup>13</sup> Indeed, by writing the carbonyl group at position 8 in the enolic form, the complete nucleus of the penicillic acids is obtained. Therefore, in order to simplify the nomenclature, Compound IV has been named 8-hydroxyphenillic acid.

Since the reaction of 6-aminopenicillanic acid with carbon dioxide takes place so readily, it seemed probable that it might be occurring in *P. chrysogenum* fermentations in which 6-aminopenicillanic acid is an intermediate or end-product. Indeed,

(11) H. T. Clarke, J. R. Johnson and R. Robinson, Editors, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, pp. 859, 891.

(12) J. C. Sheehan and J. P. Ferris, *J. Am. Chem. Soc.*, **81**, 2912 (1959).

(13) H. T. Clarke, J. R. Johnson and R. Robinson, Editors, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J. 1949, p. 453.