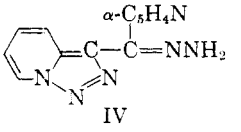
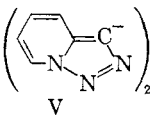


IV



V

Infrared absorption data for III have been obtained from potassium bromide discs and from chloroform solution. Lack of absorption from 3.5 to 6.0 mμ clearly indicates the absence of an aliphatic diazo group in both the solid state and in solution at ordinary temperature.

EXPERIMENTAL[5]

1-α-Picolinoylpyridotriazole (III, R = C_5H_4NCO). According to the directions of Eistert and Schade[2] for the preparation of azipyridil, 1-α-picolinoylpyridotriazole (III. R = C_5H_4NCO), m.p. 151° was obtained in 66% yield.

Infrared absorption for 1-α-picolinoylpyridotriazole from (a) a potassium bromide disc (cm.$^{-1}$, % transmission): 3086, 18.5; 3040, 18.0; 1658, 7.1; 1634, 12.5; 1587, 28.6; 1572, 28.0; 1511, 7.4; 1479, 30.0; 1427, 15.2; 1416, 10.6; 1355, 29.9; 1328, 33.9; 1309, 42.2; 1271, 26.2; 1245, 27.1; 1225, 10.3; 1159, 21.7; 1151, 27.4; 1110, 39.1; 1091, 17.5; 1052, 34.9; 1010, 41.5; 993, 27.0; 940, 7.9; 890, 23.4; 812, 41.6; 768, 4.5; 752, 20.0; 742, 17.2; 723, 43.7; 703, 26.0; 673, 16.1; 648, 46.6; and (b) a chloroform solution (cm.$^{-1}$, absorptivity): 3425, 0.03; 2967, 0.15; 2445, 0.03; 1653, 0.82; 1634, 0.70; 1585, 0.34; 1572, 0.26; 1499, 0.33; 1471, 0.11; 1412, 0.40; 1359, 0.19; 1325, 0.21; 1274, 0.28; 1145, 0.36; 1107, 0.17; 1091, 0.42; 1045, 0.05; 1008, 0.31; 995, 0.36; 964, 0.06; 939, 0.70; 886, 0.50.

1-α-picolinoylpyridotriazole 3,5-dinitrobenzoate. A solution of 2.25 g. (0.01 mol.) of 1-α-picolinoylpyridotriazole and 2.12 g. (0.01 mol.) of 3,5-dinitrobenzoic acid in 75 ml. of *o*-xylene was heated at 110° for 2 hr. Upon cooling the crude salt, *1-α-picolinoylpyridotriazole 3,5-dinitrobenzoate,* m.p. 154–159° (dec.) separated in 75% yield. It recrystallized from ethyl acetate–ethanol as pale yellow needles, m.p. 158–159 (dec.).

Anal. Calcd. for $C_{19}H_{12}N_6O_7$: C, 52.30; H, 2.77; N, 19.28; O, 25.66. Found: C, 52.40; H, 2.69; N, 18.98; O, 25.68.

After treating 1.0 g. (0.002 mol.) of this salt with 10 ml. of 10% sodium hydroxide with stirring for 10 min., a solid was removed by filtration. Upon acidifying the filtrate, 0.4 g. (90%) of 3,5-dinitrobenzoic acid, m.p. and mixture m.p. 204–205°, was obtained. The solid phase from the alkaline reaction mixture was identified as 1-α-picolinoylpyridotriazole, melting point and mixture melting point 151°, 0.5 g. (90%).

Attempts to alkylate 3,5-dinitrobenzoic acid with 1-α-picolinoylpyridotriazole in tetralin at 160° led to an unidentified oil.

1,1′-Bipyridotriazole. A solution of 1.0 g. (0.005 mol.) of 1-α-picolinoylpyridotriazole and 0.16 g. (0.05 mol.) of hydrazine (as 95% aqueous hydrazine) in 30 ml. of *n*-butyl alcohol was refluxed for 2 hr. Colorless needles, 0.2 g. (17% of *1,1′-bipyridotriazole,* m.p. 245° (dec.), separated upon cooling, and after recrystallization from ethanol melted at 254–255° (dec.).

Anal. Calcd. for $C_{12}H_8N_6$: C, 61.02; H, 3.41; N, 35.55. Found: C, 61.09; H, 3.34; N, 35.60.

A mixture melting point determination with a sample prepared from a dihydrazone of α-pyridil and silver oxide[4] showed no depression. The previously reported[4] m.p. 272–274° (dec.) is in error.

Upon concentration of the solvent a second product separated from the reaction mixture in *n*-butyl alcohol as pale yellow needles, 0.6 g. (51%), m.p. 172–176°. Recrystallization from ethanol gave the *hydrazone of 1-α-picolinoylpyridotriazole,* m.p. 174–175°.

Anal. Calcd. for $C_{12}H_{10}N_6$: C, 60.49; H, 4.19; N, 35.28. Found: C, 60.53; H, 4.08; N, 35.64.

When the reaction between 1-α-picolinoylpyridotriazole and hydrazine was carried out under nitrogen, the hydrazone derivative was obtained in 90% yield with no trace of 1,1′-bipyridotriazole.

Acknowledgment. We are indebted to Mr. R. T. O'Connor, Southern Regional Research Laboratory for infrared absorption data.

CHEMISTRY DEPARTMENT
TULANE UNIVERSITY
NEW ORLEANS 18, LA.

(5) Semimicro elemental analyses by Alfred Bernhardt, Mülheim (Ruhr) Germany. Melting points are uncorrected.

The Electrochemical Reduction of Michler's Ketone[1]

R. M. ELOFSON

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In connection with another project, it became necessary to reduce Michler's ketone to the corresponding pinacol (*p,p*-dimethylaminodiphenylcarbinol) and to rearrange this material to the pinacolone. After rather unsuccessful attempts to prepare the pinacol by other means it was decided to reduce Michler's ketone electrochemically. The ensuing experiments resulted in some interesting results of theoretical and practical significance for electrochemical preparations and are reported herewith.

The reduction of ketones at a variety of cathodes to form pinacols has been widely used.[2a-4] Escherlich and Moest[5] found that Michler's ketone yields the pinacol with a copper electrode while both pinacol and hydrol are formed in almost equal amounts at a nickel cathode. The chief advantage of any given electrode under the usual conditions of uncontrolled cathode potentials is to limit the cathodic potential to the hydrogen overvoltage of the metal. It was therefore deemed simplest to use the method of Allen and Corwin[6] where the reduction is conducted at a controlled potential mercury cathode.

From polarographic results,[7] it is known that in acid solutions of *p*H 1.3 benzophenone is reduced

(1) Contribution No. 109 from the Research Council of Alberta.

(2) (a) K. Elbs and K. Brand, *Z. Electrochem.,* **8,** 783 (1902). (b) J. Tafel, *Z. Electrochem.,* **17,** 972 (1911).

(3) S. Swann, Jr., N. J. Leonard, and F. C. Howard, *Trans. Electrochem. Soc.,* **67,** 6 pp. preprint (1936).

(4) N. J. Leonard, S. Swann, Jr., and C. Fuller, *J. Am. Chem. Soc.,* **75,** 5127 (1953).

(5) F. Escherlich and M. Moest, *Z. Electrochem.,* **8,** 849 (1902).

(6) M. J. Allen and A. H. Corwin, *J. Am. Chem. Soc.,* **72,** 114 (1950).

(7) R. Pasternak, *Helv. Chim. Acta,* **31,** 753 (1948).

TABLE I

ELECTROLYSES OF MICHLER'S KETONE[a]

Cathode[b] Potential, V.	Ketone Concn.	Acid Concn.	Stirring[c]	Yield Pinacol	Other Products
0.90	0.125*M*	1.5*N*	Rapid	70%	Hydrol
1.40	0.125*M*	1.5*N*	Rapid	5%	Hydrol
0.90	0.125*M*	1.5*N*	Slow	14%	Ether and viscous oil
1.05	0.125*M*	1.5*N*	Slow	None	Ether 90%, tar
1.40	0.125*M*	1.5*N*	Slow	None	Ethane 8%, ether 30%
1.50	0.125*M*	1.5*N*	None	None	Ethane 26%, ether tar
1.20	0.5*M*	1.5*N*	Rapid	85%	Hydrol 4%
1.20	0.5*M*	2.5*N*	Rapid	64%	Ether
1.35	0.5*M*	1.5*N*	Rapid	38%	Hydrol and tar
1.40	0.5*M*	2.2*N*	Rapid	45%	Ether 45%, tar
0.95	0.125 *I*	0.75 in 50% isopropyl alcohol	Rapid	74%	Recovered ketone
1.05	0.125*M*	Same	Rapid	77%	Ether
1.05	0.125*M*	Same	Slow	None	48% ether, tar

[a] 200-ml. solution. [b] Cathode area, 50 cm.^{2} [c] Temp., 20–25°.

in one electron step. In controlled potential electrolyses Pasternak showed that only benzopinacol is isolated, whereas at *p*H 4.3 a mixture of benzpinacol and benzhydrol was produced and at *p*H 8.6 mainly benzhydrol was produced. Polarographic investigation of Michler's ketone showed that in 1.5*M* hydrochloric acid a one-electron reduction occurred at a half-wave potential of −0.72 volt in solutions of $7.5 \times 10^{-4}M$ to 1×10^{-2} *M*. This indicated that electrolyses conducted with cathodic potentials of −0.90V should result in good yields of pinacol. However, the work of Allen and Corwin[8] indicated that higher yields of pinacol and lower yields of the hydrol were obtained in the reduction of *p*-aminoacetophenone with potentials as high as −1.5 volts despite the fact that polarographic results indicated that a potential of −1.1 volt would be adequate.

The results of a number of reductions of Michler's ketone under varied conditions are summarized in Table I. High pinacol yields are favored by higher concentrations of ketones, comparatively low voltages and rapid stirring. Increasing the acid concentration from 1.5*N* to 2.5*N* resulted in a decreased pinacol yield and favored formation of the ether. Lower acid concentration which might be beneficial were not investigated because of solubility considerations. While the effect of diluting the electrolyte with isopropyl alcohol seemed to increase the specificity of the reduction at −0.95 volt, the results at −1.05 volts indicate quite clearly that the same factors were operative in producing side reactions. Very high cathodic potentials with no stirring resulted in appreciable yields of the ethane. Because of the possibility of pinacol-pinacolone rearrangement, the temperature was maintained in the 20–25° range although Allen, Fearn, and Levine[8] found that high temperatures favored pinacol formation.

Isomerization of the pinacol to the pinacolone. First attempts to prepare the pinacol resulted in the isolation of some pinacolone as contaminating material. It was determined that this material arose from isomerization of the pinacol hydrochloride when this material was isolated according to the method of Allen and Corwin. In subsequent experiments the electrolyzed solution was neutralized with sodium bicarbonate, the precipitated pinacol extracted with chloroform and precipitated with benzene, care being exercized not to heat any of the solutions. That isomerization of the pinacol did not take place during the electrolysis was indicated by the fact that no pinacolone was detected with the latter isolation technique. However, some isomerization of the pinacol occurred when heated on the steam cone for 2 hr. in 2*N* hydrochloric acid although 50% of the starting material was recovered unchanged. On the other hand, warming the pinacol to 50° for 15 min. in glacial acetic acid resulted in complete destruction of the pinacol and a higher yield of pinacolone. Heating for longer periods resulted in extensive decomposition of the pinacolone. The facile rearrangement of the pinacol in acetic acid but not in hydrochloric acid is presumably due to the fact that the free amine groups in acetic acid solution labilize the system toward the pinacol-pinacolone rearrangement.[9] On the other hand, in hydrochloric acid these amino groups exist as cations which stabilize the system towards rearrangement.

From the polarographic results it is certain that the primary electrode process is a rapid one electron reduction of Michler's ketone to form a ketyl radical. The results reported in Table I demon-

(8) M. J. Allen, J. E. Fearn, and H. A. Levine, *J. Chem. Soc.*, 2220 (1952).

(9) W. E. Bachmann and H. R. Steinberger, *J. Am. Chem. Soc.*, **56**, 170 (1934).

TABLE II

DIAGNOSTIC BANDS[a] OF MICHLER'S KETONE AND REDUCTION PRODUCTS[b]

Ketone	1361 (st)	1321 (st)	1289 (st)	1230	1183 (st)	1169	1064	947	927 (st)	833 (st)	819	768 (st)	682
Hydrol	3570	1349 (st)	1227	1182	1162 (st)	1058	1018	939	948	813 (st)	797 (st)		750
Pinacol	3540	1348 (st)	1227	1206	1156		1058	1032	948	813 (st)	797 (st)		757
Pinacolone	1665 (st)	1349 (st)	1242	1163	1060	1027	948	822	805 (st)	765	747		674 (st)
Ether	1348 (st)	1226	1184	1162 (st)	1131	1060 (Broad)		948	816 (st)	800	756		
Ethane (Nujol)	1620	1521	1354	1236	1206	1168	1123	1064	950	805	793		752

[a] Cm.$^{-1}$ [b] Carbon disulfide solution.

strate that this radical forms a complex[10a] with the electrode which has been formulated by Brewster[10b] according to Equation 1:

$$Ar_2C{=}O \xrightarrow[Hg^-]{H^+} Ar_2COH \quad (Hg) \qquad (1)$$

Under the influence of stirring, the free radical is apparently freed from the surface of the electrode and dimerization occurs to form the pinacol according to Equation 2:

$$2Ar_2COH\ (Hg) \longrightarrow 2Ar_2\dot{C}OH \longrightarrow Ar_2COH\ |\ Ar_2COH \qquad (2)$$

This mechanism explains why high yields of pinacol are only obtained with rapid stirring. Slow stirring or dilute solutions, both of which inhibit dimerization, may present an opportunity for further reduction. In particular, higher cathodic potentials encourage reduction to the hydrol, which is easily converted to the ether in acid solutions, and to the ethane. This occurs very easily in the case of Michler's ketone. These results are at variance with the results of Corwin for *p*-aminoacetophenone where high pinacol yields were favored by higher cathodic potentials.

A recent paper by Mandell, Powers, and Day[11] has produced convincing evidence of a rate controlling reaction for the second step of the reduction of phenyl ketones in alkaline solutions. The existence of a stereospecific reaction indicated the existence of a complex between the ketyl radical and the mercury surface. The effect of stirring reported here gives independent substantiation to the existence of such a complex and demonstrates that the mechanism is operative in acid solution.

EXPERIMENTAL

The electrolyses were carried out in a 600-ml. beaker with a layer of mercury, stirred by a magnetic stirrer, as cathode. The beaker was cooled to 20–25° by means of a copper water bath through which tap water flowed. The anolyte was 1.5*N* hydrochloric acid containing hydrazine as an anodic depolarizing agent. The anolyte compartment was made from an alundum thimble 4.5 × 16 cm. outside dimensions soaked in sodium silicate followed by sulfuric acid accorded to Allen and Corwin. The cathode potential was controlled manually.

After completion of electrolyses as indicated by a fall of the current to a low value, or evolution of hydrogen, or both the solution was poured into a sodium bicarbonate solution, extracted with chloroform, and the chloroform solution dried over sodium sulfate, and reduced in volume at reduced pressure to produce a 10% solution. To the dried chloroform solution was added three volumes of benzene and the solution cooled in the refrigerator. The pinacol, filtered off and

(10) (a) No attempt is made herein to define the actual nature of such a complex. Presumably it is not an adsorption complex because the polarographic results indicate a normal diffusion wave. (b) J. H. Brewster, *J. Am. Chem. Soc.*, **76**, 6361 (1954).

(11) L. Mandell, R. M. Powers, and R. A. Day, Jr., *J. Am. Chem. Soc.*, **80**, 6284 (1958).

dried melted at 192–193° when carried out under optimum conditions. Reduction of volume to a small volume and addition of ethyl alcohol precipitates the ether. Identification of material was largely by means of infrared analyses in carbon disulfide solution. Diagnostic bands of isolated compounds are listed in Table II.

Preparation of pinacolone. A 2-g. sample of pinacol was dissolved in 40 ml. acetic acid and warmed to 50° on steam cone for 15 min. The acetic acid solution was poured into water, neutralized with sodium carbonate, and extracted with benzene. The benzene extract was dried over sodium sulfate, reduced in volume and diluted with petroleum ether 40–60°. Yield of crude pinacolone m.p. 220° 1.6 g. After recrystallization from benzene–petroleum ether, it melted at 230–232°.

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RESEARCH COUNCIL OF ALBERTA
87TH AVENUE AND 114TH STREET
EDMONTON, ALTA.

Chondroitin Sulfate Modifications. II.[1] Peracetylated Sodium Chondroitin Sulfate A

M. L. WOLFROM AND J. W. SPOORS[2]

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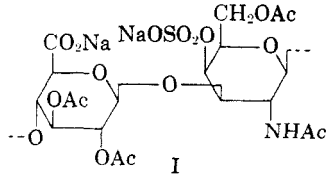
The acetylation of the acidic polysaccharides, pectin[3] and hyaluronic acid,[4] as effected with pyridine and acetic anhydride in formamide, has been reported. We find that this acetylating system can be applied to sodium chondroitin sulfate A under conditions in which the reaction is entirely homogeneous. It is essential that all moisture be excluded. The polysaccharide salt is peracetylated without desulfation and the product (I), after purification by precipitation methods and dialysis, can be isolated as a white, fluffy powder on freeze-drying. This polymeric peracetate is remarkable in being readily soluble in water, formamide and 1:1 water-ethanol. It is insoluble in acetone, chloroform, ethanol, and ether. It may be readily de-*O*-acetylated to yield the original material and can thus be of use in the purification of the polysaccharide.



I

(1) Part I, *J. Am. Chem. Soc.*, **82**, in press (1960).

(2) National Science Foundation Research Associate under Grant NSF G584 to The Ohio State University.

(3) J. F. Carson, Jr., and W. D. Maclay, *J. Am. Chem. Soc.*, **67**, 787 (1945).

(4) Z. Hadidian and N. W. Pirie, *Biochem. J.*, **42**, 266 (1948); R. W. Jeanloz and E. Forchielli, *J. Biol. Chem.*, **186**, 495 (1950).

EXPERIMENTAL

Peracetylated sodium chondroitin sulfate A (I). An amount of 3.8 g. of sodium chondroitin sulfate A, purified essentially as described previously,[5] was finely pulverized and dried over phosphoric anhydride at 70° and 0.05 mm. for 24 hr. This dry powder was dissolved in 24 ml. of dry, freshly distilled formamide by shaking overnight in a sealed flask. To this solution was added, with agitation, 24 ml. of dry, freshly distilled pyridine followed by 10 ml. of acetic anhydride. The sealed solution was shaken at room temperature for 12 hr. when a further quantity of 13 ml. of acetic anhydride was added, and shaking was continued for a total of 24 hr., during which time the color of the solution became a medium red-brown. The solution was then poured with stirring into 500 ml. of ethanol at 0° and then 400 ml. more ethanol was added to yield a white, flocculent precipitate which was collected by filtration and washed with ethanol. The product was further purified by pouring its solution in 100 ml. of water into 500 ml. of ethanol. Precipitation was effected on the addition of 3–5 ml. of a saturated aqueous sodium chloride solution. This procedure was twice repeated and the final product was dissolved in 100 ml. of water and dialyzed for 2 days against distilled water. Recovery of the product as a fluffy, white, amorphous solid was effected by freeze-drying; yield 3.5 g. (72%), $[\alpha]_D^{30}$ −25° (*c* 1.14, water).

This material was insoluble in acetone, chloroform, ether, ethanol, and methanol but was soluble in water, formamide and 1:1 (by vol.) water-ethanol. It was non-reducing toward Benedict solution and exhibited a positive sulfate test only after hydrolysis with dilute hydrochloric acid. The ninhydrin test for the free amino group was negative; positive tests were obtained for uronic acid and hexosamine. Infrared absorption spectral examination showed the strong acetate ester peak at 1740 cm.$^{-1}$ The prominent bands at 3500 cm.$^{-1}$ and 1670 cm.$^{-1}$ may be attributed to the water of hydration.[6]

Anal. Calcd. for $C_{12}H_{12}NaO_6(NHCOCH_3)(OCOCH_3)_{3.25}(OSO_2ONa\cdot 2H_2O)_{0.75}$: C, 38.38; H, 4.52; N, 2.18; Na, 6.28; CH_3CO, 28.52. Found: C, 37.83; H, 4.53; N, 2.34; Na, 6.14; CH_3CO,[7] 28.05.

De-O-acetylation of peracetylated sodium chondroitin sulfate A. An amount of 600 mg. of the above-described peracetylated sodium chondroitin sulfate A was added at 0° to a filtered solution of 3.0 g. of barium hydroxide octahydrate in 50 ml. of water, and the resultant solution was maintained at 0–5° for 1.5 hr. The solution was then carbonated, filtered, and barium ion was removed exactly with sulfuric acid. The centrifuged, neutral solution was dialyzed against distilled water for 48 hr. and its solid content was recovered as a white powder by freeze-drying; yield 300 mg. (64%), $[\alpha]_D^{32}$ −16° (*c* 1.08, water). The product exhibited a negative ninhydrin reaction for the free amino group.

Anal. Calcd. for $C_{12}H_{16}NaO_6(NHCOCH_3)(OH)_{3.25}(OSO_2ONa\cdot 2H_2O)_{0.75}$: N, 2.77; ash (as sulfate), 24.62; CH_3CO, 8.52. Found: N, 2.50; ash, 24.42; CH_3CO,[7] 8.15.

DEPARTMENT OF CHEMISTRY
THE OHIO STATE UNIVERSITY
COLUMBUS 10, OHIO

(5) M. L. Wolfrom and K. Onodera, *J. Am. Chem. Soc.*, **79**, 4739 (1957). In footnote 23 of this reference the product is designated incorrectly as sodium chondroitin sulfate C. Our preparation contained 0.8 sulfate group per disaccharide unit.

(6) S. A. Barker, E. J. Bourne, and D. H. Whiffen, *Methods of Biochem. Anal.*, **3**, 213 (1956).

(7) A. Chaney and M. L. Wolfrom, *Anal. Chem.*, **28**, 1614 (1956).