[CONTRIBUTION FROM THE WHITMORE LABORATORY OF THE COLLEGE OF CHEMISTRY AND PHYSICS, THE PENNSYLVANIA STATE UNIVERSITY]

The Preparation and Dehydration of 6-Hydroxyspiro[4,5]decane, a Neopentyl System

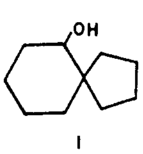
BY PAUL A. NARO[1] AND JOSEPH A. DIXON

RECEIVED AUGUST 27, 1958

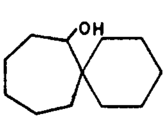
Rearrangements of neopentyl-type alcohols of the spiro series must lead to changes in ring size. The preparation and alumina- and acid-catalyzed dehydration of 6-hydroxyspiro[4,5]decane are described. While the alumina dehydration led to 42.2% normal and 47.1% rearranged products, the acid-catalyzed reaction yielded only 79.8% rearranged products and 13.8% unreacted alcohol. These results are discussed in the light of previous work.

Introduction

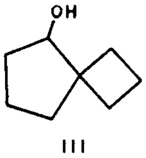
Although there have been numerous dehydration studies of neopentyl-type alcohols, only five[2-6] have been reported in the spiro series. Three of the most interesting examples are 6-hydroxyspiro-[4,5]decane (I), 7-hydroxyspiro[5,6]dodecane (II) and 5-hydroxyspiro[3,4]octane (III). All were dehydrated using acidic catalysts.



I

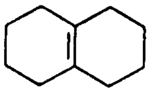


II

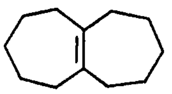


III

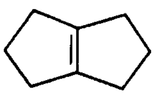
These alcohols are unique in that the neopentyl system is also a part of an alicyclic ring, and any rearrangements which occur must result in changes of ring size. Upon dehydration these alcohols might be expected to yield, in addition to other products, some bicyclo[0,4,4]decene-1(6)(IV), bicyclo[0,5,5]-dodecene-1(7) (V) and bicyclo[0,3,3]octene-1(5)-(VI), respectively. Thus, dehydrations of these spiranols might conceivably provide new synthetic routes to fused ring compounds.



IV



V



VI

The dehydration and rearrangement of the spiranol I has been studied by Jacquier and Christol[2] in connection with their studies of the Ritter[7] reaction. These workers reported that the only product obtained when compound I was treated with either zinc chloride or polyphosphoric acid was IV, and *it was produced in a yield of 95%*. No trace of the $\Delta^{1,9}$-isomer was found. In addition, these authors were unable to dehydrate the alcohol II even on heating with twice its weight of zinc chloride at 140°, and the use of polyphosphoric acid yielded only a small quantity of cyclohexylcyclohexene. Unfortunately, the study was reported without the benefit of a description of the experimental procedures and data. In contrast to these observations, Laber[5] has reported that the spiranol II is dehydrated readily by zinc chloride, giving an 80% yield of cyclohexylcyclohexene. Although Laber conducted the reaction under reduced pressure, his conditions of temperature and time were almost identical with those of Jacquier and Christol.

In a more recent, more extensive, and more fully documented study,[3] however, Christol, Jacquier and Mousseron now report that traces of isomeric octalins were found in the dehydration of I with the same reagents as before. It is interesting to note that the constants reported for the $\Delta^{9,10}$-isomer in their study do not agree with those obtained by other workers.[8] By subjecting their $\Delta^{9,10}$-octalin to the conditions of the Ritter reaction they obtained only 9-formylaminodecalin. The same product could have resulted had the olefin actually been a mixture of the $\Delta^{9,10}$- and $\Delta^{1,9}$-isomers. A second attempt to dehydrate the spiranol II met with the same results as before. Because of these surprising results and because of the aforementioned possible application of the dehydration of such spiranols to the synthesis of difficulty obtainable fused five- and seven-membered ring systems, it appeared desirable to study the preparation and dehydration of 6-hydroxyspiro[4,5]decane.

The dehydration of pinacolyl alcohol (VII) provides the closest aliphatic analogy to the dehydration of the spiranols. The dehydration of this compound in the vapor phase over alumina has been described by various workers.[9-12] Although the results vary widely, their studies indicate that the use of temperatures in excess of 300° and the presence of acidic impurities in the alumina tend to increase the amounts of rearranged products. Keulemans,[11] for example, was able to obtain a 75% yield of the normal dehydration product at 285°. By use of activated alumina at higher temperatures, however, Petrov[9] observed total rearrangement, obtaining 65% tetramethylethylene (VIII) and 35% methyl isopropyl ethylene (IX). Since alumina can act as a Lewis acid, it can cause rearrangements in much the same way, although in general to not as great an extent, as acidic catalysts.[13a] It therefore seemed advisable to also

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[1] American Petroleum Institute Fellow, 1956–1958.

[2] R. Jacquier and H. Christol, *Bull. soc. chim. France*, 556 (1954).

[3] H. Christol, R. Jacquier and M. Mousseron, *ibid.*, 1027 (1957).

[4] I. Vogel, *Chem. Ber.*, **85**, 25 (1952).

[5] G. Laber, *Ann.*, **588**, 79 (1954).

[6] B. Belleau, THIS JOURNAL, **75**, 1159 (1953).

[7] J. J. Ritter, *et al.*, *ibid.*, **70**, 4045 (1948); **70**, 4048 (1948); **71**, 4128 (1949).

[8] S. Dev, *J. Indian Chem. Soc.*, **31**, 1 (1954); J. R. Durland and H. Adkins, THIS JOURNAL, **61**, 429 (1939); W. G. Dauben, E. C. Martin and G. J. Fonken, *J. Org. Chem.*, **23**, 1205 (1958).

[9] A. A. Petrov, *Doklady Akad. Nauk, S.S.S.R.*, **73**, 1205 (1950) *C. A.*, **45**, 2878^h (1951).

[10] P. L. Cramer and A. L. Glasebrook, THIS JOURNAL, **61**, 230 (1939).

[11] A. I. M. Keulemans, *Chem. Weekblad*, **39**, 330 (1942); *C. A.*, **40**, 4039^e (1946).

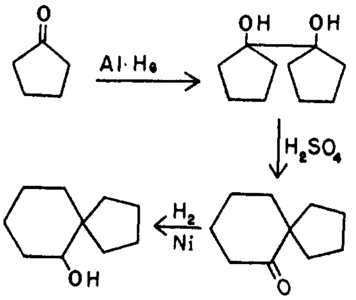
[12] E. A. Kelso, G. Wash, J. T. Horeczy, B. Shive and W. A. Felsing, THIS JOURNAL, **63**, 2273 (1941).

[13] (a) G. W. Wheland, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 489; (b) p. 519.

study the alumina dehydration of spiranols in an effort to determine whether or not analogies could be drawn between such cyclic and aliphatic systems.

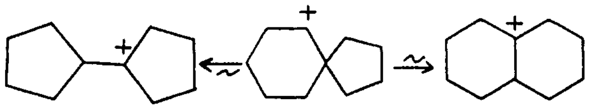
Discussion and Results

The present paper describes the preparation and dehydration of 6-hydroxyspiro[4,5]decane (I). The synthesis was carried out according to the scheme



1,1′-Dihydroxy-1,1′-dicyclopentyl was prepared by a slight modification of the method of Walter.[14] Dropwise addition of a benzene solution of the diol to 50% sulfuric acid with simultaneous steam distillation gave 72% 6-ketospiro[4,5]decane. Finally, catalytic reduction of the ketone yielded the alcohol I.

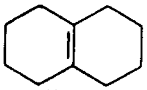
The following intermediates can result upon dehydration of the spiranol



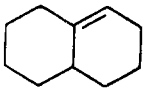
XII X XI

These species could give rise to the olefins

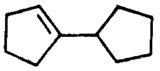
XIII



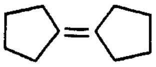
XIV



XV



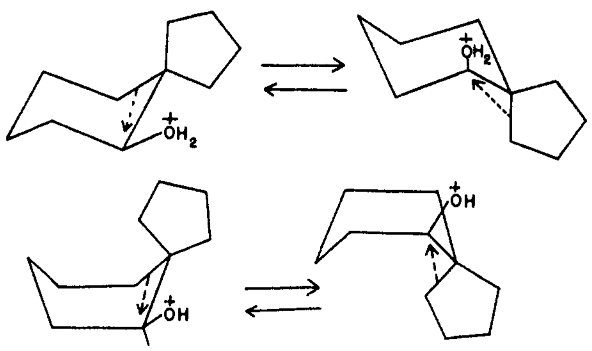
XVI



XVII

By examination of molecular models it appears that the chair form of the cyclohexane ring places rather stringent steric requirements on the hydroxyl group. The axial hydroxyl seems to be more hindered than the equatorial, and it should therefore be expected that the equatorial form would predominate at room temperature, but not necessarily at reaction temperature. The boat form, though highly strained due to the interactions imposed by the cyclopentane ring, presents a different situation. Both the axial and equatorial hydroxyls appear to have approximately equal steric requirements.

However, if one considers the Whitmore mechanism[13b] of 1,2-shifts, it also appears that a rearward attack by an electron pair from the cyclopentyl ring on the carbon atom involved is possible only in the case of the axial alcohol and leads to XI. The equatorial alcohol allows a rearward attack only for the electron pair which is part of the cyclohexane ring, and leads to an intermediate of the type XII. Thus it could be predicted that if the alcohol reacts in its equatorial form, the products would be XIII and/or XVI and/or XVII, and if it reacted in its axial form they would be XIII and/or XIV and/or XV. That both XIV and XV are products of both dehydrations, together with the fact that no bicyclopentyl derivative was found in either case, is strongly suggestive that the alcohol reacts in its axial form.



These conclusions are further substantiated by the studies of Rowe, *et al.*,[15] on the dehydration of 6-methyl-6-hydroxyspiro(4,5)decane with boron trifluoride etherate. In a matter of seconds, these workers obtained a quantitative conversion of the spiranol to 10-methyl-$\Delta^{1,9}$-octalin, thus demonstrating the ease of dehydration and rearrangement when the hydroxyl group is constrained to the more favorable axial conformation.

Dehydration over Alumina.—The dehydration was carried out in the vapor phase at 350°, and the resulting mixture of olefins was fractionally distilled. Only one compound was separated and a mixture of at least two others was shown to be present. The single compound isolated (42.2%) exhibited principal bands in the infrared at 2975, 2860, 1695, 1650, 1460, 1440, 1177, 1038, 940, 903, 869 and 732 cm.$^{-1}$, and was readily identified as spiro-(4,5)deca-6-ene (XIII) (or a position isomer thereof) by quantitative hydrogenation to a hydrocarbon whose infrared absorption spectrum and properties are exactly identical with an authentic sample of spiro(4,5)decane, prepared by Wolff–Kishner reduction of the corresponding ketone.

It was not possible to completely identify the small forecut (10.7%) of olefins which distilled before the spirodecene. However, that the material was of the form of XIII was indicated by catalytic hydrogenation of the mixture to yield, as one of the products, spiro(4,5)decane.

The remainder of the olefin product (47.1%) was characterized by the preparation of two and only two nitrosochlorides. These were shown to be the nitrosochlorides of the octalins XIV and XV. No trace of the nitrosochlorides of compounds XVI or XVII could be found.

Dehydration with Sulfuric Acid.—The dehydration was effected by azeotropic distillation of the olefins and water from a solution of the alcohol and a few milliliters of sulfuric acid at 100° and atmospheric pressure. The olefin mixture was then fractionally

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[14] C. R. Walter, This Journal, **74**, 5185 (1952).

[15] J. W. Rowe, A. Melera, D. Arigoni, O. Jeger and L. Ruzicka, *Helv. Chim. Acta*, **40**, 1 (1957).

distilled as in the alumina dehydration. The products were a mixture of the octalins XIV and XV (79.8%), unreacted alcohol (13.8%) and polymeric material (4.3%). The octalins were characterized by means of the nitrosochlorides as before.

Thus, it has been shown that both the acid-catalyzed and alumina-catalyzed dehydration of 6-hydroxyspiro(4,5)decane led to a mixture of $\Delta^{9,10}$- and $\Delta^{1,9}$-octalin. No quantitative estimation of the amounts of each isomer present based on the weights of nitrosochlorides was made since the reaction is not quantitative and the products are difficult to purify. It was observed, however, that the blue nitrosochloride prepared from the $\Delta^{9,10}$-isomer predominated in the higher boiling fractions while the white nitrosochloride from the $\Delta^{1,9}$-isomer predominated in the lower fractions. This, together with the fact that the refractive index of $\Delta^{9,10}$-octalin reported by Christol, Jacquier and Mousseron[3] (n^{25}D 1.4918) is intermediate among the distillation data obtained in this study, strongly suggests that their compound is actually a mixture of the two expected isomers.

The fact that unreacted alcohol was found in the acid-catalyzed dehydration is not evidence that the compound is rather stable toward dehydration. The unreacted alcohol simply steam distilled out of the acidic medium with the liberated water.

In view of the results obtained by Petrov,[9] it was surprising that 42.2% of the normal product was obtained from the alumina-catalyzed dehydration. This strongly suggests that ring enlargements in such spiranols are not easily effected in the presence of weakly acidic catalysts in contrast to the more facile rearrangements which occur in the aliphatic alcohols.

Experimental[16]

Preparation of 1,1′-Dihydroxy-1,1′-dicyclopentyl.—In a large flask equipped with an efficient copper-coil condenser and a heavy-duty stirrer were placed 1500 ml. of anhydrous benzene and 120 g. (4.45 moles) of aluminum granules. The mixture was heated to boiling, the heating mantle quickly removed, and a solution of 100 g. (0.368 mole) of mercuric chloride in 1 kg. (11.9 moles) of cyclopentanone was added at once. The reaction began in a few seconds and was extremely violent, but experience in this Laboratory has shown that it is necessary to operate in this fashion in order to obtain the maximum yield. Cooling should be used only if necessary. The gray mixture refluxed for 1.5 hours and was then heated at reflux for an additional hour with stirring. The mixture was cooled, diluted with 2 l. of benzene and decomposed by dropwise addition of 1 l. of saturated salt solution (exothermic). The resulting mixture was filtered with suction while hot and the filter cake was extracted 3 times with boiling benzene. After the bulk of the solvent was removed by distillation, cooling the brown sirupy residue gave brown crystals. These were washed with cold hexane, and two recrystallizations from a 50–50 benzene–hexane mixture yielded 303 g. (30%) of white prisms, m.p. 111.4–112.4°, reported[14] m.p. 109–111°.

Preparation of 6-ketospiro(4,5)decane.—A solution of 120 g. (0.71 mole) of the aforementioned diol in 2 l. of benzene was added dropwise to a solution of 100 ml. of water and 100 ml. of concentrated sulfuric acid which was simultaneously being steam distilled. When no more organic material appeared in the distillate the two layers were separated and the aqueous layer was saturated with sodium chloride and extracted 3 times with ether. The original organic layer and extracts were combined, washed with 5% bicarbonate solution, and dried. The ether was then distilled and the residual liquid was fractionally distilled through a packed column.[17] There was obtained 77.6 g. (72.3%) of a pale yellow liquid,[18] b.p. 95° (8 mm.), n^{25}D 1.4820, n^{20}D 1.4840, d^{20}_{4} 0.9888, η^{20} 4.23 cp.; *M*D calcd. 44.01, found 44.05. The DNPH was prepared in the usual way,[19] m.p. 121–122° (reported[20] m.p. 116–117°).

Anal. Calcd. for $C_{16}H_{20}N_4O_4$: N, 16.86. Found: N, 16.77.

Preparation of 6-Hydroxyspiro(4,5)decane.—The spiranone (310 g., 2.04 moles) was hydrogenated using a nickel-on-kieselguhr catalyst[21] at 130° and 1000 p.s.i. Filtration of the catalyst and fractional distillation of the filtrate yielded 250.7 g. (81%) of 6-hydroxyspiro(4,5)decane. The spiranol is a water-white viscous liquid with a pungent camphoraceous odor, b.p. 124° (30 mm.), n^{25}D 1.4951, n^{20}D 1.4966, d^{20}_{4} 0.9963; *M*D 45.53 (calcd.), 45.27 (found). The 3,5-dinitrobenzoate has m.p. 135.6–136.8°. The α-phenylurethan has m.p. 79–80°.

Anal. Calcd. for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.39; H, 11.53.

Dehydration over Alumina.—The apparatus used consisted of a horizontal 36-inch, 30 mm. i.d. Pyrex tube with 3 separately controlled heating sections. The alumina (4–8 mesh, Alorco) was activated by heating overnight at 450° in a stream of nitrogen. The spiranol (163 g., 1.07 moles) was added to the tube at a rate of about 20 drops/min. while maintaining the three sections at 250, 300 and 350°, respectively. After all the material had been added to the tube a slow stream of nitrogen was passed through to sweep out any remaining olefins and water. A total of 153.4 g. (92%) of material was collected, of which 18.1 g. (94% of the theoretical) was water. The olefin mixture (143 g., n^{25}D 1.4894) was then distilled from hydroquinone (3 mg.) through a spinning band column[22] at atmospheric pressure. Only one product was isolated, n^{25}D 1.4856, b.p. 184° (735 mm.). The remainder of the material was a mixture of olefins having n^{25}D 1.4857–1.4977 and b.p. 185–197° (740 mm.).

Dehydration with Sulfuric Acid.—A mixture of 148.5 g. (0.96 mole) of the spiranol and 5 ml. of concentrated sulfuric acid was carefully heated to 100°, at which point the bulk of the olefins and water distilled. The water was separated and the organic material was washed twice with 5% bicarbonate solution and dried. The dry product (123.4 g., 94.1%) was then distilled from hydroquinone through a spinning band column[22] at 732 mm. No single compound was isolated, the distillate being a mixture of olefins having n^{25}D 1.4897–1.4978, b.p. 188–195° (732 mm.). The undistilled residue contained 13.8% unreacted spiranol.

Preparation of Nitrosochlorides.—A solution of 1 g. of the olefin, 2 g. of *n*-butyl nitrite and 3 ml. of glacial acetic acid was cooled to −70° and 2 ml. of concentrated hydrochloric acid was added dropwise with stirring. Treatment of selected fractions from both the acid- and alumina-catalyzed dehydrations yielded light blue crystals. After 3 recrystallizations from acetone a pure white nitrosochloride, m.p. 120.5–121°, was obtained. The melting point was found to be greatly dependent upon the method of heating. Analogous behavior has been observed by Bartlett, *et al.*,[23] who give a melting point for bicyclo(0,4,4)decene-1(2)nitrosochloride of 121°. Concentration of the blue mother liquors gave, after standing three days at 0°, large blue prisms, m.p. 89–90°. Cope and Holzman[24] give a melting point for bicyclo(0,4,4)decene-1(6)nitrosochloride of 89–90°.

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[16] All melting points are corrected. Micro analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

[17] The packed section of this column is 90 cm. long with an inside diameter of 25 mm., and is packed with 0.24 × 0.24 inch protruded metal packing. The efficiency is estimated to be approximately 15 theoretical plates.

[18] The yellow color can be removed by percolation through activated silica gel. There is, however, no detectable change in the physical constants.

[19] R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 171.

[20] M. Mousseron, R. Jacquier and H. Christol, *Compt. rend.*, **239**, 1805 (1954).

[21] Supplied by the Universal Oil Products Co., Chicago, Ill.

[22] This column is manufactured by the Nester–Faust Co., Exton, Pa. The packed section is 36 inches long with an internal diameter of 11 mm. The band is a spiral of 300 mesh stainless steel screen.

[23] P. D. Bartlett, F. E. Condon and A. Schneider, THIS JOURNAL, **66**, 1531 (1944).

[24] A. C. Cope and G. Holzman, *ibid.*, **72**, 3067 (1950).

Anal. Calcd. for $C_{10}H_{16}NOCl$ (blue); N, 6.94; Cl, 17.58. Found: N, 6.78; Cl, 17.87.

Anal. Calcd. for $C_{10}H_{16}NOCl$ (white): Cl, 17.58. Found: Cl, 17.20.

Hydrogenation of Spiro(4,5)deca-6-ene.—The olefin (7 g., 0.052 mole, $n^{25}D$ 1.4856, b.p. 184° (735 mm.), d^{20}_4 0.8995; MD 43.53 (calcd.), 43.62 (found)), 50 ml. of heptane and 0.5 g. of Baker PtO_2 catalyst was shaken for 7 hours at 66° and 2 atm. of hydrogen. It absorbed 97.4% of the theoretical amount of hydrogen. The platinum was removed by filtration and the filtrate was distilled to yield 5.1 g. (73%) of hydrocarbon, b.p. 87° (40 mm.), $n^{25}D$ 1.4686. Its infrared absorption spectum is identical with that of spiro(4,5)decane, $n^{25}D$ 1.4687, b.p. 97° (50 mm.).

Acknowledgment.—The authors express their appreciation to the American Petroleum Institute for the grant which made this research possible.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY]

Anomalous Reactions of Kojic Acid and Related Compounds with Acrylonitrile and Acrylic Ester

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RECEIVED SEPTEMBER 10, 1958

Some 3-hydroxy-1,4-pyrones satisfying certain structural requirements were found to undergo anomalous reactions with acrylonitrile and methyl acrylate. The scope and conditions of the former reaction have been investigated in some detail.

The well-known reactions of phenols with acrylonitrile[3] or acrylic esters in the presence of base normally involve addition at the phenolic oxygen; but some phenols, notably phloroglucinol, resorcinol[4] or 2-naphthol[5] that are capable of keto-enol tautomerism undergo cyanoethylation ortho to the phenolic hydroxyl. Such a cyanoethylation is presumably through the anion of the keto form, since ketones containing α-hydrogens are cyanoethylated at their α-positions.

Kojic acid (Ia) is phenolic, and under alkaline conditions is known to react through either of the resonance forms of its anion.[6] Cyanoethylation might have been expected, therefore, and indeed a claim was made[7,8] for such a reaction by Woods but this claim was proved invalid.[9]

We have discovered, however, that kojic acid does react readily with acrylonitrile, but the reaction is far from a simple cyanoethylation. The product, labeled "compound A," melted with decomposition at 261–262°. It analyzed for $C_{15}H_{14}O_9$ and presented an intriguing structural problem.

Compound A gave a positive ferric chloride enolic test and could be titrated as a weak monobasic acid. It could be acetylated and benzoylated. It was inert toward the usual carbonyl reagents and yielded tars with a number of other reagents (thionyl chloride, bromine, sodium bromoacetate, methyl iodide and silver oxide, succinic anhydride and sodium succinate, phosphorus pentachloride, thionyl chloride). Its infrared spectrum (Fig. 1) showed a strong hydroxyl band at 2.94, carbonyl bands at 5.63 and 5.78, along with pyrone bands at 6.02, 6.18 and 6.36 μ.

The difficulty in approaching the structure of A lay in the absence of nitrogen and presence of many oxygens in the molecule. With nitrogen absent it would obviously be troublesome to determine which part of the molecule had arisen from the original acrylonitrile. The band at 5.63 μ suggested a γ-lactone and support for this contention was found on isolating a material by slight modification of the conditions of reaction, which contained labile nitrogen and had carbonyl bands at 5.76 and 5.93 μ. When this material was allowed to stand with concentrated acid at room temperature, crystals of A separated. The quantity of material was too small for anything but spectral study, but it is safe to assume that it is a direct precursor of A, probably an imido lactone that changed to the lactone itself on hydrolysis.

As the lactonization seemed to involve reaction between the nitrile group and a hydroxymethyl group, it appeared promising to circumvent the lactonization by the use of an appropriate derivative of kojic acid incapable of such reaction, and from which the results could be extrapolated to kojic acid.

α-Chloro-α-deoxykojic acid (Ib) was selected first since it was accessible. On reaction with acrylonitrile it yielded a well defined material, called compound C. Its infrared spectrum showed bands at 3.03, 4.38, 5.77, 6.12 with shoulder at 6.07 and 6.24 μ. Of particular significance was the presence of the nitrile band at 4.38 and the absence of the lactone band at 5.63 μ. The compound was difficult to purify in view of its sparing solubility in most solvents. After recrystallization from boiling acetic acid it analyzed for $C_{15}H_{13}Cl_2NO_6$, although carbon was 0.7% high and nitrogen 0.5% low, indicating some solvolysis during purification.

This result did support the initial hypothesis that loss of nitrogen in the formation of A was caused by lactonization and that the hydroxymethyl group is not necessary for the abnormal reaction with acrylonitrile. To test the generality of this anomalous reaction several α-keto enols were prepared and in particular a number of 3-hydroxy-1,4-pyrones, since this was apparently the nucleus responsible for the unusual course of reaction.

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[1] Corn Products Refining Co. Fellow, 1947–1949.

[2] Allied Chemical and Dye Corp. Fellow, 1957–1958.

[3] H. A. Bruson, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 79.

[4] G. S. Misra and R. S. Asthana, *Ann.*, **609**, 240 (1957).

[5] A. F. Hardman, U. S. Patent 2,421,837, *C. A.*, **41**, 5901 (1947).

[6] A. Bećlik, *Adv. Carbohydrate Chem.*, **11**, 170 (1956).

[7] L. L. Woods, THIS JOURNAL, **74**, 3959 (1952).

[8] L. L. Woods, *ibid.*, **75**, 1510 (1953).

[9] C. D. Hurd and S. Trofimenko, *ibid.*, **80**, 2526 (1958).