1,3-butanedione in 12.5 ml. of acetic acid containing 0.5 ml. of concentrated hydrochloric acid was refluxed for 15 minutes. Volatile material was removed from the reaction mixture by evaporation under reduced pressure on the steam-bath. The residue was triturated with ether and the mixture was filtered. The solid product weighed 1.9 g. (yield 81%) and melted at 157–162°. Four recrystallizations from 50% alcohol gave a yellow crystalline compound, m.p. 167–169°. The analytical data for this compound are given in Table II.

INDIANAPOLIS, INDIANA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

Dinitrophenylhydrazones of α-Halo Ketones

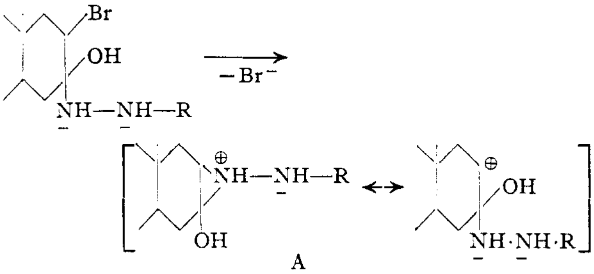
BY FAUSTO RAMIREZ AND ARTHUR F. KIRBY[1]

RECEIVED MARCH 10, 1952

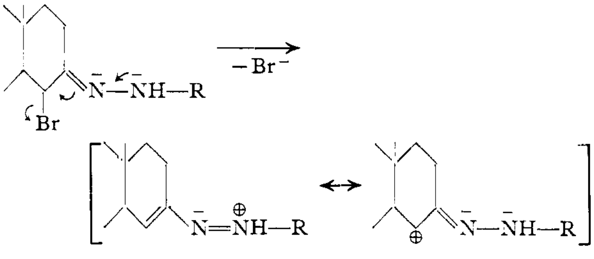
In a study of the behavior of α-halo ketones toward the usual carbonyl reagents the following dinitrophenylhydrazones (DNPH) were prepared. DNPH of: 2-chlorocyclohexanone (Ia), 2-bromocyclohexanone (IIa), 6,6-dimethyl-2-bromocyclohexanone (IIIa), 2-bromo-1-tetralone (IVa) and 2-bromo-1-keto-1,2,3,4-tetrahydrophenanthrene (Va). When solutions of the halo hydrazones Ia, IIa or IIIa in acetic acid were kept at their boiling points for five minutes, smooth dehydrohalogenation took place with formation of the corresponding α,β-unsaturated hydrazone. Loss of hydrogen halide occurred on similar treatment of the halo ketones with 1 mole of dinitrophenylhydrazine in acetic acid solution. No elimination from the halo hydrazone or the halo ketone was observed in those cases (IVa and Va) in which an aromatic ring was conjugated to the phenylhydrazone group. The methoxyhydrazones were easily obtained from the halo hydrazones on short warming in methanol. From Ia, IIa and IIIa osazones were obtained on treatment with excess dinitrophenylhydrazine. These observations suggest the formation of an intermediate halo hydrazone in the Mattox–Kendall reaction used to introduce the Δ^4-3-keto system in some steroids and are consistent with a recently stated picture of the reaction involving a solvolysis of the halogen facilitated by the electron-donor character of the nitrogen atom α to the phenyl in the phenylhydrazone.

The behavior of α-halo ketones toward the usual carbonyl reagents presents some interesting features. Hantzsch[2] described the formation of osazones and 1,2-dioximes from compounds of the type R_1–CHX–CO–R_2 using 1–3 moles of phenylhydrazine and hydroxylamine, respectively. Curtin and Tristram[3] established the formula $C_{28}H_{24}N_4$ for the product of the reaction between α-haloacetophenones and phenylhydrazine and furnished evidence in favor of a tetrahydropyridazine structure for that product. With hydroxylamine, α-bromoacetophenone is reported to form the dioxime of phenylglyoxal.[4] An unsuccessful attempt to prepare the (*p*-carboxyphenyl)-hydrazone of 2-chlorocyclohexanone has been recorded[5] and this is in agreement with the isolation of a dinitrophenylosazone[6] and of a 1,2-dioxime[7] on treatment of 2-chlorocyclohexanone with the corresponding carbonyl reagent.

A recent communication by Mattox and Kendall[8] reporting the formation of α,β-unsaturated dinitrophenylhydrazones from steroidal α-bromo ketones by means of dinitrophenylhydrazine in acetic acid solution, has prompted further studies on the course of this smooth and useful dehydrohalogenation.[9,10] Djerassi[9a] pictures the reaction as proceeding *via* a cyclic immonium intermediate A, without initial formation of a hydrazone of the bromo ketone.



On the other hand, Mattox and Kendall[9b] favor the formation of an α-bromo hydrazone in which the reactivity of the halogen atom is explained as



In one case,[9b] bromination of the dinitrophenylhydrazone of the parent ketone in chloroform solution led to a rather unstable α-bromo hydrazone which eliminated hydrogen bromide in acetic acid solution. The α-bromo hydrazones were not isolated from the reaction between the corresponding α-halo ketone and the carbonyl reagent.

The present communication deals with the preparation of the dinitrophenylhydrazones of several simple α-halo ketones of varied structure and re-

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[1] From the Ph.D. thesis of Arthur F. Kirby. Presented at the 121st National Meeting of the American Chemical Society, Buffalo, N. Y., March, 1952.

[2] A. Hantzsch and W. Wild, *Ann.*, **289**, 285 (1896).

[3] D. Y. Curtin and E. W. Tristram, THIS JOURNAL, **72**, 5238 (1950).

[4] R. Scholl and G. Matthaiopoulos, *Ber.*, **29**, 1550 (1896). The 2,4-dinitrophenylhydrazone of α-bromoacetophenone has just been described (G. D. Johnson, THIS JOURNAL, **73**, 5888 (1951)).

[5] H. W. Murphy and G. L. Jenkins, *J. Am. Pharm. Assoc.*, **32**, 83 (1943).

[6] R. B. Loftfield, THIS JOURNAL, **73**, 4707 (1951).

[7] N. Tokura and R. Oda, *Bull. Inst. Phys. Chem. Research (Tokyo)*, **22**, 844 (1943); *cf.* A. F. Childs, L. J. Goldsworthy, G. F. Hardings, S. G. P. Plant and G. A. Weeks, *J. Chem. Soc.*, 2320 (1948).

[8] V. R. Mattox and E. C. Kendall, THIS JOURNAL, **70**, 882 (1948).

[9] (a) C. Djerassi, *ibid.*, **71**, 1003 (1949); (b) V. R. Mattox and E. C. Kendall, *ibid.*, **72**, 2290 (1950).

[10] These studies have been carried out in the steroid field. Recently, W. W. Rinne, *et al.* (*ibid.*, **72**, 5759 (1950)) prepared 2-methyl-2-cyclohexen-1-one dinitrophenylhydrazone from an unidentified mixture of bromo ketones obtained by bromination of 2-methylcyclohexanone. For a recent application in the morphine series see M. Gates and G. Tschudi, *ibid.*, **74**, 1110 (1952).

ports some observations on their behavior under different conditions. Table I summarizes the ultraviolet absorption data of the compounds dealt with in this investigation.

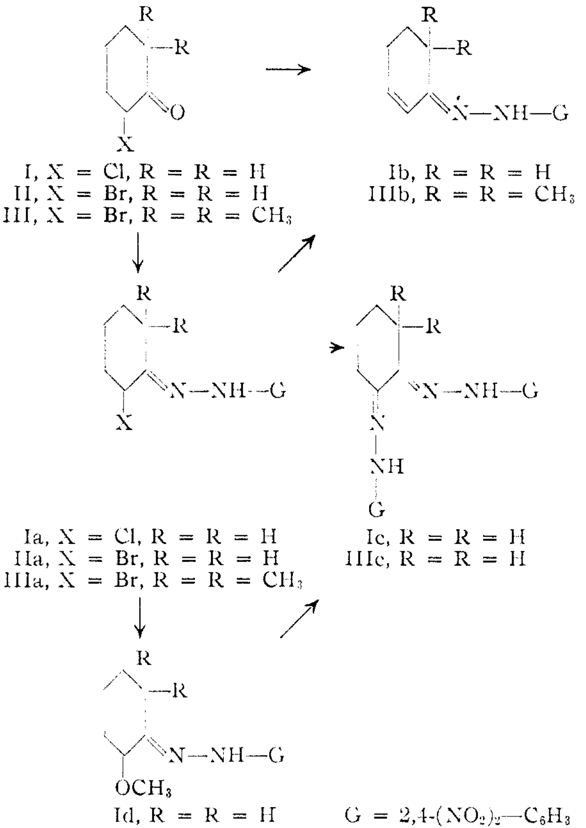
TABLE I

2,4-Dinitrophenylhydrazone of:	λ_{max}, mμ	log ϵ_{max} (chloroform)
Cyclohexanone	366	4.37
2-Chlorocyclohexanone (Ia)	357	4.37
2-Bromocyclohexanone (IIa)	360	4.39
2-Methoxycyclohexanone (Id)	373	4.39
6,6-Dimethylcyclohexanone	367	4.36
6,6-Dimethyl-2-bromocyclohexanone (IIIa)	364	4.37
6,6-Dimethyl-2-methoxycyclohexanone (IIId)	373	4.40
2,2-Cyclohexen-1-one (Ib)	378	4.43
6,6-Dimethyl-2-cyclohexen-1-one (IIIb)	378	4.43
1-Tetralone	385	4.45
2-Bromo-1-tetralone (IVa)	387	4.45
2-Methoxy-1-tetralone (IVd)	389	4.49
1-Keto-1,2,3,4-tetrahydrophenanthrene	391	4.51
2-Bromo-1-keto-1,2,3,4-tetrahydrophenanthrene (Va)	393	4.51
2,4-Dinitrophenylosazone of:		
1,2-Cyclohexanedione (Ic)	351	4.50
	392	4.39
6,6-Dimethyl-1,2-cyclohexanedione (IIIc)	351	4.50
	385	4.41

The α-halo dinitrophenylhydrazones were prepared in good yields by means of an aqueous methanolic solution of 2,4-dinitrophenylhydrazine sulfate containing excess sulfuric acid (Brady reagent).[11] In general these compounds proved to be quite stable when pure or in solutions of nonhydroxylic solvents. When solutions of the α-halo hydrazones Ia, IIa or IIIa in acetic acid were kept at their boiling points for five minutes, smooth dehydrohalogenation took place with formation of Ib[12] or IIIb, respectively. The same results were obtained on similar treatment of solutions of the α-halo ketones I, II or III in acetic acid with one mole of 2,4-dinitrophenylhydrazine; the products isolated were the α,β-unsaturated dinitrophenylhydrazones. The elimination of hydrogen halide appeared to proceed slowly if at all at room temperature. These observations are consistent with the view[9b] that in the Mattox-Kendall reaction the formation of the α-halo hydrazone precedes the dehydrohalogenation step.

In the two cases studied (IVa and Va) in which an aromatic ring was conjugated to the dinitrophenylhydrazone group, no hydrogen bromide was eliminated under conditions comparable to or more drastic than those described above.[13] As shown by the behavior of IIIa, the degree of substitution on a position adjacent to the hydrazone group seems to play no significant role in the elimination.[14]

The lability of the α-halogen atom in the hy-



I, X = Cl, R = R = H
II, X = Br, R = R = H
III, X = Br, R = R = CH$_3$

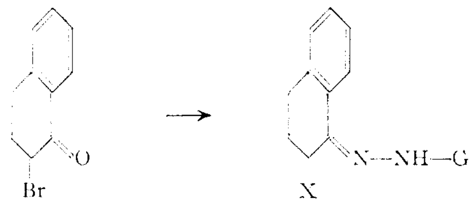
Ib, R = R = H
IIIb, R = R = CH$_3$

Ia, X = Cl, R = R = H
IIa, X = Br, R = R = H
IIIa, X = Br, R = R = CH$_3$

Ic, R = R = H
IIIc, R = R = H

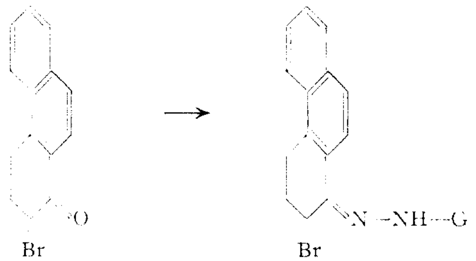
Id, R = R = H
IIId, R = R = CH$_3$

G = 2,4-$(NO_2)_2$—C_6H_3



IV

IVa, X = Br
IVd, X = OCH$_3$



V

Va

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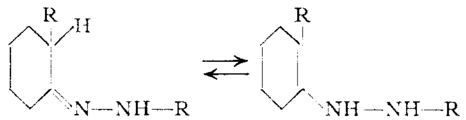
(11) O. L. Brady, *J. Chem. Soc.*, 757 (1931).

(12) From IIa, Ib was obtained in the form of its rather unstable hydrobromide.

(13) Bearing in mind the picture of the reaction suggested by Mattox and Kendall[9b] this difference in reactivity between IVa and IIa (or any two such structures) could perhaps be correlated with the additional resonance stabilization associated with the conjugated aromatic ring in IVa. This additional resonance stabilization would presumably be of more significance in the reactant than in the charged transition state of IVa, resulting in a lower reactivity relative to IIa

(14) In an early interpretation of the Fischer indole synthesis, Robinson conceived a preliminary enolization of the hydrazone (or ketimine to enamine change)



Cf. G. M. Robinson and R. Robinson, *J. Chem. Soc.*, **113**, 639 (1918); **125**, 827 (1924); R. B. Carlin, THIS JOURNAL, **74**, 1077 (1952). Such enolization might introduce an additional feature in the reactions of unsymmetrically substituted halo hydrazones.

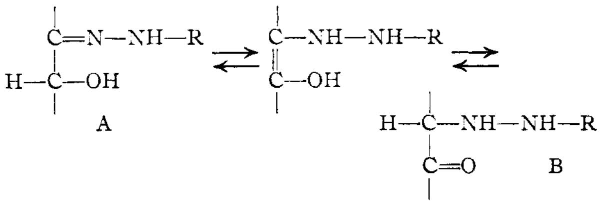
TABLE II

Compound	M.p., °C.	Formula	Analyses, % Calcd. C	H	N	X[f]	Found C	H	N	X
Ia	154–155[a]	$C_{12}H_{13}O_4N_4Cl$	46.1	4.2	17.9	11.3	46.3	4.3	17.9	11.2
IIa	129–130[a]	$C_{12}H_{13}O_4N_4Br$	40.4	3.7	15.7	22.4	40.5	3.6	15.7	22.1
IIIa	143–144[a]	$C_{14}H_{17}O_4N_4Br$	43.6	4.4	14.5	20.7	43.8	4.4	14.3	20.5
IVa	183–184[b]	$C_{16}H_{13}O_4N_4Br$	47.4	3.2	13.8	19.7	47.5	3.3	14.0	19.6
Va	209–210[c]	$C_{20}H_{15}O_4N_4Br$	52.7	3.3	12.3	17.5	52.8	3.2	12.3	17.4
Id	134–135[a]	$C_{13}H_{16}O_5N_4$	50.6	5.2	18.2		50.8	5.2	18.5	
IIId	144–145[a]	$C_{15}H_{20}O_5N_4$	53.6	6.0	16.7		53.8	6.2	16.9	
IVd	230–231[a]	$C_{17}H_{16}O_5N_4$	57.3	4.5	15.7		57.5	4.7	15.8	
IIIb	171–172[d]	$C_{14}H_{16}O_4N_4$	55.3	5.3	18.4		55.3	5.1	18.4	
Ic	227–228[a]	$C_{18}H_{16}O_8N_8$	45.8	3.4			45.9	3.4		
IIIc	237–238[e]	$C_{20}H_{20}O_8N_8$	48.0	4.0	22.4		48.0	3.9	22.4	

[a] Solvent: ethyl acetate. [b] Solvent: chloroform–methanol. [c] Solvent: toluene. [d] Solvent: ethyl acetate–methanol. [e] Solvent: chloroform–methanol. [f] X = halogen.

drazone is apparent in the behavior of Ia, IIa and IIIa toward methanol. In this solvent formation of the corresponding α-methoxy hydrazone (Id or IIId) was essentially complete on warming for a few minutes. The same treatment applied to IVa led also to an α-methoxy hydrazone (IVd). Mattox and Kendall[9b] have noted the formation of an α-methoxy hydrazone (in addition to an α,β-unsaturated hydrazone) in the reaction of a steroidal α-bromo ketone with 2,4-dinitrophenylhydrazine in methanolic solution.

The α-halo hydrazones (Ia, IIa and IIIa) and the α-methoxy hydrazones (Id and IIId) were converted into the corresponding osazones (Ic and IIIc) by an excess of Brady reagent. The osazone Ic has been described as the only product of the action of aqueous solutions of dinitrophenylhydrazine on 2-hydroxy- and 2-alkoxycyclohexanones.[15] In the mechanism of osazone formation proposed by Weygand[16] one of the essential steps is the enaminization A → B



$$\begin{array}{c} | \\ \mathrm{C{=}N{-}NH{-}R} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{A} \end{array} \rightleftarrows \begin{array}{c} | \\ \mathrm{C{-}NH{-}NH{-}R} \\ \| \\ \mathrm{C{-}OH} \\ | \end{array} \rightleftarrows \begin{array}{c} | \\ \mathrm{H{-}C{-}NH{-}NH{-}R} \\ | \\ \mathrm{C{=}O} \\ | \end{array} \; \mathrm{B}$$

Whether the transformations of the α-halo and α-alkoxy hydrazones into the osazone involves an intermediate α-hydroxy hydrazone is under investigation. Osazones have been postulated by Letsinger and Collat[17] as intermediates in the reactions of α-amino ketones with hydrazine and phenylhydrazine. These authors emphasized the similarities in the behavior of α-halo and α-amino ketones toward certain carbonyl reagents.

Experimental[18]

Preparation of Halo Ketones.—With one exception described below the halo ketones used have been previously prepared.[19] 2-Bromocyclohexanone,[20] b.p. (0.1 mm.) 54–55°, n^{25}D 1.5082, was prepared from cyclohexanone using N-bromosuccinimide according to directions kindly furnished by Dr. L. L. McCoy of this Department.

2,2-Dimethylcyclohexanone.—The method of Johnson and Posvic[21] was followed. The ketone, b.p. (760 mm.) 168–170°, n^{20}D 1.4486 formed a semicarbazone, m.p. 198–198.5°; reported[21] m.p. 199–199.5°. The **2,4-dinitrophenylhydrazone** prepared using Brady reagent[11] melted at 142–143° (methanol).

Anal. Calcd. for $C_{14}H_{18}O_4N_4$: C, 54.9; H, 5.9. Found: C, 55.0; H, 6.1.

2-Bromo-6,6-dimethylcyclohexanone.—A solution of 10.16 g. of bromine in 40 ml. of dry chloroform was added slowly, with mechanical stirring, to a solution of 8.00 g. of 2,2-dimethylcyclohexanone in 125 ml. of chloroform kept at 0°. After stirring 15 minutes at room temperature, the mixture was poured into cold water containing some sodium bisulfite. The chloroform layer was washed successively with 5% sodium bicarbonate and water and dried over sodiun sulfate. Distillation of the chloroform yielded 10 g. of crude ketone, m.p. 56–57°. The m.p. did not change on recrystallization from *n*-heptane.

Anal. Calcd. for $C_8H_{13}OBr$: C, 46.8; H, 6.4; Br, 39.0. Found: C, 46.9; H, 6.6; Br, 39.0.

General Procedure for the Preparation of the Halo 2,4-Dinitrophenylhydrazones.—One mole of the halo ketone alone or dissolved in the minimum amount of methanol was treated at room temperature with freshly prepared Brady reagent[11] containing one mole of 2,4-dinitrophenylhydrazine. Per gram of 2,4-dinitrophenylhydrazine, 2 ml. of concentrated sulfuric acid, 15 ml. of methanol and 5 ml. of water were used. The precipitated hydrazone was filtered within 5–10 minutes, washed well with cold aqueous methanol, dried and recrystallized from a suitable solvent. The yields were above 80%. The constants of the hydrazones are summarized in Table II.

2,4-Dinitrophenylhydrazones.—From samples of authentic ketones, the following were prepared. They have been described elsewhere. 2,4-Dinitrophenylhydrazone of: cyclohexanone, m.p. 161–162°, reported[22] m.p. 160°; 2-cyclohexene-1-one, m.p. 168–169°, reported[23] m.p. 167.5–169°; 1-tetralone, m.p. 259–260°, reported[24] m.p. 262–263°; 1-keto-1,2,3,4-tetrahydrophenanthrene, m.p. 285°, reported[25] m.p. 283–285°.

General Procedure for the Dehydrohalogenation of the Halo Hydrazones.—A solution of the halo hydrazone (0.5–1.0 g.) in the minimum amount of hot acetic acid was kept at its boiling point for 5 minutes. The solution was cooled until the acetic acid began to crystallize and the crystals which separated were collected. The recrystallized material was compared by mixed melting points and absorption spectra with authentic samples of the α,β-unsaturated hy-

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[15] A. Kotz, K. Blendermann, R. Rosenbusch and E. Sirringhaus, *Ann.*, **400**, 55 (1913); H. Adkins and A. G. Rossow, THIS JOURNAL, **71**, 3836 (1949).

[16] F. Weygand, *Ber.*, **73**, 1284 (1940).

[17] R. L. Letsinger and R. Collat, THIS JOURNAL, **74**, 621 (1952).

[18] All melting points are corrected. The microanalyses were carried out by Micro-Tech Laboratories, Skokie, Ill., and Schwarzkopf Microanalytical Laboratories, Middle Village, New York. The ultraviolet absorption spectra were taken in chloroform solution in a Cary Recording Spectrophotometer, Model 11.

[19] (a) A. L. Wilds, THIS JOURNAL, **64**, 1424 (1942); (b) A. L. Wilds and J. A. Johnson, *ibid.*, **68**, 87 (1946).

[20] P. Z. Bedoukian, *ibid.*, **67**, 1430 (1945).

[21] W. S. Johnson and H. Posvic, *ibid.*, **69**, 1361 (1947).

[22] C. F. H. Allen, *ibid.*, **52**, 2955 (1930).

[23] K. Dimroth and K. Resin, *Ber.*, **75B**, 322 (1942).

[24] G. D. Johnson, THIS JOURNAL, **73**, 5888 (1951).

[25] N. L. Drake and W. C. McVey, *J. Org. Chem.*, **4**, 464 (1939).

drazones and the starting materials. In this way it was established that Ia, IIa and IIIa eliminated hydrogen bromide while IVa and Va were recovered unchanged. The constants of the unsaturated hydrazones are included in Table II.

When the above procedure was applied to IIa, a yellow substance m.p. 168° (dec.), λ_{max} 378 mμ, log ϵ_{max}^{chlf} 4.43, was obtained. This substance gave a positive Beilstein test for halogen. When its solution in chloroform was washed with water an equivalent amount of bromide ion was found present in the aqueous layer. The yellow substance was the hydrobromide of the hydrazone Ib which was recovered halogen-free from the chloroform solution. Va was extremely insoluble in glacial acetic acid.

Reaction of Halo Ketones with 2,4-Dinitrophenylhydrazine in Acetic Acid.—To a solution of the halo ketone in glacial acetic acid there was added 1 mole of 2,4-dinitrophenylhydrazine and the solution kept at its boiling point for 5 minutes. The product which precipitated on cooling was characterized by comparison with authentic samples of the dinitrophenylhydrazones of the starting material or the corresponding α,β-unsaturated ketone. Here again the hydrobromide of Ib was obtained from IIa. Under these conditions, the formation of Va from V is sluggish and is accompanied by acetylation of 2,4-dinitrophenylhydrazine.

Reaction of Halo Hydrazones with Methanol.—The halo hydrazone was dissolved in methanol and the solution refluxed for 15–30 minutes. After removal of the solvent the yellow methoxy hydrazone was shown to be halogen-free in the Beilstein test. The constants of the methoxy hydrazones are included in Table II.

Formation of Dinitrophenylosazones.—A mixture of the halo hydrazone or the methoxy hydrazone was refluxed with excess of Brady reagent for 3–4 hours. The bright red osazone precipitated during the reaction. The mixture was cooled and the osazone collected and recrystallized as indicated in Table II.

NEW YORK 27, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF AGRICULTURAL CHEMISTRY, PURDUE UNIVERSITY]

A Polymer-homologous Series of Crystalline Oligosaccharide Acetates from Xylan Hydrolysate[1]

BY ROY L. WHISTLER AND CHEN-CHUAN TU

RECEIVED FEBRUARY 29, 1952

The series of crystalline oligosaccharides from xylobiose to xylohexaose is converted to the corresponding series of oligosaccharide acetates, all of which are obtained crystalline in the β-D′-configuration. The melting points and specific rotations of these derivatives are correlated with their degrees of polymerization.

A series of crystalline oligosaccharides composed only of D-xylopyranose units uniformly joined by (1 → 4)-β-D′-linkages has been isolated from xylan hydrolysate.[2] The series extends from xylobiose to xylohexaose inclusive. These are the first crystalline oligosaccharides to be isolated which are composed solely of pentose sugar units. The series is of special interest since its members are structurally identical to the corresponding members of the series from cellulose, except that the xylo-oligosaccharides lack the projecting primary alcohol group on each ring unit characteristic of the gluco-oligosaccharides. Comparisons between the two series may therefore be expected to indicate the effect of the primary alcohol group on molecular properties. Such comparisons including rates of hydrolysis are now in progress. As a further aid for comparison of the two series and to obtain further characterization of the xylo-oligosaccharides, they were converted to their crystalline acetates. Each member of the series was acetylated in a hot mixture of acetic anhydride and sodium acetate in such a way as to preserve unaltered the general structural arrangement and to esterify free anomeric hydroxyls in the β-D′-configuration. Hence, all anomeric carbon atoms within the structures have the same relative steric configurations.

TABLE I

PREPARATION AND YIELD OF β-OLIGOSACCHARIDE ACETATES

Sugar, xylo-	G. taken	NaAc, g.	Ac$_2$O, g.	Reflux, hr.	Yield, g.
Biose	1.50	2.00	20	3.0	2.10
Triose	0.80	0.90	17	4.5	1.32
Tetraose	.80	1.36	17	5.5	1.42
Pentaose	.90	1.41	19	6.5	1.25
Hexaose	.40	0.70	10	7.5	0.46

Optical rotations, melting points and molecular weights of the various β-D′-acetates are shown in Table I. Although the molecular weights determined by Rast method, using the precautions cited by Smith and Young[3] and Meldrum, Saxer and Jones,[4] are in agreement with the expected values, the accuracy of the determination apparently decreases as the molecular weight increases. The melting points increase progressively with degree of polymerization and tend to approach the softening temperature of xylan diacetate. Optical rotations vary uniformly with the degree of polymerization of the oligosaccharide. Freudenberg and coworkers[5] have shown that if the type of linkage in a polymer-homologous series is uniform, the expression $[M]_n/n$ plotted against $(n - 1)/n$ (where $[M]$ is the molecular rotation and n is the degree of polymerization) yields a straight line for $n \geqq 2$. When the molecular rotations of the present series are plotted against the suggested function of degree of polymerization, a linear relation is found to exist as shown in Fig. 1. This finding is further evidence for the presence of uniform linkages in the series members.

The acetyl content of the β-D-acetates was deter-

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(1) Journal Paper No. 602 of the Purdue University Agricultural Experiment Station.

(2) R. L. Whistler and C. C. Tu, THIS JOURNAL, in press.

(3) J. H. C. Smith and W. G. Young, *J. Biol. Chem.*, **75**, 289 (1927).

(4) W. B. Meldrum, L. P. Saxer and T. O. Jones, THIS JOURNAL, **65**, 2023 (1943).

(5) K. Freudenberg, "Tannin. Cellulose. Lignin," J. Springer, Berlin, 1933, pp. 90, 104.