

TABLE I<sup>a</sup>  
THE DIRECTION OF ENOLIZATION OF  $\alpha$ -FORMYL CYCLIC KETONES

No.	Ketone	$\delta^0$ ( $\tau$ ) <sup>b</sup>	K	(% Ib)	No.	Ketone	$\delta^0$ ( $\tau$ ) <sup>b</sup>	K	(% Ib)
1	Cyclopentanone	2.73	3.54	78	7	Cyclododecanone	1.49	0.39	28
2	Cyclohexanone	1.39	0.32	24	8	2-Isopropylcyclohexanone	1.49	.39	28
3	Cycloheptanone	2.43	1.94	66	9	4,4-Dimethyl-2-cyclohexenone	2.57	2.45	71
4	Cyclooctanone	1.89	0.79	44	10	2-Benzal-4- <i>t</i> -butylcyclohexanone	1.05	0.11	10
5	Cyclononanone	1.57	.45	31	11	Bicyclo[2:2:2]octanone	2.98	7.34	88
6	Cyclodecanone	1.24	.22	18	12	Camphor	3.29		100

<sup>a</sup> All measurements were made on 10% solutions (by weight) in carbon tetrachloride at  $25 \pm 1^\circ$  and at 40 Mc. <sup>b</sup>  $\pm 0.01$  p.p.m.

expectation that the high strain in the internal double bond of Ia would provide the impetus for the exclusive preference for Ib. The low field part of the n.m.r. spectrum of II is shown in Fig. 1. The signal at  $-0.15 \tau$  is assigned to the hydroxyl proton (disappears upon deuterium exchange) and the doublet at 0.32 and 0.38  $\tau$  is assigned to the *exo*- and *endo*- non-enolized (6%) aldehyde proton (splitting remains upon  $\alpha$ -hydrogen deuterium exchange). The absorptions at 2.61 and 3.29  $\tau$  have a total area equal to that of the hydroxyl absorption. The relative absorption area  $2.61/3.29 \tau$  increases from 5/95 for a 10% to 31/69 for a 26% solution (by weight) of II in  $CCl_4$  to 78/22 for a 14% solution of II in  $CCl_4$  containing 8% dimethyl sulfoxide.<sup>5</sup> The absorptions at 2.61 and 3.29  $\tau$  are consequently assigned to the vinyl proton of IIa and IIb, respectively. The separation between these absorptions (0.68 p.p.m.) is comparable to the separation between the vinyl protons of 2-methylenecycloalkanes.<sup>6</sup> The value of 3.29  $\tau$  now may be assigned to  $\delta_b$ . Using the experimental values for  $\delta_a$  and  $\delta_b$ , the percentage of Ib and the equilibrium constant, *K*, were estimated for a series of cyclic  $\beta$ -keto aldehydes at  $25^\circ$ . These data are given in Table I. The  $\beta$ -keto aldehydes were found to be >99% enolized except for no. 1 (89% enol), no. 11 (98% enol), and no. 12. For several of the enols,  $H_b$ , O-H proton spin coupling was observed at  $25^\circ$ . This coupling was determined for the other enols at reduced temperatures.<sup>7</sup> A plot of this coupling as a function of the percentage of Ib is shown in Fig. 2. The linear relationship and the intercept of near zero coupling substantiate the reliability of the models employed and the derived equilibrium constants. It is of interest that the only slight deviation from the line of the point for II (no. 12) in Fig. 2 suggests that the magnitude of this coupling is not strongly dependent upon the strength of the hydrogen bond.<sup>8</sup>

The data in Table I clearly show that the direction of enolization of cyclic  $\beta$ -keto aldehydes is strongly dependent upon structure. The trends (excluding no. 9 and 10) may be rationalized in terms of  $\pi$ -strain (the strain in double bonds). Further details of this work (including acyclic systems) will be discussed soon.<sup>9</sup>

(5) Intermolecular hydrogen bonded enol forms of I were not observed for the other systems investigated.

(6) Unpublished results from this Laboratory. See also L. M. Jackman, "Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, New York, N. Y., 1959, p. 123.

(7) The observed coupling is a weighted average of the contributions from Ia and Ib. At temperatures below  $25^\circ$ , 10% solutions in carbon disulfide were used. There were no effects on chemical shifts upon changing to this solvent.

(8) The chemical shifts of the enol protons ranged between  $-0.15$  (no. 12) and  $-5.15 \tau$  (no. 7).

(9) NOTE ADDED IN PROOF.—The n.m.r. study of  $\alpha$ -formyl ketones by Forsén and Nilsson [*Arkiv Kemi*, **19**, 569 (1962); **20**, 41 (1963)] has been noticed. They report proton spin coupling between  $H_b$ , O-H for several acyclic derivatives and erroneously consider that this coupling should vanish upon rapid intramolecular O-H exchange (Ia, Ib equilibrium fast). When this coupling was observed, the exchange was considered slow and since, in these instances, no absorption representative of the aldo enol form was seen, the formyl ketone was thought to exist in the hydroxymethylene form. For no. 2, no such coupling was observed and they somehow reasoned that this material exists in the aldo enol form (in qualitative agreement with results

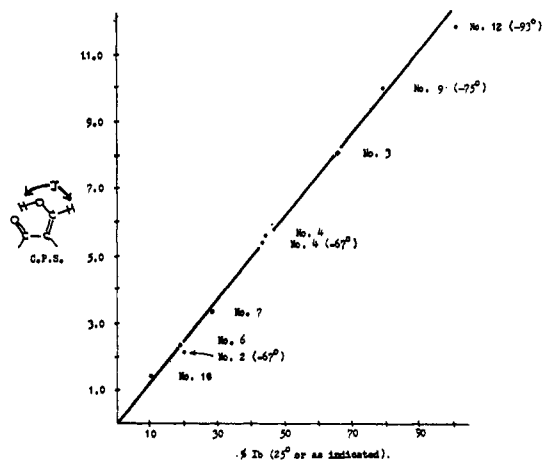


Figure 2.

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presented here). Nuclear spin state averaging resulting from rapid proton exchange should occur only for the intermolecular process.

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#### D-ribo-HEXOS-3-ULOSE, A NEW DICARBONYL-SUGAR<sup>1,2</sup> Sir:

A new crystalline disaccharide was isolated recently from culture media of the crown-gall tumor-inducing organism *Agrobacterium tumefaciens* grown on sucrose as the carbon source.<sup>3</sup> It was characterized by a variety of physical, chemical and enzymatic techniques and evidence has been presented to prove the structure of the new keto compound to be  $\alpha$ -D-ribo-hexopyranosyl-3-ulose  $\beta$ -D-fructofuranoside (referred to below as "3-ketosucrose"). When the conversion of sucrose to 3-ketosucrose was first reported,<sup>4</sup> D-fructose was the only product identified following hydrolysis with acid or enzyme. When crystalline 3-ketosucrose became available,<sup>3</sup> hydrolysis in 0.05 N  $H_2SO_4$  or with  $\beta$ -D-fructofuranoside fructohydrolase (3.2.1.26)<sup>5</sup> resulted in the identification of two products, one of which was identical chromatographically with fructose while the other gave a deep red color with urea phosphate<sup>6</sup> and

(1) Issued as Microbiology Research Institute No. 557.

(2) The new sugar was named in accordance with the "Rules of Carbohydrate Nomenclature," published by the American Chemical Society, see *J. Org. Chem.*, **28**, 251 (1963).

(3) S. Fukui, R. M. Hochster, R. Durbin, E. E. Grebner and D. S. Feingold, *Bull. Res. Council Israel*, **11A4** (Hestrin Memorial Issue), 262 (1963).

(4) D. S. Feingold, R. Durbin and E. E. Grebner, Abstracts of the 140th National Meeting of the American Chemical Society, 1961, p. 3D.

(5) Usage as recommended by the Commission on Enzymes of the International Union of Biochemistry, 1961.

(6) C. S. Wise, R. J. Dimler, H. A. Davis and C. E. Rist, *Anal. Chem.*, **27**, 33 (1955).

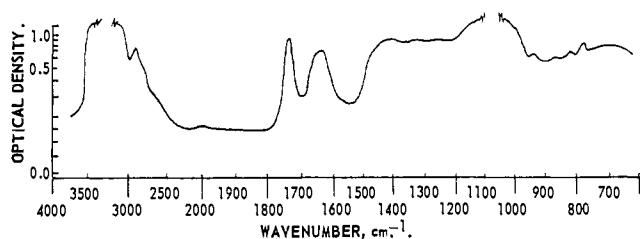


Fig. 1.—Infrared spectrum of D-ribo-hexos-3-ulose (2 mg. in 400 mg. KBr).

always moved faster than fructose. We now wish to report the successful isolation of the previously unidentified component of the enzymatic hydrolysis product of 3-ketosucrose and to present data on its isolation, physical constants and structure.

Crystalline 3-ketosucrose (200 mg.) was hydrolyzed with  $\beta$ -D-fructofuranoside fructohydrolase (3 mg.) at pH 5.0 in 0.01 M acetate buffer for 2 hr. at room temperature. The non-fructose moiety of the reaction product reacted readily at room temperature in the arsenomolybdate reaction of Nelson<sup>7</sup> (while fructose required heating at 100° before it would show a positive reaction with this reagent). When the hydrolysis mixture was passed through a charcoal bed (Darco G-60, acid-washed) most of the fructose was found in the effluent while the non-fructose moiety was chiefly retained on the charcoal. The latter component was removed from charcoal with 50% ethanol (v./v.) and concentrated to a sirup (at 32°). Adsorption and elution from charcoal was repeated four times because a small quantity of fructose remained behind on each previous passage. The combined sirups were finally dissolved in water-saturated butanol and, following removal of water under reduced pressure (at 35–37°), the product was precipitated from butanol by refrigeration at –25° for 1–2 weeks. Recrystallization from *n*-butyl alcohol was repeated three times whereupon the product was obtained, fructose-free, in approximately 45% yield as highly hygroscopic, colorless, rhombic crystals.

The crystalline material gave a single spot of  $R_f$  0.42 ( $R_{fructose}$  1.16) on chromatography in acetone–AcOH–water (4:1.2:10)<sup>8</sup> and of  $R_f$  0.51 ( $R_{fructose}$  1.36) in methyl ethyl ketone–acetone–water (3:1:0.6).<sup>9</sup> M.p. (in presence of drying agent to reduce hygroscopicity) 58–60° (uncor.),  $[\alpha]_D^{26} +14.8^\circ$  (c1, H<sub>2</sub>O). *Anal.* Calcd. for C<sub>6</sub>H<sub>10</sub>O<sub>6</sub>·0.5H<sub>2</sub>O: C, 38.5; H, 5.9. Found: C, 38.9; H, 6.24. Infrared spectrum (KBr disk) gave sharp bands at 1730 and 1626 cm.<sup>-1</sup> indicative of the presence of a free carbonyl group and water, respectively (Fig. 1).

Periodate oxidation<sup>10</sup> of the new substance consumed 2.9 moles of periodate per mole of starting material with the concomitant formation of 1.7 moles of titrable free acid. Reduction of the isolated material with NaBH<sub>4</sub><sup>11</sup> produced two polyols which were identified by paper chromatography and paper electrophoresis as sorbitol and allitol.

From the above data the newly isolated non-fructose product of the enzymatic hydrolysis of 3-ketosucrose is identified as D-ribo-hexos-3-ulose ("3-ketoglucose").

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(7) H. Nelson, *J. Biol. Chem.*, **153**, 375 (1944).

(8) S. Burrows, F. S. M. Grylls and J. S. Harrison, *Nature*, **170**, 800 (1952).

(9) G. Höström, *Acta Chem. Scand.*, **11**, 743 (1957).

(10) Gottlieb, C. G. Caldwell and R. M. Hixon, *J. Am. Chem. Soc.*, **62**, 3342 (1940).

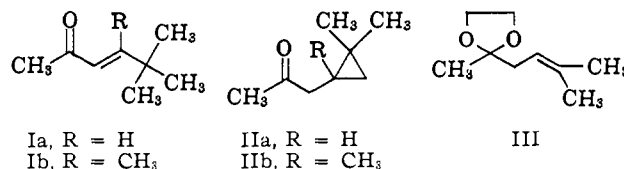
(11) M. Abdel-Akher, J. K. Hamilton and F. Smith, *ibid.*, **73**, 4691 (1951).

(12) National Research Council of Canada Fellow in collaboration with the Canada Department of Agriculture, 1961–1963.

## A NOVEL PHOTOCHEMICAL REACTION. CONVERSION OF $\alpha,\beta$ -UNSATURATED KETONES TO ACETONYLCYCLOPROPANES

Sir:

In contrast to the extensive investigations undertaken on photochemical reactions of cyclic  $\alpha,\beta$ -unsaturated carbonyl compounds,<sup>1</sup> the photochemistry of simple acyclic  $\alpha,\beta$ -unsaturated ketones, other than *cis-trans* isomerization, has not been explored.<sup>2</sup> As part of our systematic study of the photochemistry of such ketones, we have examined the photochemical behavior of ketones Ia and Ib. We wish to report that these undergo a novel photochemical reaction, resulting in the formation of derivatives of acetonycyclopropane.



Irradiation of 5,5-dimethyl-3-hexen-2-one (Ia) (5.0 g. in 400 ml. of ether) by means of a Hanovia 450-watt light source, employing a Pyrex filter, led first to a *cis-trans* isomerization, reaching a photostationary state in 2 hr.,<sup>3</sup> followed by the slow formation of a third ketone. The reaction was followed by vapor phase chromatography until the yield of the new ketone reached a maximum, after 46 hr. Distillation, b.p. 52° (15 mm.), and further purification by vapor phase chromatography, afforded 1.5 g. of isomeric ketone (38% based on reacted starting material; approximately 20% of starting ketone recovered) (found: C, 76.11; H, 11.30);  $\gamma_{max}^{CCl_4}$  3055 and 1724 cm.<sup>-1</sup>; semicarbazone, m.p. 145–146° (found: C, 59.03; H, 9.31; N, 22.64). The n.m.r. spectrum exhibited the following peaks: a two-proton doublet at 7.75  $\tau$  ( $J_{AB} = 7.4$  c.p.s.); three-proton singlets at 7.97, 8.97 and 9.05  $\tau$ ; a broad multiplet in the 9.1  $\tau$  to 9.7  $\tau$  region and a broad triplet at 10.12  $\tau$ , corresponding to a total of three hydrogens. This spectrum, in particular the characteristic absorption of cyclopropane methylenic hydrogens at high field, suggested the formulation of the structure of this ketone as IIa. This structure assignment was confirmed by an independent synthesis of 3-(2,2-dimethylcyclopropyl)-2-propanone, carried out in the following manner. Isobutyrideneacetone was converted to the ethyleneketal III, shown by n.m.r. analysis to be the  $\beta,\gamma$ -unsaturated isomer.<sup>4</sup> The ketal was treated in a Simmons–Smith reaction with methylene iodide and zinc–copper couple,<sup>5</sup> resulting in an 80% yield of IIa, identical in every respect with the ketone obtained from the irradiation of Ia.

(1) See, for example, P. De Mayo and S. T. Reid, *Quart. Rev.*, **15**, 393 (1961), for early references; H. E. Zimmerman and D. I. Schuster, *J. Am. Chem. Soc.*, **84**, 4527 (1962); W. W. Kwie, B. A. Shoulders and P. D. Gardner, *ibid.*, **84**, 2268 (1962); J. J. Hurst and G. H. Whitham, *Proc. Chem. Soc.*, 160 (1959); 116 (1961).

(2) A report by R. Ya. Levina, V. N. Kostin and P. A. Gembitskii, *Zh. Obshch. Khim.*, **29**, 2456 (1959), describing the conversion of 1-acetylcyclohexene and of ketone Ib to their respective  $\beta,\gamma$ -unsaturated isomers could not be substantiated in our present work. The photochemistry of methyl propenyl ketone in the vapor phase has been investigated [R. S. Tolberg and J. N. Pitts, Jr., *J. Am. Chem. Soc.*, **80**, 1304 (1958)]; at room temperature the principal reaction was found to be *cis-trans* isomerization.

(3) The *cis* isomer was isolated by vapor phase chromatography and identified by comparison of its infrared spectrum with the published spectrum of the *cis* ketone, cf. R. Heilman, G. de Gaudemaris and P. Arnaud, *Bull. soc. chim. France*, [5], 119 (1957). The *cis-trans* equilibrium ratio was approximately 45:55.

(4) It was shown that double bond migration from the  $\alpha,\beta$ -position to the more stable  $\beta,\gamma$ -position occurred in the  $\alpha,\beta$ -unsaturated ketal under the ketalization conditions.

(5) R. S. Shank and H. Shechter, *J. Org. Chem.*, **24**, 1824 (1959).