chains run in one direction, half in the other direction. This is most probably the case with starch too, and one of the above arrangements of the chains is probably approximately correct even if the starch structure is only pseudo-orthorhombic.

If adjacent glucose residues along the starch chain are identical in their configurations, the periodicity along the chain requires that adjacent glucose residues be rotated about b_0, so that the (CH_2OH) groups on adjacent glucose residues are *trans* to each other (Fig. 2). (This is also found to be the case in cellulose[16] and chitin,[13] where the glucosidic link is β.) The *trans* arrangement for starch in the "B" modification does not necessitate this arrangement in the "V" modification, where the chains assume a helical configuration.[15] Indeed, it is probable that a rotation about the glucosidic bond to the *cis* configuration accounts for the very different shape of the chains in these modifications of starch.

In contrast to the case of chitin,[14] odd-ordered reflections ($h00$), ($00l$) and (hOl) are quite intense on the "B" diffraction patterns. This must mean that the chains are unequally spaced along a_0 and c_0 (Figs. 1 and 2).

Chains running in opposite directions through the unit may be displaced with respect to each other in arbitrary amount along b_0. The reflection (020) appears to be very weak or missing, since it does not appear on the fiber diagram. It is likely, then, that the displacement is approximately $^1/_4\ b_0$.

The structure shown in Fig. 2 is in accord with these qualitative observations of intensities. It is based on the space group D_2^1, but a similar structure, based on D_2^2, with every other chain translated $^1/_2$ along b_0 is equally likely. Even if the structure is not truly orthorhombic the spacing and orientation of the chains should approximate, in its gross aspects, the structure shown in Fig. 2.

Bear and French[2] have established a close relationship between the "A," "B" and "C" modifications of starch. This relationship is independent of the validity of their unit cells, so that it should be found that the "A" and "C" unit cells resemble closely that reported here for the "B" modification.

It seems well to point out that in contrast to cellulose, the configuration of the starch chain depends upon how the starch is treated. The chains, fully extended in the "B" modification, become helices in the "V" modification and the starch–iodine complex, and assume an intermediate, crumpled form in the fibers prepared by the use of certain plasticizers.[9]

Summary

1. Methods for preparing films and fibers of the "B" modification of starch are outlined.

2. Film and fiber diffraction patterns of the "B" modification of starch have been prepared. The fiber axis is 10.6 Å.

3. A new unit cell for the "B" modification has been found, with $a_0 = 16.0$, $b_0 = 10.6$, $c_0 = 9.2$ Å. The structure is probably orthorhombic. There are 8 glucose residues per unit; the density of the crystalline portion of starch is about 1.6 g./cc.

4. A rough structure of the "B" modification of starch has been proposed on the basis of the unit cell dimensions and qualitative consideration of the intensities (Fig. 2).

5. It is pointed out that plasticizers useful in producing starch fibers generally alter the starch structure materially, and unlike the case of cellulose, the fiber spacing of starch is easily altered by treatment of the starch.

AMES, IA. RECEIVED JUNE 18, 1943

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

α,β-Diamino Ketones. I. Reactions of Heterocyclic Secondary Amines with α-Bromo-β-aminoketones[1]

BY NORMAN H. CROMWELL, CHARLES E. HARRIS AND DONALD J. CRAM

The reactions of α-bromo-α,β-unsaturated ketones with primary and secondary amines have been the subjects of several investigations in this Laboratory.[2] The development of an excellent method of preparing mixed α,β-diamino ketones from α-bromo-α,β-unsaturated ketones is one of the results of these investigations. From a knowledge of the mechanisms[2f] of these reactions it is possible to arrange the conditions in such a manner as to allow the preparation of many specific mixed diamino ketones of possible chemotherapeutic interest.

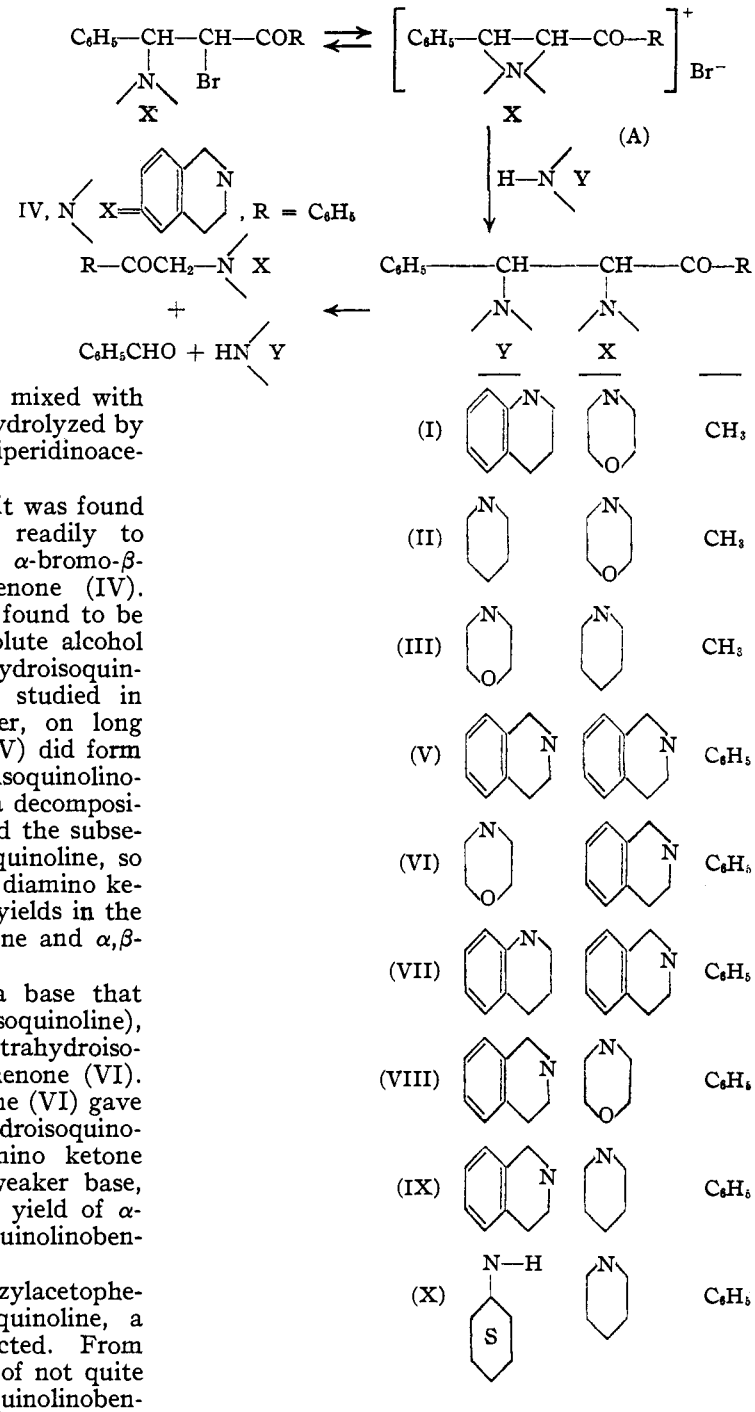
α-Bromo-β-morpholinobenzylacetone[2c] reacted readily with tetrahydroquinoline (which is a weaker base than morpholine) to give good yields of the expected α-morpholino-β-tetrahydroquinolinobenzylacetone (I). The structure of (I) was established by hydrolysis to give α-morpholinoacetone, isolated as its oxime. This same bromo amino ketone reacted in dry ether with piperidine (which is a stronger base than morpholine) to give very poor yields of α-morpholino-β-piperidino-

(1) Presented before the Division of Organic Chemistry, American Chemical Society, Pittsburgh, Pa., September 6, 1943.

(2) (a) Cromwell, *et al.*, THIS JOURNAL, **62**, 1672 (1940); (b) **62**, 2897 (1940); (c) **62**, 3470 (1940); (d) **63**, 837 (1941); (e) **63**, 2984 (1941); (f) **65**, 301 (1943); (g) **65**, 308 (1943); (h) **65**, 312 (1943).

benzylacetone (II). In alcohol solution the product from this reaction seemed to be a mixture of all of the possible diamino ketones.[2d]

α-Bromo-β-piperidinobenzylacetone[2g] reacted readily either in dry ether or absolute alcohol with morpholine to give fair yields of the expected α-piperidino-β-morpholinobenzylacetone (III). Compound (III) was obtained in a high and a low melting form, probably the two possible racemates. Either of these two forms of (III) lowered the melting point of (II) considerably, when mixed with it. The diamino ketone (III) was hydrolyzed by acid solution to give the known α-piperidinoacetone, isolated as its oxime.[2f]



In the benzylacetophenone series it was found that tetrahydroisoquinoline added readily to α-bromobenzalacetophenone to give α-bromo-β-tetrahydroisoquinolinobenzylacetophenone (IV). This bromo amino ketone (IV) was found to be more stable in the presence of absolute alcohol than the analogous α-bromo-β-tetrahydroisoquinolinobenzylacetone which has been studied in a previous investigation.[2f] However, on long standing, alcoholic suspensions of (IV) did form small amounts of α,β-ditetrahydroisoquinolinobenzylacetophenone (V), indicating a decomposition of the bromo amino ketone, and the subsequent reaction of the tetrahydroisoquinoline, so formed, with unchanged (IV). The diamino ketone (V) was also prepared in good yields in the usual way from tetrahydroisoquinoline and α,β-dibromobenzylacetophenone.

(IV) reacted with morpholine (a base that seems to be weaker than tetrahydroisoquinoline), giving a fair yield of the expected α-tetrahydroisoquinolino-β-morpholinobenzylacetophenone (VI). Acid hydrolysis of this diamino ketone (VI) gave a good yield of the known ω-tetrahydroisoquinolinoacetophenone.[3] This bromo amino ketone (IV) also reacted readily with a weaker base, tetrahydroquinoline, to give a good yield of α-tetrahydroisoquinolino-β-tetrahydroquinolinobenzylacetophenone (VII).

When α-bromo-β-morpholinobenzylacetophenone[2b] reacted with tetrahydroisoquinoline, a mixed product was obtained as expected. From this mixed product a small amount of not quite pure α-morpholino-β-tetrahydroisoquinolinobenzylacetophenone (VIII) was separated.

α-Bromo-β-piperidinobenzylacetophenone[4] reacted with tetrahydroisoquinoline (which is a weaker base than piperidine) to give good yields of α-piperidino-β-tetrahydroisoquinolinobenzylacetophenone (IX). The structure of (IX) was established by acid hydrolysis. When this same bromo amino ketone reacted with cyclohexylamine (a weaker base than piperidine) a fair yield of α-piperidino-β-cyclohexylaminobenzylacetophenone (X) was obtained. This is the first mixed diamino ketone containing a primary amino group that has been prepared in these investigations.

Certain theoretical studies as well as several further practical applications of these reactions to prepare specific compounds are the subjects of other investigations in these Laboratories.

(3) Allewelt and Day, *J. Org. Chem.*, **6**, 384 (1941).
(4) Dufraisse and Moureu, *Bull. soc. chim.*, (4e) **41**, 457 (1927).

TABLE I

PHYSICAL AND ANALYTICAL DATA

Diamino ketones	No.	M. p., °C., dec.	Yield, %	Formula	Percentage composition Calcd. C	Calcd. H	Found C	Found H
Benzylacetones								
α-Morpholino-β-tetrahydroquinolino-[a]	(I)	173	51	$C_{22}H_{28}N_2O_2$	75.79	7.74	75.68	7.58
α-Morpholino-β-piperidino-[b]	(II)	123	10	$C_{19}H_{28}N_2O_2$	72.12	8.92	72.30	8.86
α-Piperidino-β-morpholino-	(III)	117[c]					71.75	8.87
		101[d]	32	$C_{19}H_{28}N_2O_2$	72.12	8.92	72.11	8.94
Benzylacetophenones								
α,β-Ditetrahydroisoquinolino-	(V)	187	51	$C_{32}H_{32}N_2O$	83.86	6.83	83.67	6.88
α-Tetrahydroisoquinolino-β-morpholino-	(VI)	177	30	$C_{26}H_{30}N_2O_2$	78.84	7.09	78.76	7.10
α-Tetrahydroisoquinolino-β-tetrahydroquinolino-	(VII)	164	47	$C_{32}H_{32}N_2O$	83.86	6.83	83.69	6.90
α-Morpholino-β-tetrahydroisoquinolino-	(VIII)	163	15	$C_{26}H_{30}N_2O_2$	78.84	7.09	79.23	7.20
α-Piperidino-β-tetrahydroisoquinolino-	(IX)	165	37	$C_{29}H_{32}N_2O$	82.03	7.60	82.15	7.62
α-Piperidino-β-cyclohexylamino-	(X)	155	20	$C_{25}H_{32}N_2O$	80.16	8.54	79.98	8.62

[a] N, Calcd., 7.69. Found, 7.68. [b] N, Calcd., 8.86. Found, 9.06. [c] N, Calcd., 8.86. Found, 8.90. [d] N, Calcd., 8.86. Found, 8.92.

Experimental[5]

Derivatives of Benzylacetone

α-Morpholino-β-tetrahydroquinolinobenzylacetone (I).—To 114 ml. of absolute alcohol were added 57 g. (0.183 mole) of α-bromo-β-morpholinobenzylacetone[2c] and 49 g. (0.371 mole) of tetrahydroquinoline and the mixture allowed to stand at room temperature for two days. At the end of this time the precipitate was filtered, washed and recrystallized from chloroform and alcohol giving 34.3 g. (0.0943 mole) of a white crystalline product. This compound was soluble in benzene and chloroform, slightly soluble in ether, very slightly soluble in alcohol and in dilute hydrochloric acid, and 0.1 g. was soluble in 10 ml. of absolute alcohol containing 0.95 g. of dry hydrogen chloride gas. This preparation was repeated using ether as a solvent. A white crystalline product was obtained, in 20.4% yield, which was identical with (I).

Hydrolysis.—Acid hydrolysis of the diamino ketone (I) in the usual way[2f] gave benzaldehyde, tetrahydroquinoline (isolated as the benzene sulfonamide) and the water soluble α-morpholinoacetone (isolated as its water soluble oxime, recrystallized from petroleum ether and benzene, m. p. 104–106°).

Anal. Calcd. for $C_7H_{14}N_2O_2$: C, 53.14; H, 8.92. Found: C, 53.42; H, 8.98.

α-Morpholino-β-piperidinobenzylacetone (II).—In 10 ml. of dry ether were placed 5 g. (0.0160 mole) of α-bromo-β-morpholinobenzylacetone[2c] and 2.8 g. (0.0320 mole) of piperidine and the mixture allowed to stand in the icebox for two days. At the end of this time the precipitate was filtered but it all proved to be water soluble. The filtrate was evaporated and the resulting oil taken up in alcohol and a white solid obtained which after four recrystallizations from alcohol and water gave 0.5 g. (0.00158 mole) of a white crystalline product m. p. 118–123°. A mixed melting point with α,β-dimorpholinobenzylacetone[2c] gave m. p. 108–132°, and with α,β-dipiperidinobenzylacetone[2g] gave m. p. 100–110°. This reaction was also carried out in alcohol but a mixture impossible to separate was obtained.

α-Piperidino-β-morpholinobenzylacetone (III).—To 25 ml. of absolute alcohol were added 12 g. (0.0387 mole) of α-bromo-β-piperidinobenzylacetone[2g] and 6.74 g. (0.0775 mole) of morpholine and the mixture allowed to stand at room temperature. The reaction took place with evolution of heat and was complete in about three hours. At the end of this time the precipitate was filtered and the product recrystallized three times from alcohol and water giving 2.4 g. of white needles, m. p. 115–117°. A mixed melting point experiment with this compound and α-morpholino-β-piperidinobenzylacetone (II) gave m. p. 90–111°; with α,β-dipiperidinobenzylacetone,[2g] m. p. 95–116°; and with α,β-dimorpholinobenzylacetone,[2c] m. p. 95–140°.

The reaction mixture filtrate was concentrated and cooled and a second crop of crystals came out, which, after recrystallization from alcohol and water, gave 1.5 g. of white crystalline compound, m. p. 100–101°. A mixed melting point of the two racemates gave m. p. 102–114°; a mixed melting point of the lower melting racemate with α,β-dipiperidinobenzylacetone[2g] gave m. p. 92–116°; with α,β-dimorpholinobenzylacetone,[2c] m. p. 93–140°; and with α-morpholino-β-piperidinobenzylacetone (II), m. p. 90–110°.

This reaction was also carried out in ether solution and a 40.2% yield of product was obtained, m. p. 102–114°, which when mixed with a mixture of the two racemates gave m. p. 103–114°. An analysis of this product also agreed with the formula, $C_{19}H_{28}N_2O_2$.

Hydrolysis.—Acid hydrolysis of the mixed racemates of (III) in the usual way gave α-piperidinoacetone, isolated as its oxime, m. p. 122–123°.[2f] No α-morpholinoacetone was detected.

Derivatives of Benzylacetophenone

α-Bromo-β-tetrahydroisoquinolinobenzylacetophenone (IV).—In 20 ml. of a 50% ether–petroleum ether (b. p. 37°) solution was dissolved 10 g. (0.035 mole) of α-bromobenzalacetophenone[2b] and the solution cooled to −10° in an ice–salt mixture. Previously cooled tetrahydroisoquinoline (0.035 mole (4.65 g.)) was added to the cold mixture with shaking. The resulting solution was allowed to stand well-corked for two hours at −10°. The white product (12.5 g.) was filtered off, washed with 50% ether-petroleum ether, and dried *in vacuo*, m. p. 117°, yield 85%.

(5) All m. p. are corrected and determined by placing sample in bath 10° below m. p. and heating at the rate of 3° per minute. Micro Dumas analyses for nitrogen and semimicro carbon–hydrogen analyses by the Analytical Laboratory, Department of Chemistry, University of Nebraska, under the supervision of H. Armin Pagel.

Anal. Calcd. for $C_{34}H_{32}NOBr$: C, 68.57; H, 5.28. Found: C, 68.80, 68.52; H, 5.36, 5.42.

This bromo amino ketone reacted with sodium ethoxide in the usual way to give a red oily product which was probably the α-tetrahydroisoquinolinobenzalacetophenone. All attempts to crystallize this oil failed.

When a sample of (IV) was allowed to stand in absolute alcohol at room temperature for one week a small amount (about 20%) of the addition product decomposed[2f] to give α-bromobenzalacetophenone and tetrahydroisoquinoline. This was shown by the isolation of a 10% yield of α,β-ditetrahydroisoquinolinobenzylacetophenone (V), m. p. 184–186°, identical with that prepared from α,β-dibromobenzylacetophenone as described below.

α,β-Ditetrahydroisoquinolinobenzylacetophenone (V).—In 20 ml. of absolute alcohol was suspended 5 g. (0.0136 mole) of α,β-dibromobenzylacetophenone and the mixture cooled to 0°. Tetrahydroisoquinoline (8 g. (0.060 mole)) was added rapidly while shaking. The solution at first remained white, but then changed to an orange color. After allowing it to stand for two days at room temperature, during which time the mixture was shaken and worked with a spatula, the white precipitate was filtered off and washed well with petroleum ether and then with water. The crude product was recrystallized twice from benzene–petroleum ether (b. p. 80°) mixtures to give 4.4 g. of a white product.

α-Tetrahydroisoquinolino-β-morpholinobenzylacetophenone (VI).—In 15 ml. of dry ether and 5 ml. of absolute alcohol, were suspended 5 g. (0.012 mole) of (IV) and 3.6 g. (0.024 mole) of morpholine added. After standing overnight at room temperature the red-colored solution was filtered, the precipitate washed with petroleum ether and then with water. After three recrystallizations from a chloroform–alcohol mixture and two from a benzene–petroleum ether mixture, 1.7 g. of pale yellow crystals was obtained.

Hydrolysis.—Acid hydrolysis (40 ml., 15% sulfuric acid) of the diamino ketone (VI) (4.0 g.) in the ordinary manner[2e] gave 1.65 g. of ω-tetrahydroisoquinolinoacetophenone, identical with a sample prepared from ω-bromoacetophenone.[3]

Other mixed diamino ketones prepared by essentially[6] this same procedure were: (VII) from (IV) and two equivalents of tetrahydroquinoline; (VIII) from α-bromo-β-morpholinobenzylacetophenone[2b] and tetrahydroisoquinoline (mixed m. p. of (VI) with (VIII), 150–163°; hydrolysis of (VIII) gave mainly ω-morpholinoacetophenone[2b] and traces of ω-tetrahydroisoquinolinoacetophenone[3] along with tetrahydroisoquinoline and benzaldehyde); (IX) from α-bromo-β-piperidinobenzylacetophenone[4] and tetrahydroisoquinoline (hydrolysis of (IX) gave ω-piperidinoacetophenone, isolated as its hydrochloride[2d]); (X) from α-bromo-β-piperidinobenzylacetophenone[4] and cyclohexylamine.

Summary

1. The preparation of one new α-bromo-β-amino ketone and nine new diamino ketones has been described.

(6) The amount of absolute alcohol in the reaction medium and the time for reaction varied slightly in each individual case.

LINCOLN, NEBRASKA RECEIVED JUNE 7, 1943

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 938]

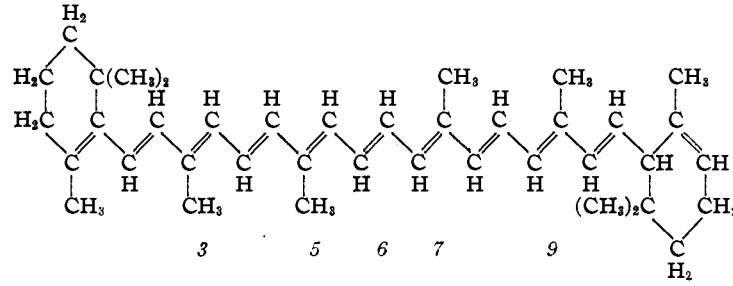
cis–trans Isomerization and *cis*-Peak Effect in the α-Carotene Set and in Some Other Stereoisomeric Sets

BY L. ZECHMEISTER AND A. POLGÁR

As far as we know, no up-to-date study of the stereoisomerization of α-carotene[1] is available while a more detailed investigation has been presented for β-carotene.[2] The α-carotene molecule includes five double bonds which are available for *trans*→*cis* rotations (see the formula), the number of stereoisomers being thirty-two.[3]

It was first assumed[4] that the all-*trans* member of a stereoisomeric hydrocarbon set possesses greater adsorption affinity than any other member of the set but this postulate must now be abandoned for both carotene sets mentioned.

A re-investigation of α-carotene showed the presence of the eleven isomers listed in Table I of which neo-α-carotene U and W have been crystallized.



All-*trans*-α-carotene. (The double bonds available for a *trans*→*cis* shift are numbered.)[5]

The ratio of stereoisomers is dependent on the method of isomerization (Table II).

(1) A. E. Gillam, M. S. El Ridi and S. K. Kon, *Biochem. J.*, **31**, 1605 (1937).

(2) A. Polgár and L. Zechmeister, THIS JOURNAL, **64**, 1856 (1942).

(3) L. Pauling, *Fortschr. Chem. organ. Naturstoffe*, **3**, 203 (1939); *cf.* L. Zechmeister, A. L. LeRosen, F. W. Went and L. Pauling, *Proc. Natl. Acad. Sci.*, **27**, 468 (1941).

(4) L. Zechmeister and P. Tuzson, *Ber.*, **72**, 1340 (1939); L. Zechmeister, L. Cholnoky and A. Polgár, *ibid.*, **72**, 1678 (1939).

(5) The following *nomenclature* is proposed. Each double bond of the *conjugated system* will be assigned an *italicized* number in order to avoid confusion with the numbering of carbon atoms: *e. g.*, *3,6*-di-*cis*-β-carotene. The lowest number will be given to the double bond in the β-ionone ring or, if the double bond of this ring is not part of the chromophore, to the conjugated double bond nearest the β-ionone ring. In the absence of such a system an α-ionone ring receives preference over an aliphatic terminal group.