the components by assuming it a linear function of the composition, *i.e.*, the heat of formation of the compound was zero. The value of T_0 thus calculated along with the experimentally determined melting points of the four substances are given in the last column of Table II.

TABLE II

MELTING POINTS AND EUTECTIC POINTS

Compound	T_{100} experimental, °K.	T_0 (calcd.), °K.
4-Chloro-3-heptanone (A)	210.2	212.05[a]
A_3B_2	207.2	208.60
Eutectic of A with A_3B_2 comp. 25.4% B	202.3	204.45 (25% B)
AB	211.0	212.47
Eutectic of AB with B comp. 54.2% B	210.4	211.6 (55% B)
2-Chloro-3-heptanone (B)	224.2	225.90[a]

[a] From calorimetric data

From the data obtained as above a temperature of 204.45° and composition of 25% total per cent. B of the eutectic formed between 4-chloro-3-heptanone and compound A_3B_2, undepressed by the presence of any impurity was calculated. Similarly T_0 of the eutectic formed from AB with 2-chloro-3-heptanone was determined as 211.6° at 55 total per cent. B. These points are marked on the phase diagram Fig. 1, as asterisks, as are the melting points of the original components and the compounds A_3B_2 and AB. These points on connection as shown by the dotted curve yield a representative phase diagram for pure components A and B.

The eutectic points, depressed by the presence of the known amounts of impurities, were calculated as 203.03 and 210.18°, respectively, and are denoted by (+) immediately below those denoting the pure eutectics. The lowering of the eutectic point was calculated using equation (3), where X is the mole per cent. of total impurity other than the two chloroketones and

$$\Delta H_f = N_A \Delta H_{f_A} + N_B \Delta H_{f_B}$$

where N_A and N_B are the mole fractions of the two chloroketones and ΔH_{f_A} and ΔH_{f_B} are their heats of fusion.[6]

Theoretically these points should agree with the eutectics plotted on the phase diagram as determined from the warming curves. The eutectic temperatures and the melting points of the compounds A_3B_2 and AB obtained from the phase diagram (Fig. 1), uncorrected for lowering, as well as the melting points of A and B obtained from the warming curves, without correction for impurity, are given in the second column of Table II.

(6) Lewis and Randall, "Thermodynamics," McGraw-Hill Book Co., Inc., New York, N. Y., p. 240, Exercise 3.

STATE COLLEGE, PENNA. RECEIVED JANUARY 16, 1950

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS, THE PENNSYLVANIA STATE COLLEGE]

α-Halo Ketones. IV. The Isomeric α-Chloroketones Derived from 3-Heptanone

BY J. G. ASTON AND J. D. NEWKIRK

A suitable resonance intermediate has been proposed to explain rearrangements during metathesis of α-haloketones which predicts the same products from the two α-isomers. The preparation of 4-chloro-3-heptanone is described for the first time. The product of chlorination of 3-heptanone consists of 74% of the 2-chloro and 26% of the 4-chloro isomer as determined by a warming curve. The product obtained from both isomers by the action of anhydrous sodium methylate in ether is the methyl ester of 2-ethylvaleric acid. It has not been possible to ascertain the composition of the chlorination or bromination product of isopropyl isobutyl ketone.

The investigation of McPhee and Klingsberg[1] has done much to clarify the theoretical basis of the rearrangement of α-haloketones to esters by the action of sodium alcoholates and to acids by the action of sodium hydroxide. A more general formulation of their mechanism is shown.

In this scheme IIIra, IIIrb are the two resonance forms arising separately by ionization of the keto and enol forms of the fragment derived from I by loss of X^-, while IIIrc and IIIrd are the corresponding forms derived from III. However, there is no assumption made concerning the initial point of attack which may be by the removal of X^- or by the removal of H^+. The significant assumption is that the reaction intermediate in the rearrangement is stabilized by resonance between four forms and this may explain the preference for rearrangement over direct replacement which presumably involves an intermediate of the type $\overset{-}{Y}\overset{+}{R}\overset{-}{X}$. The ester (or acid) finally obtained is that at the end of the most favorable path.

The reaction of aqueous sodium hydroxide on α-haloketones usually produces replacement of halogen by hydroxyl. If this replacement also involves the common intermediate III, the same hydroxy ketone will result from I and II, namely, that most readily derived from III. *Since the structure of α-bromoketones as obtained by bromination has hitherto been assigned on the basis of the products of hydrolysis*[2] we are left with no certain knowledge of which α-carbon atom is substituted when a ketone is halogenated.

In order to ascertain the nature of the chlorination product of 3-heptanone, 2-chloro- and 4-chloro-3-heptanone have been synthesized by the reaction of the appropriate cadmium alkyl on the required chloro acid chloride using the method devised by Cason.[3]

The solid equilibrium diagram has been previously determined from warming curves on mixtures of these isomers.[4] By taking the warming

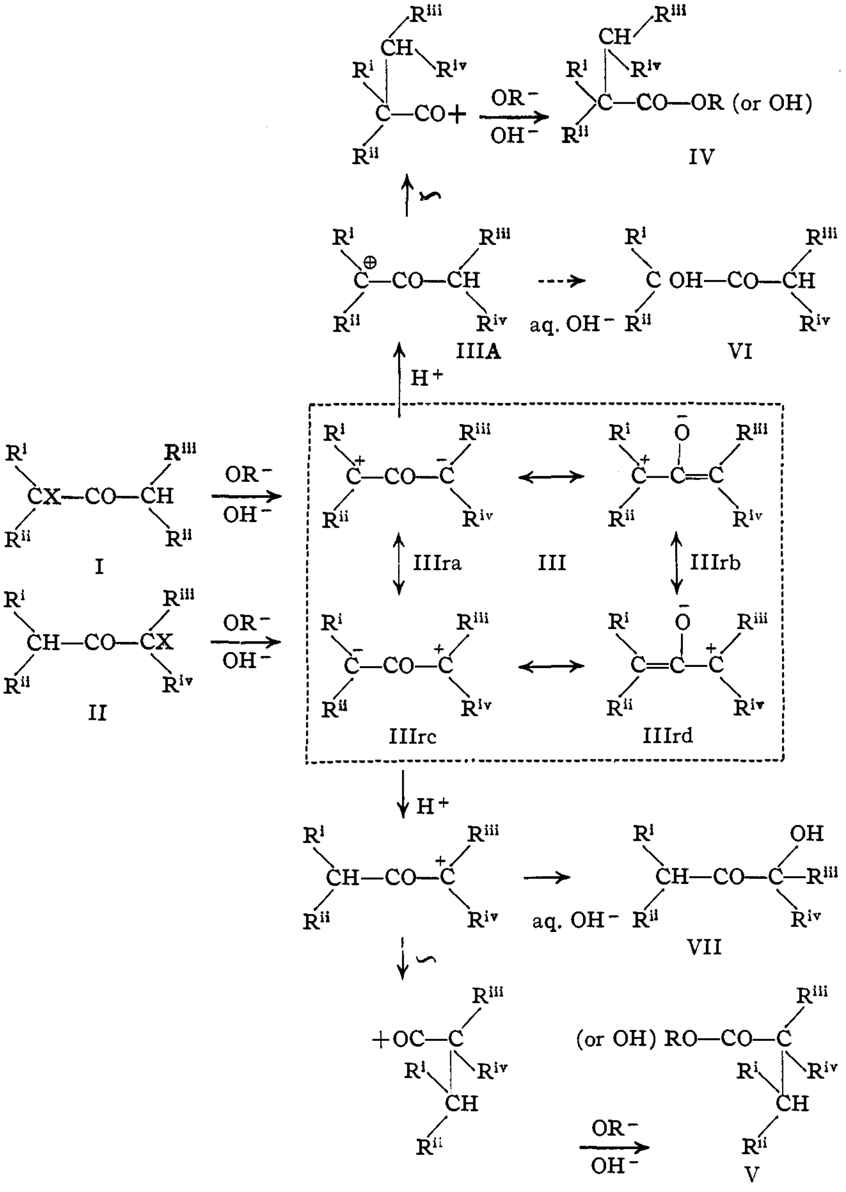
---

(1) McPhee and Klingsberg, THIS JOURNAL, **66**, 1132 (1944).

(2) Favorskii, *J. prakt. Chem.*, [2] **88**, 641 (1913).

(3) Cason, THIS JOURNAL, **68**, 2078 (1946).

(4) Newkirk and Aston, *ibid.*, **73**, 3898 (1951).



curve on the solidified product of chlorination of 3-heptanone and comparing the result with this equilibrium diagram it has now been found that chlorination of this ketone yields 74% of the 2-chloro and 26% of the 4-chloro compound.

Both of these products yield the same ester upon rearrangement, namely, the methyl ester of 2-ethylvaleric acid.

Attempts were made to prepare α-chloroisopropyl isobutyl ketone by the same method as well as by the action of isobutylmagnesium bromide on α-chloroisobutyryl chloride without any success so that it was not possible to ascertain the position of the entering chlorine when isopropyl isobutyl ketone was chlorinated using the warming curve technique.

An attempt was made to prepare an oxime from the bromination product of this ketone without success. It had been our plan, had we been able to obtain this oxime, to subject it to the Beckmann rearrangement which would have removed one of the alkyl groups in the ketone from the tautomeric system and thus make it possible to ascertain the position of the bromine atom by metathesis without complication by rearrangement of the type discussed at the beginning of this paper.

It seems likely from the foregoing that this bromoketone is a mixture of bromoketones. The fact[5] that the bromoketone obtained by the action of phosphorus tribromide on isobutyroin has the same melting point as the bromination product and produces no lowering of the melting point of the bromination product is no evidence of identity in view of the fact that the isomeric chlorination products of 3-heptanone form compounds with each other which would indicate a similar possibility in the case of the bromination products of isopropyl isobutyl ketone. The products of the action of alkali and sodium methylate on the products of bromination of isopropyl isobutyl ketone and the compound obtained by the action of phosphorus tribromide on isobutyroin are described in a succeeding paper.[5]

Experimental

4-Chloro-3-heptanone and 2-Chloro-3-heptanone.—A Grignard solution was prepared from 360 g. of ethyl bromide and 72.9 g. of magnesium in 800 ml. of ether. To the Grignard was added in small portions 303 g. of anhydrous cadmium chloride. A negative Gilman test was obtained at the end of one hour and 50 minutes. The solvent was removed by distillation and replaced with 1250 ml. of dry benzene. To the chilled solution was added 324 g. of α-chlorovaleryl chloride in an equal volume of benzene. After three hours in an ice-bath the solution was warmed to 32° for 20 minutes and poured onto 3 l. of ice. The organic layer was washed successively with water, with excess 5% sodium carbonate solution, with water and dried over anhydrous sodium sulfate. The solvent was removed by distillation and the residue vacuum distilled yielding approximately 150 g. of distillate. Several such distillates were combined and fractionated through a column of about 20 theoretical plates. The pure 4-chloro-3-heptanone was obtained in 28.2% yield based on magnesium, b.p. 61° (12 mm.), $n^{20}\mathrm{D}$ 1.4351.

Anal. Calcd. for $C_7H_{13}OCl$: Cl, 23.86. Found: Cl, 23.41, 23.46.

The 2,4-dinitrophenylhydrazone, crystallized from alcohol–ethyl acetate, melted at 112–113°.

Anal. Calcd. for $C_{13}H_{17}O_4N_4Cl$: C, 47.49; H, 5.21; Cl, 10.79. Found: C, 47.80; H, 5.18; Cl, 11.15.

The isomeric 2-chloro-3-heptanone was prepared similarly in 27.4% yield, b.p. 55° (8 mm.), $n^{20}\mathrm{D}$ 1.4348.

The 2,4-dinitrophenylhydrazone of 2-chloro-3-heptanone melted at 64.5–66°.

Anal. Calcd. for $C_{13}H_{17}O_4N_4Cl$: C, 47.49; H, 5.21; Cl, 10.79. Found: C, 47.78; H, 5.18; Cl, 10.67.

---

[5] Abraham A. Sacks and J. G. Aston, THIS JOURNAL, 73, 3902 (1951).

Rearrangement of 4-Chloro-3-heptanone.—A stirred suspension of 73.5 g. of sodium methylate in 400 ml. of dry ether below 10° was treated during one hour and 15 minutes with 200 g. of 4-chloro-3-heptanone. The solution was then refluxed for 40 minutes when 200 ml. of water was added to dissolve the salts. The organic layer was separated, combined with two ethereal extracts of the aqueous layer and dried over anhydrous sodium sulfate. The ether was removed by distillation and the residue fractionated yielding 147.3 g. (76.8%) of the methyl ester of 2-ethylvaleric acid, b.p. 79–80° (55 mm.), $n^{20}\text{D}$ 1.4080. Saponification of the ester yielded methyl alcohol as identified by its 3,5-dinitrobenzoate. The acid was liberated, separated and converted to the chloride thence to the amide. Melting point and mixed melting point with an authentic sample of the amide of 2-ethylvaleric acid was 100–101°. Another sample of the acid chloride was converted to the *p*-toluide. Melting point and mixed melting point with an authentic sample of the *p*-toluide of 2-ethylvaleric acid was 128–129°.

Rearrangement of 2-Chloro-3-heptanone.—The residue from the rearrangement of 112.5 g. after treatment as described above yielded 70.3 (64.5%) of the methyl ester of 2-ethylvaleric acid. Saponification of this ester yielded methyl alcohol identified by its 3,5-dinitrobenzoate. The amide was prepared from the liberated acid; melting point and mixed m.p. of this derivative with an authentic sample of the amide of 2-ethylvaleric acid was 100–101°. The *p*-toluide was also prepared. Melting point and mixed m.p. of this derivative with an authentic sample of the *p*-toluide of 2-ethylvaleric acid was 128–129°.

Chlorination of 3-Heptanone.—Chlorine gas (140 g.) was added to 225 g. of 3-heptanone below 5°. Nitrogen gas was then bubbled through the solution for 4.5 hours. The residue was fractionated through a column of about 30 theoretical plates yielding 161.2 g. (54.7%) of the monochloro derivative of 3-heptanone, b.p. 70° (17 mm.), $n^{20}\text{D}$ 1.4351.

Anal. Calcd. for $C_{17}H_{13}OCl$: Cl, 23.86. Found: Cl, 24.13, 24.22, 24.26.

A warming curve was run on 30 ml. of this sample and of a mixture of 30 ml. of this compound with 5 ml. of 2-chloro-3-heptanone. The liquidus points on both systems are tabulated.

Chlorinated product		
Liquidus point, °K.		217.43
2-Chloro-3-heptanone, %	(found from diagram)	74.0
Chlorinated product with 5 ml. 2-chloro-3-heptanone added to 30 ml.		
Liquidus point, °K.		218.50
2-Chloro-3-heptanone, %	found (from diagram)	77.8
	calcd. (from diagram)	77.8

STATE COLLEGE, PA. RECEIVED JANUARY 16, 1950

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS, THE PENNSYLVANIA STATE COLLEGE]

α-Halo Ketones. V. The Preparation, Metathesis and Rearrangement of Certain α-Bromoketones

BY ABRAHAM A. SACKS[1] AND J. G. ASTON

Certain bromoketones have been treated with sodium alcoholates to give esters in good yields. The bromo compounds from isopropyl propyl, isopropyl isobutyl and isopropyl neopentyl ketones give an ester corresponding to the bromine being removed from the α-carbon of the group other than isopropyl but, on hydrolysis, yield the hydroxyketone corresponding to the bromine being removed from the isopropyl group. The remainder behave "normally."

Further studies of the action of aqueous sodium hydroxide and of sodium methylate on certain α-bromoketones have been made. The results are reported in the present paper.

The α-bromoketone obtained from bromination of isopropyl isobutyl ketone gives an 80% yield of the methyl ester of diisopropylacetic acid by the reaction of sodium methoxide on its ether solution. If the bromoketone be treated with sodium hydroxide the product is α-hydroxyisopropyl isobutyl ketone as proved by oxidation to acetone and isovaleric acid.

Assuming direct replacement this indicates that the bromoketone is α-bromoisopropyl isobutyl ketone and that ester formation corresponds to a rearrangement from I to V in the scheme previously outlined.[2,3]

Since isobutyroin is oxidized to diisobutyryl, there is no doubt as to its structure. By the action of PBr_3, isopropyl α-hydroxyisobutyl ketone (VII in the above scheme) is converted into an α-bromoketone. If no rearrangement occurs, this bromoketone is isopropyl α-bromoisobutyl ketone (II in the above scheme) and for the present this doubtful assumption will be made.

Experimentally, this bromoketone does not lower the melting point of that derived from isopropy isobutyl ketone by direct bromination. However, in view of the fact that the bromoketone may be a mixture of the two bromoketones which could form compounds or solid solution, this fact is of little significance. The fact that it also gives methyl diisopropylacetate by the action of sodium methylate is, of course, no proof of identity. On hydrolysis, naturally, it gives α-hydroxyisopropyl isobutyl ketone (VI in the above scheme) which is not in conflict with the assigned structure.

Thus, it is possible that the bromoketone obtained by bromination of isopropyl isobutyl ketone is isopropyl α-bromoisobutyl ketone and corresponds to II in the above scheme. This is, of course, in violation of the "rules" for bromination of ketones.[4] However, these rules were based on a structure proof which disregarded rearrangements such as occur in going from II to VI.

There is another reaction which has a bearing on this point, namely, the action of nitrous acid on ketones in acid media, the conditions being not unlike those of bromination.[5]

In a series of ketones with isopropyl as the common group and the other group methyl, ethyl, propyl, *n*-butyl and isobutyl, respectively, substitution occurs exclusively on the α-carbon of the isopropyl group only when the other group is methyl. Thus,

---

(1) Abraham A. Sacks died suddenly on December 18, 1943. This paper was written from his thesis material.

(2) J. G. Aston and J. D. Newkirk, THIS JOURNAL, **73**, 3900 (1951).

(3) McPhee and Klingsberg, *ibid.*, **66**, 1132 (1944).

(4) Favorski, *J. prakt. Chem.*, [2] **88**, 641 (1913).

(5) Aston and Mayberry, THIS JOURNAL, **57**, 1888 (1935).