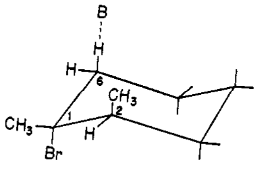
by the addition of hydrogen bromide to 1,2-dimethylcyclohexene in pentane, reacted very much more rapidly with strong bases than did mixtures. By kinetic analysis it was possible to show that the mixtures contained two components, one of which reacted approximately 12 times as fast as the other in second-order elimination reactions. The data reported in Table IV show furthermore that the fast component is converted exclusively to 1,2-dimethylcyclohexene, whereas the isomer gives relatively little of the symmetrical olefin. On this basis the assignment of the *trans* structure to the more reactive component seems unambiguous.

It is of interest to note that no more than trace amounts of 2,3-dimethylcyclohexene are formed from either bromide in bimolecular eliminations. While equilibration studies have not been carried out, it seems probable that the standard free energy of the exomethylene olefin is higher than that of the unsymmetrical endocyclic isomer.[15]

It is not difficult to rationalize the fact that the *cis*-bromide gives largely the exomethylene olefin in the E_2 reaction. Although *trans* elimination could go through a planar transition state much as II the methyl group at C_2 is so close to the *trans*-hydrogen on C_6 that some steric strain should exist between B and the methyl hydrogens.



II

The *trans*-bromide was allowed to react with a series of bases, pyridine, 2-picoline and 2,6-lutidine since it seemed possible that relatively large amounts of the exomethylene isomer might be formed as steric requirements were increased. No such trend was observed when the reactions were carried out at room temperature although the reaction rate was obviously decreased as the bulk of the base was increased. At 100°, picoline and lutidine, especially the latter, gave appreciable amounts of exomethylene compound. This may indicate that the activation energy of the E_2 reaction at the methyl group is becoming close enough to that of the reaction at the ring C–H to allow the former reaction to become competitive at the higher temperature. However, it is not possible to distinguish this from a similar increase in the competition from a carbonium ion mechanism at the higher temperatures.

Synthesis of Tertiary Acetates.—It is worth noting that highly efficient conversions of the tertiary alcohols to esters was achieved by acetylation with acetyl chloride in dimethylaniline as solvent. The more common procedure in which pyridine is used instead of dimethylaniline was found to be completely unsatisfactory.

Acknowledgment.—We are indebted to Miss Katherine Douglas for aid in the infrared spectroscopy and to the Iowa State Institute for Atomic Research for the use of the instrument. One of us (T.D.N.) is grateful for the partial support of this study by a fellowship grant from the Iowa State Research Institute.

AMES, IOWA

---

[15] This is based upon the assumption that the usual difference in the strain energy in endo- and exocyclic isomers[16] is not outweighed by repulsion between methyl groups.

[16] W. Hückel, "Theoretische Grundlagen der organischen Chemie," 2nd ed., Akademische Verlagsgesellschaft, Leipzig, 1934, p. 72.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

The Use of Monosubstituted Acetoacetic Esters in the Robinson Reaction[1]

BY ALBERT V. LOGAN, ELLIOT N. MARVELL, RICHARD LAPORE[2] AND DAVID C. BUSH[2]

RECEIVED MARCH 15, 1954

A series of 2-oxo-3-alkyloctahydronaphthalenes has been prepared by Robinson's method using the methiodide of the Mannich base derived from cyclohexanone, formaldehyde and dimethylamine, and a series of substituted acetoacetic esters. Further substitution has been achieved by means of Grignard reaction with the keto group in the two position. The Robinson reaction has been shown to proceed reasonably well when alkyl-substituted acetoacetic esters are employed but to fail with aryl-substituted esters. Isomeric ketones were isolated when ethyl methylacetoacetate was used. A mechanism for the Robinson reaction is proposed.

It was originally shown by Robinson[3] that quaternary salts derived from Mannich bases may be employed conveniently for the alkylation of certain active-hydrogen containing molecules. The method has since found successful application,[4,5] and has been termed the α-acylethylation reaction by Lions.[5] With Mannich bases derived from cyclohexanone Robinson[3] was able to alkylate acetoacetic ester, the initial alkylation being followed by a ring closure of the aldol type. This process proved useful as a means for the synthesis of the decalin ring system.[3,6] However, there appears to be no record of any substituted aceto-

---

[1] This work was supported by the Atomic Energy Commission under contract with Oregon State College and by a fellowship from E. I. du Pont de Nemours and Co., Inc., during 1952-1953 (R.L.P.). Published with the approval of the Monographs Publications Committee, Oregon State College, as Research Paper No. 246, School of Science, Department of Chemistry.

[2] This work was abstracted from theses submitted by Richard LaPore (du Pont Fellow in Chemistry 1952-1953) and David C. Bush in partial fulfillment of the requirements for the Doctor of Philosophy degree at Oregon State College.

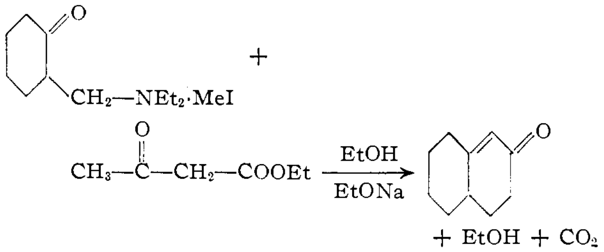
[3] E. C. DuFeu, F. J. McQuillan and R. Robinson, *J. Chem. Soc.*, 53 (1937).

[4] H. R. Snyder and L. Katz, THIS JOURNAL, **69**, 3140 (1947); E. E. Howe, A. J. Zambito, M. R. Snyder and M. Tishler, *ibid.*, **67**, 38 (1945); H. R. Snyder and L. Hamlin, *ibid.*, **72**, 5082 (1950).

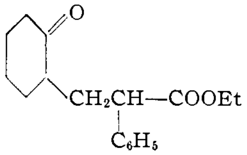
[5] N. S. Gill, K. B. James, F. Lions and K. T. Potts, *ibid.*, **74**, 4923 (1952).

[6] N. S. Gill and F. Lions, *ibid.*, **72**, 3468 (1950).

acetic esters being employed in this synthesis. As a part of other work in this Laboratory it became desirable to study the use of substituted acetoacetic esters in the Robinson reaction.



When the unsubstituted acetoacetic ester is alkylated the yields range from 60–80%.[3,6] Table I shows that the alkyl-substituted acetoacetic esters can be employed in the Robinson reaction, but that the yields are lower. An attempt was made to use ethyl phenylacetoacetate in the reaction, but the presence of the phenyl group made the initial alkylation product sensitive to the basic catalyst and ethyl 2-phenyl-3-(2-oxocyclohexyl)-propionate (I) was the only product isolated.



I

TABLE I

ALKYL-SUBSTITUTED ACETOACETIC ESTERS

Substituent	Methyl	Ethyl	Propyl	Benzyl	Allyl
Yield,[a] %	41	35	32	42	26

[a] Figures are based on amount obtained after a single distillation.

The conditions under which the reaction may occur were studied in an attempt to improve the yield. It seemed reasonable to test the effect of changing base strength of the catalyst, since the less acidic substituted acetoacetic ester might react more readily with a catalyst of greater base strength. Table II lists the results of a series of runs carried out under similar conditions using ethyl methylacetoacetate and various catalysts. There is little evidence that the use of a stronger base as catalyst improves the yield. However, the maximum yield obtained with ethyl methylacetoacetate (59%) occurred when sodium isopropoxide was used as a catalyst, but under conditions differing from those in the runs of Table II.

TABLE II

EFFECT OF THE BASE STRENGTH OF THE CATALYST[a]

Catalyst	Solvent	Yield,[b] %
EtONa	EtOH	39–42
i-PrONa	*i*-PrOH	41
t-BuOK	*t*-BuOH	15
Na	Xylene	0

[a] Ethyl methylacetoacetate used throughout. [b] *Cf.* Table I.

The time of reaction also appears to have little significance in determining the yield. The results shown in Table III indicate the general lack of correlation between the reaction time and the yield. Such a result was unexpected since the methiodide of the Mannich base of cyclohexanone was not appreciably soluble in the reaction mixture.

TABLE III

EFFECT OF REACTION TIME ON YIELD[a]

Time, hr.	4.0	4.5	5.5	5.75	7.5
Yield,[a] %	42	32	38	41	30

[a] Ethyl methylacetoacetate and sodium ethoxide used.

TABLE IV

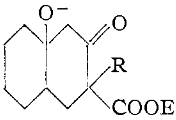
EFFECT OF EXCESS CATALYST ON THE YIELD[a]

Methiodide, mole	Ester, mole	Catalyst, mole	Solvent	Yield, %
0.11	0.14	0.14	*i*-PrOH	41
.11	.28	.28	*i*-PrOH	59
.11	.42	.42	*i*-PrOH	36
.3	.6	.6	*i*-PrOH	55

[a] Ethyl methylacetoacetate used.

The product isolated from these reactions is the unsaturated ketone which results from dehydration of the original aldol product. If water is set free during this dehydration step it would account for the lower yields with substituted acetoacetic esters, since substitution may retard the initial alkylation rate enough to permit both the cyclization and dehydration reactions to be going on in the mixture concurrently. In that case the water could destroy the active anion of the substituted acetoacetic ester. Accordingly the reaction was carried out in the presence of excess base and ester. The data of Table IV indicate that the use of two moles of ester and two of base leads to an optimum yield.

It is not necessary, however, to assume that water is a product of the formation of the unsaturated ketone. Thus the anion of the aldol product II can undergo intramolecular transesterification followed by a base-catalyzed ring opening and decarboxylation. It is interesting to note that no unsaturated ester has been isolated from this reaction, and that a carbethoxyl group not appropriately situated for the transesterification comes through the reaction intact.[3] A similar example is to be found in the preparation of 3,5-dimethyl-4-carbethoxy-2-cyclohexen-1-one[7] where a carbethoxyl *para* to the hydroxyl is eliminated with the hydroxyl while an *ortho* carbethoxyl group is retained.



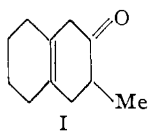
II

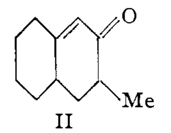
In all cases the product isolated directly from the reaction was not pure and could not be completely purified by distillation with simple fractionating columns. However, the use of a Stedman packed column of greater efficiency permitted the separation of the product obtained with ethyl methylacetoacetate into three distinct fractions. The high boiling fraction appeared to be a mixture and was not identified. The other two fractions, b.p. 63.5–65° (0.34 mm.) and 72.5–74.5° (0.30 mm.) had identical compositions, and were identified as unsaturated ketones. The lower boiling ketone was assigned the structure I and the higher boiling

---

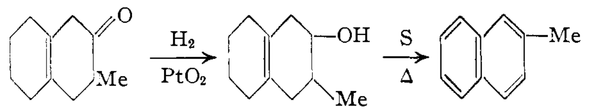
(7) E. C. Horning, M. O. Denekas and R. E. Field, *Org. Syntheses*, **27**, 27 (1947).

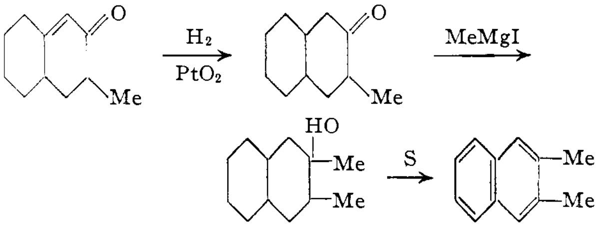
one the structure II. The evidence for this assignment is threefold. The molecular refractivity of the ketone I agrees with the calculated value but that of II shows an exaltation of 1.38 units. The


I


II

ketone I absorbs strongly at 1712 cm.$^{-1}$ whereas its isomer absorbs at 1668 cm.$^{-1}$. Saturated ketones absorb at 1705-1720 cm.$^{-1}$ and α,β-unsaturated ketones[8] at 1665-1700 cm.$^{-1}$. Hydrogenation of ketone I gives an unsaturated alcohol which can be dehydrated and dehydrogenated by the action of sulfur to give 2-methylnaphthalene. Since double bonds common to two rings are known to be difficult to hydrogenate[9] this preferential reduction of the ketone indicates that the 9-10 position for the double bond is most likely. Hydrogenation of the isomeric ketone under similar conditions gave a saturated ketone (absorption band at 1704 cm.$^{-1}$) which was treated with methylmagnesium iodide and the product heated with sulfur. That treatment gave 2,3-dimethylnaphthalene.





Infrared spectra of the ketones isolated when ethyl ethylacetoacetate and ethyl propylacetoacetate were used indicate that similar mixtures of isomeric ketones are present. No separation and identification of products was attempted in those cases.

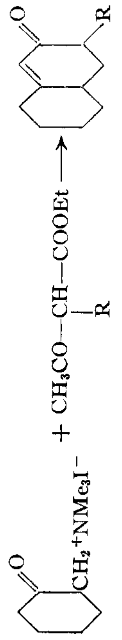
Experimental

2-Dimethylaminomethylcyclohexanone Methiodide.—The hydrochloride of 2-dimethylaminomethylcyclohexanone was prepared in 75% yield by the method of Mannich and Braun.[10] An aqueous solution of that salt was made alkaline with 30% sodium hydroxide and the free base extracted with ether. The ether solution was dried over KOH pellets and methyl iodide (equimolar amount) was added at such a rate that the temperature did not exceed 30°. The methiodide precipitated as a creamy solid which was isolated by suction filtration. After being dried *in vacuo* the product was suitable for preparative use.

2-Oxo-3-alkyloctahydronaphthalenes.—The general procedure described below was used for the preparation of a series of 3-alkylated products. Data for the compounds prepared are given in Table V.

A solution of sodium alkoxide (ethoxide or isopropoxide depending on whether ethanol or isopropyl alcohol was used as the solvent) in the absolute alcohol was prepared

TABLE V



R	B.p., °C.	$n^{20}D$	Yield[a]	Analyses, % Calcd. C	Analyses, % Calcd. H	Analyses, % Found C	Analyses, % Found H	2,4-Dinitrophenylhydrazone M.p., °C.	2,4-Dinitrophenylhydrazone Analyses, % Calcd. C	Calcd. H	Found C	Found H	Semicarbazone M.p., °C.	Semicarbazone Analyses, % Calcd. C	Calcd. H	Found C	Found H
	63.5-65[b] (0.34 mm.)	1.4983[b]				80.97[b]	9.73[b]	151-156[b]			59.21[b]	5.78[b]					
Methyl	72.5-74.5[c] (0.30 mm.)	1.5131[c]	40-50	80.44	9.84	80.28[c]	9.68[c]	173-178[b]	59.29	5.86	59.83[c]	5.87[c]					
Ethyl	105-107 (2.3 mm.)	1.5086	35-40	80.8	10.2	80.23	10.4	163-166	60.32	6.19	60.07	6.01	190-191.5	66.34	9.0	66.70	8.90
Propyl	117-121 (2.3 mm.)	1.5023	30-35	81.2	10.5	79.4[e]	9.8[e]	157-160	61.13	6.50	60.76	6.44	183-185	67.43	9.3	66.34	9.0
Benzyl[d]	140-145 (1 mm.)		35-40	84.9	8.38	84.6	8.10	160-164	65.7	5.77	65.67	5.77					
Allyl	140-145 (0.5 mm.)		20	82.2	9.53	81.6	9.30	166-172	61.7	6.0	60.9	5.9					

[a] Yields expressed in % based on amount of quaternary salt consumed. [b] Data for ketone I: d^{25}_4 0.9981, M_D calcd. 48.16, found 48.22. [c] Data for ketone II: d^{25}_4 0.9962, M_D calcd. 48.16, found 49.54. [d] Approx. 40% of the ethyl benzylacetoacetate was converted to ethyl dihydrocinnamate. [e] No sample of analytical purity was obtained although several samples were prepared.

---

[8] See for example N. H. Cromwell, F. A. Miller, A. R. Johnson, R. L. Frank and D. J. Wallace, THIS JOURNAL, 71, 3337 (1949).

[9] J. R. Durland and H. Adkins, *ibid.*, 60, 1501 (1938).

[10] C. Mannich and R. Braun, *Ber.*, 53, 1874 (1920).

in a three-necked flask fitted with reflux condenser and stirrer and protected from atmospheric moisture. To this solution was added dropwise an equimolar amount of ethyl α-alkylacetoacetate. The resultant solution was heated to 70–80° and a slurry containing one-half molar amount of 2-dimethylaminomethylcyclohexanone methiodide in absolute alcohol was added slowly over a period of about one to two hours. After all the methiodide had been added the solution was heated and stirred for four to six hours. One-half of the solvent was removed under reduced pressure and a volume of water equal to the amount of residue was added. The product was isolated by continuous extraction with ether in a liquid–liquid extractor and distilled under reduced pressure.

3-Methyl-1,2,3,4,5,6,7,8-octahydro-2-naphthol.—A solution of 11.2 g. (0.069 mole) of the low-boiling ketone I from the 3-methyl product in 75 ml. of absolute ethanol was hydrogenated over platinum oxide (0.25 g.) at 30 p.s.i. The product was distilled under reduced pressure giving two fractions b.p. 88–91.5 (1.5 mm.), $n^{27}D$ 1.5025 and b.p. 91.5–93 (1.5 mm.), $n^{27}D$ 1.5060. After standing for several hours the second fraction solidified, m.p. 40–45°. The solid gave a positive xanthate test, absorbed bromine, and showed an intense absorption band at 3280 cm.$^{-1}$. Since the solid alcohol could not be purified for analysis a *m*-nitrophenylurethan was prepared, m.p. 150–154°.

Anal. Calcd. for $C_{18}H_{22}N_2O_4$: C, 65.44; H, 6.72. Found: C, 65.02; H, 6.62.

The liquid product of fraction one was identified as the ketone described below.

2-Oxo-3-methyldecahydronaphthalene.—A solution of 8.2 g. (0.05 mole) of the higher-boiling ketone II from the 3-methyl product (Table V) in 50 ml. of absolute ethanol was hydrogenated over platinum oxide (0.25 g.) at 30 p.s.i. The ketone absorbed one mole of hydrogen and the product was distilled under reduced pressure, b.p. 83–85° (1.5 mm.), $n^{26}D$ 1.4840. This material gave a positive phenylhydrazine test and showed strong absorption at 1704 cm.$^{-1}$.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.55; H, 10.82. Found: C, 78.97; H, 10.54.

A 2,4-dinitrophenylhydrazone was formed, m.p. 130–138°.

Anal. Calcd. for $C_{17}H_{22}N_4O_4$: C, 58.94; H, 6.43. Found: C, 59.26; H, 6.35.

β-Methylnaphthalene.—A mixture of 0.2 g. of 3-methyl-1,2,3,4,5,6,7,8-octahydro-2-naphthol and 0.1 g. of sulfur was heated for two hours at 250°. Several drops of liquid were collected on a cold finger condenser. A picrate was prepared from the product, m.p. 113–116°. A mixture of this picrate and picric acid melted at 104–109°. The picrate of β-methylnaphthalene is reported[11] to melt at 115°.

2,3-Dimethylnaphthalene.—Two grams (0.012 mole) of 2-oxo-3-methyldecahydronaphthalene was added dropwise to an excess (0.05 mole) of methylmagnesium iodide in dry ether. After being heated for four hours the product was poured onto a mixture of ice and 10% ammonium chloride solution. The organic layer was separated, washed with dilute sodium thiosulfate and dried over Drierite. Part of the crude alcohol (0.2 g.) obtained by this procedure was mixed with 0.1 g. of sulfur and heated at 250° for two hours. A small amount of solid, m.p. 101–102°, collected on the cold finger condenser. A melting point of 102° is reported[12] for 2,3-dimethylnaphthalene. No depression of melting point was observed when the above solid was mixed with an authentic sample of 2,3-dimethylnaphthalene.

Infrared Spectra.—The infrared spectra were measured with a Perkin-Elmer 12C spectrometer remodelled to function as a double-beam continuous recording instrument. Sodium chloride cells were employed and thin films of pure liquids were used.

---

(11) E. J. H. Chu and Z. I. Shen, *J. Chinese Chem. Soc.*, **10**, 119 (1943); *cf. C. A.*, **38**, 2951 (1944).

(12) W. Thiele and G. Trautmann, *Ber.*, **68B**, 2245 (1935).

CORVALLIS, OREGON

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MICHIGAN]

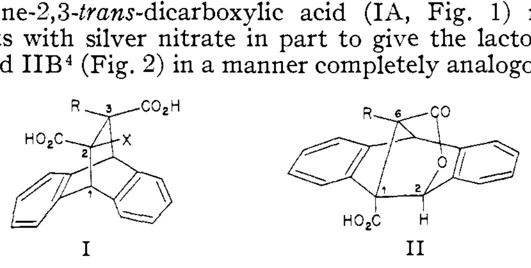
Reactions of Hindered α-Substituted Succinic Acids. IV. Further Reactions Involving the Wagner-Meerwein Rearrangement[1,2]

BY WYMAN R. VAUGHAN AND RANDEL Q. LITTLE, JR.[3]

RECEIVED DECEMBER 5, 1953

The rearrangements of 2-bromo- and 2-chloro acids and anhydrides in the dibenzo[2,2,2]bicycloöctadiene-2,3-dicarboxylic acid series to 2-hydroxy derivatives of the 3,4,7,8-dibenzo[3,2,1]bicycloöctadiene-1,6-dicarboxylic acid series by means of silver nitrate or silver oxide are discussed and are compared with the analogous base-induced reactions.

The fact that 2-bromodibenzo[2,2,2]bicycloöctadiene-2,3-*trans*-dicarboxylic acid (IA, Fig. 1) reacts with silver nitrate in part to give the lactone acid IIB[4] (Fig. 2) in a manner completely analogous to the reaction of 2-hydroxy-3-methyldibenzo[2,2,-2]bicycloöctadiene-2,3-*trans*-dicarboxylic acid with 48% hydrobromic acid to give the lactone acid IIC[5] (Fig. 2) has led us to investigate the behavior of other haloacids and haloanhydrides in this series with silver nitrate and with silver oxide.



I

A, R = H; X = Br
B, R = H; X = OH
C, R = CH_3; X = OH

II

A, R = H (hydroxy acid)
B, R = H
C, R = CH_3

Figs. 1 and 2.

The behavior of IA with silver nitrate is completely analogous to its behavior with alkali, except for the ratio of products[1] (IIIA, Fig. 3, and IIA, Fig. 2) and the fact that the rearranged product is obtained as the lactone acid IIB, instead of the free hydroxyacid. However, certain striking differences were observed with each of the other halo compounds in the series. In particular, the bromoanhydride, IVA (Fig. 4), with silver nitrate affords a rearranged hydroxyacid (VA, Fig. 5) instead of IIIA; the chloroanhydride, IVC (Fig. 4), affords a rearranged hydroxyacid (VB, Fig. 5) *in addition to* IIIB (Fig. 3) and a lactone acid, IIC (Fig. 2), *instead of* IC (Fig. 1), when treated with silver oxide;

---

(1) Preceding paper, W. R. Vaughan and R. Q. Little, Jr., THIS JOURNAL, **76**, 2952 (1954).

(2) Abstracted from a portion of the Ph.D. Dissertation of Randel Q. Little, Jr., University of Michigan, 1953.

(3) American Brake Shoe Company Fellow, 1952–1953.

(4) W. R. Vaughan, M. V. Andersen, Jr., and R. Q. Little, Jr., THIS JOURNAL, **76**, 1748 (1954).

(5) W. R. Vaughan and K. M. Milton, *ibid.*, **74**, 5623 (1952).