[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Introduction of the Angular Methyl Group. The Preparation of *cis*- and *trans*-9-Methyldecalone-1[1]

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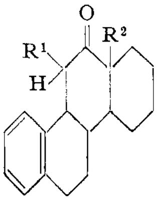
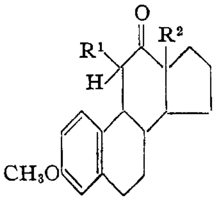
In the synthesis of steroid-like structures one of the significant problems which has challenged the ingenuity of the chemist is that of producing substances containing the so-called angular methyl group. For the most part[2] this has been accomplished by methods involving simultaneous synthesis of the polycyclic nucleus.[3] In this communication is described a method for introducing the methyl group in place of the angular hydrogen atom at the 9-position of the *preformed* bicyclic system, decalone-1 (VII). Since a number of similar nuclei having steroid-like structures, but lacking the angular methyl substituent, are relatively accessible,[3] the method may have added significance.

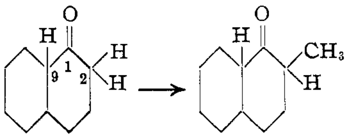
Peak and Robinson[4] have reported the introduction of the angular methyl group directly into the polycyclic ketones I and II by treatment with potassium *t*-butoxide and methyl iodide. While angular methylation may have been realized to give the products III and IV,[5] the method, nevertheless is not general. Cook and Lawrence,[6] for example, attempted to prepare 9-methyldecalone-1 by the methylation of decalone-1 (VII). However, only a trace of the desired isomer was detected in the complex mixture which resulted, and the chief product of monomethylation was 2-methyldecalone-1 (VIII).



I ($R^1 = R^2 = H$)
III ($R^1 = H, R^2 = CH_3$)
V ($R^1 = CH_3, R^2 = H$)



II ($R^1 = R^2 = H$)
IV ($R^1 = H, R^2 = CH_3$)
VI ($R^1 = CH_3, R^2 = H$)



VII VIII

In the present work a method was devised to prevent methylation from taking place at carbon-2. The process involves three steps: (1) protection of the methylene (C-2) group by substitution of the hydrogens by an appropriate residue, (2) methylation (which now can involve only the 9-position), (3) removal of the protective residue to regenerate the methylene group. In order for the method to be practical it is requisite that the protective group be (a) readily introduced, (b) inert to the methylation reaction, (c) easily removed. These conditions appear to be satisfied, at least in part, by the benzal group.

Crystalline *trans*-2-benzaldecalone-1 (IX) was prepared from decalone-1 and benzaldehyde in 88% yield. Methylation by the action of potassium *t*-butoxide[4,13] and methyl iodide in an atmosphere of nitrogen produced a mixture of two isomers, one melting at 104° and the other at 94°. The former composed the major portion (three-fourths) of the product, and being the less soluble readily was obtained pure. By careful fractional crystallization the isomers were obtained in 68 and 23% yields, repectively, thus accounting for 91% of methylated material. When an inert atmosphere was not employed during the reaction this yield was considerably lower.

Since it may be assumed[7] that methylation took place exclusively at the 9-position, the existence

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[1] This work was assisted in part by a grant from the Wisconsin Alumni Research Foundation.

[2] For an exception see Woodward, THIS JOURNAL, **62**, 1208 (1940).

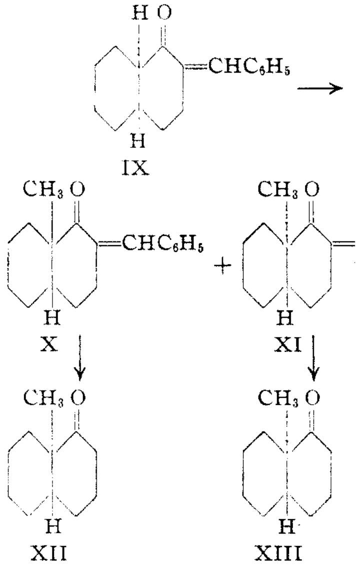
[3] For complete reviews through 1939 see Linstead, *Annual Reports Chem. Soc.*, **33**, 312 (1936), and Springall, *ibid.*, **36**, 286 (1939).

[4] Peak and Robinson, *J. Chem. Soc.*, 1581 (1937); see also McGinnis and Robinson, *ibid.*, 404 (1941).

[5] The structures III and IV were assigned to the methylation products mainly because these after reduction and dehydrogenation gave chrysene and 1,2-cyclopentenophenanthrene, respectively. This evidence is valid only on the assumption that if the methylated ketones had the alternative structures V and VI, the methyl groups would have been retained through the dehydrogenation. That there is some reason to question the validity of such an assumption is implied by the work of Jones and Ramage, *J. Chem. Soc.*, 1853 (1938). These authors found that the principal product of dehydrogenation of hydrochrysene derivatives containing a methyl group at the 5-position (as in formula V) was chrysene rather than 5-methylchrysene. Fieser, Joshel and Seligman, THIS JOURNAL, **61**, 2134 (1939), have reported the loss of a methyl group similarly situated in the chrysene nucleus upon dehydrogenation of the cyclodehydration product from 1-(2′-methylcyclohexyl)-2-(α-naphthyl)-propanol-1. A sound proof of structure for the methylation products of Peak and Robinson[4] and McGinnis and Robinson[4] therefore seems to be lacking.

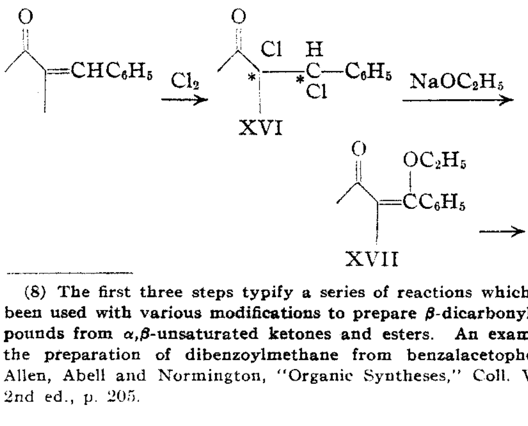
[6] Cook and Lawrence, *J. Chem. Soc.*, 817 (1937).

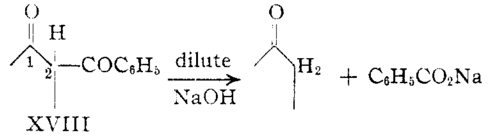
[7] The improbability that methylation occurred at any point other than the 9-position is supported by the work of Koebner and Robinson,[13] who found that 6-methoxy-2-benzaltetralone-1 was recovered unchanged after submission to methylation conditions. Proof of the premise, however, rests on the degradation to the 9-methyldecalones XII and XIII.



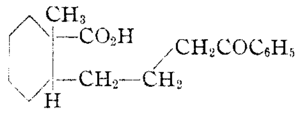
of two isomers may be accounted for by (1) a *cis–trans* isomerism of the decalin type at the juncture of the two rings (represented by formulas X and XI), or (2) geometric isomerism involving the benzal group, the ring configuration being the same in both isomers, or (3) an isomerism involving both types (1) and (2). All attempts to interconvert the two substances failed; thus preparation of the dibromides followed by thermal debromination[16] regenerated the original isomer in each case. This suggested that the isomerism was not of type (2), which indeed proved to be the case, as shown by the degradation of each to two different 9-methyldecalones (XII and XIII). The latter on condensation with benzaldehyde gave back the respective starting ketones X and XI showing that no rearrangement had occurred during the transformations.

The removal of the benzal group from the methylated ketones was effected by means of the following reactions[8]





Although a number of steps are involved, in practice the intermediate products need not be isolated and *the whole operation may be performed in a single day.* Thus the benzal derivative melting at 104° rapidly absorbed chlorine in carbon tetrachloride solution yielding on evaporation an oily mixture of diastereoisomeric dichlorides XVI. This on warming with alcoholic sodium ethoxide was converted to the enol ether XVII which was rapidly hydrolyzed by acidifying and warming the reaction mixture. The resultant β-diketone XVIII, which formed an insoluble copper enolate, was not isolated, but was directly cleaved by steam distillation from dilute alkaline solution. The oil in the distillate amounted to a 71% yield of a pure 9-methyldecalone-1 identified as the known[6,9] (see Table I) isomer, probably[9c] of *cis*-configuration (formula XII). Acidification of the alkaline residue gave benzoic acid and a small amount (4.4%) of a keto acid $C_{18}H_{24}O_3$ which evidently has the structure XIV arising from the alternative cleavage of XVIII between carbons 1 and 2.



XIV (CH_3/H *cis*)
XV (CH_3/H *trans*)

Similar treatment of the 94° benzal ketone gave a new 9-methyldecalone-1 to which the *trans* configuration (formula XIII) is now tentatively assigned. This substance is different from that presumed to be XIII by Nenitzescu, Ciŏranescu and Przemetzky.[9d] Their material was prepared by a method which has failed in the hands of other workers[6,9c,10] and seems to leave the structure in doubt.[11] In the *trans* series the inter-

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[8] The first three steps typify a series of reactions which have been used with various modifications to prepare β-dicarbonyl compounds from α,β-unsaturated ketones and esters. An example is the preparation of dibenzoylmethane from benzalacetophenone, Allen, Abell and Normington, "Organic Syntheses," Coll. Vol. I, 2nd ed., p. 205.

(9) (a) Chuang, Tien and Ma, *Ber.*, **69**, 1494 (1936); (b) Kon, Linstead and Simnns, *J. Chem. Soc.*, 814 (1937); (c) Elliott and Linstead, *ibid.*, 660 (1938); (d) Nenitzescu, Ciŏranescu and Przemetzky, *Ber.*, **73**, 313 (1940); (e) Plentl and Bogert, *J. Org. Chem.*, **6**, 669 (1941).

(10) Robinson and Walker, *J. Chem. Soc.*, 60 (1937).

(11) The material presumed to be XIII by Nenitzescu, *et al.*, was isolated as the semicarbazone, m. p. 185°, in 4% yield from a ketonic fraction resulting from an unusual cyclization, involving simultaneous reduction, of γ-(2-methyl-$\Delta^{1,2}$-cyclohexenyl)-butyric acid in cyclohexane. The ketone had a b. p. which at 5 mm. was 10° below that of *cis*-9-methyldecalone obtained in the same experiment. There seems to be some question regarding the homogeneity of the methylcyclohexenylbutyric acid of the Rumanian workers, as may be inferred from their experimental description. If any of the isomeric γ-(1-methyl-$\Delta^{2,3}$-cyclohexenyl)-butyric acid was present

mediate β-diketone XVIII apparently was cleaved in both directions in approximately equal amounts, for the ketone and keto acid XV were obtained in the same (26%) yields. It should be pointed out that the ester of the keto acid XV could be recyclized by the Dieckmann method to the β-diketone XVIII, thus providing a source of additional *trans*-9-methyldecalone-1. A comparison of the two 9-methyldecalones is found in Table I.

TABLE I

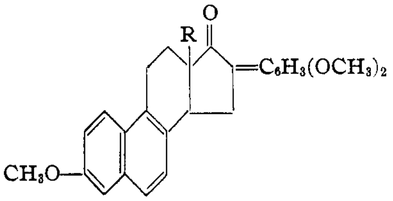
9-Methyldecalone-1

	Cis[a]		
	Cook and Lawrence[6]	Present work[18a]	*Trans*[a]
B. p. °C.	118	116	119
B. p. Mm.	20	14–15	14–15
Oxime, m. p., °C.	108.5–111	109–110 114.5–115.5[c]	141.5–142[b]
Semicarbazone, m. p., °C.	224–225	226–227	219–220
2,4-Dinitrophenylhydrazone, m. p., °C.	159–160	164.5–165.5	171.5–172
Benzal derivative, m. p., °C.	....	104–104.5	93.5–94

[a] Probable configuration. [b] The proximity of this m. p. to that (139–139.5°) of an oxime isolated by Cook and Lawrence[6] from the direct methylation of decalone suggests that the two may be identical. As pointed out by these authors, however, the 139–139.5° compound could be the 2-methyldecalone-1 derivative, epimeric with the known isomer.[6] [c] Polymorphic modifications.

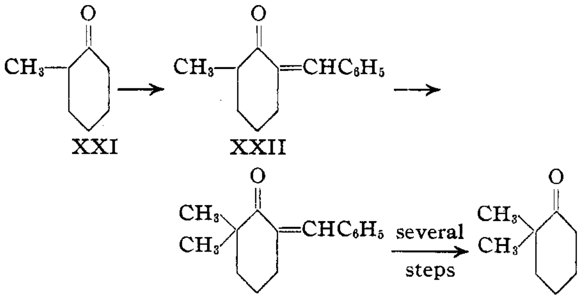
A distinct difference was observed in the relative rates of semicarbazone formation between the two decalones as well as the benzal derivatives X and XI, the *trans* isomers reacting more rapidly in each case. Another manifestation of a difference in reactivity between the carbonyl groups of the stereoisomers is found in the proportion of cleavage products of the β-diketones XVIII: the ratio of ketone to keto acid was approximately 16 to 1 in the *cis* and 1 to 1 in the *trans* series. Since the pairs of stereoisomers in each case differ from each other only in the spatial arrangements of the atoms and therefore have the same groups to activate the carbonyl function, the causes of the differences in reactivity must be subtle. Ordinary molecular models of *cis*- and *trans*-9-methyldecalone-1 fail to show any pronounced difference in degree of hindrance of the carbonyl group by the angular substituents.[12]

The work presented in this communication seems to afford additional justification for the structure XX assigned by Koebner and Robinson[13] to the substance produced by methylation of the piperonal condensation product XIX from synthetic norequilenin methyl ether. These workers prepared the former substance XX in an effort to establish its identity with the corresponding derivative of natural equilenin, but the material did not have the expected properties, and therefore, as pointed out by them, should correspond to *dl*-isoequilenin. It seems entirely possible that the desired equilenin derivative actually was formed to a small extent, but was not found, due to the preponderance of the known isomer. The ready availability of norequilenin[14] suggests an interesting application of the method described in this paper.



XIX (R = H)
XX (R = CH$_3$)

Another application is found in the conversion of 2-methylcyclohexanone (XXI) into the *gem*-dimethyl compound XXIV. The study was conducted preliminary to the work in the decalone series already described. This afforded an advantage in that the intermediates contained fewer centers of asymmetry, thus facilitating the isolation of pure substances for a study of the individual reactions. Methylation of the benzal derivative XXII gave the known[15] homolog



XXI XXII XXIII XXIV

(this could arise if in the previous step, acylation had occurred at position-1 of methylcyclohexene) this on cyclization might give the isomeric 10-methyldecalone-1. This is suggested as a possible structure for their ketone.

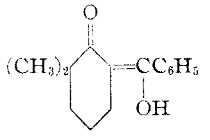
(12) The steric hindrance concept, however, does suggest a correlation between the differences in the rate of semicarbazone formation and the extent of β-diketone cleavage. The former is typical; and the cleavage of β-diketones has been studied by Kutz and Adkins, THIS JOURNAL, **52**, 4036 (1930), who found that "increased branching in the radical at one end of the diketone molecule decreased the cleavage on that side."

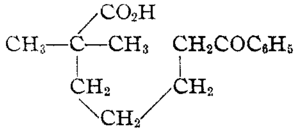
(13) Koebner and Robinson, *J. Chem. Soc.*, 566 (1941).

(14) Koebner and Robinson, *ibid.*, 1994 (1938).

(15) (a) v. Auwers and Krollpfeiffer, *Ber.*, **48**, 1226 (1915); (b) Haller and Cornubert, *Compt. rend.*, **170**, 700 (1920); (c) Haller, *ibid.*, **157**, 179 (1913).

XXIII in 95% yield. This was quantitatively converted to an easily separable mixture of two diastereoisomeric dichlorides (XVI). By the action of sodium ethoxide followed by acid the predominant α-isomer was converted to the β-diketone XVIII,[16] which was isolated as the insoluble copper enolate in 45 to 50% yields. The latter on shaking with mineral acid was decomposed to an easily separable mixture of diketo (formula XVIII) and enol (probably XXV[17]) modifications. These were readily cleaved by dilute alkali to give the known 2,2-dimethylcyclohexanone (XXIV), identified through derivatives, and the alternate cleavage product ε-benzoyl-α,α-dimethylcaproic acid (XXVI). The ratio of these products was approximately 3 to 5.


XXV


XXVI

Grateful acknowledgment is due to Theodore H. Meltzer and Kenneth L. Temple for their assistance in the preparation of starting materials, and to Arthur Goldman who carried out many of the analyses.

Experimental Part[18]

2-Benzal-6-methylcyclohexanone (XXII).—Cornubert and Louis[19] have prepared this substance in 67% yield by condensation of benzaldehyde with *o*-methylcyclohexanone in a methanolic solution of sodium methoxide. In the present work it was found easier to duplicate yields of 65 to 70% by using an aqueous-alcoholic solution of sodium hydroxide. A mixture of 2-methylcyclohexanone (15 g.), benzaldehyde (20 cc.), water (80 cc.), sodium hydroxide (8.8 g.) and 95% alcohol (48 cc.) was heated with mechanical stirring for three hours on the steam-bath. The insoluble oil was extracted with ether and submitted to distillation at reduced pressure. In a typical run the fraction boiling at 153–160° (mostly at 153–154°) at 4 mm. amounted to 18.4 g. (69%), m. p. 56–60°. This material was satisfactory for the next step. Recrystallized it melted at 61–62° (literature[19] m. p. 62°).

2-Benzal-6,6-dimethylcyclohexanone (XXIII).—A flask containing a solution of 19.5 g. of potassium in 500 cc. of *t*-butyl alcohol, previously dried by distillation from potassium *t*-butoxide, was evacuated and filled with dry, oxygen-free[20] nitrogen. The benzal derivative XXII (33.0 g.) was added at room temperature, and after swirling a few minutes solution was complete. The mixture was chilled (nitrogen being admitted) in an ice-salt bath and 58 cc. of methyl iodide added. After the initial vigorous reaction terminated, the mixture (containing precipitated potassium iodide) was heated under reflux (mercury trap) on the steam-bath for one and one-half hours and the solvent removed at reduced pressure. Water was added and the crystalline residue filtered and washed with water. The damp cake on crystallization from methanol–water solution gave 31.3 g. of colorless plates, m. p. 79–80°. A second crop obtained from the mother liquors amounted to 2.2 g., m. p. 78–79.5°, making the total yield 95%. A sample sublimed at reduced pressure and recrystallized from methanol formed flat needles, m. p. 79.5–80°. Previously reported melting points[15] range from 78°[15c] to 82–83°.[15a]

Anal. Calcd. for $C_{15}H_{18}O$: C, 84.07; H, 8.46. Found: C, 84.14; H, 8.45.

When the methylation was carried out as above but without the nitrogen, the yield dropped to 83%. Also in contrast an oily acidic fraction was obtained, doubtless an oxidation product.

Addition of chlorine to the above benzal ketone XXIII (31.3 g.) was carried out in carbon disulfide (150 cc.) with cooling in an ice–salt bath. When the gas ceased to be absorbed rapidly, the solvent was removed at reduced pressure and the colorless oil dissolved in 100 cc. of methanol. On cooling the solution deposited 26.2 g. of the **α-isomer of 2-benzal-6,6-dimethylcyclohexanone dichloride (XVI)**, m. p. 81–83°. An additional 5.2 g. of the same material, m. p. 78–81.5° was obtained from the concentrated mother liquor, making the yield 75%. Recrystallized for analysis the substance formed colorless elongated prisms from methanol, m. p. 82–83°.

Anal. Calcd. for $C_{15}H_{18}OCl_2$: C, 63.17; H, 6.36. Found: C, 62.98; H, 6.36.

The mother liquor from above proved to be supersaturated with the diastereoisomeric **β-dichloride,** and, when crystallization was induced, 8.2 g. (20%) of the crude substance, m. p. 58–79° was obtained. A single recrystallization from methanol gave 5.9 g. of colorless prisms, m. p. 83–84°, mixed with the α-isomer 55–65°. Further recrystallization did not raise the m. p.

Anal. Calcd. for $C_{15}H_{18}OCl_2$: C, 63.17; H, 6.36. Found: C, 62.98; H, 6.07.

An additional 0.8 g. of the mixture of dichlorides, m. p. 55–65°, was obtained from the filtrate, making the total yield 97%.

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[16] In contrast, the dibromide of XXIII reacted rapidly with sodium ethoxide, but only the starting benzal derivative XXIII (yield about 25%) and none of the expected enol ether XVII was found. This suggests the presence of "positive" bromine in the dibromide. A similar debromination was observed by Abell, *J. Chem. Soc.*, 989, 1002 (1912), in the case of dibromobenzalacetophenone. One bromine was easily eliminated in the form of hydrogen bromide to give $C_6H_5COCH{=}CBrC_6H_5$; this on treatment with sodium alkoxides gave in addition to the expected enol ether of dibenzoylmethane, a small amount of benzalacetophenone. In the present work the dibromide of XXIII was also converted to XXIII in small yield by heating the former at 145° for a few minutes. The reaction was accompanied by the evolution of hydrogen bromide, not bromine. Thus intermolecular bromination must have occurred, perhaps also due to positive halogen.

[17] *Cf.* the structure of benzoylacetone, Scheiber and Herold, *Ann.*, **405**, 295 (1914).

[18] (a) All melting points are corrected. (b) The use of the terms *cis* and *trans* in this section is not intended to imply that the configurations have been established; indeed they refer only to the *probable* configurations used in the first part of the work.

[19] Cornubert and Louis, *Bull. soc. chim.*, [5] **5**, 520 (1938).

[20] Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 2nd ed., part II, p. 395.

2-Benzal-6,6-dimethylcyclohexanone dibromide was formed by treating a solution of XXIII (2.1 g.) in carbon tetrachloride with the calculated amount (1.6 g.) of bromine. On evaporation and treatment of the residue with alcohol a single substance (3.1 g.) m. p. 86–87° was obtained in 83% yield. The pure dibromide crystallized from methanol in colorless plates, m. p. 86.5–87.5°.

Anal. Calcd. for $C_{15}H_{18}OBr_2$: C, 48.15; H, 4.85. Found: C, 47.97; H, 4.89.

When this substance (3.7 g.) was treated with sodium ethoxide (from 0.46 g. of sodium) as described below for the dichloride, 0.5 g. of XXIII could be crystallized from the oily product. The latter even after treatment with acid failed to give a ferric chloride test, and no coloration or derivative was obtained with cupric acetate.

Thermal decomposition of the dibromide of XXIII was carried out by heating (oil-bath) 0.2 g. in a test-tube containing a thermometer. At 145° a vigorous evolution of hydrogen bromide was observed. This continued for about fifteen minutes as the temperature gradually rose to 150°. The oily residue which had darkened to some extent was dissolved in methanol, and on cooling deposited crystals of the benzal ketone XXIII, m. p. 79–80° after recrystallization. The yield was small, and the residue was not further investigated since it failed to crystallize readily.

2-Benzoyl-6,6-dimethylcyclohexanone XVIII and XXV.—A mixture of the α-dichloride of XXIII (2.80 g.) and sodium ethoxide from 0.46 g. of sodium and 6.0 cc. of ethanol (dried by distillation from magnesium ethoxide[21]) was allowed to reflux (excluding moisture) on the steam-bath for two hours during which darkening and precipitation of sodium chloride was observed. After most of the alcohol was removed, water was added and the oil extracted with ether. Treatment of the acidified (with nitric acid) aqueous layer and washings with silver nitrate gave 2.66 g. of silver chloride, accounting for 95% of the chlorine. Evaporation of the ether solution gave an oil probably containing the enol ether XVII, since the ferric chloride test, at first negative, developed slowly on standing to give an intense purple color. This suggests that the material was slowly hydrolyzing in the presence of the test solution to the enol XXV which gives an instantaneous color with ferric chloride. The enol ether was hydrolyzed with hydrochloric acid (1.0 cc. concd.) in 30 cc. of alcohol and 10 cc. of water by refluxing on the steam-bath for forty minutes. The solution was concentrated to remove most of the alcohol, water added and the oil extracted with ether. This material now gave an immediate color with ferric chloride solution, and on shaking with a saturated aqueous solution of cupric acetate, green crystals of the copper enolate of the β-diketone gradually precipitated. After standing overnight 1.02 g. of this substance was filtered from the ether layer. The latter was concentrated and again shaken with cupric acetate solution. In this way a total of 1.19 g. (46%) of the copper derivative was isolated. Some β-diketone still remained in solution as shown by the ferric chloride test, but no more could be isolated in the manner described above even after again submitting the organic residue to hydrolytic conditions. The more volatile fraction obtained on evaporative distillation at 0.1 mm. of the oily residue yielded an additional 0.02 g. of copper enolate. This derivative crystallized from benzene–ether solution in green prisms, m. p. 214–216.5° dec. On shaking with dilute sulfuric acid (1 part concd. acid and 4 parts water) and ether it was quantitatively decomposed to a mixture (1.05 g.) of enol and diketo forms. The latter separated on crystallization from 40–60° petroleum ether, m. p. 71–75°, yield 0.13 g. (an additional 0.10 g. was obtained after removal of the enol form described later). It was believed to be the **diketo modification XVIII,** because the test with ferric chloride was at first negative, but developed gradually to the characteristic purple color. The recrystallized material formed colorless needles from petroleum ether (40–60°), m. p. 76–77°.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.54; H, 7.81.

The solvent was removed from the filtrate, and the residue crystallized from methanol in which the diketo form is very soluble. Thus the **enol XXV** was obtained in yellowish needles, m. p. 63–66°; yield 0.64 g. Two recrystallizations from the same solvent gave almost colorless needles, m. p. 65–65.5°. This substance showed a m. p. depression on mixing with the diketo form, and gave an instantaneous intense purple color with ferric chloride.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 77.92; H, 7.76.

Alkaline Cleavage of 2-Benzoyl-6,6-dimethylcyclohexanone.—The mixture of diketo and enol forms obtained directly from the decomposition of the copper enolate was used. A suspension of 0.6 g. in 40 cc. of 1% sodium hydroxide solution was slowly steam distilled, maintaining the volume constant by heating, until the distillate was no longer cloudy. The latter (about 50 cc.), which contained an insoluble colorless oil with a camphor-like odor, was treated with 0.5 g. each of semicarbazide hydrochloride and sodium acetate. After a short while at room temperature the **semicarbazone of 2,2-dimethylcyclohexanone** began to crystallize, and in a few hours it was collected; yield 0.14 g. (29%), m. p. 195–199°. Recrystallized from methanol–petroleum ether (40–60°) it formed felted colorless needles, m. p. 201–202°.[18a] (Previously reported melting points[22] range from 197–198°[22d] to 202–204°.[22b]) The **oxime** prepared in a similar manner crystallized from 40–60° petroleum ether in colorless plates, m. p. 92.5–93[18a] (literature m. p. 93.5–94°[23] cor.).

The homogeneous alkaline residue from the steam distillation gave on acidification a crystalline precipitate of **ϵ-benzoyl-α,α-dimethylcaproic acid (XXVI)** amounting to 0.30 g. (46%), m. p. 101–105°. A solution of the acid in dilute sodium bicarbonate, was treated with Norit, filtered, acidified and the product recrystallized from aqueous methanol. It formed colorless needles, m. p. 105–105.5° and gave a precipitate with 2,4-dinitrophenylhydrazine solution.

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.29; H, 8.00.

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[21] Fieser, *ibid.*, p. 359.

[22] (a) Elliott and Linstead, *J. Chem. Soc.*, 776 (1938); (b) Bartlett and Pöckel, THIS JOURNAL, **59**, 820 (1937); (c) Meerwein, *Ann.*, **405**, 129 (1914); (d) v. Auwers and Lange, *ibid.*, **401**, 303 (1913).

[23] Haller and Cornubert, *Bull. soc. chim.*, [4] **41**, 367 (1927).

The original acidic filtrate from the crude keto acid was extracted with ether from which benzoic acid was isolated and identified.

2-Benzaldecalone-1 (IX) has been prepared in unspecified yield by Hückel and Brinkmann.[24] Their procedure using sodium methoxide as the condensing agent did not give as good results as a modification of the procedure of Vorländer and Kunze[25] for preparing dibenzalcyclohexanone.

Decalone-1 (152 g.), readily prepared in 90% yield by chromic acid oxidation[26] of decalol-1,[27] was dissolved in 1 liter of 95% alcohol. To the cooled solution was added with swirling in the following order, 400 cc. of 15% sodium hydroxide, 113 cc. of freshly distilled benzaldehyde and 100 cc. of water. The homogeneous, pale yellow solution was seeded with a little 2-benzaldecalone-1 and allowed to stand at room temperature for two days, during which time a copious crystalline precipitate formed. After chilling, it was filtered, washed with 300 cc. of 60% alcohol, triturated with water to remove traces of alkali, again filtered, and washed with water. The colorless product amounted to 154.3 g., m. p. 90.5–92°. A sample recrystallized from ether–petroleum ether (40–60°) melted at 91–92° (literature m. p. 91°[24]). The filtrate from the first crop on standing for four days at room temperature deposited an additional 24.3 g. of almost colorless material, m. p. 88–91°. The total yield based on decalone was therefore 75%. Since 23 g. of ketone of good purity could be recovered as described below, the yield based on the decalone consumed was 88%.

The filtrate from the second crop of benzal derivative was acidified with 140 cc. of concentrated hydrochloric acid, the alcohol removed and the residue, containing a suspended oil, steam distilled. The oil in the distillate was separated by ether extraction and distilled at reduced pressure. Thus 23 g. of decalone boiling at 97–102° (8–9 mm.) was obtained. The non-steam-volatile residue was extracted with ether and washed with 10% potassium carbonate solution which removed 4.3 g. of crude benzoic acid. The neutral fraction was dried over potassium carbonate, concentrated, and 40–60° petroleum ether added, whereupon 11.0 g. of colorless felted needles, m. p. 137–138°, separated. Twice recrystallized from ether solution the product had the m. p. 139.5–140°, not raised by further recrystallization. As a tentative structure for this compound, **2-(α-hydroxybenzyl)-decalol-1** is suggested.

Anal. Calcd. for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.08, 78.42; H, 9.20, 9.18.

2-Benzaldecalone-1 semicarbazone formed quantitatively in methanol solution using semicarbazide hydrochloride and pyridine. It crystallized from methanol in colorless needles, m. p. 212.5–214° dec. (introduced in bath at 208°).

Anal. Calcd. for $C_{18}H_{23}ON_3$: C, 72.70; H, 7.79. Found: C, 72.32; H, 7.78.

Methylation of 2-benzaldecalone-1 was carried out following the same procedure as described above for 2-benzal-6-methylcyclohexanone. The quantities employed were 20.0 g. of potassium, 500 cc. of *t*-butyl alcohol, 60 cc. of methyl iodide, and 31.67 g. of recrystallized (m. p. 91–92°) benzaldecalone IX. The crude methylation product amounted to 33.58 g. (quantitative yield), m. p. about 73–90°. This was dissolved in 250 cc. of methanol, and after standing for seven hours at room temperature 19.00 g. of ***cis*-2-benzal-9-methyldecalone-1 (X)** separated in heavy colorless prisms, m. p. 98–102°. The m. p. of the purified material was 104–104.5°.

Anal. Calcd. for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.90; H, 8.57.

The filtrate was concentrated to 200 cc., and was seeded with the *trans* isomer (previously obtained pure from pilot runs). After several hours 4.12 g. of colorless plates, m. p. 91–93°, had separated. A single recrystallization from methanol gave pure ***trans*-2-benzal-9-methyldecalone (XI)** as colorless lozenge-shaped plates, m. p. 93.5–94°, depressed on mixing with 2-benzaldecalone-1.

Anal. Calcd. for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.68; H, 8.75.

The filtrate from the second crop was further fractionated, and a summary of the results appears in Table II. The combined yields of methylated products amounted to 91%.

TABLE II

FRACTIONAL CRYSTALLIZATION OF THE METHYLATION PRODUCT OF 2-BENZALDECALONE-1

All of the fractions were carefully checked as to identity. Thus fraction no. 6 consisted of well-formed plates, m. p. 86–92° which was depressed to 72–91° on mixing with pure X; mixed with pure XI, the m. p. was 90–93°. A single recrystallization of No. 6 from methanol gave material melting at 91–93°.

Fraction	Volume of solution in cc.	*cis* Isomer X (prisms) G.	*cis* Isomer X (prisms) M. p., °C.	*trans* Isomer XI (plates) G.	*trans* Isomer XI (plates) M. p., °C.
1	250	19.00	98–102		
2	200			4.12	91–93
3	140	2.07	96–101		
4	95			2.06	91–92.5
5	65	1.07	96–101		
6	45			1.24	86–92
7	25	0.49	93–100		
8	10			0.41	87.5–91
9	7	0.17	93–100		
	Total	22.80 g. (68%)		7.83 g. (23%)	

Semicarbazone of *trans*-2-Benzal-9-methyldecalone-1.—A mixture of the *trans*-benzal derivative XI (0.30 g.), semicarbazide hydrochloride (0.30 g.) and pyridine (1.0 cc.) was heated in methanol (9 cc.) solution on the steam-bath for one hour. The semicarbazone obtained on the addition of water (5 cc.) amounted to 0.32 g. or 87%, m. p. 208–210°, with previous softening. The derivative crystallized from methanol in colorless prisms, m. p. 209–210° dec. (introduced in bath at 200°).

Anal. Calcd. for $C_{19}H_{25}ON_3$: C, 73.28; H, 8.09. Found: C, 73.39; H, 7.78.

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[24] Hückel and Brinkmann, *Ann.*, **441**, 21 (1925).

[25] Vorländer and Kunze, *Ber.*, **59**, 2078 (1926).

[26] According to the procedure for the oxidation of menthol to menthone, Sandborn, "Organic Syntheses," Coll. Vol. I, 2nd ed., p. 340.

[27] Musser and Adkins, THIS JOURNAL, **60**, 664 (1938).

Semicarbazone of *cis*-2-Benzal-9-methyldecalone-1.—When the identical procedure described above was applied to the *cis* isomer X, unreacted ketone was recovered, and only a 33% yield of semicarbazone was obtained. However, when the reaction period was extended to six and one-quarter hours the yield was raised to 92%. The pure derivative crystallized from methanol in colorless prisms, m. p. 191–192° dec.

Anal. Calcd. for $C_{19}H_{25}ON_3$: C, 73.28; H, 8.09. Found: C, 73.35; H, 8.05.

The difference in rates of semicarbazone formation noted in the preceding two experiments has been used to separate mixtures of the methylated isomers X and XI. Such a procedure made it possible to obtain relatively quickly the more soluble isomer XI from mixtures which after removal of the first crops, were difficult to separate. The method involved heating the residue in methanol with about one-half the calculated amount of semicarbazide hydrochloride and pyridine for thirty minutes. The semicarbazone which crystallized from the solution was rich in the *trans* isomer. In a typical experiment 8.3 g. of semicarbazone, m. p. 205–208°, thus obtained was heated with 30 cc. each of water and concentrated hydrochloric acid for thirty minutes under reflux. The oil solidified on cooling, and was crystallized from methanol. The first crop amounted to 4.5 g. of XI, m. p. 90–94° (not depressed on mixing with pure XI). Further fractions contained some of the higher melting isomer.

***cis*-9-Methyldecalone-1 (XII).**—Chlorine gas was bubbled rapidly into a chilled solution of 22.0 g. of *cis*-2-benzal-9-methyldecalone-1 (X) in 110 cc. of carbon tetrachloride until the rate of absorption markedly decreased. The solvent was then removed at diminished pressure, and to the colorless oily residue was added a solution of sodium ethoxide from 6.6 g. of sodium and 132 cc. of dry[21] ethanol. The apparatus was evacuated, filled with nitrogen, and the solution was allowed to reflux for three hours[28]; sodium chloride precipitated as the solution darkened. The mixture was acidified (to congo red) with dilute (1:1) hydrochloric acid and refluxing was continued for thirty minutes. The alcohol was removed, and the residue steam distilled slowly from a solution of 20 g. of sodium hydroxide in 1500 cc. of water. Approximately 1500 cc. of distillate was collected before no more oil came over. The latter, which had a camphor-like odor, was extracted with ether, dried over anhydrous potassium carbonate, and after removing the solvent through a short Vigreux column, was distilled at diminished pressure. The boiling range was 99.5–100° (7–8 mm.) and the colorless *cis*-9-methyldecalone-1 amounted to 10.2 g. or 71%. On redistillation it boiled at 116° (14–15 mm.); $n^{25.0}_{D}$ 1.4897; $d^{25.0}_{4}$ 0.9930. Cook and Lawrence[6] give $n^{18.8}_{D}$ 1.4903; $d^{18.8}_{4}$ 0.9953. The small residue from the first distillation on treatment with semicarbazide hydrochloride and sodium acetate in dilute alcohol gave 0.31 g. of the **semicarbazone** of *cis*-9-methyldecalone-1, m. p. 221–225° (crude). This derivative was also prepared from the pure ketone XII, and in agreement with Elliott and Linstead[9c] the rate of reaction was observed to be slow at 30°, and rapid on warming. The recrystallized substance had the m. p. 226–227°[18a] dec. (introduced in bath at 220°). Previously reported melting points[6,9] range from 223°[9b,d] to 225–226°.[9a]

The **oxime** of *cis*-9-methyldecalone-1 crystallized from aqueous methanol in colorless lozenge-shaped plates, m. p. 109–110°, which on standing for several weeks underwent a polymorphic change to prisms, m. p. 114.5–115.5°. The latter remelted at 108.5–110° (literature m. p. 108.5–111°[6]; 106°[9c]). Besides the 106° oxime, Plentl and Bogert[9e] reported a second isomer m. p. 88°. None of the latter was encountered in the present work.

The **2,4-dinitrophenylhydrazone** of XII crystallized from ethyl acetate–methanol solution in orange plates, m. p. 164.5–165.5°[18a] (literature m. p.[6] 159–160°).

The **benzal derivative** of XII was prepared by treating a solution of 0.20 g. of the ketone in 1.3 cc. of 95% alcohol with 0.53 cc. of 15% sodium hydroxide solution followed by 0.15 cc. of benzaldehyde. After standing at room temperature overnight 0.28 g. (92%) of colorless prisms separated, m. p. 102–104°. One recrystallization from methanol raised the m. p. to 104–105°; no depression on mixing with methylation product X.

***cis*-1-Methyl-2-(γ-benzoylpropyl)-cyclohexane-2-carboxylic Acid (XIV).** The alkaline solution remaining after the steam distillation in the above preparation of XII contained an oil which was extracted with ether. This fraction was not further investigated; the aqueous layer on acidification gave a mixture of benzoic acid and the keto acid XIV. The latter was easily separated by its insolubility in hot water and amounted to 1.11 g., m. p. 90–105° (crude). It was purified by solution in dilute sodium bicarbonate and reprecipitation, evaporative distillation at 165° (0.1 mm.), and recrystallization from methanol. The keto acid crystallized from dilute alcohol in small colorless leaflets, m. p. 131–133°.

Anal. Calcd. for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.80; H, 8.40.

***trans*-9-Methyldecalone-1 (XIII)** was prepared by the procedure already described for the *cis* isomer, starting with 8.60 g. of *trans*-2-benzal-9-methyldecalone-1 (m. p. 93–94°) in 43 cc. of carbon tetrachloride. Sodium methoxide from 5.9 g. of sodium and 130 cc. of methanol was used and the mixture was heated at this stage for eighteen hours.[29] The decalone fraction from the steam distillation

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(28) The time required to complete the elimination of chlorine from the intermediate XVI was determined by pilot runs which were interrupted after the ethoxide treatment, and acidified with nitric acid. The aqueous layers and washings from ether extraction were treated with silver nitrate. From 1.00 g. of *cis*-2-benzal-9-methyldecalone-1, 0.91 g. (81%) of silver chloride was obtained after refluxing for two hours; 1.02 g. (91%) after three hours. The ether layer was shaken with a saturated solution of cupric acetate and allowed to stand, with occasional shaking, for several days. On evaporation of the ether and addition of petroleum ether 0.49 g. of the green copper enolate of 2-benzoyl-*cis*-9-methyldecalone-1 separated. It could be precipitated in an amorphous condition from a benzene solution by addition of petroleum ether, m. p. 150–153° dec. *Anal.* Calcd. for $C_{36}H_{42}O_4Cu$: C, 71.79; H, 7.03. Found: C, 70.23; H, 6.94.

(29) Later experiments show that sodium ethoxide can be used instead of methoxide to shorten the reaction period. Thus by the chloride precipitation method as described above[28] for the *cis* series, three hours of refluxing with ethoxide gave 1.08 g. (96%) of silver chloride starting with 1.00 g. of the *trans*-benzal derivative XI. The copper enolate of 2-benzoyl-*trans*-9-methyldecalone-1 was also obtained. It was soluble in benzene and precipitated on addition of ether as a green amorphous solid, m. p. 235–238° dec. *Anal.* Calcd. for $C_{36}H_{42}O_4Cu$: C, 71.79; H, 7.03. Found: C, 70.49; H, 6.98.

also had a camphor-like odor and amounted to 1.19 g., b. p. 119–120° (14–15 mm.).

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.85; H, 10.92.

The residue from the diminished pressure distillation yielded some additional ketone in the form of the semicarbazone; 0.33 g., m. p. 219–220°. Thus a total of 26% of XIII was accounted for. In contrast to the *cis* isomer, the pure *trans*-9-methyldecalone-1 reacted rapidly with semicarbazide at room temperature to yield the **semicarbazone.** It formed colorless needles from methanol, m. p. 219–220° dec. (introduced in bath at 215°).

Anal. Calcd. for $C_{12}H_{21}ON_3$: C, 64.54; H, 9.48. Found: C, 64.67; H, 9.55.

The **oxime** of XIII crystallized from methanol in prismatic needles, m. p. 141.5–142°. It sublimes slowly at 60° (0.1 mm.).

Anal.[30] Calcd. for $C_{11}H_{19}ON$: C, 72.88; H, 10.56. Found: C, 73.21; H, 10.60.

The **2,4-dinitrophenylhydrazone** of XIII formed elongated orange prisms from ethyl acetate–methanol solution, m. p. 171.5–172°.

Anal. Calcd. for $C_{17}H_{22}O_4N_4$: C, 58.94; H, 6.40. Found: C, 59.01; H, 6.28.

The **benzal derivative** of XIII was prepared by the same procedure described above for the *cis*-ketone, using one-half quantities. The crystalline product amounted to 1.03 g. (67%), m. p. 88–91°, softening at 85°. Once recrystallized the substance formed the characteristically lozenge-shaped plates, m. p. 93–93.5°, not depressed on mixing with the methylation product XI.

***trans*-2-Benzal-9-methyldecalone-1 Dichloride.**—In one experiment the oily mixture of diastereoisomeric dichlorides from the addition of chlorine to XI partially solidified. One of the isomers separated readily on crystallization from methanol. A second isomer could be separated from the mother liquor, but was not further investigated. The more insoluble substance was recrystallized twice from ethyl acetate–methanol solution, forming a mixture of plates and short prismatic needles, m. p. 160–161°.

Anal. Calcd. for $C_{18}H_{22}OCl_2$: C, 66.46; H, 6.82. Found: C, 66.60; H, 6.57.

***trans*-1-Methyl-2-(γ-benzoylpropyl)-cyclohexane-1-carboxylic Acid (XV).**—In the preparation of XIII above, the portion which was not volatile with steam was worked up as described previously for the *cis* keto acid XIV. The crude keto acid XV amounted to 2.51 g. (26%), m. p. 160–165°. After sublimation at 160° (0.1 mm.) and recrystallization from alcohol, it formed colorless plates, m. p. 167–168° (softening at 162°).

Anal. Calcd. for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 75.06; H, 8.26.

The **oxime** of XV formed colorless prisms from methanol–petroleum ether (40–60°), m. p. 166–166.5°. The **semicarbazone** crystallized from methanol in colorless felted needles, m. p. 184–185°.

Anal. Calcd. for $C_{19}H_{27}O_3N_3$: C, 66.06; H, 7.88. Found: C, 66.30; H, 7.73.

The **methyl ester** of the keto acid XV was prepared by reaction with diazomethane. This derivative separated from chilled (ice–salt bath) methanol in small colorless plates, m. p. 42–43°, resolidifying as the temperature continued to rise and remelting at 46–47°.

Anal. Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.65; H, 8.53.

Dieckmann Cyclization of Keto Ester.—Following the procedure of Bachmann, Cole and Wilds[31] for the preparation of the methyl ether of 16-carbomethoxy-*dl*-equilenin, 1.0 g. of the above methyl ester was treated with sodium methoxide (from 0.20 g. of sodium) in 10 cc. of dry benzene by refluxing in an atmosphere of nitrogen for two hours. After acidification the organic layer was washed with water, sodium bicarbonate solution, and again with water. The benzene was evaporated, replaced by ether, and the mixture was shaken with a saturated solution of cupric acetate and allowed to stand for two days. The green copper enolate which precipitated amounted to 0.6 g., m. p. 230–234° dec. After solution in benzene and reprecipitation with ether, the material had the m. p. 235–238° dec. (*cf.* footnote[29]).

Summary

A method has been devised for introducing the angular methyl group into decalone-1. The process involves three steps: (1) protection of the reactive methylene group by condensation with benzaldehyde, (2) methylation of the resultant benzal derivative in which substitution has been shown to occur exclusively at the angular position, (3) removal of the benzal residue by conversion into the benzoyl group to give 2-benzoyl-9-methyldecalone-1, and alkaline cleavage of the latter into sodium benzoate and 9-methyldecalone-1.

The new method provides a convenient source of the previously known 9-methyldecalone-1, and has made possible the isolation and characterization of the hitherto unknown stereoisomeric 9-methyldecalone-1 (configuration probably *trans*).

The generality of the method has been supported by successful application to the formation of 2,2-dimethylcyclohexanone.

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[30] Microanalysis by Mr. E. Shelberg.

[31] Bachmann, Cole and Wilds, THIS JOURNAL, **62**, 824 (1940).