the basis of two experiments in which the polymerization yield was carefully determined, and because our brittle points agreed with those of Trommsdorff,[21] it is believed that the properties of our polymers were not greatly influenced by monomeric esters.

Summary

Higher *n*-alkyl acrylates having two to sixteen carbon atoms in the alkyl group were prepared in high yields by the alcoholysis of methyl acrylate. The monomeric esters were emulsion polymerized, and the coagulated polymers were examined briefly to determine the influence of chain length of the alkyl group upon the properties of the polymer. As the chain length of the alkyl group increased, the polymers became softer and tackier at room temperature (up to and including tetradecyl acrylate). The polymer of *n*-hexadecyl acrylate was a wax-like solid at room temperature but soft and tacky above 35°. As the molecular weights increased, the brittle points of the first eight polyalkyl acrylates became lower; beyond octyl acrylate, which had a brittle point of −65°, the brittle points became higher.

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[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

Some New Aspects of the Ortho Effect. Cyclic Ketones Related to Acetophenone

BY RICHARD G. KADESCH[1]

The failure of certain diortho-substituted acetophenones to react with hydroxylamine and other typical carbonyl reagents is well known. Feith and Davies[2] were unable to obtain an oxime from acetomesitylene or propiomesitylene and failure was likewise encountered by Claus and Foecking[3] with acetodurene and by Baum[4] with acetoisodurene and acetopentamethylbenzene. This inertness was also shown toward other carbonyl reagents such as hydrazine, phenylhydrazine and semicarbazide. However, the carbonyl group in acetomesitylene is not completely devoid of reactivity toward additive reagents, as on heating with hydroxylamine hydrochloride and alcohol in a sealed tube for six hours at 160° N-acetylmesidine was obtained.[2] The amide was undoubtedly produced by the Beckmann rearrangement of the oxime. The only typical carbonyl reaction displayed by acetomesitylene under normal conditions is reduction to mesitylmethylcarbinol or ethylmesitylene. A further abnormality of acetomesitylene was found[5] in its behavior toward the Grignard reagent to form a salt which regenerated the ketone on hydrolysis. This salt was shown[6] to be the enolate[7] of the ketone and its formation to be as follows

$$C_9H_{11}\overset{O}{\overset{\|}{C}}CH_3 + RMgX \longrightarrow C_9H_{11}C(OMgX)=CH_2 + RH$$

The inertness of diortho-substituted acetophenones toward carbonyl reagents was interpreted by the early workers as an additional example of hindrance to reaction due to the size of the ortho substituents in shielding the reacting group from the attacking reagent. This classical theory of steric hindrance,[8] due to Kehrmann and Victor Meyer, is inadequate in many cases—actually, the "ortho effect" is one of great complexity involving the simultaneous operation of several different factors.[8b] That the classical bulk effect may often be of secondary importance is shown by the many examples now known in which ortho substituents increase the rate of reaction.

The abnormal behavior of acetomesitylene toward the Grignard reagent was first explained[6] on the basis of steric hindrance to normal addition, thus allowing the competing enolization reaction sufficient time to occur. The mesityl group was believed neither to assist nor retard the enolization process.[9] In opposition to this latter view there have since been observed numerous instances in which the enol form of a mesityl ketone was formed more rapidly and was more stable than the enol of the corresponding phenyl ketone.[10]

The steric effects usually associated with diortho-substituted aromatic ketones are not shown by 4,7-dimethyl-α-indanone.[11] A survey of the

(1) Present address: Pittsburgh Plate Glass Co., Columbia Chemical Division, Barberton, Ohio.

(2) Feith and Davies, *Ber.*, **24**, 3546 (1891).

(3) Claus and Foecking, *ibid.*, **20**, 3097 (1887).

(4) Baum, *ibid.*, **28**, 3207 (1895).

(5) Klages, *ibid.*, **35**, 2635 (1902).

(6) Kohler, Stone and Fuson, THIS JOURNAL, **49**, 3181 (1927).

(7) The enolate shows reactions corresponding to either of the two structures having magnesium attached to oxygen or to carbon. The best representation of the structure involves a resonating anion partaking of structures containing the negative charge on the oxygen or the carbon atom. See Fuson, Fugate and Fisher, *ibid.*, **61**, 2362 (1939); Fuson, Fisher, Ullyot and Fugate, *J. Org. Chem.*, **4**, 111 (1939).

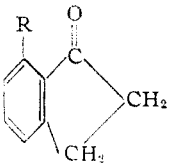
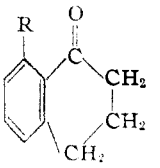
(8) (a) Stewart, "Stereochemistry," Longmans, Green and Co., New York, N. Y., 1907, pp. 314–444; (b) Vavon in Grignard, "Traité de Chimie Organique," Masson et Cie., Paris, 1936, Vol. 2, Part 2, pp. 851–876.

(9) Kohler and Baltzly, THIS JOURNAL, **54**, 4015 (1932).

(10) Kohler and Sonnichsen, *ibid.*, **60**, 2650 (1938); Kohler and Thompson, *ibid.*, **59**, 887 (1937); Kohler, Tishler and Potter, *ibid.*, **57**, 2517 (1935); Kohler and Potter, *ibid.*, **58**, 2166 (1936); Fuson, *et al.*, *ibid.*, **62**, 2962 (1940); **63**, 1500, 1679 (1941), and preceding papers; Zucker and Hammett, *ibid.*, **61**, 2779 (1939); Brown, Kharasch and Sprowls, *J. Org. Chem.*, **4**, 442 (1939).

(11) Moureu, *Bull. soc. chim.*, [3] **9**, 572 (1893); *Ann. chim.*, [7] **2**, 204 (1894); Cocroft, M.S. Dissertation, University of Chicago, 1940; Cocroft, *Proc. Iowa Acad. Sci.*, **48**, 245 (1941).

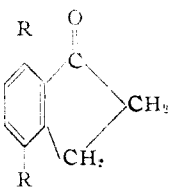
literature reveals numerous other instances of compounds of the types

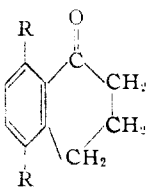



in which R may be methyl or some larger alkyl group, which form carbonyl derivatives such as oximes and semicarbazones in a normal manner.[12] No such compounds containing a 7-membered alicyclic ring have been described in the literature.

These cyclic ketones may be regarded as diortho-substituted acetophenone derivatives formally related to acetomesitylene in which the second ortho substituent has become a part of the alicyclic ring. Since the size of the ortho substituents present in these molecules is as great as those in acetomesitylene, other factors must be operating here which lead to an enhanced reactivity. It has been the purpose of the present work, therefore, to investigate the nature of the ortho effect in such cyclic ketones with the possibility that the knowledge gained might be applied in interpreting the ortho effect generally.

The behavior of a series of cyclic ketones of the type mentioned, in which the alicyclic ring is 5-, 6- or 7-membered, has been examined with the idea of determining the relation between the coplanarity of the carbonyl group with the aromatic nucleus and the observed steric effects. Thus, in α-indanone (I, R = H) and 4,7-dimethyl-α-indanone (I, R = CH_3) the carbonyl


I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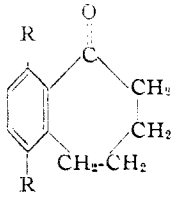

III

group must of necessity be coplanar with the benzene nucleus due to its incorporation into the rigid 5-membered alicyclic ring. In α-tetralone (II, R = H) and 5,8-dimethyl-α-tetralone (II, R = CH_3) the carbonyl group will, at the most, deviate only slightly from the coplanar position. In benzosuberone (III, R = H) and 6,9-dimethylbenzosuberone (III, R = CH_3) the steric requirements of the 7-membered alicyclic ring are such that the carbonyl group cannot attain the coplanar configuration. The relative positions in space of the 9-methyl group and the carbonyl group in 6,9-dimethylbenzosuberone are considerably different than is the case when the alicyclic ring is 5- or 6-membered. It was thought that 6,9-dimethylbenzosuberone, in which the steric relationships are more nearly like those in acetomesitylene, might also exhibit a large hindrance to carbonyl reactions in contrast to the 7-substituted α-indanones and 8-substituted α-tetralones. This has actually been found to be the case both for reactions with methylmagnesium iodide and with hydroxylamine.

The behavior of the cyclic ketones, and of some open chain ketones for purposes of comparison, toward methylmagnesium iodide has been studied

TABLE I

REACTIONS OF KETONES WITH METHYLMAGNESIUM IODIDE

Compound	Moles per mole of ketone[a] Active H	Addition
α-Indanone	0.12 (5)	0.97 (3)
4,7-Dimethyl-α-indanone	.21 (5)	.67 (5)
5,7-Dimethyl-α-indanone	.16 (6)	.66 (6)
4-Methyl-7-*i*-propyl-α-indanone	.22 (4)	.51 (4)
α-Tetralone	.17 (4)	.57 (4)
5,8-Dimethyl-α-tetralone	.17 (2)	.60 (2)
Benzosuberone	.25 (4)	.61 (4)
6,9-Dimethylbenzosuberone	1.01 (2)	.0 (2)
Acetophenone	0.09 (3)	.76 (2)
o-Methylacetophenone	.14 (2)	.58 (2)
2,4-Dimethylacetophenone	.19 (2)	.55 (2)
Acetodurene	.81 (1)	.00 (1)
Acetomesitylene	.73 (1)	..
α-Naphthyl methyl ketone	.06 (2)	0.74 (2)
β-Naphthyl methyl ketone	.15 (1)	1.17 (1)
1-Acetyl-2-methylnaphthalene	1.02 (2)	0.0 (2)

[a] Each value represents the average of several determinations, the figures in parentheses giving the number of runs which were made in determining this average.

TABLE II

OXIMATION OF CYCLIC AND OPEN CHAIN KETONES

Solvent: 75% ethanol, acetate buffer, temperature 0°C.

Compound	% Ketone reacted in hr. 0.5	1	2	4	7	10
α-Indanone	8	14	23	34	45	55
4,7-Dimethyl-α-indanone	0	0	1	1	2	3
5,7-Dimethyl-α-indanone	0	0	0	1	3	3
α-Tetralone	7	10	17	28	39	47
5,8-Dimethyl-α-tetralone	7	9	11	14	16	17
Benzosuberone	9	16	24	36	51	59
6,9-Dimethylbenzosuberone[a]	0	1	1	1	3	2
Acetophenone	20	31	45	62	75	82
o-Methylacetophenone	1	3	6	11	18	22
2,4-Dimethylacetophenone	1	2	3	10	16	22
Acetomesitylene	0	0	1	1	1	2
n-Butyrophenone	13	21	32	47	61	69
α-Naphthyl methyl ketone	5	11	17	28	38	46
β-Naphthyl methyl ketone	16	24	37	54	69	77
1-Acetyl-2-methylnaphthalene[a]	0	1	1	1	1	1

[a] In a separate experiment this ketone failed to yield an oxime or semicarbazone after nine hours at 95°.

(12) Smith and Prichard, THIS JOURNAL, **62**, 771, 779 (1940); Whittleston, *ibid.*, **59**, 825 (1937); Cook, Hewitt, Mayneord and Roe, *J. Chem. Soc.*, 1727 (1934); Carter and Slater, *ibid.*, 546 (1938); Barnett and Sanders, *ibid.*, 434 (1933); Harland and Robertson, *ibid.*, 937 (1939); Mayer, Phillipps, Rüppert and Schmitt, *Ber.*, **61B**, 1966 (1928); Schroeter, *ibid.*, **63B**, 1308 (1930); v. Auwers and Risse, *Ann.*, **502**, 282 (1933); Ruzicka, *et al.*, *Helv. Chim. Acta*, **16**, 268 (1933); **5**, 710 (1922); Smith and Spillane, THIS JOURNAL, **65**, 202 (1943).

by the use of a modified Zerewitinoff apparatus. The amounts of enolization (active hydrogen) and addition to the carbonyl group so determined are listed in Table I. Data on the reactivity of the same group of ketones toward hydroxylamine are given in Tables II and III.

TABLE III

OXIMATION OF CYCLIC KETONES

Solvent: 75% ethanol, acetate buffer: temperature, 7°C.

Compound	% Ketone reacted in hr. 5	10	25	51	100
4,7-Dimethyl-α-indanone	4	4	9	15	20
5,7-Dimethyl-α-indanone	4	5	8	12	16
5,8-Dimethyl-α-tetralone	13	16	19	25	33
6,9-Dimethylbenzosuberone	3	4	7	5	4

Discussion of Results

The quantitative data concerning the reactions of the 7-substituted α-indanones and 8-substituted α-tetralones with methylmagnesium iodide are in agreement with the qualitative information already outlined in indicating the lack of any great steric hindrance in these compounds. Benzosuberone, which contains a 7-membered ring, showed about the same amount of enolization and addition as did the α-indanones and α-tetralones. The presence of an ortho methyl group in 6,9-dimethylbenzosuberone, in contrast to its effect in α-indanone or α-tetralone, leads to a typical highly hindered compound of the acetomesitylene type.

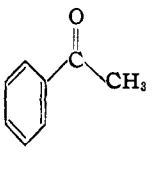
The results for the reactions of the cyclic ketones with hydroxylamine were qualitatively the same as for reactions with methylmagnesium iodide, although the differences were not as striking. The differences in reactivity between 4,7- or 5,7-dimethyl - α - indanone and 6,9-dimethylbenzosuberone, for example, did not appear after ten hours at 0°. A reaction time of one hundred hours at 7° was necessary before 6,9-dimethylbenzosuberone remained alone as a highly hindered compound.

From a comparison of the reactivities of the cyclic and open chain ketones toward methylmagnesium iodide and hydroxylamine, certain general features become apparent: (1) The simple cyclic ketones (α-indanone, α-tetralone, benzosuberone) are very similar to acetophenone and *n*-butyrophenone; (2) 4,7- and 5,7-dimethyl-α-indanone and especially 5,8-dimethyl-α-tetralone are to be classed with *o*-methylacetophenone and 2,4-dimethylacetophenone; (3) 6,9-dimethylbenzosuberone is similiar to acetomesitylene, acetodurene, etc. In other words, the introduction of an ortho methyl group into one of the cyclic ketones has about the same effect as in acetophenone except when the alicyclic ring is 7-membered.[13]

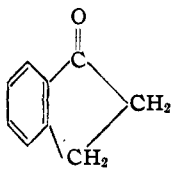
(13) A similar case in which a 7-membered ring compound (N-methyltetrahydro-homo-quinoline) shows a unique behavior is given by (a) Brown, Widiger and Letang, THIS JOURNAL, **61**, 2597 (1939); and (b) Brown and Fried, *ibid.*, **65**, 1841 (1943).

These generalizations may be explained by considering the orientations and configurations prevailing in these molecules. As a result, certain factors hitherto not considered in this connection, are revealed as playing a part in the phenomenon of the ortho effect in aromatic ketones.

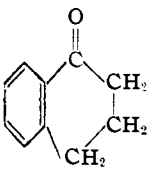
First, it may be considered very probable that the acetophenone molecule is predominantly coplanar, the resonance contributions of the quinoid structures[14] being sufficient to prevent free rotation of the acetyl group to a large extent. Acetophenone (IV), then, exists in a configuration



IV



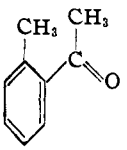
V



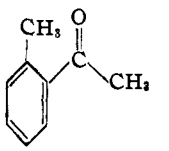
VI

like that of α-indanone (V), which is absolutely coplanar, or α-tetralone (VI), which probably may deviate only slightly from coplanarity. This is supported by the fact that the absorption band at about 2800 Å. corresponding to quinoidal resonance has about the same intensity in all three ketones.[15] The fact that all three show about the same reactivity means that the ortho methylene group (earlier "formally" regarded as an ortho substituent) has no appreciable retarding effect on the carbonyl group.

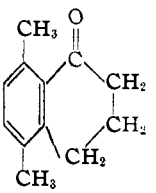
In *o*-methylacetophenone there are two coplanar configurations which we may write. Structure VIII is to be preferred since it has been shown



VII



VIII



IX

from dipole moment data[16] that the hindrance between ortho methyl and acetylmethyl involved in VII is prohibitive. That *o*-methylacetophenone is actually coplanar, as represented by VIII, like acetophenone is indicated by the finding that the absorption spectra of acetophenone and 2,4-dimethylacetophenone are almost identical.[17] Further, the spectra of *o*-methylpropiophenone, α-indanone and α-tetralone have all been found to be very similiar.[15] In VIII the spacial relationship between the ortho methyl and carbonyl groups is like that existing in 4,7- and 5,7-dimethyl-α-indanones or in 5,8-dimethyl-α-tetralone (IX). This gives a logical explanation for the similiar steric effect of the ortho methyl group

(14) Pauling, "Nature of the Chemical Bond," 1st ed., Cornell University Press, 1939, p. 131, 143.

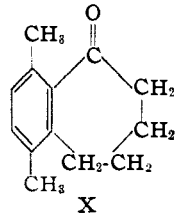
(15) Ramart-Lucas and Hoch, *Bull. soc. chim.*, [5] **2**, 327 (1935).

(16) Kadesch and Weller, THIS JOURNAL, **63**, 1310 (1941).

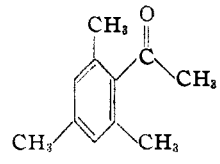
(17) O'Shaughnessy and Rodebush, *ibid.*, **62**, 2906 (1940).

in the two cases. It is not necessary to postulate a chelation similar to that suggested for *o*-toluic acid[18] to account for the stabilization of structure VIII. Further, it can be seen why the pseudo ortho substituent in α-indanone does not act as a genuine ortho methyl group to hinder reaction. The configuration in each case is very different; in α-indanone it corresponds to VII but the genuine monoortho-substituted ketone is like VIII.

When the alicyclic ring is 7-membered, as in 6,9-dimethylbenzosuberone (X), the configuration is no longer like that of VIII and IX but is like that of acetomesitylene (XI). That is, the



X



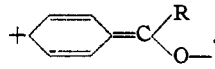
XI

carbonyl group is not coplanar with the benzene ring in either case. From a scale model it can be seen that the steric requirements of the 7-membered ring prevent X from being coplanar. The non-coplanarity of XI has been demonstrated from dipole moment measurements,[16] the absorption spectrum[17] and the Raman spectrum.[19]

It appears logical to conclude that the non-coplanarity of X underlies its behavior as a highly hindered ketone, since it is this feature which distinguishes it from IX and the 7-substituted-α-indanones. This non-coplanarity enables the 9-methyl group and the ortho-methylene group to be sterically much more effective than they would be otherwise. The carbonyl carbon atom is no longer exposed to attack[20] from the side (along a line perpendicular to the benzene ring) as in the completely planar molecules, but must now be attacked along a line more nearly blocked by the 9-methyl and ortho-methylene groups.[21] Further, it is possible that the mobile nature of X leads to a lower entropy of activation compared to relatively rigid molecules. The significance of this factor in the carbonyl reactions of rigid and mobile ketones has been pointed out and discussed by Price and Hammett.[22]

The extension of this concept to acetomesitylene leads to a more precise interpretation of the nature of the steric hindrance in this ketone. It seems probable that the hindrance is classical in the sense that it depends on the sheer bulk of the ortho substituents in shielding the carbonyl group from attack. The ortho groups are enabled to exert their maximum effect because they, at the same time, force the acetyl group out of the plane of the benzene ring. This forces the reagent to attack along a line more nearly blocked by the ortho methyl groups. Thus, the proximity of the ortho groups is not sufficient in itself to establish a high degree of steric hindrance, but orientation with respect to the reacting group is of importance as well. Since one ortho methyl group is not sufficient to force the acetyl group from a coplanar position, we see why its hindering effect is smaller than that resulting from the introduction of a second ortho methyl group.

Although no quantitative data are available for mesityl aldehyde, it is likely that its ability to react[23] with typical carbonyl reagents is due in considerable part to the fact that the —CHO group is too small[16,19] to be blocked from the coplanar position by the two ortho methyl groups. The coplanar position allows attack on the carbonyl carbon atom from the side and is the position in which the ortho methyl groups are least effective sterically.

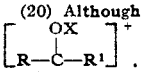
The non-coplanarity of X and XI may also be connected with the importance of quinoidal resonance involving structures of the type  . Since such structures must be completely coplanar,[16,17,19] they will contribute little to the state of X and XI while they will be of maximum importance in I (R = CH_3) and IX. This factor alone should operate to make X more reactive than the corresponding planar ketones since it is not necessary to overcome the resonance stabilization to form the transition complex.[22] Obviously this factor is greatly overshadowed by those considered above.

The inertness of X as compared to I (R = CH_3), IX and 5,7-dimethyl-α-indanone supplements the evidence[24] indicating that the ortho effect in hindered ketones of the acetomesitylene type chiefly involves a bulk effect. The electrostatic influence of the methyl substituents in slowing reaction is of secondary importance.

The behavior of 1-acetyl-2-methylnaphthalene as a highly hindered ketone shows that the CH group of the fused aromatic ring, when in the ortho position, acts in the same way as a *bona fide* ortho group in retarding reaction.[25] Accord-

(18) Dippy, Evans, Gordon, Lewis and Watson, *J. Chem. Soc.*, 1421 (1937).

(19) Saunders, Murray and Cleveland, THIS JOURNAL, **63**, 3121 (1941).

(20) Although the actual attack is made on an entity.  , *cf.* Hammett, "Physical Organic Chemistry," McGraw-Hill Book Company, New York, N. Y., 1940, p. 333; John R. Johnson in Gilman's, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1943, 2nd ed., p. 1880) which contains no carbonyl group as such, this reasoning is none the less applicable.

(21) During the preparation of this manuscript a paper appeared (ref. 13b) in which the ortho effect in quaternary salt formation from aromatic tertiary amines was regarded as operating in a closely similar manner.

(22) Price and Hammett, THIS JOURNAL, **63**, 2387 (1941).

(23) Gattermann, *Ann.*, **347**, 374 (1906).

(24) Baker and Tweed, *J. Chem. Soc.*, 796 (1941); Brown, Kharasch and Sprowls, *J. Org. Chem.*, **4**, 442 (1939); Zucker and Hammett, THIS JOURNAL, **61**, 2779 (1939).

(25) This behavior of the CH group of an adjoining ring has long been known in carboxylic acids and their esters; Bergmann and Hirshberg, *J. Chem. Soc.*, 331 (1936); V. Meyer, *Ber.*, **27**, 1580 (1894); **28**, 182, 1262 (1895); Mayer and Sieglitz, *ibid.*, **55**, 1851 (1922).

ing to the idea developed above, the ortho CH group is large enough to block the methyl of the acetyl group, preventing the latter from attaining the coplanar position. Similar results were obtained by Adams and Binder[25a] who found that 1-acetyl- and 1-propionyl-2-methylnaphthalenes reacted with methylmagnesium iodide to give the iodomagnesium enolates of the ketones rather than the normal carbonyl addition products. Contrary results exist in the report[25b] of the preparation of the oximes and semicarbazones of both 1-propionyl- and 1-acetyl-2,6-dimethylnaphthalene. Since the conditions employed for the formation of these derivatives are unknown to the writer, it cannot be said whether or not this is really irreconcilable with the results of Adams and Binder and those of the present paper.

Experimental

Treatment of Ketones with Methylmagnesium Iodide.—The ketones were examined in the Grignard Machine[26] to determine both the active hydrogen and addition to carbonyl. The procedure[26] was modified so that a reaction period of seven minutes was used and seven minutes was allowed for the decomposition of the unreacted Grignard reagent by aniline. The reactions were carried out at room temperature (24–28°) using 0.4–0.5 *N* methylmagnesium iodide in dibutyl ether. About 0.0001 mole (15–25 mg.) of the ketone was dissolved in 0.8 cc. of isoamyl ether and 0.4–0.5 cc. of the Grignard reagent run in. The blank value was generally about 0.25 cc. of methane.

Oxime Formation.—The determinations of the extent of reaction of the ketones with hydroxylamine were made essentially in the manner of Ruzicka and Buijs.[27] The reaction medium was 75% ethanol and the initial concentrations of ketone and hydroxylamine were approximately 0.05 *M*. The ketone (0.00095 mole) was weighed into a 50-cc. Erlenmeyer flask, 0.00098 mole of hydroxylamine hydrochloride (crystallized from alcohol) in ethanol was added from a buret, the volume was made up to 50 cc. with ethanol and 5 cc. of an aqueous acetate buffer (0.6 *M* in sodium acetate and in acetic acid) was added from a pipet. At the desired intervals a 2-cc. portion was withdrawn and run into 50 cc. of aqueous phosphate buffer for titration. Ten cc. of 0.03 *N* iodine was added and back-titration accomplished with 0.02 *N* sodium thiosulfate.

Acetophenone Derivatives.—Acetophenone, acetomesitylene and acetodurene were the same as materials used previously.[16]

o-Methylacetophenone was prepared by adding 35 g. of *o*-toluoyl chloride (b. p. 95–98° (18 mm.)) to a cooled toluene–ethyl acetate solution of methylzinc iodide (from 36 g. of methyl iodide)[28] according to the method of Baker.[29] Eighteen grams (yield 60%) of the ketone was obtained and distilled twice *in vacuo* from a Claisen flask, b. p. 107–108° (25 mm.).

2,4-Dimethylacetophenone, prepared in 86% yield from acetic anhydride and *m*-xylene by the method of Noller and Adams,[30] was distilled twice *in vacuo* from a Claisen flask, b. p. 115° (18 mm.), 122–123° (23 mm.).

n-Butyrophenone was prepared from *n*-butyryl chloride and benzene in the presence of aluminum chloride and distilled twice *in vacuo* from a modified Claisen flask, b. p. 122–124° (26 mm.).

α-Indanone (V).—Eastman Kodak Co. hydrocinnamic acid (30 g.) was cyclized through the acid chloride by the procedure given for the preparation of α-tetralone from γ-phenylbutyric acid.[31] The crude product (24.5 g.) was distilled *in vacuo* and the material collected at 118–126° (13 mm.) was crystallized from ligroin, m. p. 40–41.5°.

4,7-Dimethyl-α-indanone (I, R = CH_3).—It was prepared according to the procedure of Mayer and Müller[32] by condensing β-chloropropionyl chloride with *p*-xylene. The β-chloropropionyl chloride was obtained by the method of Kharasch and Brown.[33] The chloro ketone so obtained was cyclized by heating in concd. sulfuric acid and the product was recrystallized repeatedly from aqueous methanol, m. p. 77–78°.

3,5-Dimethylbenzylmalonic Acid.—First, ω-bromomesitylene was prepared by the bromination of mesitylene.[34] In addition to maintaining the hydrocarbon at 135–155°, side-chain bromination was further favored by passing bromine vapor, well diluted with air, slowly into the reaction mixture. This was done by passing air through the bromine, vaporizing it slowly, and thence into the bottom of the hot reaction mixture through a capillary tube. In this way 140 g. of bromine was passed into 109 g. of mesitylene during 5.5 hours. The mixture was distilled *in vacuo* and the ω-bromomesitylene collected at 156–170° (90 mm.). The yield was 86 g. (49%).

Eighty-six grams of ω-bromomesitylene was added with stirring to 75 g. of malonic ester and 10 g. of sodium in 400 cc. of absolute ethanol during one-half hour at 60–70° and the stirring continued one-half hour longer. The mixture was poured into water, the oil separated, washed with water, the aqueous layer washed with ether and the combined extracts dried over anhydrous sodium sulfate. Distillation *in vacuo* yielded 37 g. of 3,5-dimethylbenzyl malonic ester at 198–205° (24 mm.). Hydrolysis to the acid was effected by barium hydroxide. A portion was crystallized from benzene, m. p. 147–148°.

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35; neut. eq., 111. Found: C, 64.61; H, 6.35; neut. eq., 114.

3,5-Dimethylbenzylacetic Acid.—The 3,5-dimethylbenzylmalonic acid was decarboxylated by heating for one-half hour at 175–185°. Twenty-two grams (96% yield from 3,5-dimethylbenzylmalonic ester) of 3,5-dimethylbenzylacetic acid was collected at 168–178° (13 mm.) by distillation of the oil. A portion was crystallized from benzene, m. p. 45–46.5°.

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92; neut. eq., 178. Found: C, 73.61; H, 7.65; neut. eq., 189, 184.

5,7-Dimethyl-α-indanone.—Cyclization of 15 g. of 3,5-dimethylbenzylacetic acid was effected through the acid chloride[31] to give 8.3 g. (62% yield) of crude 5,7-dimethyl-α-indanone after concentration of the combined extracts. Repeated recrystallization from aqueous methanol gave white needles, m. p. 76–77°. A mixed melting point determination with 4,7-dimethyl-α-indanone gave m. p. 46–52°.

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 81.85; H, 7.03.

2-Methyl-5-isopropylbenzylmalonic Acid.—The chloromethylation of *p*-cymene as directed by Whittleston[35] yielded 59% of 2-chloromethyl-*p*-cymene distilling at 118–121° (14 mm.).

Anal. Calcd. for $C_{11}H_{15}Cl$: Cl, 19.43. Found: Cl, 18.60.

The condensation of 44 g. of 2-chloromethyl-*p*-cymene with a 50% excess of sodiomalonic ester yielded 46.5 g. (63% yield) of 2-methyl-5-isopropylbenzylmalonic ester, b. p. 186–196° (13 mm.). Hydrolysis of 15.5 g. of the ester with barium hydroxide gave 2-methyl-5-isopropylbenzyl-

(25a) Adams and Binder, THIS JOURNAL, **63**, 2773 (1941).

(25b) Dziewonski, Stec and Zagala, *Chem. Abs.*, **33**, 1713 (1939).

(26) Niederl and Niederl, "Micromethods of Quantitative Organic Elementary Analysis," John Wiley and Sons, New York, N. Y., 1938, pp. 206–213.

(27) Ruzicka and Buijs, *Helv. Chim. Acta*, **15**, 8 (1932).

(28) Houben, "Die Methoden der organischen Chemie," 2nd ed., Vol. IV, G. Thieme, Leipzig, 1924, p. 899.

(29) Baker, *J. Chem. Soc.*, 447 (1938).

(30) Noller and Adams, THIS JOURNAL, **46**, 1889 (1924).

(31) "Organic Syntheses," Vol. XV, 1935, p. 77.

(32) Mayer and Müller, *Ber.*, **60B**, 2278 (1927).

(33) Kharasch and Brown, THIS JOURNAL, **62**, 925 (1940).

(34) Wispek, *Ber.*, **16**, 1577 (1883); see also Weiler, *ibid.*, **33**, 334 (1900).

(35) Whittleston, THIS JOURNAL, **59**, 825 (1937).

malonic acid, m. p. 163° (from benzene). This acid has been prepared as an intermediate twice previously but never isolated.[35,36]

Anal. Calcd. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25; neut. eq., 125. Found: C, 67.30; H, 7.41; neut. eq., 121.

2-Methyl-5-isopropylbenzylacetic Acid.—The decarboxylation of 2-methyl-5-isopropylbenzylmalonic acid by heating at 190–200° for thirty minutes gave 2-methyl-5-isopropylbenzylacetic acid which was distilled *in vacuo*, b. p. 171–181° (13 mm.), m. p. 83–83.5° (softens at 69°). This acid has been prepared previously but was not analyzed.[35,36]

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79; neut. eq., 206. Found: C, 75.26; H, 8.45; neut. eq., 202.

4-Methyl-7-isopropyl-α-indanone.—The 2-methyl-5-isopropylbenzylacetic acid was cyclized through its acid chloride[31] to give 3.5 g. (37% yield from 2-methyl-5-isopropylbenzylmalonic ester) of 4-methyl-7-isopropyl-α-indanone. Crystallization from aqueous methanol yielded almost colorless, pale orange-yellow needles, m. p. 107°.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.51; H, 8.86.

α-Tetralone (VI) was prepared by the oxidation of tetralin by air.[37] The product was fractionated carefully *in vacuo* using a good column and the material collected at 76.0–77.0° (1 mm.) used.

5,8-Dimethyl-α-tetralone (IX).—β-(2,5-Dimethylbenzoyl)-propionic acid was prepared by the Friedel and Crafts reaction of succinic anhydride with *p*-xylene.[38] The crude acid (53.5 g.) was reduced by the Clemmensen method[39] to yield 46 g. of γ-(2,5-dimethylphenyl)-butyric acid. All of this acid was cyclized by heating in 85% sulfuric acid[40] to give, after distillation, 15.5 g. of 5,8-dimethyl-α-tetralone, light yellow oil, b. p. 172–174° (25 mm.). Four crystallizations from ligroin gave a colorless product, m. p. 31.5–32.5°, $n^{34}D$ 1.5626, d^{34}_4 1.0665, M_D calcd. 51.82, M_D observed 53.03.

Benzosuberone (III, R = H).—Cinnamylideneacetic acid was obtained in 27% yield by the condensation of cinnamaldehyde with malonic acid.[41] It was recrystallized twice from alcohol, m. p. 160–164°, and hydrogenated[42] over colloidal palladium catalyst. The resulting δ-phenylvaleric acid was recrystallized from ligroin, m. p. 56–58°, and 13 g. was cyclized by way of the acid chloride.[43] The ring closure proceeded with difficulty and was accompanied by considerable tar formation. The benzosuberone was fractionated twice *in vacuo* from a modified Claisen flask. The material collected at 141.5–143° (14 mm.) weighed 3.1 g. (27% yield) and was colorless. It became colored on standing; d^{20}_4 1.0827, $n^{20}D$ 1.5636; M_D calcd. 47.21, M_D observed 48.10.

β-2,5-Dimethylbenzoylethylmalonic Acid.—ω-Chloro-2,5-dimethylpropiophenone was prepared by the condensation of β-chloropropionyl chloride with *p*-xylene.[32] Eighty-six grams of the chloro ketone was added with stirring during fifty minutes to 19 g. of sodium and 148 g. of malonic ester in 550 cc. of absolute ethanol at about 75° and the stirring continued for three hours longer. On cooling, the mixture was poured into water, the oil separated, the aqueous layer extracted with ether and the combined extracts dried over anhydrous sodium sulfate. The β-2,5-dimethylbenzoylethylmalonic ester obtained was found to boil at 215–218° (15 mm.) with considerable decomposition. Consequently, the crude ester, obtained after removal of everything boiling up to 215° at 15 mm., was treated directly with barium hydroxide. The resulting β-2,5-dimethylbenzoylethylmalonic acid was an oil which could be crystallized from benzene or by cooling. A portion was crystallized five times from benzene to give colorless needles with m. p. 117–118° (dec.).

Anal. Calcd. for $C_{14}H_{16}O_5$: C, 63.62; H, 6.10; neut. eq., 132. Found: C, 63.84; H, 6.06; neut. eq., 127.

γ-(2,5-Dimethylbenzoyl)-butyric Acid.—β-2,5-Dimethylbenzoylethylmalonic acid was decarboxylated by heating at 170–190° for forty-five minutes. The γ-(2,5-dimethylbenzoyl)-butyric acid obtained was distilled *in vacuo* and 42 g. (63% yield based on β-chloropropionyl chloride) of light yellow oil collected which solidified in the receiver, b. p. 170–180° (1 mm.). Colorless needles were obtained by crystallizing once from aqueous methanol and four times from ligroin, m. p. 72–73°.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32; neut. eq., 220. Found: C, 71.11; H, 7.34; neut. eq., 209.

The acid was also prepared from glutaryl chloride and *p*-xylene by the method of Borsche,[44] m. p. 71–72.5°. A mixed melting point with the acid from the decarboxylation of β-2,5-dimethylbenzoylethylmalonic acid gave m. p. 71–73°.

δ-(2,5-Dimethylphenyl)-valeric Acid.—Forty grams of γ-(2,5-dimethylbenzoyl)-butyric acid was reduced by the Clemmensen method.[39] Distillation of the product *in vacuo* gave 26.5 g. of a thick, almost colorless oil with a bluish tinge, b. p. 155–167° (1 mm.), which crystallized after standing one day. It crystallizes from low-boiling ligroin in star-shaped clusters of colorless needles, m. p. 36.5–37.5° (after three crystallizations).

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.70; H, 8.80; neut, eq., 206. Found: C, 75.88; H, 8.78; neut. eq., 196.

6,9-Dimethylbenzosuberone (X).—The acid chloride obtained from 22.5 g. of δ-(2,5-dimethylphenyl)-valeric acid by treatment with thionyl chloride was dissolved in 200 cc. of carbon disulfide, cooled in ice and 17 g. of aluminum chloride added during one hour with stirring.[42] The reaction seemed to proceed more readily and with less tar formation than the corresponding ring closure of δ-phenylvaleric acid. After allowing the mixture to stand for sixteen hours protected by a calcium chloride tube, it was decomposed by ice and acid. The extracts were made alkaline with sodium carbonate and steam distilled. The steam distillate was extracted with benzene and 8.5 g. (41% yield) of 6,9-dimethylbenzosuberone obtained by distilling *in vacuo* from a Claisen flask. Three distillations gave an almost colorless oil with a light, sweet odor, b. p. 121–131° (1 mm.), $n^{20}D$ 1.5507, d^{20}_4 1.0475, M_D calcd. 56.44, M_D observed 57.32.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.11; H, 8.63.

On standing, the material took on a light yellow color, a behavior also shown by benzosuberone. 6,9-Dimethylbenzosuberone failed to form an oxime when heated with hydroxylamine hydrochloride and sodium acetate in aqueous alcohol for twenty-three hours at 60° or for nine hours in a sealed flask at 95°. It also failed to form a semicarbazone when heated with semicarbazide hydrochloride and sodium acetate in aqueous alcohol for nine hours in a sealed flask at 95°.

α-Naphthyl Methyl Ketone.—It was prepared by the method of Pfau and Ofner[45] by the reaction of naphthalene with acetyl chloride in carbon disulfide, the solvent which yields the highest proportion of the α-ketone. The product was distilled *in vacuo*, b. p. 172–173° (18 mm.), and the α-isomer isolated as the picrate. The pure, colorless α-naphthyl methyl ketone was obtained by decomposing the picrate and was distilled three times *in vacuo* from a Claisen flask, b. p. 163–164° (14 mm.), $n^{20}D$ 1.6276.

β-Naphthyl Methyl Ketone.—This was obtained from the Eastman Kodak Company and used without further purification.

1-Acetyl-2-methylnaphthalene.—First, fifty-three grams of 2-methylnaphthalene was brominated in the dark in

(36) Rapson and Short, *J. Chem. Soc.*, 128 (1933).
(37) "Organic Syntheses," Vol. XX, 1940, p. 94.
(38) *Ibid.*, Vol. XIII, 1933, p. 12; Vol. XV, 1935, p. 92.
(39) *Ibid.*, Vol. XV, 1935, p. 64.
(40) Barnett and Sanders, *J. Chem. Soc.*, 434 (1933).
(41) Hinrichsen and Triepel, *Ann.*, **336**, 197 (1904).
(42) Borsche, *Ber.*, **45**, 621 (1912).
(43) Borsche and Roth, *ibid.*, **54**, 174 (1921).
(44) Borsche, *ibid.*, **52**, 2079 (1919).
(45) Pfau and Ofner, *Helv. Chim. Acta*, **9**, 669 (1926).

carbon disulfide[46] to yield 71 g. of 1-bromo-2-methylnaphthalene which was distilled twice *in vacuo*, b. p. 152–158° (15 mm.).

It was attempted to prepare 1-acetyl-2-methylnaphthalene by the addition of acetyl chloride to the Grignard reagent from 1-bromo-2-methylnaphthalene in the manner found by Kohler and Blanchard[47] to be successful for the preparation of 2,4,6-triphenylacetophenone. The only products were 2-methylnaphthalene (49%) and 1-bromo-2-methylnaphthalene (33%). When, instead, the Grignard reagent was added to acetyl chloride the same two products were obtained, 1-bromo-2-methylnaphthalene predominating in the ratio of 1.4–1. In addition, density measurements showed that the product contained a maximum of 10% of 1-acetyl-2-methylnaphthalene. This behavior of 2-methyl-1-naphthylmagnesium bromide is very similar to that of the Grignard reagents of other sterically hindered aryl bromides. It was found[48] that the addition of acetyl chloride to the Grignard reagent of bromomesitylene or bromopentamethylbenzene yielded none of the methyl ketone while the addition of the Grignard reagent of bromopentamethylbenzene to acetyl chloride yielded only 6% of acetopentamethylbenzene.

Another method involving reaction between 2-methyl-1-naphthoyl chloride and methylmagnesium iodide proved successful. The Grignard reagent[46] was prepared from 41 g. of 1-bromo-2-methylnaphthalene, the ether solution diluted with dry benzene and carbon dioxide passed in for five and one-half hours. Solid carbon dioxide was then added to complete the reaction and on working up the mixture 24 g. of 2-methyl-1-naphthoic acid was obtained. The acid was treated with thionyl chloride and converted to the acid chloride, b. p. 115–120° (1–2 mm.). 2-Methyl-1-naphthoyl chloride (15.2 g.) in 50 cc. of ether was added dropwise with stirring during ninety minutes to methylmagnesium iodide (from 42 g. of methyl iodide) in 200 cc. of ether. The stirring was continued for thirty minutes longer at the boiling point. On working up the mixture 11.2 g. (82% yield) of 1-acetyl-2-methylnaphthalene was obtained and distilled twice *in vacuo*, b. p. 122–126° (1 mm.), $n^{20}D$ 1.6040, d^{20}_4 1.0842. M_D calcd. 55.51, M_D observed 58.44.[49]

Anal. Calcd. for $C_{14}H_{12}O$: C, 84.75; H, 6.57. Found: C, 86.11, 85.10; H, 7.32, 6.98.

1-Acetyl-2-methylnaphthalene failed to form an oxime when heated with hydroxylamine hydrochloride and sodium acetate in aqueous alcohol for twenty-three hours at 60° or for nine hours in a sealed flask at 95°. It also failed to form a semicarbazone when heated with semicarbazide hydrochloride and sodium acetate in aqueous alcohol for nine hours in a sealed flask at 95°.

Benzal-1-acetyl-2-methylnaphthalene.—1-Acetyl-2-methylnaphthalene and benzaldehyde were condensed in the manner employed for the preparation of benzal-2,4,6-triethylacetophenone.[50] After thirty hours of shaking, yellow crystals were obtained which were crystallized from ethanol, m. p. 136.5–137.5°.

Anal. Calcd. for $C_{20}H_{16}O$: C, 88.24; H, 5.88. Found: C, 88.37; H, 6.04.

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Summary

1. 6,9-Dimethylbenzosuberone, which contains a 7-membered alicyclic ring, has been shown to be a highly hindered ketone of the acetomesitylene type in contrast to the corresponding 5- and 6-membered ring compounds, 4,7-dimethyl-α-indanone and 5,8-dimethyl-α-tetralone.

2. A theory has been proposed to account for the inertness of 6,9-dimethylbenzosuberone toward additive reagents. The low reactivity is believed to arise from the fact that the carbonyl group is forced out of the plane of the benzene ring because of its incorporation into the 7-membered alicyclic ring. This non-coplanarity (which is not present to any important degree in the corresponding 5- and 6-membered ring compounds) forces any attacking reagent to approach the carbonyl carbon atom along a line more nearly blocked by the ortho groups. The theory has been extended to explain more precisely the nature of the steric effects operating in acetomesitylene. It also offers a possible explanation of the absence of strong steric effects in mesityl aldehyde. Thus, the proximity of ortho groups is a necessary condition for the operation of strong shielding effects in retarding reaction but not a sufficient one. An additional factor of importance is the orientation of the ortho groups with respect to the carbonyl group.

3. 1-Acetyl-2-methylnaphthalene was found to be a highly hindered ketone showing that the CH group of the adjoining nucleus is effective sterically as in the corresponding carboxylic acids and their esters.

4. Nine new compounds, not previously described in the literature, have been prepared.

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(46) Mayer and Sieglitz, *Ber.*, **55**, 1851 (1922).

(47) Kohler and Blanchard, THIS JOURNAL, **57**, 370 (1935).

(48) Smith, Webster and Guss, *ibid.*, **59**, 1078 (1937).

(49) After this work was completed (June, 1941) there was reported the preparation of 1-acetyl-2-methylnaphthalene by the same series of reactions, Adams and Binder, *ibid.*, **63**, 2773 (1941). These authors obtained the ketone in 89% yield with b. p. 125–130° (3–4 mm.), $n^{30}D$ 1.6037, d^{30}_4 1.084.

(50) Fuson and Corse, *ibid.*, **60**, 2063 (1938).