[Contribution from the Department of Chemistry of the University of Oregon]

The Reformatsky Reaction in Syntheses of ω,ω-Diarylalkanoic Acids and Related Compounds[1,2]

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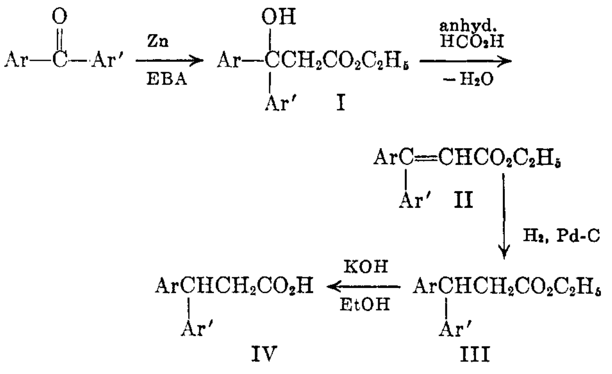
By the sequence of reactions illustrated in Scheme II benzophenone was condensed (Reformatsky reaction) with methyl γ-bromocrotonate (MBC) and thence converted to δ,δ-diphenylvaleric acid (VII) and 9-phenylbenzosuber-5-one (VIII). For structural proof, VIII was reduced to 5-phenylbenzosuberan, identical in infrared spectrum with an authentic sample of this compound prepared from benzosuber-5-one.

3-Methoxy-; 4-methoxy-; 4,4′-dimethoxy-; and 3,4,5,3′,4′-pentamethoxybenzophenones readily underwent Reformatsky reaction with ethyl bromoacetate (EBA) but failed to react significantly with MBC. The hydroxyesters resulting from the reaction with EBA were transformed into β,β-diarylpropionic acids by the general method of Scheme I. For the series starting with 4,4′-dimethoxybenzophenone, the intermediate compound ethyl β,β-bis(4-methoxyphenyl)propionate was also converted to the corresponding δ,δ-diarylvaleric acid XV via Scheme III.

Despite widespread usage of the Reformatsky reaction for condensations involving aldehydes, cycloalkanones, dialkyl ketones, and alkyl aryl ketones, there has been very little investigation of this reaction employing diaryl ketones. In this paper we report the results of our experiments on the Reformatsky reaction between (*a*) benzophenone and various methoxy-substituted benzophenones and (*b*) the bromoesters ethyl bromoacetate (EBA) and methyl γ-bromocrotonate (MBC). An attempt is made to correlate these data with others reported in the literature.

The elegant method of Gardner[4] for production of 4-methoxybenzophenone through benzoylation of anisole by means of benzoic acid in the presence of polyphosphoric acid was repeated and extended to the syntheses of 4,4′-dimethoxybenzophenone (82% yield) and 3,4,5,3′,4′-pentamethoxybenzophenone (60% yield from veratrole and trimethylgallic acid). These ketones, as well as 3-methoxybenzophenone, were treated according to Scheme I.



Scheme I

The Reformatsky condensation with EBA (used in excess) proceeded readily in refluxing benzene in every case. The intermediate hydroxyesters I were successively dehydrated to the unsaturated esters II in good yield by treatment with anhydrous formic acid, hydrogenated to the esters III (presumably in quantitative yield) at low pressure using 30% palladium-charcoal as catalyst and glacial acetic acid as solvent, and hydrolyzed to the acids IV in essentially quantitative yield *via* alcoholic potassium hydroxide. Examination of Table I shows that the yields of hydroxyesters are notably higher in the cases of benzophenone and 3-methoxybenzophenone than they are for the other ketones listed. Such a relationship is consistent with the point of view that the Reformatsky reaction, like the addition of a Grignard reagent to a carbon-oxygen double bond, occurs *via* nucleophilic attack of the halogen-bearing carbon onto the carbonyl carbon. Such attack is hindered by an electron-donating ortho or para methoxy group but is facilitated (if

TABLE I

Percentage Yields for Reformatsky Reaction of Methoxy-Substituted Benzophenones With Ethyl α-Bromoacetate

Position(s) of Methoxy Substituent(s)	Yield of Hydroxyester (I), %	Over-all Yield[a] of Diarylpropionic Acid (IV), %
None	*ca.* 95[b]	. .
2-	60–70[c]	. .
3-	95–100[d]	88
4-	78	67
4,4′-	69	56
3,4,3′,4′-	*ca.* 81[e]	. . .[f]
3,4,5,4′-	*ca.* 70[e]	. . .[g]
3,4,5,3′,4′-	. . .[h]	59

[a] From ketone and ethyl α-bromoacetate. [b] H. Rupe and E. Busolt, *Ber.*, **40,** 4537 (1907). The percentage yield given in ref. 5, p. 26 appears to be in error. [c] R. Stoermer and E. Friderici, *Ber.*, 41, 324 (1908). [d] Estimated. [e] Crude yield of liquid product, see ref. 13. [f] Over-all yield of diarylacrylic acid (from hydrolysis of II) was 59%. [g] Over-all yield of diarylacrylic ester was 39%. [h] Not isolated.

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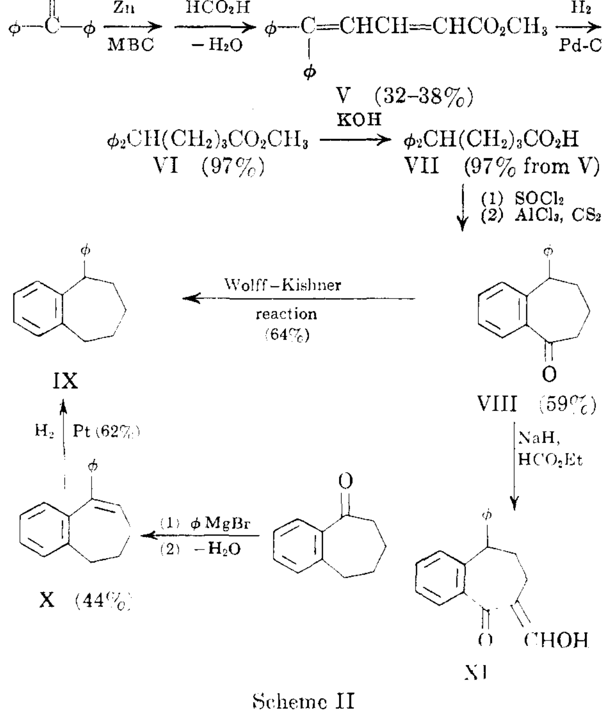
(2) Abstracted from the Ph.D. dissertation of George M. Bower, University of Oregon, June, 1957.

(3) Research assistant, 1954–1956.

(4) P. D. Gardner, *J. Am. Chem. Soc.*, **76,** 4550 (1954).

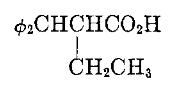
anything) by an electron-withdrawing meta methoxy group. It is apparent that for Ar and Ar′ = phenyl or a methoxy-substituted phenyl group Scheme I represents a suitable synthetic approach to the production of β,β-diarylpropionic acids (and their ethyl esters) as well as of ethyl β,β-diarylacrylates (and the corresponding β,β-diarylacrylic acids). The facile dehydration (even during vacuum distillation) of many Reformatsky hydroxyesters,[5] however, is still occurrent here so that production of esters of type I in high yield and purity is accomplished only in selected cases.

Judging from the preceding results one would anticipate that these diaryl ketones likewise ought to react readily with MBC, though perhaps to give somewhat lower yields than with EBA due to an increasing number of possible side reactions with the former reagent. Indeed, when benzophenone was treated with MBC in benzene-ether and the intermediate product was dehydrated (*cf.* Scheme II) a low yield of the crystalline dienic ester V resulted. Hydrolysis of the ester produced the corresponding dienic acid. Catalytic hydrogenation of V gave the saturated ester VI, hydrolyzable to δ,δ-diphenylvaleric acid (VII), obtained in 31–37% overall yield for the three-step process. In further transformations VII was converted to its acid chloride and cyclized by a high-dilution Friedel-Crafts technique to 9-phenylbenzosuber-5-one (VIII) which was (*a*) formylated with ethyl formate to give XI and (*b*) reduced by the Wolff-Kishner method to 5-phenylbenzosuberan (IX).

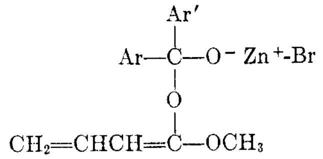


Scheme II

In consideration of the observations of Dreiding and Pratt[6] that, depending on reaction conditions, one might get either α- or γ-addition (or both) of MBC to the carbonyl group, it seemed pertinent to ascertain if VII (expected for γ-addition) were, indeed, the correct formulation for the product formed. That the alternative structure XII (expected for α-addition) was inappropriate was indicated by the fact that microanalysis of the compound failed to show the presence of a C-methyl group. Positive evidence for the assignment of structure VII was then obtained through synthesis of the hydrocarbon IX by an unequivocal route involving dehydration to an alkene (presumably X) of the intermediate carbinol resulting from interaction of phenylmagnesium bromide with benzosuberone and subsequent catalytic hydrogenation of the alkene. The liquid hydrocarbons (IX) from the two pathways exhibited identical infrared absorption spectra which showed no absorption at 7.27 ± 0.05μ (C—methyl deformation) but did show strong absorption at about 13.9μ—perhaps due to —$(CH_2)_4$—deformation.[7]


$\phi_2CHCH(CH_2CH_3)CO_2H$

XII


$Ar—C(Ar')(O^- Zn^+\text{-}Br)—O—C(OCH_3)=CHCH=CH_2$

XIII

Attempts to apply the same conditions as used for Reformatsky reaction of MBC with benzophenone to the reaction of MBC with the four methoxy-substituted benzophenones previously found by us to condense readily with EBA, however, gave only very small quantities of crude resinous products (possibly of types V–VII) which were not amenable to purification by distillation or crystallization. Alteration of the refluxing solvent used, the time of reaction, and the molar ratio of MBC to ketone (from a considerable excess of the former to a molar excess of the latter) were of no greater avail. In fact, usually 60–80% of the total original amount of ketone used was recovered from these runs. Stork[8] likewise observed a high (48%) recovery of ketone (plus a 48% yield of Reformatsky product) from interaction of 6-methoxy-1-tetralone with MBC in the molar ratio of 1:2 (ketone:MBC). The low reactivity of our methoxy-substituted benzophenones toward MBC may be the consequence of molecular compound (π-complex) formation between the aryl ring of the ketone and the electron-attracting carbon-carbon double bond of MBC or its zinc derivative. The presence of one or more methoxy groups on the aryl moiety should

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[5] R. L. Shriner, *Org. Reactions*, **I**, 11 (1942). See also **ref. 10.**

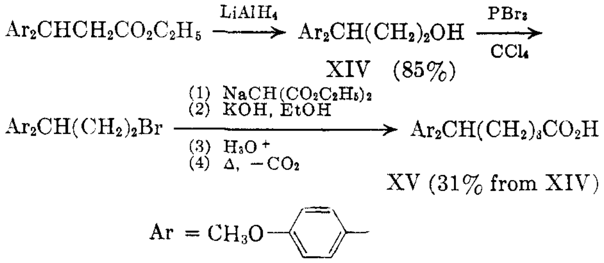
[6] A. S. Dreiding and R. J. Pratt, *J. Am. Chem. Soc.*, **75**, 3717 (1953).

[7] F. A. Miller in H. Gilman, *Organic Chemistry*, John Wiley and Sons, Inc., New York, 1953, Vol. III, pp. 143–145.

[8] G. Stork, *J. Am. Chem. Soc.*, 69, 2936 (1947).

greatly enhance such complex formation.[9] From Fisher-Hirschfelder-Taylor models one notes that, especially if the BrZn— end of the complexed MBC (with its alkenic system in planar parallelism to the aryl ring) were to coordinate with the methoxy oxygen, the carbomethoxy group of MBC could easily assume the appropriate stereorelationship for formation of an intermediate (XIII) of the type suggested by Jones, O'Sullivan, and Whiting.[10] On acidification of the reaction mixture one would regenerate the starting ketone. EBA, devoid of a carbon-carbon double bond, ought not give such a molecular compound. The success in reactions (of MBC) with 6-methoxy-1-tetralone and 3,4,5-trimethoxybenzaldehyde (46% yield of Reformatsky product)[6,11] might then be ascribed to the absence in these molecules of a second aryl group, with its attendant effects of steric hindrance to attack at the carbonyl carbon (due to the nonplanarity of benzophenones) and its complexing properties.

Failure to achieve Reformatsky reaction between the methoxy-substituted benzophenones and MBC led us to investigate an alternate pathway for preparation of δ,δ-diarylvaleric acids, pursued only in the case of the starting ketone 4,4′-dimethoxybenzophenone. In this approach the diarylpropionic ester, formed by means of the EBA reaction, was converted to the desired acid XV (15% overall yield from 4,4′-dimethoxybenzophenone) in the manner depicted in Scheme III.



$$Ar_2CHCH_2CO_2C_2H_5 \xrightarrow{LiAlH_4} \underset{\text{XIV (85\%)}}{Ar_2CH(CH_2)_2OH} \xrightarrow[CCl_4]{PBr_3}$$

$$Ar_2CH(CH_2)_2Br \xrightarrow[\substack{(3)\ H_3O^+ \\ (4)\ \Delta,\ -CO_2}]{\substack{(1)\ NaCH(CO_2C_2H_5)_2 \\ (2)\ KOH,\ EtOH}} \underset{\text{XV (31\% from XIV)}}{Ar_2CH(CH_2)_3CO_2H}$$

Ar = CH_3O—

Scheme III

EXPERIMENTAL[12]

4,4′-Dimethoxybenzophenone. Following the general procedure of Gardner[4] an equimolar mixture of anisic acid (57 g.) and anisole (41 g.) was stirred with 540 g. of polyphosphoric acid (Victor Chemical Co.) at 70° for 2 hr. and then poured into ice and water. The precipitate was washed with 500 ml. of 5% aqueous sodium hydroxide and then with water, dried, and recrystallized once from ethanol; yield 75.4 g. (82%) of needles, m.p. 144–146°; reported[13] m.p. 144–145°.

3,4,5,3′,4′-Pentamethoxybenzophenone. By the foregoing procedure a mixture of 41 g. of trimethylgallic acid,[14] 25 g. of veratrole, and 430 g. of polyphosphoric acid gave 36 g. (60%) of slightly tan prisms, m.p. 117–119°; reported m.p. 118°,[15] 119–120°.[16]

Ethyl β-hydroxy-β,β-bis(4-methoxyphenyl)propionate. To a stirred, warmed (to just below ebullition temperature) mixture of 50 g. (0.76 g.-atom) of activated (with hydrochloric acid)[17] 20-mesh zinc, 58.3 g. (0.24 mole) of 4,4′-dimethoxybenzophenone, 400 ml. of anhydrous benzene, and a crystal of iodine there was added over a period of 30 min. (at such a rate as to maintain refluxing) a solution of 70 g. (0.42 mole) of ethyl α-bromoacetate in 20 ml. of benzene. After an additional 15 min. the mixture was treated with *ca.* 200 ml. of 10% acetic acid. The combined organic layer and benzene extracts of the aqueous phase were washed successively with water, excess 1.5% aqueous ammonia, and water, dried (magnesium sulfate), and evaporated. Crystallization of the residue from ethanol gave 55 g. (69%) of needles, m.p. 87–91°. An analytical sample was obtained by recrystallization from ethyl acetate, m.p. 92–93°.

Anal. Calcd. for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.07; H, 6.76.

Ethyl β,β-bis(4-methoxyphenyl)propionate. To a warm solution of 14.4 g. of the preceding hydroxyester in 140 ml. of anhydrous benzene was added 20 ml. of anhydrous formic acid. After the transient bright red color had faded (30 sec.) the mixture was boiled for 5 min. and evaporated (air blast). The residual unsaturated ester was hydrogenated in glacial acetic acid (90 ml.) using 2.5 g. of 5% palladium-charcoal and hydrogen at 3.5–4 atm. for 30 min. The liquid from evaporation of the filtered solution crystallized from absolute ethanol to yield 11.4 g. (83%) of saturated ester as plates, m.p. 46–49°. Several recrystallizations of a sample from the same solvent raised the melting point to 49.5–50.5°.

Anal. Calcd. for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.31; H, 7.17.

β,β-Bis(4-methoxyphenyl)propionic acid. Hydrolysis of the preceding saturated ester by refluxing with a 3% solution of potassium hydroxide in 75% ethanol for 1 hr., followed by concentration of the solution, acidification with dilute hydrochloric acid, and filtration, gave a 97% yield of product (m.p. 129–131°); obtained as needles, m.p. 138.5–139.5°, after several recrystallizations from absolute ethanol; reported m.p. 138–139°,[18] 139–141°.[19]

Anal. Calcd. for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.57; H, 6.51.

β,β-Bis(4-methoxyphenyl)acrylic acid. Hydrolysis in the foregoing manner of the crude unsaturated ester obtained from dehydration of 5 g. of the preceding hydroxyester gave 4.1 g. (95%) of product (m.p. 141–146°); obtained as needles, m.p. 146.5–147.5°, after several recrystallizations from dilute methanol; reported[18] m.p. 142°.

Anal. Calcd. for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 72.09; H, 5.84.

3,3-Bis(4-methoxyphenyl)propanol (XIV). To a stirred suspension of 3.3 g. (0.087 mole) of lithium aluminum hydride in 400 ml. of anhydrous ether was added, at such rate as to maintain gentle refluxing, a solution of 29 g.

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[9] L. J. Andrews and R. M. Keefer, *J. Am. Chem. Soc.*, **75**, 3776 (1953); W. G. Barb, *Trans. Faraday Soc.*, **49**, 143 (1953).

[10] E. R. H. Jones, D. G. O'Sullivan, and M. C. Whiting, *J. Chem. Soc.*, 1415 (1949).

[11] E. C. Horning, M. G. Horning, J. Koo, M. S. Fish, J. A. Parker, G. N. Walker, R. M. Horowitz, and G. E. Ullyot, *J. Am. Chem. Soc.*, **72**, 4840 (1950).

[12] Unless otherwise designated microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill. Results on biological tests (conducted in a different laboratory) of selected compounds described in this section will be reported elsewhere.

[13] E. C. Horning and J. A. Parker, *J. Am. Chem. Soc.*, **74**, 3870 (1952).

[14] F. Mauthner, *Org. Syntheses*, **Coll. Vol. I,** 537 (1941).

[15] S. v. Kostanecki and J. Tambor, *Ber.*, **39**, 4022 (1906).

[16] W. H. Perkin and C. Weizmann, *J. Chem. Soc.*, **89**, 1649 (1906).

[17] Ref. 5, p. 16.

[18] F. Bergmann, M. Weizmann, E. Dimant, J. Patai, and J. Szmuskowicz, *J. Am. Chem. Soc.*, **70**, 1612 (1948).

[19] G. A. Holmberg, *Acta Chem. Scand.*, **6**, 607 (1952).

(0.092 mole) of ethyl β,β-bis(4-methoxyphenyl)propionate in 110 ml. of ether. The mixture was refluxed 1 hr. longer, treated first with ethyl acetate and then (cautiously) with 200 ml. of cold 3*N* hydrochloric acid. Combined ethereal solutions (from separation and extraction of the aqueous phase with 150 ml. of ether) were washed thrice with water, dried (magnesium sulfate), and evaporated. The viscous residue crystallized from ether at −5° as needles which were collected by suction-filtration in a cold room at 5°;[20] yield 15 g. (first crop) of m.p. 54–56° and 6.2 g. (second crop) of m.p. 48–52° (85% total). Further recrystallizations of a sample from ether changed the m.p. to 54–55°.

Anal. Calcd. for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.96; H, 7.44.

The 3,5-dinitrobenzoate[21a] crystallized from benzene–petroleum ether (60–90°) as yellow needles, m.p. 116–117°.

Anal. Calcd. for $C_{24}H_{22}N_2O_8$: N, 6.01. Found: N, 6.15.

δ,δ-Bis(4-methoxyphenyl)valeric acid (XV). To a stirred solution of 55 g. (0.2 mole) of the preceding alcohol in 250 ml. of carbon tetrachloride at −5° was added, over a period of 2 min., 27 g. (0.1 mole) of freshly distilled phosphorus tribromide. Thirty minutes later stirring was stopped. The solution was allowed to stand at room temperature overnight, then warmed to 50° for 20 min. and treated with water. The combined carbon tetrachloride layer and extracts of the aqueous phase were washed repeatedly with water, dried (calcium chloride), and evaporated to leave a slightly yellow viscous liquid bromide. A solution of this liquid in 200 ml. of absolute ethanol was further dried by azeotropic distillation with 20 ml. of anhydrous benzene until the distilling temperature reached 78° and then added to the ethanolic sodiomalonic ester obtained from 4.6 g. (0.2 g.-atom) of sodium, 350 ml. of absolute ethanol, and 32 g. (0.2 mole) of diethyl malonate. The mixture was refluxed for 5 hr. and the decanted (from sodium bromide) supernatant liquid was treated with a solution of 28 g. of potassium hydroxide in 100 ml. of water. After a further 2 hr. of refluxing the mixture was concentrated, diluted with water, washed with ether, and acidified. The resultant immiscible liquid (presumably the monosubstituted malonic acid) which crystallized on standing was evaporatively distilled (with decarboxylation) at 240–270° (1 mm.). Crystallization of the distillate from ethyl acetate gave 19.3 g. (31%) of needles, m.p. 98–101°. Several recrystallizations from the same solvent gave an analytical sample, m.p. 103.5–104°.

Anal. Calcd. for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05; neut. equiv., 314. Found: C, 72.60; H, 7.28; neut. equiv., 314.

Ethyl β-(3,4-dimethoxyphenyl)-β-(3,4,5-trimethoxyphenyl)-propionate. Following the same sequence of transformations as used with 4,4′-dimethoxybenzophenone, the crude hydroxyester from Reformatsky reaction of 15 g. of zinc, 25 g. of 3,4,5,3′,4′-pentamethoxybenzophenone, and 15 g. of ethyl bromoacetate was dehydrated with 50 ml. of anhydrous formic acid and the resultant yellow liquid was hydrogenated (using 200 ml. of hot glacial acetic acid and 2 g. of 30% palladium-charcoal). Crystallization of the liquid product from absolute ethanol gave 18 g. (59% over-all yield) of solid, m.p. 79–81°. Repeated recrystallizations of a sample from the same solvent gave very fine prisms, m.p. 81.5–82.5°.

Anal. Calcd. for $C_{22}H_{28}O_7$: C, 65.33; H, 6.98. Found: C, 65.25; H, 7.04.

β-(3,4-Dimethoxyphenyl)-β-(3,4,5-trimethoxyphenyl)propionic acid. Hydrolysis of the foregoing ester with aqueous ethanolic potassium hydroxide as described above gave a 98% yield of product, m.p. 95–98°. Further purification[22] was effected by two recrystallizations from ethyl acetate displacement by means of benzene-hexane (1:1 by volume) through a column of Mallinckrodt silicic acid, two recrystallizations from benzene-hexane, and drying at 80° for 12 hr. at 1 mm. to a powder, m.p. 128.5–130°.

Anal. Calcd. for $C_{20}H_{24}O_7$: C, 63.82; H, 6.43. Found: C, 64.04; H, 6.36.

Ethyl β-hydroxy-β-phenyl-β-(4-methoxyphenyl)propionate. Using the Reformatsky reaction in the aforementioned manner there was obtained (from 15 g. of zinc, 21.2 g. of 4-methoxybenzophenone,[4] and 25 g. of ethyl α-bromoacetate), after one recrystallization from ethanol, 23.5 g. (78%) of needles, m.p. 79–81°. Several recrystallizations of a sample from ethyl acetate changed the m.p. to 79–80°.

Anal. Calcd. for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 72.08; H, 6.61.

β-Phenyl-β-(4-methoxyphenyl)propionic acid. Successive steps of dehydration, hydrogenation (30% palladium-charcoal), and hydrolysis (according to the previous procedures, but starting with 3 g. of the preceding hydroxyester) gave 2.2 g. (86%) of acid, m.p. 120–122° (without recrystallization), highest reported[19] m.p. 124–125°.

β-Phenyl-β-(3-methoxyphenyl)propionic acid. Repetition of the same transformations on 3-methoxybenzophenone[23] (8.5 g.) as conducted on its isomer 4-methoxybenzophenone produced 9.1 g. (88%) of crude yellow acid, m.p. 92–98°. Several recrystallizations of a sample from ethyl acetate–petroleum ether (90–120°) gave white prisms, m.p. 99–100°.

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.90; H, 6.18.

δ-Phenylvaleric acid. Following the general procedure of Huang-Minlon[24] a mixture of 10 g. of γ-benzoylbutyric acid,[25] 7.5 g. of sodium hydroxide, 7.5 ml. of 95% hydrazine, and 80 ml. of diethylene glycol gave 8.4 g. (90%) of brown solid, m.p. 51–54°. Recrystallization of a small sample from ether–petroleum ether (30–60°) gave platelets, m.p. 56.5–57.5°; mixture melting point with the product (m.p. 53–56°) from Clemmensen reduction[26] on the same starting material 53–56°.

Methyl δ,δ-diphenylpentadienoate (V). A mixture of 4.4 g. (0.067 g.-atom) of activated 20-mesh zinc (*vide supra*), 20 g. (0.11 mole) of benzophenone, 55 ml. of anhydrous benzene, 35 ml. of anhydrous ether, and a crystal of iodine was treated with a solution of 10 g. (0.056 mole) of methyl γ-bromocrotonate[27] in 25 ml. of benzene, added over a period of 1 hr. An additional 2 g. of zinc was then added. The mixture was stirred and refluxed for 2 hr. longer and then treated with 45 ml. of 2*N* acetic acid. The organic layer was washed with 5% aqueous sodium bicarbonate and then water, dried (sodium sulfate), and evaporated. The residual oil was warmed with twice its volume of anhydrous formic acid for 15 min.[28] The residue from evaporation of the resultant mixture by means of an air-blast was fractionally distilled to give a viscous liquid, b.p. 135–165° (0.8 mm.), which crystallized from methanol; best yield 5.6 g. (38%), av. yield 32%, m.p. 84–86°. Several recrystallizations of a sample from methanol produced needles, m.p. 86–87°.

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[20] Efforts to obtain crystals by filtration at room temperature were unsuccessful.

[21] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, *The Systematic Identification of Organic Compounds*, 4th ed., John Wiley and Sons, Inc., New York, 1956, (a) p. 212, (b) p. 254.

[22] Procedure devised by Dr. C. D. Lind of this laboratory.

(23) L. H. Klemm and T. Largman, *J. Am. Chem. Soc.*, **76**, 1688 (1954).

(24) Huang-Minlon, *J. Am. Chem. Soc.*, **68**, 2487 (1946).

(25) L. F. Fieser and J. Szmuszkovicz, *J. Am. Chem. Soc.*, **70**, 3352 (1948).

(26) A. Ali, R. D. Desai, R. F. Hunter, and S. M. M. Muhammad, *J. Chem. Soc.*, 1013 (1937).

(27) Prepared by the method of K. Ziegler A. Späth, E. Schaaf, W. Schumann, and E. Winkelmann, [*Ann.*, **551**, 80 (1942)] as modified by H. Schmid and P. Karrer [*Helv. Chim. Acta*, **29**, 573 (1946)]. It was found advisable to use recrystallized (obtained as white plates from water) *N*-bromosuccinimide in this preparation.

(28) Sometimes dehydration was effected merely by heating at 125°.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 82.00; H, 6.11.

δ,δ-Diphenylpentadienoic acid. Acidification of the solution obtained by refluxing the preceding ester with a slight excess of 2% methanolic potassium hydroxide for 2 hr. gave a quantitative yield of product, m.p. 176–186°. Several recrystallizations of a sample from toluene gave needles, m.p. 190–191°.

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 82.02; H, 5.90.

Methyl δ,δ-diphenylvalerate (VI). A solution of 15 g. of methyl δ,δ-diphenylpentadienoate in 150 ml. of glacial acetic acid was shaken with 3 g. of 5% palladium-charcoal for 10 min. under hydrogen at 3.5–4-atm. pressure. The filtered solution (negative permanganate test) was distilled to give 14.7 g. (97%) of colorless liquid, b.p. 145–150° (0.5 mm.).

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 81.39; H, 7.51.

δ,δ-Diphenylvaleric acid (VII). Hydrolysis of the preceding saturated methyl ester in the manner used for the dienic ester produced a quantitative yield of product, m.p. 89–92°. Several recrystallizations of a sample from 60% ethanol gave needles, m.p. 92.5–93.5°.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.23; H, 7.30; C-methyl,[29] none.

9-Phenylbenzosuber-5-one (VIII). In an adaptation of published[30] high-dilution Friedel-Crafts intramolecular acylations, a solution of δ,δ-diphenylvaleryl chloride [prepared from 10 g. (0.039 mole) of the foregoing acid and 8 ml. of thionyl chloride] in 250 ml. of purified[31] carbon disulfide was added (*via* the attachment described by Leonard and Sentz)[32] over a period of 10 hr. to a stirred, refluxing mixture of 750 ml. of carbon disulfide and 2.7 g. of anhydrous aluminum chloride. At 3-hr. intervals 2.7-g. portions of aluminum chloride (total used 10.8 g., 0.081 mole) were added. After 12 hr. the dark red mixture was treated with water and filtered. The benzene solution of the residual oil from distillation of the organic layer was washed with excess 10% aqueous potassium carbonate and then with water, dried (magnesium sulfate), and evaporated. Evaporative distillation of the residue at 190–200° (0.5 mm.) gave 5.47 g. (59%) of ketone. Several recrystallizations of a sample from dilute ethanol gave needles, m.p. 71.0–71.5°.

Anal. Calcd. for $C_{17}H_{16}O$: C, 86.40; H, 6.83. Found:[29] C, 86.82; H, 6.99.

The oxime[21b] was obtained in the form of prisms from benzene–petroleum ether (30–60°), m.p. 152.5–153.5°.

Anal. Calcd. for $C_{17}H_{17}NO$: N, 5.57. Found: N, 5.47.

5-Phenylbenzosuberan (IX). (*a*) *From 9-phenylbenzosuber-5-one.* The diluted mixture from the Huang-Minlon reaction[24] on 2 g. of the preceding ketone was extracted with benzene. Distillation of the water-washed and dried (magnesium sulfate) extract yielded 1.2 g. (64%) of light yellow liquid, b.p. 132–135° (1 mm.). A re-distilled sample for infrared analysis was obtained almost colorless, b.p. 149–150° (2 mm.). After long standing it yielded prisms, m.p. 41–45°.

(*b*) *From benzosuber-5-one.* To the ice-cold Grignard reagent from 0.4 g. of magnesium (16 mg.-atoms), 2.4 g. (15 mmoles) of bromobenzene, and 75 ml. of ether was slowly added a solution of 2 g. (8.5 mmoles) of benzosuber-5-one (obtained by cyclization of δ-phenylvaleric acid with polyphosphoric acid)[33] in 20 ml. of ether. The mixture was stirred in the cold for 30 min. and then refluxed for 1 hr. Hydrolysis, collection of carbinol, and dehydration with formic acid followed the method of Klemm and Ziffer[34] to give, after fractional distillation at 1.5 mm., 0.4 g. of colorless ketonic liquid (presumably recovered starting material), b.p. 95–110°, and 1 g. (44%) of permanganate-reducible liquid (presumably *5-phenylbenzosuber-5-ene,* X), b.p. 115–135°.

A solution of 0.9 g. of the preceding alkenic fraction in 25 ml. of glacial acetic acid was shaken with 0.1 g. of Adams' platinum oxide under hydrogen at 4 atm. pressure for 2 hr. (whereupon the solution no longer reduced permanganate). Distillation of the filtered solution yielded 0.56 g. (62% from the alkene) of colorless liquid, b.p. 115° (0.6 mm.). A sample for analysis was redistilled at 149–150° (2 mm.).

Anal. Calcd. for $C_{17}H_{18}$: C, 91.84; H, 8.16. Found: C, 91.51; H, 8.34.

The infrared absorption spectra[35] of the products from (*a*) and (*b*) were identical; strong to very strong bands at 3.26–3.52 (C—H stretching), 6.24 and 6.71 (phenyl), 6.90 (CH_2-deformation), *ca.* 13.35 (ortho disubstituted benzene), *ca.* 13.9 (tetramethylene deformation), and *ca.* 14.35μ.

6-Hydroxymethylene-9-phenylbenzosuber-5-one (XI). A mixture of 2.36 g. (0.01 mole) of 9-phenylbenzosuber-5-one, 1.48 g. (0.02 mole) of ethyl formate, and a few ml. of anhydrous benzene was stirred and warmed with 0.5 g. (0.02 mole) of sodium hydride in an atmosphere of nitrogen. Vigorous evolution of gas occurred. The red pasty contents were diluted with 10 ml. of benzene, stirred at 50° for 1.5 hr., and treated successively with 3 ml. of glacial acetic acid and 30 ml. of water. The benzene layer was separated, washed with water, and extracted with 100 ml. of 10% aqueous sodium carbonate. Acidification of the alkaline extract gave 2.1 g. of solid, recrystallized once from ethyl acetate, m.p. 101.5–102.5°. Several recrystallizations of a sample from benzene–petroleum ether (60–90°) gave prisms, m.p. 102–102.5°.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.46; H, 6.12.

EUGENE, ORE.

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(29) Analyzed by Clark Microanalytical Lab., Urbana, Ill.

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(32) N. J. Leonard and R. C. Sentz, *J. Am. Chem. Soc.*, **74**, 1704 (1952).

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(34) L. H. Klemm and H. Ziffer, *J. Org. Chem.*, **20**, 182 (1955).

(35) Obtained by Samuel P. Sadtler and Son, Inc., Philadelphia, Pa. See spectrum No. 67257 in their catalog.