(1-cyclopentenyl)-piperidine to produce a 74% yield of mixed 2,3,4,5,6,7- and 2,3,4,4a,5,6,-hexahydro-1-methyl-1H-1-pyrindine, b.p. 65–66° (6 mm.), confirmed by analysis (calcd. for $C_9H_{15}N$: C, 78.77; H, 11.02. Found: C, 78.71; H, 11.19) and by infrared absorption of the free base and of the perchlorate salt, m.p. 215–217°. Similarly, N-methyl-3-bromopropylamine hydrobromide reacts with 1-(1-cyclohexenyl)-piperidine to produce a 73% yield of mixed 1,2,3,4,5,6,7,8- and 1,2,3,4,4a,5,6,7-octahydro-1-methylquinoline, b.p. 82–84° (6 mm.), confirmed by infrared studies and by catalytic reduction to *cis*-1-methyldecahydroquinoline (picrate salt, m.p. 199–201°, reported m.p. 199–200°,[3] *anal.* calcd. for $C_{10}H_{19}N\cdot(NO_2)_3C_6H_2OH$: C, 50.25; H, 5.80. Found: C, 50.35; H, 5.71).

Further studies are under way to determine the scope of this reaction.

(3) M. Ehrenstein and W. Bunge, *Ber.*, **67**, 1715 (1934).

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RECEIVED FEBRUARY 16, 1959

SYNTHESIS OF ARYLDICHLOROBORANES

Sir:

We have found a simple and direct synthesis of aryldichloroboranes from boron trichloride and aromatic hydrocarbons.[1]

These halides were prepared by charging a stainless steel-lined pressure vessel (400 ml. internal capacity) with 100–125 g. of aromatic hydrocarbon, 2–30 g. of aluminum powder, 0.1 g. of aluminum chloride, iodine, or methyl iodide, and 60 g. of boron trichloride[2] and heating the vessel, under autogenous pressure and with agitation to 120–150° for 5–60 min. or to 30–50°[3] for 24–48 hours. The product, usually a liquid slurry, was filtered and the filtrate was distilled. In the case of benzene, the conversion to purified $C_6H_5BCl_2$ ranged from 60 to 72%, b.p. 95° (48 mm.). *Anal.* Calcd. for $C_6H_5BCl_2$: C, 45.38; H, 3.17; B, 6.79; Cl, 44.66. Found: C, 45.87; H, 3.54; B, 7.39; Cl, 44.31. Variations in the C_6H_6 to BCl_3 ratio had no significant effect on the nature of the products, and there was no evidence for the formation of $(C_6H_5)_2BCl$ or $C_6H_4(BCl_2)_2$. Polysubstitution in the aromatic nucleus undoubtedly is unfavorable because the strongly electronegative BCl_2 group deactivates the ring.[4]

Tolyldichloroborane was obtained from toluene in 60% conversions at 140°. Hydrolysis of the dichloride and cleavage of the B–C bond with hydrogen peroxide gave *p*- and *m*-cresol in a 3:2 molar ratio (infrared determination); no *o*-cresol was present in detectable quantities. When prepared at 35°, the ratio of *para* to *meta* isomers in tolyldichloroborane was about 4.6:1. The aryldichloroboranes formed from the isomeric xylenes at 35° were: *meta*, 3,5-xylyl- with trace amounts of 2,5-xylyl-; *ortho*, 3,4-xylyl-; and *para*, 2,5-xylyl-. Mesitylene at 140° gave largely 2,5-xylyldichloroborane (~15% yield) with a small amount of the 2,4- isomer. At 35°, mesitylene reacted to form traces of mesityldichloroborane. Durene was inactive at 140°. At 30°, naphthalene and also biphenyl appeared to give more than one type of arylboron derivative.

The distribution of isomers in this synthesis of arylboranes is comparable to that in Friedel–Craft reactions that are run in the presence of aluminum chloride.[5] Accordingly, it is suggested that the active species in this synthesis may be BCl_2^+ or $ArH\cdot BCl_2^+$. Such species would be stabilized by the formation of the $AlCl_4^-$ anion, and reaction of the cation complex with the active aluminum surface would then produce the $ArBCl_2$ compound. The aspect of reaction mechanism is being investigated.

(1) The classical methods for the preparation of aryldihaloboranes have been discussed in a recent review by M. F. Lappert, *Chem. Rev.*, **56**, 1049 (1956). E. Pace (*Atti Accad. Lincei*, **10**, 193 (1929)) reported the synthesis of $C_6H_5BCl_2$ from benzene and boron trichloride over palladium black at 500–600°. The Pace synthesis has been studied by W. L. Ruigh, *et al.* (WADC Technical Report 55-26, Parts III–IV (1956), P.B. Nos. 121,374 and 121,718. U. S. Dept. of Commerce, Washington, D. C.). They found that, with charcoal-supported palladium catalysts, the yields were variable, probably due to sensitivity of the catalyst to poisons.

(2) Boron tribromide and triiodide also proved operable, but boron trifluoride did not react under these conditions.

(3) In one experiment with benzene, an exothermic reaction set in at 3° and the internal temperature flashed to 120°. A 66% conversion to $C_6H_5BCl_2$ was obtained. Variations in reaction rate are attributed to variations in the activity of the aluminum surface.

(4) The BCl_2 group should be at least as effective as Cl in deactivating the ring, and chlorobenzene itself was found to be inert to the BCl_3–Al reagents at 50°.

(5) Aluminum chloride is a co-product in this synthesis of arylboron chlorides.

CONTRIBUTION NO. 530 FROM THE
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ON THE MECHANISM OF FATTY ACID SYNTHESIS[1]

Sir:

Recently we have reported[2–3] that the first step in fatty acid synthesis is the carboxylation of acetyl CoA to malonyl CoA catalyzed by the biotin containing R_{1gc} fraction in the presence of ATP and Mn^{++}.

Malonyl CoA readily is converted to palmitate in the presence of R_{2gc} and TPNH.[2] This conversion can be followed spectrophotometrically or isotopically. The addition of acetyl CoA will significantly increase the rate and extent of synthesis of palmitate. Furthermore, a significant amount of C^{14}-acetyl CoA is incorporated into palmitate when unlabeled malonyl CoA is used (Table I). The amount of label introduced into palmitate corresponds to about one eighth of the total amount of "C_2 units" converted to palmitate (measured by TPNH oxidation). Unlabeled acetaldehyde does not reduce the amount of C^{14}-acetyl CoA incorporated into palmitate and acetaldehyde is not formed by the enzymic reduction of acetyl CoA by TPNH.[4] Not only acetyl CoA but also C^{14}-butyryl CoA and C^{14}-octanoyl CoA can be incorporated into palmitate in presence of malonyl CoA.

(1) This work was supported in part by several grants: 2G-88 and RG-5873, Division of Research Grants (NIH); H-2236(C3), National Heart Institute (NIH); G-3227, National Science Foundation; and AEC Contract AT(11-1)-64, Project 4.

(2) S. J. Wakil, THIS JOURNAL, **80**, 6465 (1958).

(3) S. J. Wakil and J. Ganguly, *Fed. Proc.*, **18**, 346 (1959).

(4) R. O. Brady, *Proc. Nat. Acad. Sci.*, **44**, 993 (1958).

TABLE I

Additions	TPNH oxidized (mμmoles)	C^{14}-substrate incorporated into palmitate (mμmoles)
None	18.0	..
1-C^{14}-acetyl CoA (12 mμmoles)	32.2	1.80
same + acetaldehyde (1000 mμmoles)	32.2	1.90
1-C^{14}-acetate (320 mμmoles)	18.0	0.00
2-C^{14}-malonate (1000 mμmoles)	18.2	0.00
1-C^{14}-butyryl CoA (30 mμmoles)	18.2	1.10
1-C^{14}-octanoyl CoA (50 mμmoles)	20.0	3.00

Each cuvette contained 20 μmoles of potassium phosphate buffer *p*H 6.5, 50 mμmoles of TPNH, 50 mμmoles of synthetic unlabeled monomalonyl CoA, other substrates as indicated, 200 μg. of R_{2gc} and H_2O to 0.4 ml. Incubated for 10 min. at 38°.

R_{2gc}, as prepared, does contain an enzyme which decarboxylates malonyl CoA to CO_2 and acetyl CoA (as measured by the enzymatic formation of citrate). This would explain why malonyl CoA in the absence of added acetyl CoA can form palmitate in the presence of R_{2gc} and TPNH (Table I). R_{2gc} does not contain enoyl hydrase, β-hydroxyacyl dehydrogenase or thiolase nor does it catalyze the oxidation of TPNH by acetyl CoA, acetoacetyl CoA, β-hydroxybutyryl CoA, crotonyl CoA, butyryl CoA, Δ^{2-3}-hexenoyl CoA and octanoyl CoA. The oxidation of TPNH in this system requires the combined presence of malonyl CoA and some unsubstituted fatty acyl CoA (C_2, C_4, C_6 etc.). None of the substituted intermediates of the β-oxidation sequence can replace these fatty acyl CoA esters. These observations suggest a possible mechanism of fatty acid synthesis

$$CH_3COCoA + CO_2 + ATP \xrightarrow[R_{1gc}]{\text{Biotin-containing}} HOOCCH_2COCoA$$

$$CH_3COCoA + HOOCCH_2COCoA \xrightarrow{R_{2gc}} \left[CH_3COCH(COOH)COCoA \xrightarrow{TPNH} CH_3CHOHCH(COOH)COCoA \xrightarrow{-H_2O} CH_3CH{=}C(COOH)COCoA \xrightarrow{TPNH} CH_3CH_2CH(COOH)COCoA \longrightarrow\right] CH_3CH_2CH_2COCoA + CO_2$$

The butyryl CoA formed can condense with another molecule of malonyl CoA with the formation of the β-ketodicarboxylic acid as indicated above.

(5) Postdoctoral Trainee of the Institute for Enzyme Research, University of Wisconsin.

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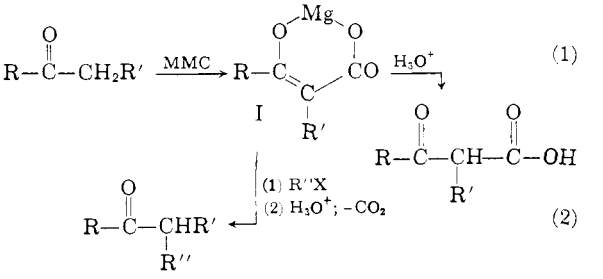
CHELATION AS A DRIVING FORCE IN SYNTHESIS. II. USE OF MAGNESIUM METHYL CARBONATE IN THE CARBOXYLATION AND ALKYLATION OF KETONES

Sir:

A previous communication[1] described the use of magnesium methyl carbonate (MMC) for the carboxylation of nitroparaffins. Further investigation has revealed that this reagent readily converts ketones to β-keto acids (eq. 1). Equally important from a practical standpoint is our finding



(1)

(2)

that the intermediate magnesium salts of β-keto acids (I) may be alkylated *in situ*. Thus the path indicated by eq. 2 is experimentally a simple method for the alkylation of ketones.

Treatment of acetophenone with 3–4 molar equivalents of MMC in dimethylformamide at 110–120° for one hour, and then acid hydrolysis, furnished a 68% yield of benzoylacetic acid, m.p. 99–100° dec. (reported,[2] 100° dec.). 1-Indanone was converted in 91% yield by the same technique to 1-indanone-2-carboxylic acid, m.p. 100–101° dec. (reported,[3] 98–100° dec.).

Cyclohexanone (1.82 g., 0.0186 mole) was heated with 80 ml. of 1.94 *M* MMC solution at 120–130° for 6 hours. After hydrolysis the crude product was extracted into ether, dried, and treated with ethereal diazomethane. Crystallization from methanol gave 1.90 g. (48%) of dimethyl cyclohexanone-2,6-dicarboxylate, m.p. 139–140° (reported[4] m.p. 142–143°) identical with an authentic specimen.[5] Alternatively the free diacid, m.p. 123° dec., neut. equiv., 99.5 (reported[6] m.p. 120–140° dec.) could be isolated by crystallization from ether–petroleum ether. Evidence for the importance of the coördinating properties of magnesium in these reactions may be seen by comparing this result with that obtained[7] by treatment of cyclohexanone with sodium ethyl carbonate.

1-Tetralone was treated with MMC solution at 120–130° for one hour, and to the cooled mixture an excess of benzyl bromide was added. Heating on the steam-bath for 6 hours, acid hydrolysis, and decarboxylation provided a 72% yield of 2-benzyl-1-tetralone, b.p. 150–155°(0.4 mm.), m.p. 51–53° (reported,[8] b.p. 176°(1 mm.), m.p. 53–54°).

When acetophenone was heated with MMC (4 equiv.) as described above, followed by methyl iodide (3 equiv.), a 74% yield of isobutyrophenone was obtained after decarboxylation. Propiophenone was not isolated, even when less than two equivalents of alkylating agent was used. Evidently the chelate salt from 2-benzoylpropionic acid (I, R = C_6H_5, R′ = CH_3), which would be formed rapidly from the initial alkylation product

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(4) F. F. Blicke and F. J. McCarty, *J. Org. Chem.*, in press.

(5) Sample provided through the courtesy of Drs. R. E. Ireland and P. W. Schiess.

(6) J. W. Cook, J. D. Loudon, and D. K. V. Steel, *J. Chem. Soc.*, 530 (1954).

(7) J. I. Jones, *Chem. and Ind. (London)*, 228 (1958).

(8) W. Borsche, P. Hofmann and H. Kühn, *Ann.*, **554**, 23 (1943).