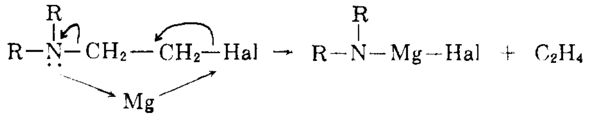
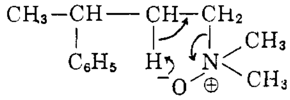
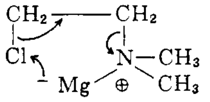
concluded that no Grignard reagent is actually formed. Instead a mechanism for this elimination is suggested whereby coördination of the metal with nitrogen occurs resulting in a displacement in the direction shown.



Further, we note the similarity between the elimination described here (I) and that observed in the Cope elimination of *N*-oxides (II),[7a,b] where retention of configuration was observed.



II



I

Experimental

All melting points are corrected.

I. **Preparation of 2-Dimethylaminoethyl Chloride.**—2-Dimethylaminoethyl chloride was isolated from its hydrochloride by addition of excess ice-cold sodium hydroxide to a cold concentrated solution of the amine hydrochloride covered with a layer of ether (in hood). The two phases were separated, the aqueous phase further extracted with ether, and the combined ether extracts dried over anhydrous sodium sulfate. Final drying was achieved by storage over calcium hydride. The free base was obtained by distillation at atmospheric pressure without a column. A fraction, b.p. 106–110°, was collected and stored over calcium hydride until used. In several 0.5-mole and 2-mole runs, yields of 54 to 67% of free 2-dimethylaminoethyl chloride were thus obtained. The yield is low because this amino chloride undergoes dimerization to form *N,N,N',N'*-tetramethylpiperazinium dichloride.[8]

II. **Reaction of 2-Dimethylaminoethyl Chloride (DAEC) and Magnesium.**—Two preliminary experiments were carried out. In the first, 0.15 g.-atom of magnesium was allowed to react with 0.05 mole of ethylene bromide in ether, followed by reaction with 0.1 mole of 2-dimethylaminoethyl chloride. A white precipitate formed which prevented further reaction. In the second, 1.75 g.-atoms of magnesium was found to react spontaneously with a portion of 1.34 moles of 2-dimethylaminoethyl chloride in 72 g. of tetrahydrofuran (THF), when the mixture was warmed to 55–60°. Additional portions of the 2-dimethylaminoethyl chloride and tetrahydrofuran were added. Evolution of a gas, took place, which decolorized bromine in chloroform. The gas was not absorbed by aqueous hydrochloric acid. Addition of 1.0 mole of benzaldehyde, and reflux, was followed by the usual Grignard work-up procedure. No benzaldehyde derivative was isolated, but 0.44 g.-atom of magnesium was recovered unchanged.

Further study was carried out in a conventional Grignard reactor, except that the condenser exit was connected in series with a Dry Ice trap, a safety flask to protect against pressure variations, and two bromine absorption flasks, respectively. The first bromine flask was immersed in an ice bath, and the second vented into the hood.

To 5.35 g. (0.22 g.-atom) of magnesium contained in the reaction flask was added portionwise one quarter to one half of 23.8 g. (0.22 mole) of dry 2-dimethylaminoethyl chloride (b.p. 108–110°) along with 10–15 ml. of pure dry tetrahydrofuran. Since the reaction did not commence on heating to 70°, additional 2-dimethylaminoethyl chloride was added portionwise until all was added. The reaction did not proceed. At this point 2–3 ml. of a reacting mixture of magnesium, tetrahydrofuran, and *ca.* 0.5 ml. of ethylene bromide was added. The reaction commenced vigorously with gas evolution and frothing. When the activity ceased, 8.2 g. (0.34 g.-atom) of magnesium turnings was added. This was followed by the dropwise addition of 36.1 g. (0.337 mole) of 2-dimethylaminoethyl chloride, along with the separate addition of 125 ml. of tetrahydrofuran. At the end of the exothermic stage the mixture was refluxed 40 min. further. It was then cooled and unchanged magnesium was removed by decantation of the supernatant liquid without exposure to the atmosphere. The recovered magnesium was washed with ether several times, dried, and weighed 4.46 g. (0.184 g.-atom). The Dry Ice trap was found to contain 12.4 g. of liquid which gave, when distilled through a 6-in. Vigreux column, 11.7 ml. of tetrahydrofuran, b.p. 64–67°, further identified by its infrared spectrum. A 2.7-ml. forerun was not investigated. The bromine from the absorption flasks was combined and distilled through a 6-in. Vigreux column. Isolated was 39.8 g. of ethylene bromide (0.212 mole), b.p. 127–131°, 55.3% based upon the magnesium consumed. It was identified by comparison of its infrared spectrum with that of an authentic sample of 1,2-ethylene dibromide. The residue of black tar remaining in the distillation flask weighed 10.0 g. and was not further investigated.

The tetrahydrofuran reaction mixture gave a negative Gilman–Grignard reagent test. It was hydrolyzed by addition of a solution of 100 g. of concd. hydrochloric acid in 500 ml. of water. This was followed by addition of a solution of 80 g. of sodium hydroxide in 160 ml. of water. During the hydrolysis and neutralization no gases were evolved which were soluble in ice-cold ether contained in an absorption flask. The aqueous alkaline hydrolysate was next extracted with four 150-ml. portions of ether. The combined extracts were dried over anhydrous potassium carbonate, and dry hydrogen chloride was passed in until no more precipitation occurred. The solid was removed by filtration and dried *in vacuo* over phosphorus pentoxide. It weighed 12.94 g. when dry and decomposed at 261–266°.

Anal.[9] Calcd. for $C_6H_{18}N_2Cl_2$: N, 14.82. Found: N, 14.43.

Recrystallization of 6.0 g. of this hydrochloride from methanol gave 3.6 g. of m.p. 295–296° dec.

Anal. Calcd. for $C_6H_{18}N_2Cl_2$: Cl, 37.49; N, 14.82. Found: Cl, 37.66; N, 14.69.

One gram of the hydrochloride was converted to the dipicrate, m.p. 258°. These facts identify the amine as *N,N,N',N'*-tetramethylethylenediamine.[10]

The alkaline hydrolysate remaining after extraction with ether was filtered and neutralized to pH 8. A solution of 30 g. of picric acid in 2 l. of water was added and the picrate obtained weighed 16.5 g. when dry and melted at 232–240°. Excess picric acid did not cause further precipitation. One gram of this material gave 0.87 g. of crystals, m.p. 253–254° dec., when recrystallized from water. Infrared spectra of all of the picrates prepared in this work were identical. Material recovered from earlier attempts to prepare a benzoate and urethane gave additional 2.08 g. of the dipicrate. The total of picrates and hydrochlorides thus isolated was 0.098 mole, 17.5%.

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[7] (a) A. C. Cope, T. T. Foster, and P. H. Towle, *J. Am. Chem. Soc.*, **71**, 3929 (1949); (b) D. J. Cram and J. E. McCarty, *ibid.*, **76**, 5740 (1954).

[8] P. D. Bartlett, S. D. Ross, and C. G. Swain, *ibid.*, **69**, 2971 (1947).

[9] Analyses carried out by the Analytical Department of S. B. Penick & Co., Newark, N. J.

[10] Reported: *N,N,N',N'*-tetramethylethylenediamine dihydrochloride, dec. 300°, and dipicrate, dec. 252°; L. Knorr, *Ber.*, **37**, 3496 (1904).

Decarboxylation Studies. II. Preparation of Alkyl Phenyl Ketones[1,2]

CHARLES GRANITO AND HARRY P. SCHULTZ

Department of Chemistry, University of Miami, Coral Gables, Florida

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A recently published study[1] of the preparation of symmetrical, straight chain, aliphatic ketones has been extended to a study of the preparation of alkyl phenyl ketones by the thermal decarboxylation, in the liquid phase, of iron salts of mixtures of aliphatic and aromatic carboxylic acids. To the references recorded in the earlier publication[1] should be added the work of

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[1] Paper I of this series: R. Davis and H. P. Schultz, *J. Org. Chem.*, **27**, 854 (1962).

[2] Abstracted in part from the M.S. thesis of C. G., University of Miami, 1962.

Friedel,[3] who reported the first synthesis of an alkyl phenyl ketone, acetophenone, by pyrolysis of a mixture of calcium benzoate and calcium acetate. Other than this, alkyl phenyl ketones have been prepared by pyrolysis reactions[4] in the vapor state only.

The reaction may be formulated as follows:

$$C_6H_5COOH + RCOOH + Fe \longrightarrow \text{Ferrous salts} + H_2$$

$$\text{Ferrous salts} \longrightarrow C_6H_5COR + C_6H_5COC_6H_5 + RCOR + CO_2 + FeO$$

The nature of the iron(II) salt has been discussed in the earlier work.[1] Although three ketones may possibly be obtained, this study demonstrated that the above reaction yielded mainly the alkyl phenyl ketone and little or no dialkyl ketone or benzophenone.

Fifteen representative aliphatic acids were treated with benzoic acid and iron in equimolar ratios. The alkyl phenyl ketones in the crude reaction mixtures were determined quantitatively from the ultraviolet absorption spectra by comparison with the spectra of known, pure standards; the reaction mixtures then were purified by traditional methods. Because of ease of isolation, the yields of methyl, ethyl, isopropyl, and secondary butyl phenyl ketones were not determined spectroscopically. *n*-Hexyl, *n*-heptyl, and *n*-octyl phenyl ketones have yield data based solely on spectroscopic data, because of similarity of boiling points, melting points, and solubilities of alkyl phenyl ketone and corresponding dialkyl ketone. Table I summarizes these data.

TABLE I

YIELDS OF ALKYL PHENYL KETONES BY PYROLYSIS OF IRON SALTS OF MIXED BENZOIC ACID AND ALIPHATIC CARBOXYLIC ACIDS

Alkyl substituent	Yield, %, of phenone		Weight % phenone in crude product, analyzed
	Analyzed	Isolated	
Methyl	—	33	—
Ethyl	—	50	—
n-Propyl	69	48	90
Isopropyl	—	69	—
n-Butyl	62	55	81
sec-Butyl	—	69	—
n-Pentyl	73	65	86
n-Hexyl	73	—	82
n-Heptyl	69	—	90
n-Octyl	70	—	87
n-Nonyl	62	50	89
n-Undecyl	74	50	93
n-Tridecyl	76	64	92
n-Pentadecyl	78	66	90
n-Heptadecyl	69	52	74

The reaction of benzoic acid, propanoic acid, and iron was studied, varying the molar ratios of organic reactants. It was found (Table II) that increasing the ratio of one reactant over the other, from 1:1, increased the yield of alkyl phenyl ketone. An excess of benzoic acid, however, had a more pronounced effect than an excess of propanoic acid.

TABLE II

YIELDS OF PROPIOPHENONE BY PYROLYSIS OF IRON SALTS OF VARYING RATIOS OF BENZOIC ACID AND PROPANOIC ACID.

Molar ratio		Yield, %, propiophenone, isolated
Benzoic acid	Propanoic acid	
4	1	72
2	1	60
1	1	50
1	2	55
1	4	59

Thirteen substituted benzoic acids were treated with propanoic acid and iron in equimolar ratios. A simplified, semimicro procedure was used so that a relatively large number of compounds could be screened efficiently. That some yield was sacrificed in this procedure may be noted by comparing the yields of propiophenone itself when obtained by the macro procedure (Table I) and the semimicro procedure (Table III). Propanoic acid was selected as the aliphatic acid for reaction with the substituted benzoic acids for these reasons: (1) No by-product 3-pentanone was observed in the reaction between propanoic acid and benzoic acid. (2) Propiophenone was obtained in 50% yield from the reaction between propanoic and benzoic acids; any change in yield, therefore, could be readily observed. (3) The expected nucleus-substituted propiophenones are all known compounds.

TABLE III

YIELDS OF NUCLEAR SUBSTITUTED PROPIOPHENONES FROM PYROLYSIS OF IRON SALTS OF SUBSTITUTED BENZOIC ACIDS AND PROPANOIC ACID

Aromatic substituent	Yield, %, substituted propiophenone, isolated
Hydrogen	39
o-Methyl	0
m-Methyl	22
p-Methyl	27
o-Chloro	0
m-Chloro	42
p-Chloro	20
o-Nitro	0
m-Nitro	0
p-Nitro	0
p-Amino	0
p-Bromo	21
p-Hydroxy	0
p-Methoxy	27

Data in Table III show an obvious *ortho* effect and also demonstrate that strongly positive or negative groups in the *meta* or *para* position interdict the ketonic decarboxylation. *meta*-Alkyl and *meta*-halogen substituted phenones are, however, more readily available from this reaction than *via* the traditional Friedel–Crafts reaction.

Experimental

Materials.—All organic starting materials were purchased and purified prior to use by either distillation and/or recrystallization. The iron was hydrogen reduced iron powder, produced by Fisher Scientific Company.

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(3) C. Friedel, *Jahresber. Fortschr. Chem.*, 270 (1857); F. K. Beilstein, "Handbuch der organischen Chemie," Vol. 7, 4th ed., B. Prager, P. Jacobson, P. Schmidt, and D. Stern, ed., J. Springer Verlag, Berlin, 1925, p. 272.

(4) J. B. Senderens, *Compt. rend.*, **150**, 112, 702 (1910); M. A. Mailhe, *ibid.*, **157**, 220 (1913); P. Sabatier and M. A. Mailhe, *ibid.*, **158**, 830 (1914).

TABLE IV

ULTRAVIOLET ABSORPTION DATA IN CYCLOHEXANE OF PURE ALKYL PHENYL KETONES

Alkyl moiety	λ_{max}, mμ	$\epsilon \times 10^{-4}$
n-Propyl	240	1.11
n-Butyl	240	1.12
n-Pentyl	239	1.30
n-Hexyl	239	1.34
n-Heptyl	240	1.20
n-Octyl	240	1.16
n-Nonyl	236	1.80
n-Undecyl	239	1.29
n-Tridecyl	236	1.72
n-Pentadecyl	240	1.26
n-Heptadecyl	240	1.09

Preparation of Pure Alkyl Phenyl Ketones as Analytical Standards.—Table IV lists the alkyl phenyl ketones prepared by the Friedel–Crafts procedure of Breusch and Oguzer.[5]

Preparation of Alkyl Phenyl Ketones.—The apparatus has been described.[1] One tenth mole of benzoic acid, 0.1 mole of aliphatic acid, and 0.11 mole of iron were used in reactions with aliphatic carboxylic acids of less than five carbon atoms; twice these quantities were utilized in reactions involving aliphatic acids of five or more carbon atoms. The reaction flask was heated to 250° until hydrogen evolution (100% yield in all cases) ceased—approximately 45 min. If the expected alkyl phenyl ketone had less than nine carbon atoms in the side chain, the condenser was set for downward distillation, and the flask heated until distillation ceased. Evolution of carbon dioxide and distillation occurred at a pot temperature of 280–300°; only a few drops of black tar distilled at higher temperatures. The volatile distillate was diluted with ether, washed with saturated sodium bicarbonate solution, dried, concentrated, and weighed. An accurately weighed sample of 10 mg. of crude product was dissolved in 1 l. of cyclohexane and compared at the wave length of maximum absorption with the spectrum of the corresponding pure ketone. The alkyl phenyl ketone was then distilled to separate it from possible lower boiling dialkyl ketones. From the appropriate ketones no acetone, no 3-pentanone, no 2,4-dimethylpentanone-3, 12% of 4-heptanone, no 3,5-dimethylheptanone-4, and 8% yields of 5-nonanone were obtained. The tarry, nonvolatile, red residue remaining after twenty-five different distillations were combined to give 50 g. of material. Chromatographic study of the small amount of tar (about 4 g.) boiling at 300–400° indicated (infrared spectrum) some benzophenone to be present; no other materials were identified in the tar. (Parenthetically, it was observed that when only benzoic acid and powdered iron were treated, a pot temperature of 350–400° was required to decompose the iron(II) benzoate; yields of 13% benzene, 17% benzophenone, a trace of benzaldehyde, and much tar resulted.)

If the expected alkyl phenyl ketone had nine or more carbon atoms in the side chain, ketonic decarboxylation of the iron salts was effected with the condenser attached vertically to the decarboxylation flask. After decarboxylation, the impure ketone was dissolved in 200 ml. of ether, filtered through a pad of Celite to remove particles of iron and iron oxide, washed with sodium bicarbonate solution, dried, concentrated, weighed, and analyzed for alkyl phenyl ketone. The crude red residue was dissolved in cyclohexane (10 ml./g.) and passed through a 2.5×20 cm. column of alumina, eluting the column with a double volume of cyclohexane. After the removal of solvent, the colorless, solid residue was recrystallized one to three times from 95% ethanol to give pure alkyl phenyl ketone.

The identity and purity of products were established by boiling and/or melting points, melting points of 2,4-dinitrophenylhydrazones and/or semicarbazones, and quantitative ultraviolet absorption spectra.

Semimicro Preparation of Ethyl Substituted Phenyl Ketones.—Into a 200-cm. test tube equipped with condenser, drying tube, and bubble counter were placed 0.05 mole of propanoic acid, 0.05 mole of substituted benzoic acid, and 0.054 mole of powdered iron. The tube was heated in an electric coil at 280–300° until all gas evolution ceased. No attempt was made to distil ketone as it formed. The cooled tube was broken directly into a steam distillation flask containing 500 ml. of water and 10 g. of sodium bicarbonate. After steam distillation, the distillate was extracted with chloroform, then dried, concentrated, and distilled and/or recrystallized, depending upon the properties of the expected ketone.

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(5) F. L. Breusch and M. Oguzer, *Chem. Ber.*, **87**, 1227 (1954).

Occurrence of the Isoflavone Afromosin in Cabreuva Wood[1]

JEFFREY B. HARBORNE, OTTO RICHARD GOTTLIEB, AND MAURO TAVEIRA MAGALHÃES

John Innes Institute, Bayfordbury, Hertford, Herts., England, and Instituto de Química Agrícola, Ministério da Agricultura, Rio de Janeiro, Brazil

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During a study of the extractives of "cabreuva" or "oleo pardo" wood (*Myrocarpus fastigiatus* Fr. Allem.), a companion substance to cabreuvin (7,3′,4′-trimethoxyisoflavone) was isolated and designated as C-2.[2] It has subsequently been found also in "cabreuva vermelha" or "oleo vermelho" (*Myroxylon balsamum* (L.) Harms).[3] Elementary, functional group and infrared spectral analyses revealed C-2 to be a hydroxydimethoxyflavone or isoflavone. A comparison of its chromatographic properties (Table I) with those of known representatives of these two classes[4] indicated that C-2 was probably an isoflavone. This was confirmed by demethylating it with aluminum chloride in dry ether and acetylating the product. The acetate thus produced had a spectrum which was almost identical with those of isoflavone and various acetylated hydroxyisoflavones, but which differed from the spectrum of flavone (Table II).

Up to the present, only one natural hydroxydimethoxyisoflavone has been described in the literature. This is afromosin, whose isolation from *Afrormosia elata* Harms was reported by McMurry and Theng[5] Mixed melting point, spectral and chromatographic comparisons (Tables I and III) of samples of afromosin (7-hydroxy-6,4′-dimethoxyisoflavone), its methyl ether and 6,7,4′-trihydroxyisoflavone[6] with C-2 and its appropriate derivatives showed that these two isoflavones were identical.

It has been mentioned several times in the literature that isoflavones may be distinguished from flavones by the absence of absorption maxima between 320 and 380 mμ, ascribed to the chalcone chromophore of the latter. Nevertheless, it is now appreciated that the substitution pattern of the flavonoids has a profound influence on their ultraviolet spectrum.[7] Thus'

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(1) This paper is part IV in the series "The Chemistry of Brazilian Leguminosae." Part III: W. B. Eyton, W. D. Ollis, I. O. Sutherland, L. M. Jackman, O. R. Gottlieb, and M. Taveira Magalhães, *Proc. Chem. Soc.*, 301 (1962).

(2) O. R. Gottlieb and M. Taveira Magalhães, *Anais Assoc. Brasil. Quim.*, **18**, 89 (1959).

(3) For references to the botanical literature, see ref. 2.

(4) J. B. Harborne, *J. Chromatog.*, **2**, 581 (1959).

(5) T. B. H. McMurry and C. Y. Theng, *J. Chem. Soc.*, 1491 (1960). These authors spell the species *Afromosia elata* Harms. See, however, "Index Kewensis," suplementum quintum, Oxonii e prelo Clarendoniano, 1921, p. 6.

(6) Kindly donated by Dr T B. H. McMurry.

(7) For references see O. R. Gottlieb and M. Taveira Magalhães, *J. Org. Chem.*, **26**, 2449 (1961).