changed IV, m.p. 47–49°, formed. After these crystals were removed by filtration, the residual liquid was added to the aqueous washings (15 ml.) from the reactor and the mixture was heated under reflux for several hours. Afterwards, most of the water was removed and crystals appeared, not of the expected methylphenylphosphinic acid (VI), Ph—P—CH$_3$(O)(OH), m.p. 134°[32] [from oxidation of secondary methylphenylphosphine oxide, Ph—P—H—(CH$_3$)(O)], but phenylphosphonic acid (VII), Ph—P—O(OH)$_2$, m.p. 158–159° (reported[33] m.p. 161–162°), confirmed by infrared. Compound VII probably was produced by hydrolysis of VI.

Anal. Calcd. for $C_6H_7O_3P$: C, 45.6; H, 4.4. Found: C, 45.4; H, 4.1.

Triethylphosphine Oxide (VIII).—By the method of Pickard and Kenyon,[7] 77 g. (0.5 mole) of phosphorus oxychloride was treated with 200 g. (1.5 moles) of ethylmagnesium bromide to give 38 g. (57%) of very hygroscopic VIII, m.p. 42–44° (reported[34] m.p. 44°).

Pyrolysis of Triethylphosphine Oxide (VIII).—Micropyrolysis of this oxide liberated only ethylene between 370° and 650° and the unstable secondary phosphine oxide. Pyrolysis of 20 g. (0.15 mole) of VIII at 580° gave a fuming yellow liquid (12.8 g.) which was extremely inflammable. The olefin trap gained *ca.* 3 g. with ethylene dibromide as the only product. Cautious oxidation of the liquid pyrolysate was followed by addition of 20 ml. of water. The solution was heated under reflux for 2 hr. After the water was removed, fractional distillation gave small amounts of impure ethylphosphonic acid, $C_2H_5PO(OH)_2$, m.p. 53–55° (reported[35] m.p. 61–62°), but the main product was diethylphosphinic acid, a clear liquid, b.p. 110–127° (0.4 mm.), from oxidation of the unstable pyrolysis product, diethylphosphine oxide. The phosphinic acid was confirmed by infrared analysis and formation of a silver salt from silver hydroxide. There also was obtained approximately 2 g. of unchanged VIII.

Tri-*n*-butylphosphine Oxide (IX).—While a stream of air was passed through the liquid, 100 g. (0.46 mole) of tri-*n*-butylphosphine[36] was oxidized quantitatively to IX by reflux at its boiling point (~295°). Pure IX was a hygroscopic white crystalline substance, m.p. 61.6–62.5°.

Pyrolysis of Tri-*n*-butylphosphine Oxide (IX).—Oxide IX yielded only 1-butene when pyrolyzed on the micro scale at temperatures to 550°. Above this temperature, small amounts of isomers appeared along with secondary di-*n*-butylphosphine oxide (X). Decomposition of 20 g. (0.09 mole) of IX at 560° produced *ca.* 4 g. weight increase in the olefin trap (chromatographic analysis showed the presence of only brominated butenes) and 12 g. of brown liquid pyrolysate, smelling of phosphine and fuming in air. Fractional distillation of the pyrolysate gave traces of butylphosphonic acid (XI) [$C_4H_9PO(OH)_2$], dibutylphosphinic acid (XII) [$(C_4H_9)_2PO(OH)$] and 7 g. of slightly impure di-*n*-butylphosphine oxide (XIII), m.p. 64–65° (reported[37] m.p. 66°). The oxide XIII was characterized by oxidation to dibutylphosphinic acid (XII), m.p. 67° (reported[38] m.p. 70–71°).

Trimethylphosphine Oxide (XIV).—Oxide XIV was prepared in a 38% yield from molar amounts of phosphorus oxychloride and the methyl Grignard, as described previously.[7] The pure product was a very hygroscopic white crystalline solid, m.p. 140–142°.

Pyrolysis of Trimethylphosphine Oxide (XIV).—Decomposition of oxide XIV on the micro scale between 350° and 700° produced no detectable breakdown. On a larger scale, 20 g. of the material passed through the reactor at 700° unchanged and was recovered as white crystals with only a small loss (2 to 3 g.) by hold-up in the reactor.

Triphenylphosphine Oxide (XV).—Oxidation of 100 g. (0.36 mole) of triphenylphosphine gave an almost quantitative yield of XV, m.p. 152–153°, when the reaction was carried out with heating under reflux for several hours in the presence of excess dilute nitric acid.

Pyrolysis of Triphenylphosphine Oxide (XV).—The oxide XV showed no decomposition in the microreactor to 700°, but slight discoloration was noted when it was pyrolyzed at 690° in the Vycor reactor under nitrogen. It was recovered as a pale yellow crystalline material, m.p. 150–152°.

---

[32] W. J. Pope and C. S. Gibson, *J. Chem. Soc.*, 740 (1912).

[33] A. D. F. Toy, *J. Am. Chem. Soc.*, **70**, 186 (1948).

[34] J. N. Collie and F. Reynolds, *J. Chem. Soc.*, 367 (1915).

[35] G. M. Kosolapoff, *J. Am. Chem. Soc.*, **67**, 1180 (1945).

[36] The authors are grateful to Food Machinery and Chemical Corp. for a generous supply of this compound.

[37] M. M. Rauhut, I. Hechenbleikner, H. A. Currier, and V. P. Wystrach, *J. Am. Chem. Soc.*, **80**, 6690 (1958).

[38] G. M. Kosolapoff, *ibid.*, **71**, 369 (1949).

The Migratory Group in the Jacobsen Rearrangement[1]

ELLIOT N. MARVELL AND DANIEL WEBB

Chemistry Department, Oregon State University, Corvallis, Oregon

Received May 7, 1962

1,2,4,5-Tetraethylbenzene-α-C^{14} has been submitted to the Jacobsen rearrangement and the product degraded. The ethyl group has been shown thus to migrate without rearrangement.

The Jacobsen rearrangement,[2] known since early in the 1880's[3] has evoked some interest in the fascinating art of mechanistic speculation,[4] but not any great amount of experimental confirmation. About twenty years ago Arnold and Barnes[5] presented some evidence on the basis of which they proposed the following mechanism. Since Smith and Lo tried unsuccessfully[6] to verify one possible consequence of this mechanism the subject

---

[1] Taken in part from a thesis submitted by Daniel Webb in partial fulfillment of the requirements for the M.S. degree, Oregon State University, September 1960. The authors are happy to acknowledge generous financial assistance by the Sigma Xi-RESA research fund and the general research grants of Oregon State University.

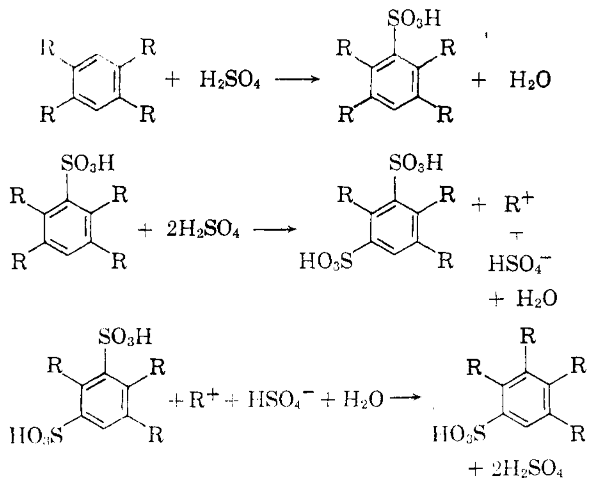
[2] For a general review see L. I. Smith, "Organic Reactions," Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 370.

[3] (a) J. Herzig, *Ber.*, **14**, 1205 (1881); (b) O. Jacobsen, *ibid.*, **19**, 1209 (1886).

[4] *Cf.*, for example, E. R. Alexander, "Ionic Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1950, pp. 257–259; and L. F. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1961, pp. 665–667.

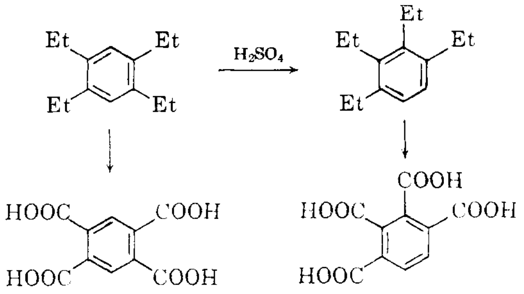
[5] R. T. Arnold and R. A. Barnes, *J. Am. Chem. Soc.*, **66**, 960 (1944).

[6] L. I. Smith and C. P. Lo, *ibid.*, **70**, 2209 (1948).



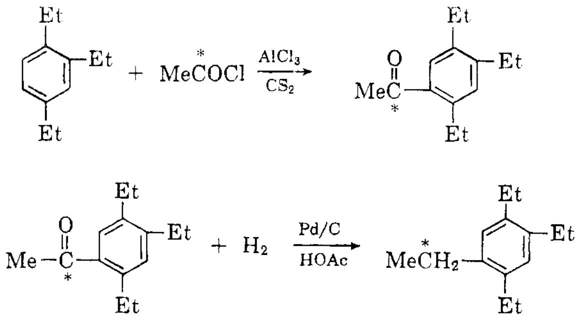
has lain virtually fallow.[7] The recent and intriguing observations of Roberts[8] on the behavior of carbonium ions ($RCl + AlCl_3$) in the presence and absence of aromatic substances suggested the investigation of a suitably labeled tetraethylbenzene under Jacobsen conditions. The results of that study will be reported in this paper.

Both 1,2,3,5- and 1,2,4,5-tetraethylbenzenes have been reported[9] to rearrange to 1,2,3,4-tetraethylbenzene in high yield. Clearly then by employing the annexed scheme with a properly labeled ethyl group, the symmetry properties of the migratory ethyl group can be examined. In the work to be described here an ethyl group labeled in the alpha position by C^{14} has been used. Although a mixture of isomeric tetraethylbenzenes has been employed for the synthesis of 1,2,3,4-tetraethylbenzene,[9c] it was not considered advisable to use the mixture in this study, because of the greater convenience of introducing the label at the latest stage in the synthesis of the starting material. Since it has never been shown that more than a single migration occurs in the course of the Jacobsen rearrangement, it is mandatory that *all four ethyl groups be identical* to ensure that the labeled group participate in the rearrangement. The choice of 1,2,4,5-tetraethylbenzene as the substrate is thus dictated.



Results

The synthesis of α-C^{14}-labeled 1,2,4,5-tetraethylbenzene was accomplished by the annexed scheme. The 1,2,4-triethylbenzene was prepared from a mixture of diethylbenzenes *via* acetylation and reduction, and was shown by gas chromatography to contain a minimum of 98% 1,2,4-triethylbenzene. Acetylation of this material gave an apparently uniform ketone which was reduced directly without attempt at careful purification. Distillation of this tetraethylbenzene gave two fractions of identical properties. Both showed only a single peak by gas chromatography and use of a melting point *vs.* composition diagram[10] for mixtures of 1,2,4,5-tetraethylbenzene (m.p. +10°) and its 1,2,3,5 isomer (m.p. −21°) indicates that this product is 98–99% 1,2,4,5-tetraethylbenzene.



This 1,2,4,5-tetraethylbenzene labeled with C^{14} on the alpha carbon was rearranged, the rearranged sulfonic acid hydrolyzed, and the crude hydrocarbon product fractionally distilled. Two fractions of identical refractive index, neither of which would crystallize in a Dry Ice bath, were obtained. While the purity of the product was not ascertained accurately, the physical properties accord well with those reported earlier.[10] The radiochemical analysis which showed this product to have the same specific activity as that of the starting material merely indicates that no unanticipated complexities occurred during the rearrangement.

The stringent requirements of the radiochemical analysis for identity and purity of the sample are met most satisfactorily for semimicro operation by a solid. Consequently the starting material and the rearrangement product were oxidized to the related tetracarboxylic acids.

Oxidation of tetraalkylbenzenes has always proved a difficult process; the difficulty apparently being associated with solubility problems. Since no single oxidation step was found to give satisfactory results, a dual process involving partial oxidation by dilute nitric acid followed by final

---

[7] *Cf.*, however, the recent study of the rates of sulfonation and desulfonation, M. Kilpatrick and M. W. Meyer, *J. Phys. Chem.*, **65**, 1312 (1961), for suggestions concerning the mechanism of the Jacobsen rearrangement.

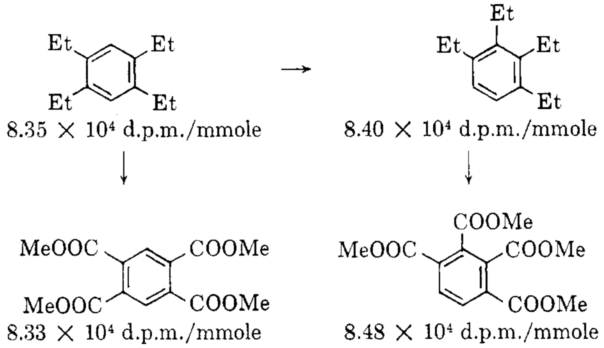
[8] (a) R. M. Roberts, G. A. Ropp, and O. K. Neville, *J. Am. Chem. Soc.*, **77**, 1764 (1955); (b) R. M. Roberts and S. G. Brandenberger, *ibid.*, **79**, 5484 (1957).

[9] (a) A. Töhl, *Ber.*, **21**, 904 (1888); (*b*) O. Jacobsen, *ibid.*, **21**, 2814, 2819 (1888); (c) L. I. Smith and C. O. Guss, *J. Am. Chem. Soc.*, **62**, 2631 (1940).

[10] L. I. Smith and C. O. Guss, *ibid.*, **62**, 2630 (1940).

oxidation with permanganate was employed. Paper chromatography showed the presence of a single acid at this point. The tetracarboxylic acid was in each case converted to the more readily purified tetraester *via* diazomethane and the ester recrystallized to a constant melting point and constant specific activity.

The results of the radiochemical assays are shown below. In each case the results reported are the average of at least two determinations and for the two solid esters were shown to be unaltered by further recrystallization. As can be seen the data lie well within a limit of error of ±1%.



8.35×10^4 d.p.m./mmole

8.40×10^4 d.p.m./mmole

8.33×10^4 d.p.m./mmole

8.48×10^4 d.p.m./mmole

Discussion

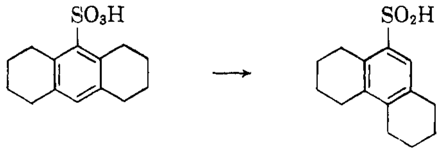
These results demonstrate unequivocally that the migratory ethyl groups maintain the functionality of the alpha carbon not less than 90% of the time. Within these limits the migratory group cannot pass through any symmetrical stage. Thus we can eliminate from consideration any process involving hydrogen-bridged ions, equilibria between the ethyl carbonium ion and ethylene, and equilibria involving hydride shifts in ethyl carbonium ions. We can now examine what this may mean in terms of mechanisms for the Jacobsen rearrangement.

As was noted earlier an important mechanistic proposal for the Jacobsen rearrangement is that of Arnold and Barnes.[5] These authors propose that the migratory group is a carbonium ion, presumably an independent entity in solution. The critical question then is—what can be said concerning the behavior of an ethyl carbonium ion in concentrated sulfuric acid? We shall adopt here the "encumbered ion" notation of Taft[11] for convenience in description. Clearly the work of Roberts, Ropp, and Neville[8a] shows that an ethyl carbonium ion encumbered to no greater degree than is provided by the ion pair $Et^+ AlCl_4^-$ in solvent ethyl chloride is capable of rapid equilibration of the ethyl carbonium ion *via*

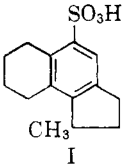
$$CH_3{-}CH_2^{\oplus} \rightleftharpoons {}^{\oplus}CH_2{-}CH_3$$

They also show that the presence of an aromatic hydrocarbon provides sufficient encumbrance, perhaps *via* a π-complex, so that equilibration is effectively prevented. There appears to be no relevant data on the nature of an ethyl carbonium ion in sulfuric acid solution,[12] and therefore in view of the behavior of the propyl system we shall assume that a solvated ethyl carbonium ion in sulfuric acid is able to undergo equilibration. The data presented here then can be interpreted on this basis as indicating that the Jacobsen rearrangement cannot occur *via* a solvated but otherwise unencumbered carbonium ion.

This interpretation draws additional support from the studies of Schroeter[13] on the rearrangement of octahydroanthracene-9-sulfonic acid. He has shown that octahydrophenanthrene-9-sulfonic acid



is obtained in this reaction in high yield and his data certainly seem to exclude the structure I for



I

his product. Since the propyl carbonium ion rearranges a primary carbonium ion functionally capable of rearranging to a secondary carbonium ion certainly should do so unless specifically encumbered so as to prevent that rearrangement.

Therefore we can now examine the mechanistic proposal made by Arnold and Barnes.[5] It is not completely clear from their paper what the nature of the migratory group was intended to be since they write $CH_3^{\oplus}\ H_2O$ while speaking of an "alkyl cation." Later, when discussing Schroeter's work they write $-CH_2.^{\oplus}$ Since the simple unencumbered carbonium ion no longer appears tenable, certain modifications of their ideas will be necessitated, but the present data in no way vitiate their entire mechanism.

One mode of migration which is in complete accord with the results of the present work is the common 1,2-alkyl migration of carbonium ion chemistry. Both the dienone–phenol rearrange-

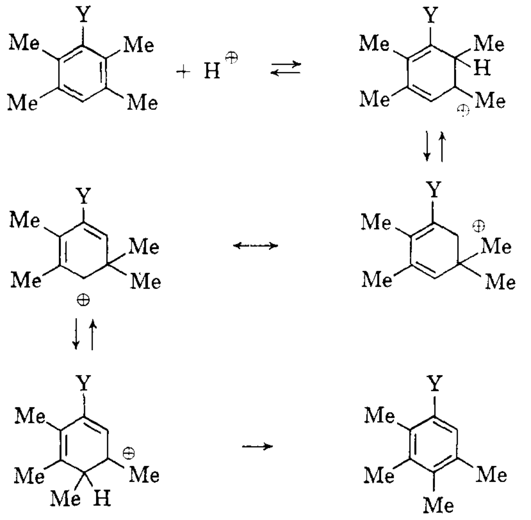
---

[11] R. H. Boyd, R. W. Taft, Jr., A. P. Wolf, and D. R. Christman, *J. Am. Chem. Soc.*, **82**, 4729 (1960).

[12] It has been reported by Gillespie [R. J. Gillespie, *J. Chem. Soc.*, 2542 (1950); R. J. Gillespie and J. A. Leisten, *Quart. Rev.*, **8**, 40 (1954)] that ethyl alcohol gives a stable solution in sulfuric acid with a ν value near to 3. The stability of this solution and the lack of polymerization of ethylene by sulfuric acid prompted Gillespie to conclude that the concentration of ethyl carbonium ions in sulfuric acid was exceedingly small. However, *n*-propyl alcohol forms a yellow solution in sulfuric acid which rapidly undergoes reactions attributed to the formation of isopropyl carbonium ions. This implies that a primary carbonium ion can form in sulfuric acid and is weakly enough encumbered so that a hydride shift from a secondary carbon is rapid.

[13] G. Schroeter and S. Götsky, *Ber.*, **60**, 2035 (1927).

ment[14] and alkyl migrations common during Friedel–Crafts alkylations[15] are familiar examples which involve aromatic rings. The migrations necessary for the Jacobsen rearrangement could occur as illustrated here, though the particular group which migrates and the direction of migration was chosen for simplicity of illustration only. The mechanism suggested by Kilpatrick and Meyer[7] is equivalent to a process of this type where Y = H. Since the studies of Smith and Cass[16] suggest that the sulfonic acid rather than the hydrocarbon rearranges the generalized substituent Y was written. It is also possible to rewrite the mechanism advanced by Arnold and Barnes[5] to permit migration of this type. Further mechanistic detail will have to await the results of new experimental tests.



Y = H or SO_3H

Experimental

1,2,4-Triethylbenzene.—A commercial mixture of diethylbenzenes (3 peaks on 6-ft. Carbowax 1500 column at 200°) was treated in 2.5-molar amounts with acetyl chloride (2.75 moles) and anhydrous aluminum chloride (2.75 moles) in 300 ml. of carbon disulfide at −5°. The mixture was allowed to stand overnight, decomposed as usual, and the ketone distilled, b.p. 130–135° (21–23 mm.); yield 81%. This ketone was reduced over palladium–charcoal (7.5% of weight of substrate) in glacial acetic acid. The product was carefully distilled through a 2-ft. Vigreux and a central cut, b.p. 53–55° (0.55 mm.), $n^{20}D$ 1.5001; yield 70% was used for further work. The literature[17] reports b.p. 99° (15 mm.), $n^{17}D$ 1.5010 for this substance. The product gave a single sharp peak indicating a purity of not less than 98% *via* GPC on a 6-ft. Carbowax 1500 column at 200°.

1,2,4,5-Tetraethylbenzene.—A sample of 1,2,4-triethylbenzene (0.185 mole) was acetylated as described above for diethylbenzene. The crude ketone was obtained in 95% yield and distilled as a clear liquid, b.p. 87–90° (0.4 mm.), $n^{17}D$ 1.5262; yield 81%. Klages[17] reports that the ketone boils at 146° (13 mm.). One-tenth mole of this ketone was hydrogenated over 1.75 g. of 10% palladium-charcoal in 40 ml. of glacial acetic acid at 40 p.s.i.g. initial pressure. The hydrocarbon was separated from acetic acid *via* dilution with water and extraction with benzene. It was purified by distillation on an 18-in. Vigreux column. A central cut, b.p. 66.8–68.0° (0.45 mm.), $n^{20}D$ 1.5056, m.p. 9.5–9.7°, was obtained in 70% yield. Smith and Guss[10] report $n^{20}D$ 1.5056, m.p. 10° for 1,2,4,5-tetraethylbenzene.

Table I

Compound	Wt. in mg.	C.p.m.	% Effic.	d.p.m./mmole × 10^4	
1,2,4,5-Tetraethylbenzene	1.831	505.7	64.2	8.17	
	1.904	529.0	65.1	8.11	av. 8.35
	1.933	578.8	64.5	8.77[a]	
1,2,3,4-Tetraethylbenzene	2.117	606.7	64.3	8.47	av. 8.40
	2.384	679.8	65.1	8.34	
Tetramethyl 1,2,4,5-benzenetetracarboxylate	1.846	332.0	65.3	8.31	av. 8.33
	2.210	388.5	65.2	8.36	
	2.046	356.4	66.2	8.16	av. 8.32[b]
	1.981	351.8	64.9	8.48	
Tetramethyl 1,2,3,4-benzenetetracarboxylate	2.171	387.6	63.2	8.78	av. 8.67
	2.026	361.3	64.5	8.57	
	1.996	351.9	63.8	8.57	av. 8.38[b]
	1.988	342.7	65.3	8.18	
	2.130	375.0	64.7	8.43	av. 8.58[c]
	2.131	394.4	65.8	8.75	

[a] Sample was frozen out, partially thawed, and the solid washed free of melt twice as a purification method before counting. [b] Samples used first were recrystallized once more. [c] Samples recrystallized a second time.

1,2,4,5-Tetraethylbenzene-α-C^{14}.—Carbonyl-labeled sodium acetate, 25.0 mg., was mixed with 20 g. of thionyl chloride in a 50-ml. three-necked flask equipped with a magnetic stirrer, dropping funnel, and reflux condenser. To this was added 5.35 g. (0.0892 mole) of acetic acid, and after the addition the solution was heated to reflux for 2 hr. The acetyl chloride was distilled through an 11-in. Vigreux column and the residue swept out twice with 3.00-g. portions of additional acetyl chloride.

The labeled acetyl chloride was used with 167 mmoles of 1,2,4-triethylbenzene to prepare 1,2,4,5-tetraethylbenzene as described above. After careful distillation 10.2 g. (54.0 mmoles) of tetraethylbenzene, b.p. 63.5–64.0° (0.40 mm.), m.p. 9.6–9.8°, was obtained. The radiochemical yield was 10%.

Jacobsen Rearrangement.—Eight grams (42 mmoles) of labeled tetraethylbenzene was mixed with 28.90 g. of reagent sulfuric acid and the mixture heated rapidly to 100°. Rapid mixing produced complete solution in about 30 min. This solution was maintained 10 min. at 100° and was then poured onto 29 g. of crushed ice. Steam distillation of the diluted mixture at 140° was carried out until only a few traces of isoluble residue remained in the still pot. The distillate was saturated with sodium chloride and extracted with ether. The ether solution was dried over calcium chloride and the hydrocarbon isolated by distillation through a 12-in. Vigreux column, b.p. 55–56° (0.25 mm.), $n^{20}D$ 1.5130, 2.52 g. (13.3 mmoles). The liquid did not solidify in a Dry Ice bath. Smith and Guss[10] report $n^{20}D$ 1.5125, m.p. −50°.

Tetramethyl Benzene-1,2,4,5-tetracarboxylate.—A mixture of 0.5 g. of 1,2,4,5-tetraethylbenzene, 7 ml. of distilled water, and 2 ml. of concentrated nitric acid was heated in a sealed tube at 155° for 8 hr. The volatile materials were removed by evaporation *in vacuo* and the residual solids were treated with 6 ml. of 1.5 *N* potassium hydroxide and 20 ml. of 5% potassium permanganate at 90°, solid permanganate being added periodically as decolorization occurred. After 8 hr. the excess oxidant was destroyed with ethanol, and the manganese dioxide removed by fil-

---

(14) R. T. Arnold and J. S. Buckley, Jr., *J. Am. Chem. Soc.*, **71**, 1781 (1949).

(15)(a) M. C. Brown and H. Jungk, *ibid.*, **77**, 5579 (1955); (b) D. A. McCaulay and A. P. Lien, *ibid.*, **74**, 6246 (1952).

(16) L. I. Smith and O. W. Cass, *ibid.*, **54**, 1614 (1932).

(17) A. Klages and R. Keil, *Ber.*, **36**, 1634 (1903).

tration. The filtrate was concentrated *in vacuo* and passed through a Dowex-50 resin column in acid cycle. The eluate was evaporated to dryness and the residue recrystallized from about 20 ml. of concentrated nitric acid. Paper chromatography using ether–acetic acid–water; 13:3:1 as solvent showed only a single spot at this point.

The combined acids from several oxidations (0.25 g.) were dissolved in 10 ml. of anhydrous methanol and treated with an excess of ethereal diazomethane. Excess diazomethane was destroyed with acetic acid and the polymethylene removed by filtration. The solution was evaporated to dryness and the residue recrystallized from aqueous methanol. Further recrystallization from benzene–hexane gave an ester, m.p. 142–144°. This ester has been reported[18] to melt at 143–144°. An authentic sample[19] did not depress the melting point of the ester so prepared.

Tetramethyl Benzene-1,2,3,4-tetracarboxylate.—Oxidation of 1,2,3,4-tetraethylbenzene followed by esterification as described above gave the desired ester, m.p. 130–131°, which did not depress the melting point of an authentic sample prepared according to the method of Read and Purves.[19] These authors report that the ester melts at 130–131°.

Determination of Radioactivity.—Radioactivity was assessed with a Packard Tri-Carb scintillation counter Model 314 using a scintillation solution containing 2.5005 g. of PPO and 0.0182 g. of POPOP in 250 ml. of toluene solution. The counting efficiency was determined by the internal standard method, and counting was carried out a sufficient time so that the standard deviation did exceed 1%. An HVT setting of 950 v. and window settings were adjusted to give a maximum for $\overline{\text{effic.}}^2$/background. The data in Table I were obtained.

---

[18] D. E. Read and C. B. Purves, *J. Am. Chem. Soc.*, **74**, 116 (1952).

[19] This authentic sample was prepared from 1,2,4,5-benzenetetracarboxylic acid kindly supplied by Dr. L. I. Smith.

Grignard Reagents from *o*-Bromobenzylamines[1]

NARIMAN B. MEHTA AND JUSTINA ZUPICICH STRELITZ

The Wellcome Research Laboratories, Burroughs Wellcome and Co. (U.S.A.) Inc., Tuckahoe, New York

Received July 19, 1962

Magnesium metal has been found to react with *o*-bromobenzylamines to form organomagnesium compounds which behave like Grignard reagents. These have been treated with aldehydes, ketones, esters, etc., to give the expected products in excellent yields.

Ehrlich[2] has shown that *p*-bromodimethylaniline in absolute ether could react with magnesium if initially activated by ethyl bromide. Subsequently, this method was employed by several other investigators,[3] but only with *p*-bromodimethylaniline. The carbonation reaction on the Grignard reagent from *o*-bromodimethylaniline studied by Holmberg[3f] gave a symmetrical ketone.

Recently, Miescher and Marxer[4] have patented a procedure for preparing aminocarbinols from Grignard reagents of halogenoaliphatic tertiary amines of the type $R_2N(CH_2)_nX$ where $n \gtrless 3$. The reaction has to be initiated by traces of ethyl bromide and is completed in the presence of ketone or aldehyde.

The formation of organomagnesium compounds of the Grignard reagent type from haloaralkyl bases does not appear to have been previously reported. Such reagents could render possible syntheses of compounds otherwise not easily accessible.[5]

Some pecularities of Grignard reagents containing tertiary amino groups might be anticipated. Barrett[6] treated aromatic Grignard reagents with ω-dialkylaminocarboxylic esters having three or more methylene groups between the amino and the ester functions and obtained the bulk of their product as ketones despite the presence of large excess of the Grignard reagent. This observation suggests stabilization of the primary reaction adduct through coordination of metal with the unshared electrons of the nitrogen.

Magnesium metal reacts with *o*-bromobenzylamines of the type I to yield the desired organomagnesium derivatives II, soluble in anhydrous ether. These respond to the Gilman test[7] with Michler's ketone and give the normal reactions of Grignard reagents with aldehydes, ketones, esters, acid chlorides, isocyanates, and isothiocyanates. In such reactions the expected products were isolated in 50–70% yields. Analytical (iodimetric)[8a] assay of solutions of Grignard reagent

---

[1] Presented before the Division of Organic Chemistry at the 140th National Meeting of the American Chemical Society, Chicago, Ill., September 1961, p. 34-G.

[2] P. Ehrlich and F. Sachs, *Ber.*, **36**, 4296 (1903). This complex with Michler's ketone gives methyl violet—a well known lecture demonstration experiment.

[3] (a) F. Sachs and L. Sachs, *ibid.*, **37**, 3088 (1904); (b) S. S. Jenkins, *J. Am. Chem. Soc.*, **53**, 3115 (1931); (c) J. S. Chamberlain and M. F. Dull, *ibid.*, **50**, 3088 (1928); (d) H. Gilman and J. Swiss, *ibid.*, **62**, 1847 (1940); (e) H. Gilman and R. H. Kirby, *ibid.*, **63**, 2046 (1941); (f) G. A. Holmberg, *Acta Chem. Scand.*, **9**, 555 (1955).

[4] (a) K. Miescher and A. Marxer, U. S. Patent 2,411,664 (November 26, 1946); (b) A. Marxer, *Helv. Chim. Acta*, **24**, 209 E (1941).

[5] After the completion of this work, F. N. Jones and C. H. Hauser [*J. Org. Chem.*, **27**, 701 (1962)] reported syntheses of a parallel nature using lithium reagents.

[6] P. A. Barrett, U. S. Patent 2,649,444 (August 18, 1953); *cf.* also British Patent 614,567 (December 17, 1948).

[7] The Gilman test was performed on the filtered ethereal solution of the Grignard complex. Traces of magnesium in acetic acid impart a greenish blue tint to the aqueous solution and can be misleading.

[8] (a) O. Job and R. Reich, *Bull. soc. chim.*, **33**, [4], 1414 (1923); *ibid.*, **37**, [4], 976 (1925); (b) The formation of a strained planar ring through the complex Mg ← N for the Grignard reagent from *o*-bromodimethylaniline has been suggested by Holmberg.[3f] High resolution n.m.r. studies are being made by Dr. B. Shapiro, Mellon Institute, Pittsburgh, Pa.