tivated enough to react with molecules as weakly basic as water molecules, thereby producing a pseudo-unimolecular reaction. The exact nature of the attacking molecule, if any, is the subject of further investigation.

STILLWATER, OKLAHOMA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

Studies in Stereochemistry. XXII. The Preparation and Reactions of Trimesitylborane. Evidence for the Non-localized Nature of the Odd Electron in Triarylborane Radical Ions and Related Free Radicals[1]

BY HERBERT C. BROWN AND VANCE H. DODSON

RECEIVED AUGUST 13, 1956

Trimesitylborane has been synthesized and its chemical behavior compared with that of triphenyl- and tri-α-naphthylboranes. In contrast to the latter compounds, trimesitylborane is far less reactive toward oxygen and water. Moreover, it fails to add either ammonia or sodium alkoxides. It is concluded that the steric effects of the three mesityl groups are so large as to hinder greatly the approach of a reacting molecule to the central atom. On the other hand, sodium reacts with trimesitylborane to form sodio derivatives analogous to those previously reported for triphenyl- and tri-α-naphthylborane. Since the vacant *p*-orbital of the boron atom is so completely blocked by the three mesityl groups, the ready formation of sodio derivatives in the case of trimesitylborane argues strongly for the entrance of the electron from the sodium atom into a non-localized orbital of the trimesitylborane molecule.

Differences in the chemical behavior of certain trialkylboranes can be correlated with the steric requirements of the alkyl groups in the boron derivative. Thus, trimethylamine forms a more stable addition compound with trimethylborane than does ammonia, whereas the reverse is true in the case of tri-*t*-butylborane.[2] Indeed, in this case trimethylamine exhibits no tendency to unite with the boron component.

It appeared of interest to examine the behavior of a borane derivative which might be expected to be even more hindered than tri-*t*-butylborane. Accordingly, the synthesis of trimesitylborane was undertaken and a study made of its chemical properties. For purposes of comparison, triphenyl- and tri-α-naphthylborane were included in the study. The behavior of these three compounds toward ammonia, sodium methoxide and *t*-butoxide, oxygen, water, sodium hydroxide and sodium metal was compared.

Results

Triphenylborane[3] and tri-α-naphthylborane[3] were prepared by treating phenylmagnesium bromide and α-naphthylmagnesium bromide, respectively, with boron trifluoride, according to the procedures previously described.[4,5] Utilization of a similar procedure for the preparation of trimesitylborane[3] resulted in the formation of dimesitylfluoroborane. Trimesitylborane could be obtained only by the use of a large excess of mesitylmagnesium bromide and forcing conditions.

Treatment of the three triarylboranes in ether solution with gaseous ammonia led to the precipitation of white crystalline addition compounds in the case of TPB and TNB ($TPB:NH_3$ and $TNB:NH_3$). However, under the same conditions TMB showed no tendency to react with ammonia. The data are summarized in Table I.

TABLE I

REACTIONS OF TPB, TNB AND TMB WITH AMMONIA

Triaryl-boron R_3B	Wt. of R_3B, g.	Wt. of combined ammonia, g.	Wt. of ammonia calcd. for $R_3B:NH_3$, g.
TPB	0.4380	0.0293	0.0308
	0.6753	.0471	.0473
TNB	1.2131	.0518	.0527
	0.5162	.0218	.0224
TMB	.1902	.0004	.0088
	.4458	.0007	.0206

Benzene solutions of TPB and TNB could be titrated stoichiometrically by standard solutions of sodium methoxide in methanol, using phenolphthalein as indicator. In the case of TNB it was demonstrated that the neutralization reaction involved the reaction of a sodium methoxide molecule with the TNB molecule by isolating the product, $TNB \cdot NaOCH_3$, presumably $Na^+[(\alpha\text{-}C_{10}H_7)_3BOCH_3]^-$. Water hydrolyzed the salt with the formation of naphthalene and di-α-naphthylborinic acid. However, the addition of anhydrous hydrogen chloride to the salt (in benzene solution) permitted the regeneration and recovery of TNB. The reactions are

$$Na^+[(\alpha\text{-}C_{10}H_7)_3B:OCH_3]^- + 2H_2O \longrightarrow C_{10}H_8 + (\alpha\text{-}C_{10}H_7)_2BOH + NaOH + CH_3OH$$

$$Na^+[(\alpha\text{-}C_{10}H_7)_3B:OCH_3]^- + HCl \xrightarrow{\text{benzene}} (\alpha\text{-}C_{10}H_7)_3B + NaCl + CH_3OH$$

In titrations of TPB and TNB with sodium *t*-butoxide in *t*-butyl alcohol the indicator changed color when less than 50% of the stoichiometric quantity of base had been added. However, benzene solutions of TMB failed to react with either base. The results of several typical titrations are summarized in Table II.

The reactivities of the triarylboranes toward oxygen were examined in α-bromonaphthalene solution. Both TPB and TNB were found to

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[1] Based upon a thesis submitted by Vance H. Dodson in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] H. C. Brown, THIS JOURNAL, **67**, 374 (1945).

[3] For convenience the following abbreviations will be used: triphenylborane, TPB; tri-α-naphthylborane, TNB; trimesitylborane, TMB.

[4] E. Krause and R. Nitsche, *Ber.*, **55**, 1261 (1922).

[5] H. C. Brown and S. Sujishi, THIS JOURNAL, **70**, 2793 (1948).

TABLE II

REACTION OF TPB AND TNB WITH SODIUM ALKOXIDES WITH PHENOLPHTHALEIN AS INDICATOR

	TPB		TNB	
Sodium alkoxide	Ml. base used	Ml. base calcd.	Ml. base used	Ml. base calcd.
Methoxide	11.10[a]	11.05	18.35[b]	18.41
	5.23[a]	5.22	15.60[b]	15.74
t-Butoxide	31.5[c]	68.3	15.1[c]	35.2
	95.2[c]	188.5	21.4[c]	51.4

[a] 0.1511 *M*. [b] 0.1149 *M*. [c] 0.0023 *M*.

react with dry oxygen gas in a molar ratio of 1 O_2 to 2 R_3B. The reaction is presumed to be

$$R_3B + {}^1/_2O_2 \longrightarrow R_2BOR$$

In the case of TPB the absorption of oxygen was complete in approximately 1 hr. at 25°, whereas TNB required 50 days for completion. TMB solutions showed no absorption of oxygen in periods as long as 15 months. The results of typical experiments are summarized in Table III.

TABLE III

REACTION OF TPB AND TNB (IN α-BROMONAPHTHALENE) WITH OXYGEN

TPB[a,c]		TNB[d,f]	
Time, hr.	Oxygen reacted ml. (S.T.P.)	Time, days	Oxygen reacted, ml. (S.T.P.)
0	0	0	0
0.25	9.9	3	7.9
0.50	11.5	17	11.9
0.75	11.6	42	12.8
1.25	12.4	54	13.2
2.25	12.4	66	13.1[e]
24.0	12.4[b]		

[a] 0.933 mmole. [b] 0.496 mmole. [c] 1.0 O_2/1.9 TPB. [d] 1.116 mmole. [e] 0.526 mmole. [f] 1.0 O_2/2.1 TNB.

TPB hydrolyzed moderately rapidly in cold water, forming a mixture of phenylboric oxide, C_6H_5BO, and phenylboronic acid, $C_6H_5B(OH)_2$. Neither TNB nor TMB showed any significant change after prolonged contact with cold water. However, refluxing water converted TNB partially into naphthalene and α-naphthylboronic acid, α-$C_{10}H_7B(OH)_2$. Dilute sodium hydroxide rapidly converted TPB into the sodium salt of phenylboronic acid and slowly converted TNB into the sodium salt of α-naphthylboronic acid. Dilute alkali had no noticeable effect on TMB in a period of four days.

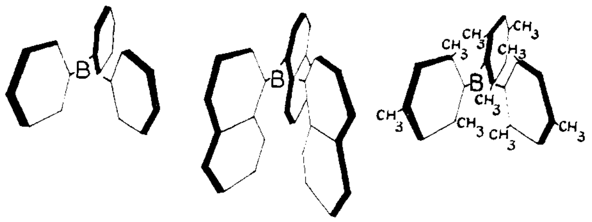
Both TPB and TNB react readily with sodium amalgam to form sodium derivatives[6,7] which have many of the characteristics of the triarylmethyl free radicals.[8]

$$(C_6H_5)_3B + Na \longrightarrow [(C_6H_5)_3B\cdot]^-Na^+$$

Treatment of TMB with sodium amalgam in dry ethyl ether led to the take-up of sodium and the formation of a colored addition compound. The amount of sodium reacted could be varied from TMB·Na to TMB·2Na, depending upon the concentration of sodium in the amalgam and the reaction time.[9]

Discussion

Examination of molecular models of the three triarylboranes indicates that the shielding of the boron atom by the three surrounding aryl groups increases in the order TPB < TNB < TMB. Simplified line drawings of the three compounds are shown in Fig. 1.



Triphenylboron Tri-α-naphthylboron Trimesitylboron

Fig. 1.—Diagrams illustrating steric situation of the central boron atom in TPB, TNB and TMB.

Support for this conclusion is provided by the available data summarized in Table IV.

Ammonia reacts with both TPB and TNB, but not with TMB, whereas the more hindered base, trimethylamine, reacts only with TPB. Even sodium methoxide, a very strong base with low steric requirements, fails to react with TMB.

The reaction of oxygen with organoboranes is believed to proceed by a direct attack on the central boron atom by the oxygen molecule.[10] The remarkable difference in the reactivities of TPB, TNB and TMB with oxygen is in accord with this interpretation.

The hydrolysis is catalyzed by acid. In the similar acid-catalyzed solvolysis of aryltrimethylsilanes,[11] it has been shown the reaction proceeds through an attack of a proton on the aromatic ring and a solvent molecule on the silicon atom. If the steric requirements of the groups on the silicon atom are maintained constant, the reaction rate increases with electron-donating substituents in a manner typical of that to be expected for an electrophilic substitution. In the present case, were the reaction to proceed through a dominant rate-determining attack of a proton on the aromatic ring, the reactivity would be predicted to vary in the order, TPB < TNB < TMB. The opposite order which is observed points to an important steric control of an attack of a water molecule on the central boron atom in the rate-determining stage.

All of the results point to a remarkable degree of steric hindrance in TMB. Indeed, an examination of the molecular model reveals that the central boron atom is completely contained within a cage of the three phenyl rings and the six *o*-methyl groups. No approach to the central boron atom appears possible without prior disruption of this protecting cage.

On this basis the ready reaction of sodium amalgam with TMB is particularly interesting.

The three alkyl or aryl groups in a borane derivative, R_3B, are believed to utilize sp^2-hybrid orbitals.

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[6] E. Krause and H. Polack, *Ber.*, **59**, 777 (1926).

[7] E. Krause and P. Nobbe, *ibid.*, **63**, 940 (1930).

[8] H. E. Bent, THIS JOURNAL, **57**, 1259 (1935).

[9] A detailed study of the reaction of TMB with sodium has recently appeared; T. L. Chu and T. J. Weismann, *ibid.*, **78**, 23 (1956).

[10] J. R. Johnson and M. G. VanCampen, *ibid.*, **60**, 121 (1938).

[11] C. Eaborn, *J. Chem. Soc.*, 3148 (1953).

TABLE IV

A COMPARISON OF THE REACTIONS OF TPB, TNB AND TMB

Reagent	Triphenylborane	Tri-α-naphthylborane	Trimesitylborane
Ammonia	Forms a 1:1 addition compound	Forms a 1:1 addition compound	No reacn.
Trimethylamine	Forms a 1:1 addition compound[a]	No reaction[b]	No reacn.
Sodium methoxide	Forms a sodium methoxide salt	Forms a sodium methoxide salt	No reacn.
Sodium *t*-butoxide	Forms a sodium *t*-butoxide salt to some extent	Forms a sodium *t*-butoxide salt to some extent	No reacn.
Oxygen	Reacts rapidly in a mole ratio $1O_2$ to 2 TPB	Reacts very slowly in a mole ratio $1O_2$ to 2TNB	No reacn.
Water (cold)	Reacts rapidly	No reaction	No reacn.
Water (hot)	Reacts very rapidly	Reacts slowly	No reacn.
Dilute NaOH	Reacts very rapidly	Reacts slowly	No reacn.
Sodium amalgam	Reacts readily[c]	Reacts readily[d]	Reacts readily

[a] Ref. 16. [b] Ref. 5. [c] Ref. 6. [d] Ref. 7.

This leaves available a vacant 2*p*-orbital. One possible interpretation of the reaction with triarylboranes involves the transfer of the electron from sodium to this vacant 2*p*-orbital.

Recently, the magnetic susceptibility of $\text{TMB}\cdot\text{Na}$ was examined.[9] The results indicate that in dilute solution in tetrahydrofuran the molecule is monomeric and possesses one unpaired electron.

However, there are difficulties in assigning this odd electron to the 2*p*-orbital. The boron atom is so completely surrounded by the three mesityl groups that this does not appear to be a reasonable electronic structure for $[\text{TMB}\cdot]^-$ unless the improbable assumption is made that the odd electron has no steric requirements. Partial or complete modification of the structure to sp^3-hybrid orbitals offers no solution to the difficulty. The only reasonable solution to the dilemma involves the assumption that the electron transferred from the sodium atom to the TMB must enter an orbital associated with the entire molecule rather than an orbital associated primarily with the boron atom.[12]

The behavior of TPB, TNB and TMB toward sodium amalgam is qualitatively quite similar. On this basis there appears to be no reason to assign a special structure or interpretation to the TMB derivative. It is concluded, therefore, that the odd electron in the monosodio derivatives of the triarylboranes is probably associated with an orbital common to the entire molecule.

It is tempting to extrapolate this conclusion to the triarylmethyls. This has, of course, been the favored interpretation of the electronic structure of these free radicals.[13] However, recent results of Weissman and Snowden appear to point to another conclusion.[14] As a result of data obtained in a magnetic resonance study of triphenylmethyl, these authors have concluded that the odd electron in this free radical appears to be relatively closely associated with the nucleus of the methyl carbon atom. If this conclusion is supported by further work, it will suggest a major difference in the electronic structures of the triarylborane radical ions and the triarylmethyl free radicals and will require a major revision of present theories regarding the electronic structures of these free radicals. The present results argue strongly for a non-localized configuration for the odd electron in the trimesitylborane radical ion and, presumably, in the related triarylmethyl free radicals.

Experimental Part

Preparation of Triarylborane Compounds. (A) Triphenylborane.—The procedure used to prepare TPB was essentially that described by Krause.[4] TPB was obtained in yields of approximately 60% as a white crystalline solid, m.p. 138° under nitrogen. The product was stored in sealed tubes and handled in a nitrogen atmosphere in subsequent experiments. The compound was analyzed for boron by the method described by Fowler and Kraus.[15] This same procedure was used in all of the boron analyses reported in this paper.

Anal. Calcd. for $C_{18}H_{15}B$: B, 4.47. Found: B, 4.51.

(B) **Tri-α-naphthylboron.**—TNB was prepared according to the procedure outlined by Brown and Sujishi.[6] Crude α-bromonaphthalene (Columbia Organic Chemicals Co.) was distilled and the fraction, b.p. 146–148° at 20 mm., was used. The TNB was crystallized from benzene and dried in a stream of nitrogen gas. The benzene of crystallization was removed by slowly warming the solid in a round bottom flask to 160° at 0.5 mm. to a constant weight. The product melted at 205–206°.

Anal. Calcd. for $C_{30}H_{21}B$: B, 2.76. Found: B, 2.74.

(C) **Trimesitylboron.**—Because of the difficulties experienced in forcing the reaction to proceed to the synthesis of trimesitylboron, the experimental procedure will be described in some detail. A standard 500-ml. three-necked flask (round bottom), equipped with a dropping funnel, ball joint stirrer, and water cooled condenser, was used. In a typical preparation, an anhydrous ethyl ether solution of bromomesitylene (0.240 mole, 47.8 g.), was added dropwise from the funnel to the flask containing magnesium turnings (0.29 g. at., 7.0 g.) and 100 ml. of anhydrous ether. The solution was refluxed during the addition period, which required approximately one hour, and for 4 to 5 hr. after the addition was complete. The solution was then allowed to stand at room temperature overnight. A slow but steady stream of nitrogen was passed through the system during the reflux period and a constant positive pressure of nitrogen gas was maintained in the system during the standing period. Dry toluene (150 ml.) was added to the flask and the mixture was heated to reflux temperature for 30 minutes to dissolve the precipitated Grignard reagent. Freshly distilled boron trifluoride etherate (0.036 mole, 5.1 g.), dissolved in 50 ml. of ether, was transferred to the dropping funnel and added to the stirred and refluxed solution of the Grignard over a period of 30 minutes. The condenser was replaced by a "goose-neck" adapter and the ether was distilled from the reaction flask. The condenser was replaced in the system and 50 ml. of toluene was added to the flask, and the solution was stirred and refluxed for 4 hr. On cooling to

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(12) In the reaction of sodium with polycyclic hydrocarbons in certain ether solvents, the electron is also assumed to enter a vacant orbital within the aromatic system, forming a free radical ion similar to that here postulated for $\text{TMB}\cdot\text{Na}$; D. Lipkin, D. E. Paul, J. Townsend and S. I. Weissman, *Science*, **117**, 534 (1953).

(13) G. W. Wheland, "Resonance in Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1955, pp. 381–393.

(14) S. I. Weissman and J. C. Sowden, THIS JOURNAL, **75**, 503 (1953).

(15) D. Fowler and C. Kraus, *ibid.*, **62**, 1143 (1940).

room temperature, the solution separated into an upper clear brick red layer and a lower yellow brown viscous layer. The entire reaction mixture was transferred to a 1-liter separatory funnel containing 300 ml. of cold water and crushed ice. After the initial hydrolysis reaction had subsided, 55 ml. of concentrated hydrochloric acid was added to dissolve the insoluble magnesium compounds and unreacted magnesium. Ice was added from time to time to keep the reaction mixture cool. After thoroughly shaking the mixture over a period of 20 minutes, the slightly turbid aqueous layer was withdrawn and the organic layer was washed with three 200-ml. portions of cold water. The yellow organic layer was then placed over calcium chloride to dry. Approximately one-half of the solvent was removed by distillation. The concentrated solution was treated with 150 ml. of 95% ethanol. A white to pale yellow solid immediately precipitated from solution. The solid was filtered and recrystallized from 300 ml. of 95% ethanol. The snow-white product weighed 4.5 g. and melted at 190.5–191.5°. Approximately two more grams of recrystallized product was obtained by evaporating the ethanol solution to one-half its original volume and allowing the solution to stand for 4 hours at room temperature.

Anal. Calcd. for $C_{27}H_{33}B$: B, 2.94; H, 9.03; C, 88.03. Found: B, 2.90; H, 9.10; C, 88.09.

Solubility of TMB.—An excess of solid TMB was added to 40 ml. of the solvent in a vessel, and the vessel was stoppered and placed in a constant temperature bath for 48 hr. During this period the mixture was shaken intermittently to facilitate saturation. Five ml. portions of the clear supernatant solution were withdrawn with a pipet and the solvent was removed by warming the solutions on a hot-plate at 60 to 70°. The results indicated a solubility per 100 ml. of solution at 25° of 6.96 g. in carbon tetrachloride, 1.25 g. in acetone, 0.08 g. in 95% ethanol, 4.98 g. in ethyl ether and 16.5 g. in benzene.

Preparation of Dimesitylboron Fluoride.—Mesitylmagnesium bromide was prepared according to the procedure outlined for TMB. Boron trifluoride etherate (0.073 mole) was added to the Grignard reagent (0.228 mole) over a period of 1.5 hr., and the reaction mixture was refluxed for 2 more hr. After standing at room temperature for 24 hr., the solution separated into two layers. The upper yellow orange ether layer was transferred, under nitrogen pressure, to a 125-ml. claisen flask and the ether was removed by distillation at atmospheric pressure. The residue was distilled at reduced pressure. A colorless liquid which distilled over the range 127–129° at 0.5 mm. pressure solidified in the receiver on cooling. The product melted at 75.5–76.0° in a sealed tube.

Anal. Calcd. for $C_{18}H_{22}BF$: B, 4.04; F, 7.09. Found: B, 3.97; F, 6.99.

When dimesitylboron fluoride was treated with water, dimesitylborinic acid was formed. After recrystallization from petroleum ether, the white crystalline solid melted at 140–141°.

Anal. Calcd. for $C_{18}H_{22}BOH$: C, 81.21; H, 8.73; B, 4.05. Found: C, 80.95; H, 8.99; B, 3.95.

Preparation of Ammonia Addition Compounds.—Anhydrous ether solutions of TPB and TNB were saturated with dry ammonia gas, and the solvent was removed at reduced pressure. The triarylboron compounds showed a gain in weight that checked well with that calculated for $TPB:NH_3$ and $TNB:NH_3$. Their melting points were in good agreement with those values given in the literature.[6,16] The very slight gain in weight shown by TMB when treated in a similar way was attributed to occluded solvent and not to reacted ammonia.

Titration with Sodium Alkoxides.—Anhydrous benzene solutions of TPB and TNB were titrated with freshly prepared and standardized sodium methoxide and sodium *t*-butoxide, using phenolphthalein as an indicator. Benzene solutions of TMB turned pink after the addition of the first drop of the alkoxide solution.

Benzene solutions of TNB which had been titrated with sodium methoxide to the phenolphthalein end-point were placed in a vacuum line, and the solvents were removed at reduced pressure. The white solid residue did not melt on heating but turned brown at 155–160° and black at 200°.

Anal. Calcd. for $Na^+[C_{30}H_{21}B:OCH_3]^-$: B, 2.42. Found: B, 2.40.

Benzene solutions of the salt were shaken with 50 ml. of distilled water and titrated with standard hydrochloric acid to a phenolphthalein end-point. The amount of titratable material, which was assumed to be sodium hydroxide, was found to be present in a mole ratio of 1:1 with respect to the original TNB. Other products formed by the hydrolysis of the salt were identified as naphthalene and di-α-naphthylborinic acid (m.p. 148–150°).

Anal. Calcd. for $C_{20}H_{14}BOH$: B, 3.85. Found: B, 3.83.

Benzene solutions of the salt were treated with a solution of hydrogen chloride dissolved in benzene. The solutions were heated on a hot-plate until all excess hydrogen chloride had been expelled, then filtered free of precipitated sodium chloride and evacuated to dryness. The solid white residue melted over the range 204–206° (TNB melts at 205–206°).

Anal. Calcd. for $C_{30}H_{21}B$: B, 2.76. Found: B, 2.73.

Reaction with Oxygen.—Weighed samples of TPB were transferred, in a nitrogen atmosphere, to the reaction bulb and dissolved in 20.0 ml. of α-bromonaphthalene. The bulb was attached to the reaction system (ball-joint), and the system was evacuated to a pressure of 0.5 mm. Pure dry oxygen gas was allowed to flow into the system and enough mercury was run into a side-arm U-tube to seal the system. The arm of the U-tube adjacent to the reaction flask was previously calibrated to represent the volume of the reaction flask and glass tubing to the mark on the side arm. A mercury-leveling device was attached to the open side of the U-tube and the pressure of the oxygen in the sealed system was adjusted to that of the atmosphere. The volume, pressure and temperature of the oxygen in the system were recorded at the beginning of the experiment and at various time intervals thereafter. Corrections for the volume of solvent in the reaction bulb were made for each reading. The reacting solution was continually agitated with a magnetic stirrer during the course of the reaction. Solutions of TNB and TMB in the same solvent were treated in a like manner.

A number of organic compounds were investigated and α-bromonaphthalene was found to fit best the needs for a solvent, having a very low vapor pressure and showing little or no signs of reacting with oxygen. A 20.0-ml. volume of the solvent was found to absorb 1.3 ml. of oxygen at S.T.P. This volume was subtracted from the final measured volume of reacted oxygen before calculating the number of moles of oxygen that had reacted.

Reaction with Water.—Mixtures of solid TPB and distilled water were shaken intermittently for a period of 8 hr. at room temperature. A pale brown residue was formed and this was filtered, dried in air and recrystallized from petroleum ether. The recrystallized material melted at 201.5–202.5° and was identified as phenylboric oxide. Evaporation of the aqueous solution produced a small amount of white solid, melting at 215°. The latter product was found to be phenylboronic acid. Refluxing a TPB and water mixture for 20 minutes produced the same materials.

Anal. Calcd. for C_6H_5BO: B, 10.41. Found: B, 10.32. Calcd. for $C_6H_5B(OH)_2$: B, 8.89. Found: B, 8.83.

TNB did not react with distilled water after treatment at room temperature for 8 hr. The melting point of the insoluble residue differed from that of the starting material by less than 1°. After refluxing in water for 1 hr., the insoluble residue was identified as a mixture of naphthalene and unreacted TNB. The aqueous solution yielded a white solid (m.p. 195°) on evaporation to dryness which was identified as α-naphthylboronic acid. A refluxing period of 2.5 hr. was required for complete conversion to these products.

Anal. Calcd. for $C_{10}H_7B(OH)_2$: B, 6.29. Found: B, 6.22.

Samples of TMB failed to react with water at room temperature after 8 hr. and after refluxing for 8 hr. The melting points of the starting material and the final product varied by less than 1°.

Reaction with Aqueous Sodium Hydroxide.—TPB was shaken with 0.05 *N* aqueous sodium hydroxide for a period of 4 hr. at room temperature. At the end of this time the samples had reacted completely and the products had gone into solution. The solution was neutralized with dilute hydrochloric acid and extracted with ether. The ether ex-

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(16) E. Krause, *Ber.*, **57**, 813 (1924).

tract was washed with water and evaporated to dryness. The residue was recrystallized from petroleum ether and identified as phenylboronic acid (m.p. 215°).

TNB was treated in the same way but the mixture was allowed to stand at room temperature for four days. The insoluble residue present was filtered and identified as a mixture of naphthalene and unreacted TNB. The filtrate was neutralized and extracted with ether. A small amount of α-naphthylboronic acid was obtained from the ether extract (m.p. 195°). TMB failed to react with 0.05 *N* sodium hydroxide after a period of 4 days at room temperature.

Reaction with Sodium Metal.—The procedures used were similar to those previously utilized for TPB[6] and TNB.[7] Since a detailed study recently has been described for the reaction of sodium with TMB,[9] we shall give only a brief summary of our observations.

A weighed sample of TMB was added to freshly prepared sodium amalgam in a dry glass bulb, and the bulb was swept out with dry nitrogen gas. Anhydrous ether was added and the bulb was sealed and set aside at room temperature. The bulb was shaken several times during the reaction period. The solution became pink, then purple and finally a yellow solid crystallized from the solution. At the end of the reaction period, the seal was broken and the ether solution was transferred to a flask containing distilled water. The bulb was rinsed several times with ether to remove all of the yellow solid adhering to the walls of the bulb. The rinses were added to the water and the ether was removed from the mixture by warming on a hot-plate. As the ether evaporated from the mixture, a white solid precipitated in the flask. The aqueous residue, containing the white precipitate, was titrated with standard hydrochloric acid to a phenolphthalein end-point. The insoluble residue was identified as TMB. The base was assumed to be sodium hydroxide. For samples that had been allowed to stand for 24 hr. the mole ratio of sodium to TMB varied from 1.09:1 to 1.53:1. A mixture of TMB and sodium amalgam which had been set aside for two months gave a 1.9 (Na) to 1 (TMB) mole ratio. No significant difference was noted between the ease of reaction of sodium with TMB as compared to TPB[6] or TNB.[7]

LAFAYETTE, INDIANA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WESTERN ONTARIO]

(±)-18-Fluoro-10-methyloctadecanoic Acid (Fluorotuberculostearic Acid)[1]

BY F. L. M. PATTISON AND R. G. WOOLFORD

RECEIVED NOVEMBER 5, 1956

Racemic fluorotuberculostearic acid (Vb) was prepared readily from 8-fluoroöctanoic acid by anodic coupling reactions. The sodium salt showed antitubercular activity *in vitro* but not *in vivo*.

From the knowledge gained from the study of fluoroacetates[2] and of other series of toxic compounds,[3] it has become increasingly apparent that certain biological systems are unable to differentiate between organic compounds containing the methyl group (CH_3^-) and the fluoromethyl group (FCH_2^-), respectively. Compounds containing the latter group, once assimilated, may then disturb or block the enzyme systems normally responsible for the metabolism of the non-fluorinated materials.

Occurring in the lipid sheath of the tubercle bacillus are a variety of fatty acids, including the levorotatory isomer of 10-methyloctadecanoic acid (tuberculostearic acid).[4] By applying the above observations regarding the fluoromethyl group to this acid, it was argued that 18-fluoro-10-methyloctadecanoic acid (fluorotuberculostearic acid) might readily be assimilated by the tubercle bacillus and that the toxic action of the fluorine atom might then result in its death. It was for this reason then that fluorotuberculostearic acid was prepared. If the racemic acid had shown high antitubercular activity, its resolution would have been undertaken; since its activity *in vivo* was low, this proved to be unnecessary. All compounds described in this article are therefore in the racemic form.

Fluorotuberculostearic acid was prepared by two routes, as is shown below. The work of Linstead, Lunt and Weedon[5] was of great value in selecting the experimental conditions. Some observations regarding symmetrical and unsymmetrical anodic coupling reactions of ω-fluorocarboxylic acids have been presented earlier.[6]

8-Fluoroöctanoic acid[6,7] (I) and methyl hydrogen β-methylglutarate[5] (II) (100% excess) on electrolysis formed a mixture of methyl 11-fluoro-3-methylundecanoate (IIIa), 1,14-difluorotetradecane and dimethyl β,β'-dimethylsuberate. The crude mixture, after hydrolysis with 10% sodium hydroxide, was separated into neutral and acidic fractions; the former gave 1,14-difluorotetradecane (20%), while the latter gave 11-fluoro-3-methylundecanoic acid (IIIb) (45%) and β,β'-dimethylsuberic acid (37%).

The anodic coupling of IIIb and methyl hydrogen azelate followed by hydrolysis of the resultant mixture gave the two symmetrical products, 1,20-difluoro-9,12-dimethyleicosane (23%) and hexadecanedioic acid (36%); a crude fraction of fluorotuberculostearic acid (Vb) also was obtained; this was found to be contaminated with azelaic acid, which had codistilled during attempted purification. Attempts to remove this impurity by preferential solubility in hot water and by treatment with alcoholic lead acetate[5] were unsuccess-

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(1) Issued as DRB Report No. SW-35.

(2) See, for example, M. B. Chenoweth, *J. Pharmacol. Exptl. Therap.*, **97**, 383 (1949); R. A. Peters, *Endeavour*, **13**, 147 (1954).

(3) F. L. M. Pattison, *Nature*, **172**, 1139 (1953); **174**, 737 (1954); F. L. M. Pattison, W. C. Howell, A. J. McNamara, J. C. Schneider and J. F. Walker, *J. Org. Chem.*, **21**, 739 (1956), and subsequent papers in the series.

(4) R. J. Anderson and E. Chargaff, *J. Biol. Chem.*, **85**, 77 (1929); M. A. Spielman, *ibid.*, **106**, 87 (1934); F. S. Prout, J. Cason and A. W. Ingersoll, THIS JOURNAL, **70**, 298 (1948); S. Ställberg-Stenhagen, *Arkiv Kemi, Mineral. Geol.*, **26A**, No. 12, (1948); G. A. Schmidt and D. A. Shirley, THIS JOURNAL, **71**, 3804 (1949).

(5) R. P. Linstead, J. C. Lunt and B. C. L. Weedon, *J. Chem. Soc.*, 3331 (1950).

(6) F. L. M. Pattison, J. B. Stothers and R. G. Woolford, THIS JOURNAL, **78**, 2255 (1956).

(7) F. L. M. Pattison, S. B. D. Hunt and J. B. Stothers, *J. Org. Chem.*, **21**, 883 (1956).