NH_4OH (6 *N*) was added at this temperature and the resulting yellow solid was collected. This material turns brown on standing in air or in solution. If placed in a desiccator under vacuum, the original yellow solid slowly turns brown over a period of several days. The yellow material, after 1 day in the desiccator, melted sharply at 75°. An analysis of this compound, assumed to be the 4′-methoxy-3-aminobiphenyl, could not be obtained. However, the uv–visible, nmr, and pK_a were consistent with those of the other 4′-substituted 3-aminobiphenyls.

Measurement of pK_a's. The pK_a's of the substituted 4-aminobiphenyls and those of three of the substituted 3-aminobiphenyls were determined spectrophotometrically[24] using a Beckman DK-2 recording spectrophotometer. Stock solutions (3×10^{-3} *M*) of these compounds (except 3-aminobiphenyl which was 1×10^{-3} *M*) were prepared by dissolving a weighed sample of each amine in 50 ml of absolute ethanol and diluting to 100 ml with deionized water. Spectra solutions (6×10^{-4} *M*; 3.5×10^{-4} for 3-aminobiphenyl) were then prepared by diluting one part of the stock solution with four parts of deionized water, buffer solution, or concentrated hydrochloric acid to form the basic, intermediate, and acid solutions, respectively. In all cases, the alcohol content of the spectra solutions was 10%.

The pK_a's were calculated from eq 1[24] where A_B represents the absorbance of the basic solution, A_A is the absorbance of the concentrated HCl solution, and A is the absorbance of an intermediate buffered acidic solution. The buffered solutions were prepared

$$\mathrm{p}K_a = \mathrm{pH} - \log\frac{A - A_A}{A_B - A} \qquad (1)$$

using Clark and Lubs hydrochloric acid buffers[25] and their pH's were measured on a Leeds and Northup research pH meter. The medium shift was minimal in all cases and the absorbance of all solutions was measured at the wavelength at which A_B was measured.

The pK_a's of the 4′-methoxy- and 4′-nitro-3-aminobiphenyls, due to solubility (nitro compound) or experimental difficulties (methoxy compound), were determined potentiometrically by measuring the pH of a solution containing exactly equivalent amounts of the amine and its salt.[26] Amine (40–50 mg) was weighed accurately into a weighing boat and then transferred to a 100-ml beaker with 10 ml of absolute ethanol. Water (70 ml) was added and the solution was stirred to ensure complete solubility of the amine. The calculated amount of 0.0977 *N* HCl needed to half-neutralize the amine present was added to the solution with a micropipet and the pH of the resulting solution was then read.

The pK_a's reported in Tables I and II are the average obtained from at least four determinations (except the 4′-methoxy- and 4′-nitro-3-aminobiphenyls which represent the average of two determinations). The maximum deviation from the mean of replicate pK_a values did not exceed 1.4% except in the case of 4′-fluoro-4-aminobiphenyl (3.3%).

Acknowledgments. This work was supported in part by the Research Corporation (Fredrick Gardner Cottrell Grant) and by the National Science Foundation Institutional Grants for Science Program (GU-3297).

Registry No.—3-Nitrobiphenyl, 2113-58-8; 4′-hydroxy-3-nitrobiphenyl, 53059-30-6; 4′-methoxy-3-nitrobiphenyl, 53059-31-7.

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Electrophilic Substitution on Metallocenes. Reactivity of the Ferrocene System in Protodeboronation and Protodesilylation

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The determination of the electrophilic reactivity of ferrocene relative to benzene has been carried out only in a few instances, such as mercuration and H–D exchange.[1,2] A major difficulty is the tendency of ferrocene to oxidation, which may interfere with the rate measurements even in those reactions where the electrophile is not a direct oxidizing agent. Thus, previous rate measurements concerning the protodesilylation reaction[3] seemed to be misled by oxidation (*vide infra*). We now wish to report rate data for the protodeboronation of ferrocenylboric acid (compound I) and the protodesilylation of trimethylsilylferrocene (compound II) as obtained under conditions whereby the incursion of side reactions could be neglected. Such data yield two independent assessments of the very high electrophilic reactivity of the ferrocene system relative to benzene.

Product analysis showed that ferrocenylboric acid was cleaved quantitatively in 5 min by 10% sulfuric acid in a 1:2 v/v water–ethanol mixture at 50°. Accordingly, on quenching with a saturated Na_2CO_3 aqueous solution, ferrocene was isolated by standard methods in 96% yield.

The reaction rate was determined under N_2 atmosphere at several acid concentrations by measuring the absorbance *decrease* in the electronic spectrum accompanying the replacement of the boric functional group by hydrogen at 440 nm. Oxidation, which eventually set in, was accompanied by an absorbance *increase*. Infinity time determinations were obtained by Mangelsdorf's method.[4] The reaction followed strictly first-order kinetics and the results were duplicated with a satisfactory degree of reproducibility under all tested conditions.

Trimethylsilylferrocene behaved similarly both from the point of view of reactivity in acidic mixed aqueous solvents and from the spectral features. These observations were clearly at variance with those reported by Marr and Webster,[3] who presumably followed the *slower*, subsequent oxidation reaction (absorbance increase) and did not correlate their product analysis (4-hr run under reflux) with the actual rate process. In fact, we found that trimethylsilylferrocene underwent complete electrophilic replacement by pro-

Table I
Dependence of First-Order Rate Constants for the Reaction of Ferrocenylboric Acid and Trimethylsilylferrocene on Acid Concentration

Protodeboronation[a]		Protodesilylation[b]	
% H_2SO_4	$10^4 \times k$, sec^{-1}	HCl, *M*	$10^3 \times k$, sec^{-1}
10	6.56	0.050	2.99
15	13.6	0.080	3.93
16	24.7	0.120	6.12
18	42.9	0.157	7.81
20	60.8	0.253	12.6
21	145	0.405	24.7
25	955	0.600	30.8

[a] λ 440 nm; $t = 44.7°$; 1:2 v/v H_2O–EtOH. [b] λ 328 nm; $t = 55.2°$; 1:4 v/v H_2O–CH_3OH.

Table II
Rate Constants for the Protodesilylation and Protodeboronation of Some Ferrocene and Benzene Derivatives

Compound	Temp, °C	*k*, sec^{-1}	k/k_0[a]	Ref
$PhB(OH)_2$	40.0	5.0×10^{-10} [b]	1	5
$(p\text{-}MeOC_6H_4)B(OH)_2$	40.0	1.35×10^{-5} [c]	2.7×10^4	7
$Fe(C_5H_5)C_5H_4B(OH)_2$ (I)	40.0	3.5×10^{-3} [d]	7×10^6	This work
$PhSiMe_3$	51.2	3.7×10^{-8} [e]	1	6
$(p\text{-}MeOC_6H_4)SiMe_3$	50.1	3.5×10^{-5} [f]	9.5×10^2	3
$Fe(C_5H_5)C_5H_4SiMe_3$ (II)	55.2	6.12×10^{-3} [f]	1.7×10^5	This work

[a] Rate relative to the reference compound, $PhB(OH)_2$ or $PhSiMe_3$. [b] Value extrapolated at aqueous 20.1% H_2SO_4. [c] In aqueous 20.1% H_2SO_4. [d] In 20% H_2SO_4–(1:2 v/v) H_2O–EtOH mixture. [e] In 0.126 *M* $HClO_4$(2:5 v/v)H_2O–MeOH mixture. [f] In 0.12 *M* HCl–(1:4 v/v) H_2O–MeOH mixture.

ton in only 4 min in 1 *M* hydrochloric acid in 1:4 v/v water–methanol solvent, at 50°. While this reaction occurred an absorbance decrease was observed also in this case. The kinetics were studied by essentially the same method as were used in the case of boric acid.

As expected,[5,6] both reactions were found to be acid catalyzed. Typical data are shown in Table I.

In protodesilylation, where mild acid conditions were used, the rate constant was found to depend linearly on the HCl concentration. Similarly, using the H_0 function for aqueous H_2SO_4, log *k* for protodeboronation was found to correlate linearly with H_0, with a slope close to unity.

The rate constants in a given concentration range are reported in Table II together with literature data for benzene derivatives under comparable experimental conditions. The two reactions provide a consistent picture for the reactivity level of the ferrocene substrate. The latter is more reactive than the benzene analog by factors of 1.7×10^5 (protodesilylation) and 7.0×10^6 (protodeboronation). Unlike Marr and Webster's results for the protodesilylation reaction, the ferrocene substrate is even much more reactive than the *p*-methoxybenzene analog, the factors being in such case 9.5×10^2 (protodesilylation) and 2.7×10^4 (protodeboronation). Protodeboronation appears to be quite significantly more selective than protodesilylation.

Electrophilic ring substitutions at the ferrocene system have been suggested to occur either by a direct attack of the reagent on the ring[8] or through a preliminary iron–electrophile interaction.[9,10] The finding that protodesilylation occurs at mild acid concentrations is in contrast with the latter hypothesis for this reaction. Recent determinations of iron protonation equilibria of ferrocene derivatives[11] allow us to calculate the concentration of the iron-protonated species as exceedingly small, *i.e.*, in the order of 10^{-10} *M*, which makes any metal participation to speed up the reaction rate quite unlikely. The nonparticipation of the iron atom may be general for ring substitutions involving hydrogen as the electrophilic reagent; H–D exchange studies[11] are indeed in agreement with this view.

Experimental Section

Trimethylsilylferrocene and ferrocenylboric acid were prepared by the methods reported in the literature.[12,13] Their structure and purity were checked by elemental analysis and electronic, infrared, and nmr spectra.

The product analysis for the protodesilylation reaction was performed as follows. Trimethylsilylferrocene (0.5 g, 2 mmol) was dissolved in 150 ml of a 1 *M* HCl solution in 1:4 v/v water–methanol mixture and warmed at 50° for 4 min. Then the solution was poured in a cold, Na_2CO_3-saturated aqueous solution, which was repeatedly extracted with petroleum ether. The ether layer was concentrated by evaporation and chromatographed on alumina with petroleum ether as eluent. Ferrocene was obtained in 96% yield and identified by elemental analysis, melting point (173–174°, lit.[14] 174°), and nmr spectrum.

As to the protodeboronation reaction, ferrocenylboric acid (0.24 g, 1.05 mmol) was made to react in 500 ml of 10% sulfuric acid solution in 1:2 v/v water–ethanol at 50°. The reaction time was 5 min, and ferrocene was isolated in 96% yield.

The rate measurements were made by recording the absorbance decrease of the reacting solutions at λ 328 and 440 nm for the protodesilylation and protodeboronation reactions, respectively. A Beckman Model DB-GT self-recording spectrophotometer was used with a tenfold expansion scale and zero suppression to allow sufficiently accurate measurements despite the small overall spectral change.

In order to avoid the interference of oxidation, the solutions of the reactants were saturated with nitrogen before mixing, and a nitrogen atmosphere was maintained in the cell compartment. For the protodesilylation reaction, the absence of the oxidation to ferricenium was indicated by the absence of any absorbance at 620 nm. In the protodeboronation reaction, a slight absorbance appeared at 620 nm only in later stages of the reaction (say beyond 75%). The wavelength (440 nm) was chosen in such a way as to keep the molar absorptivity of the ferricenium ion to a minimum. Furthermore, the absorbance data were treated by Mangelsdorf's method which neglects the infinity time absorbances.[4]

Registry No.—I, 12152-94-2; II, 12215-68-8.

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Synthesis of 6,13-Dimethyldibenz[*a*,*h*]anthracene[1]

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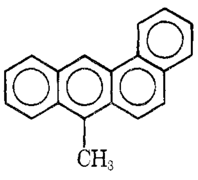
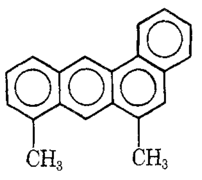
According to a hypothesis about the carcinogenic activity of benz[*a*]anthracene derivatives, the 7 position represents the main site for metabolic deactivation of members of this series.[3] The metabolic deactivation (with respect to carcinogenic activity) may be blocked by two methods: (1) substitution of a methyl group at position 7[3] and (2) substitution of methyl groups at positions 6 and 8.[4] The compounds produced by these changes, 7-methylbenz[*a*]anthracene (**1**), and 6,8-dimethylbenz[*a*]anthracene (**2**), are highly carcinogenic, presumably because the deactivation site is blocked whereas the site (position 5) at which metabolism leading to cancer occurs[3] is available for attack.



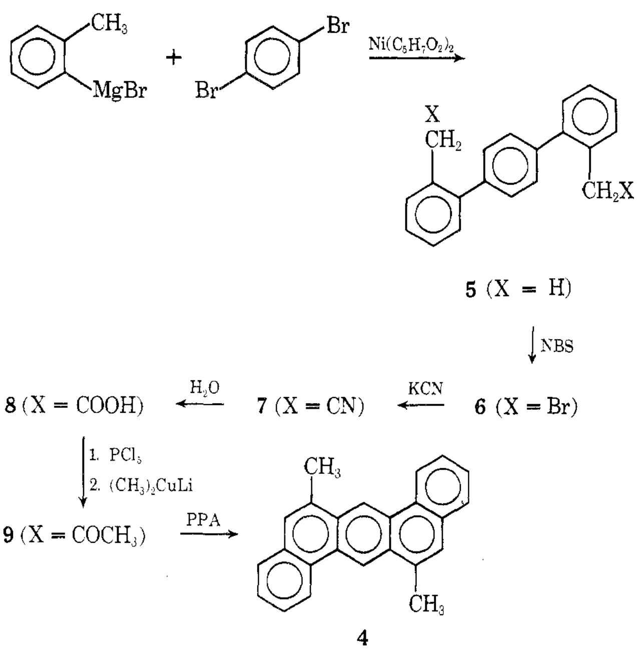
1



2

The compound dibenz[*a*,*h*]anthracene (**3**) is carcinogenic[5] and bears a structural resemblance to benz[*a*]anthracene. We were interested to see if the carcinogenic activity of **3** could be enhanced by substitution of methyl groups at positions 6 and 13 as in the case of **2**. In this paper we describe the synthesis of 6,13-dimethyldibenz[*a*,*h*]anthracene (**4**) by the route shown in Scheme I.

Scheme I



That the structure of **4** is that of a dimethyldibenz[*a*,*h*]anthracene, rather than the alternate possibility, a dimethylpicene, is indicated by the uv absorption spectrum (see Experimental Section).

Experimental Section

Generalizations. All melting and boiling points are uncorrected. Melting points were taken on a Thomas-Hoover apparatus. All compounds marked with an asterisk had ir and nmr spectra, elemental analyses (by the Galbraith Laboratories, Inc., Knoxville, Tenn., within ±0.3% of the theoretical values), and mass spectra (taken by Mr. C. R. Weisenberger on an MS-902 mass spectrometer) consistent with the assigned structures.

2,2″-Dimethyl-*p*-terphenyl (5). The Grignard reagent prepared in 1.2 l. of ether from 2.4 g of sublimed magnesium, 160 g of *o*-bromotoluene, and 2 ml of ethylene dibromide[6] was cooled to 0–5° by an ice bath and 1.0 g of nickel acetylacetonate[7] was added with stirring. A solution of 82.6 g of 1,4-dibromobenzene in 650 ml of dry ether was added during 3 hr under nitrogen. Two further additions of nickel acetylacetonate (0.5 g each) were made midway and at the conclusion of the addition of the dibromide.[8] After being held at reflux for 42 hr, the reaction mixture was worked up in a conventional way. The entire reaction product was distilled at 1 mm to remove unchanged *p*-dibromobenzene, bp 110–120°. The residue was crystallized from ethanol to yield 56.0 g (62%) of **5**, mp 137–140°, suitable for further use. A pure sample,[9] mp 142–143°, was obtained by recrystallization from ethanol-benzene.

2,2″-Bis(bromomethyl)-*p*-terphenyl* (6). A mixture of 6.95 g (0.025 mol) of **5**, 9.75 g (0.05 mol) of *N*-bromosuccinimide, and 0.3 g of benzoyl peroxide in 400 ml of carbon tetrachloride was refluxed for 30 min. After cooling, the solid was removed by filtration and the solvent evaporated from the filtrate under reduced pressure. The residue (10.2 g) was suitable for use in the next step. A sample, mp 179.5–181.0°, was obtained by recrystallization from benzene. The crude dibromide should be used soon after it is made as on standing decomposition sets in.

2,2″-Bis(cyanomethyl)-*p*-terphenyl* (7). A mixture of 10.2 g of crude **6**, 10 g of potassium cyanide, 20 ml of water, 250 ml of 2-methoxyethanol, and 150 ml of ethanol was refluxed for 20 hr. After cooling, 350 ml of water was added. After washing with water and drying the crude precipitate, 6.55 g (85% calculated on **5**), mp 228–231°, was suitable for further work. A pure sample of **7**, mp 235–237°, was obtained by recrystallization from chloroform.

2,2″-Bis(carboxymethyl)-*p*-terphenyl* (8). A solution of 24 g of crude **7** and 25 g of potassium hydroxide in 350 ml of ethylene glycol and 500 ml of water was refluxed for 20 hr. The crude acidic material obtained by acidification of the filtered (through Celite) reaction mixture weighed 23.5 g (85%) and melted at 264–268°. The analytical sample, mp 275–277°, was obtained after recrystallizations from acetic acid.

2,2″-Bis(acetonyl)-*p*-terphenyl* (9). To a stirred suspension

Table I
Ultraviolet Absorption Spectra

Compd	Uv spectra, λ_{max}, nm (log ϵ)							
10[a,b]		277 (4.63)	297 (5.20)	305 sh (4.40)	320 (4.30)	333 (4.23)	349 (4.18)	
11[a,b]		285 (4.58)	296 (4.88)	308 (4.95)	324 (4.02)	336 (4.06)	353 (4.12)	370 (4.12)
4[c]	257 (4.71)	282 (4.64)	293 (4.98)	306 (5.20)	325 (4.25)	339 (4.16)	354 (3.98)	
12[b,c]	257 (4.71)	275 (4.85)	286 (5.03)	303 (4.76)	313 (4.30)	328 (4.36)	357 (2.97)	376 (2.97)

[a] EtOH as solvent. [b] Reference 15. [c] Chloroform as solvent.