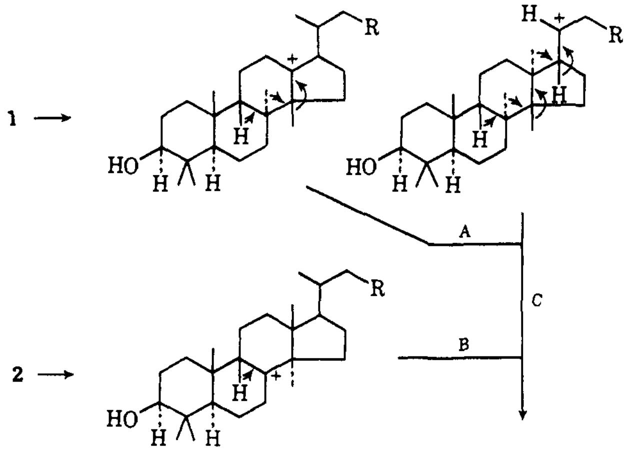
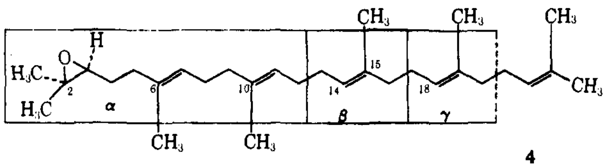
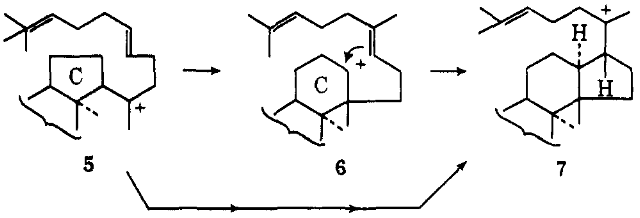
other hand, it is remarkable that cyclase action is observed in substrate cases featuring three (**1**)[8] or as few as two (**2**) olefinic links. Again, the presumed predilection for 9,10 cis (B boat) intermediate formation[7] is apparent in these cases. Furthermore, the described results indicate that partially cyclized substrate can, in the process of further enzymic cyclization, merge into (A, B) the normal methyl-hydrogen migration sequence (C) which occurs subsequent to formation of tetracycle, and proceed to the lanosterol system. These results therefore lend support to the previous suggestions[8] that the methyl-hydrogen migration sequence rests solidly on organic chemical foundations and involves behavior which can be rationalized by purely chemical means. Finally, that dihydro-9-β-$\Delta^7$-lanosterol is produced nonenzymically from **2**,[2] while the $\Delta^8$ isomer is generated in the enzyme reaction, suggests that the terminating removal of the C-9 proton may be controlled by a specific basic center in the enzyme, ensuring formation of $\Delta^8$-lanosterol. It is pertinent that a plant cyclase produces euphol ($\Delta^8$) and not isoeuphol ($\Delta^{13(17)}$), the overwhelmingly more stable product.



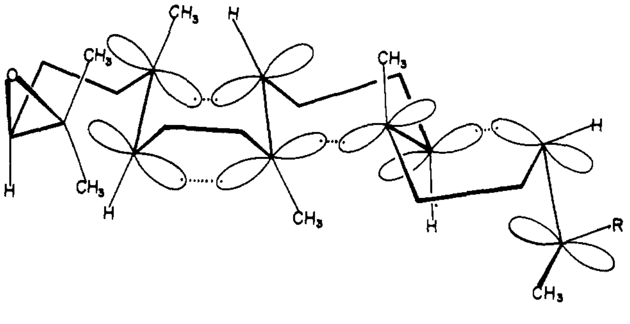
The above results, taken together with other findings,[8] indicate that, although the trisubstituted epoxide moiety is critical, individual methyls at 6,[9] 10, and 15, and π bonds at 14 and 18, are not essential for enzymic cyclization. These reactivity patterns suggest that the epoxide-tetra-π-bond sequence (α,β,γ) (**4**) constitutes the essential substrate structural requirement for sterol formation and that the epoxide-bis-π-bond moiety (α) currently represents the minimum requirement for cyclase action. In addition, special enzyme control (β) is needed at the $\Delta^{14}$ site in order to direct carbonium ion behavior and thus realize formation of a six-membered C ring. Cyclization may proceed "nonstop" to tetracycle[7,10] or may lead to discrete carbonium ion (or derivative thereof) intermediates, *e.g.*, the chemically preferred tricycle **5**. In the latter case, conversion to sterol skeleton[7] could proceed *via* chemically precedented ring expansion (**5** → **6**) to six-membered C ring or by more indirect means (**5** →→ **7**), previously considered.[11]



**4**



In terms of an extended cyclization to the protolanosterol system, the π-orbital interactions depicted in **8** would obtain; and an important function of the cyclase enzyme would be maintenance of the epoxide-π system in such a conformation as to maximize the orbital overlap permitting ultimate generation of the σ-bonding system of product sterol.[11] In this stereoelectronic interpretation, three types of π interactions can be discerned: (1) epoxide-$\Delta^6$, permitting SN2 type attack of the π electrons on C-2, (2) $\Delta^6$–$\Delta^{10}$, in which (because of the incipient B boat conformation) full overlap of nodal extremities is realized, and (3) $\Delta^{10}$–$\Delta^{14}$ and $\Delta^{14}$–$\Delta^{18}$, distinguished by perpendicular orientation of the π planes. The implications of the difference between interactions 2 and 3 will be discussed elsewhere.



**8**

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[7] A. Eschenmoser, L. Ruzicka, O. Jeger, and D. Arigoni, *Helv. Chim. Acta*, **38**, 1890 (1955).

[8] E. E. van Tamelen, R. P. Hanzlik, R. B. Clayton, and A. L. Burlingame, *J. Amer. Chem. Soc.*, **92**, 2137 (1970), and references cited therein.

[9] Unpublished results, J. A. Smaal, Stanford University.

[10] G. Stork and A. W. Burgstahler, *J. Amer. Chem. Soc.*, 77, 5068 (1955).

[11] E. E. van Tamelen, J. D. Willett, and R. B. Clayton, *ibid.*, **89**, 3371 (1967).

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## Synthesis of Aromatic Hydrocarbons *via* Intermediate Iron Complexes[1]

*Sir:*

In 1956 Fischer and Böttcher reported the synthesis of certain bisareneiron(II) salts.[2,3] Except for brief

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[1] Presented in part at the 159th National Meeting of the American Chemical Society, Houston, Tex., Feb 1970, Abstract ORGN-77.

[2] E. O. Fischer and R. Böttcher, *Chem. Ber.*, **89**, 2397 (1956).

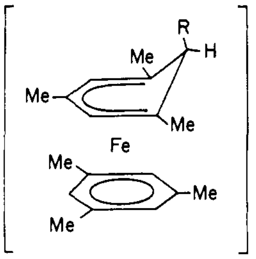

Figure 1. The structure of **2** (R = $C_6H_5$), **3** (R = *tert*-$C_4H_9$), and **4** (R = $C_2H_3$).

mention of stability trends by Tsutsui and Zeiss[4] these compounds seem to have attracted very little attention until now. We now report that bisareneiron(II) complexes undergo reactions of addition to the arene ring when treated with organolithium reagents to give interesting new complexes of iron. Furthermore, we report a simple, stepwise process for synthesis of aromatic hydrocarbons which viewed as a whole involves nucleophilic substitution of alkyl or aryl groups for hydrogen on an electron-rich aromatic ring *via* an intermediate iron complex.

The iron complexes of several arenes (*e.g.*, mesitylene, durene, *m*-xylene, hexamethylbenzene) have been prepared (eq 1) by procedures similar to that described for the mesitylene compound. Mesitylene, $FeCl_2$ powder,

$$2(\text{arene}) + FeCl_2 + 2AlCl_3 \longrightarrow (\text{arene}_2Fe)(AlCl_4)_2 \xrightarrow[H_2O]{NH_4PF_6} (\text{arene}_2Fe)(PF_6)_2 \quad (1)$$

and $AlCl_3$ powder in the mole ratio 2.5:1:3.2 were stirred vigorously under nitrogen in refluxing cyclohexane for 4 hr in a dry, silicone grease free system. After hydrolysis at 0° and filtration, treatment of the red-orange aqueous layer with aqueous $NH_4PF_6$ gave (mesitylene$_2$-Fe)($PF_6$)$_2$ (**1**) as a pale orange precipitate. Following recrystallization by addition of ether to a solution of the salt in 95% aqueous acetone the yield of pure salt was 65%. In contrast, the previous yields given by Fischer and Böttcher for synthesis of bismesityleneiron(II) salts starting from $FeBr_2$ were 30% (tetraphenylborate), 28% (reineckate), and 9% (iodide). From *m*-xylene, durene, and hexamethylbenzene we have obtained the analogous hexafluorophosphate salts in yields of 62, 78, and 57%, respectively.

The hexafluorophosphate salts react with organolithium reagents to give 1:1 or 1:2 adducts depending on the mole ratio. The reactions are conducted by addition of the organolithium reagent to a slurry of the salt in ether, pentane, or tetrahydrofuran at −70°. Reaction occurs as the mixture is allowed to warm to room temperature. Phenyllithium and **1** in a 1:1 mole ratio in ether gave a 38% yield of a brown monophenyl adduct (**2**), dec 216–217°. Similarly, from *tert*-butyllithium and **1** in petroleum ether there was obtained an 80% yield of a tan mono-*tert*-butyl adduct (**3**), dec 233–238°. Vinyllithium yields a tan monovinyl adduct (**4**), dec 195°. These adducts are assigned the structures represented in Figure 1.

The assignment of an exo geometry to the phenyl, *tert*-butyl, and vinyl groups is based partially on analogy to the phenyl adduct of cobalticinium ion for which the exo geometry has been shown by X-ray crystallography.[5] Furthermore the infrared spectra show no absorption in the region 2700–2800 cm$^{-1}$ of the kind which has been attributed to exo C–H stretching in several compounds such as π-cyclopentadienyl-π-cyclopentadienecobalt(I) and hexamethylcyclohexadienylrhenium tricarbonyl.[6] The structures are also supported by nmr and mass spectra and elemental analyses.

When bismesityleneiron(II) hexafluorophosphate is treated with 2 equiv of phenyllithium, *tert*-butyllithium, or vinyllithium, the corresponding orange, neutral diadduct may be isolated in good yield (diphenyl, **5**, 57%, mp 102–105°; di-*tert*-butyl, **6**, 75%, mp 203–204°; divinyl, **7**, 53%, mp 131–132°). The remarkable properties and structural features of these compounds warrant more detailed discussion and are described in the accompanying communication.[7]

Thermal decomposition of **2** at 216° gave a 1:1 mixture of phenylmesitylene and mesitylene. Oxidation of a petroleum ether solution of **5** with dilute aqueous $KMnO_4$ led to a 95% yield of phenylmesitylene. A conversion of mesitylene to phenylmesitylene *via* iron complexes has been effected in 35% overall yield. Probably the best previous route to phenylmesitylene, reaction of mesitylmagnesium bromide, bromobenzene, and $CoCl_2$, gave 18% yield (or 15% overall from mesitylene in two steps *via* bromomesitylene).[8]

Oxidation of a pentane solution of **7** with aqueous ceric ammonium nitrate gave 82% vinylmesitylene, an overall yield from mesitylene of 27%.

Thermal decomposition of **3** at 233° led to mesitylene with no evidence for *tert*-butylmesitylene. Oxidation of a petroleum solution of **6** with dilute aqueous $KMnO_4$ produced *tert*-butylmesitylene in 18% yield along with mesitylene. Starting from mesitylene the overall yield of *tert*-butylmesitylene is 9%. Since the oxidation could be carried out as a part of the work-up of the *tert*-butyllithium reaction, the conversion of mesitylene to *tert*-butylmesitylene could be done as a two step process with one isolated intermediate, the bisareneiron(II) salt. The only other reported route to the compound, the reaction of mesitylmagnesium bromide and *tert*-butyl chloride, provides a 5% yield[9a,b] or approximately 3% overall conversion from mesitylene in two steps *via* bromomesitylene.

It is reasonable to expect that the range of synthetic application of these reactions will not be limited to attachment of *tert*-butyl, phenyl, or vinyl groups. Rather than the usual addition–elimination sequence typical of other kinds of nucleophilic aromatic substitution, the substitution of alkyl or aryl groups for hydrogen is accomplished with an addition–oxidation sequence. The high activation energy required for direct nucleophilic substitution of aryl hydrogen atoms

$$\text{arene} \xrightarrow[2.\ NH_4PF_6]{1.\ FeCl_2,\ AlCl_3} (\text{arene}_2Fe)(PF_6)_2 \xrightarrow{2RLi} (\text{R-arene}_2Fe) \xrightarrow{(o)} \text{R-Ar} \quad (2)$$

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[3] E. O. Fischer and R. Rohrscheid, *Z. Naturforsch. B*, **17**, 483 (1962).

[4] M. Tsutsui and H. Zeiss, *Naturwissenschaften*, **44**, 420 (1957).

[5] M. R. Churchill and R. Mason, *Proc. Roy. Soc., Ser. A*, **279**, 191 (1964).

[6] P. H. Bird and M. R. Churchill, *Chem. Commun.*, 777 (1967).

[7] J. F. Helling and D. M. Braitsch, *J. Amer. Chem. Soc.*, **92**, 7209 (1970).

[8] C. E. Castro, L. J. Andrews, and R. M. Keefer, *ibid.*, **80**, 2322 (1958).

[9] (a) R. Adams and J. S. Dix, *ibid.*, **80**, 4579 (1958); (b) A. W. Burgstahler, D. J. Malfer, and M. O. Abdel-Rahman, *Tetrahedron Lett.*, 1625 (1965).

is reduced because of the positive charge resulting from coordination of ferrous ion.

Previously direct alkylation of benzene, naphthalene, and phenanthrene by lithium reagents was reported to occur very slowly even at 165°.[10] In contrast, the critical C–C bond-forming step in our sequence occurs rapidly near room temperature despite an electron-rich ring with potential problems of steric hindrance and without competing hydrogen–metal exchange. Direct substitution of aryl or vinyl groups for hydrogen on benzene rings by aryllithium or vinyllithium compounds has not been described.

Although addition of RLi compounds to other transition-metal complexes such as cobalticinium ion has been reported, it is the bisarene 2+ cations that offer a unique opportunity for organic syntheses because of their desirable combination of 2+ charge, arene complexation, and symmetry.

A broad investigation of the extensions of this chemistry is in progress.

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[10] J. A. Dixon and D. H. Fishman, *J. Amer. Chem. Soc.*, **85**, 1356 (1963).

[11] NDEA Title IV Fellow.

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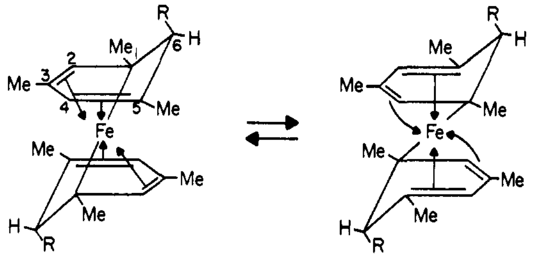
## New Fluxional Organometallic Compounds. Pseudoferrocene Systems[1]

*Sir:*

In the preceding communication[2] we reported the synthesis of bis(6-*tert*-butyl-1,3,5-trimethylcyclohexadienyl)iron(II) and bis(6-phenyl-1,3,5-trimethylcyclohexadienyl)iron(II) from the reactions of *tert*-butyllithium and phenyllithium with bismesityleneiron(II) hexafluorophosphate. We now wish to describe their properties in greater detail.

For each compound the nmr spectrum is temperature dependent. In the case of the diphenyl adduct the limiting high-temperature spectrum (Figure 1) in $CS_2$ is attained near +2° and consists of four sharp singlets and two aryl multiplets. The limiting low-temperature spectrum is reached near −75° and consists of six sharp singlets and two aryl multiplets. We believe these spectra are indicative of fluxional behavior[3] (eq 1).



(1)

Because of the simplicity of the spectra, peak assignments can be made easily (Table I). The peaks at $\tau$ 9.08 and 7.98 coalesce at about −42° to a peak which appears at $\tau$ 8.53 in the high-temperature spectrum and the peaks at $\tau$ 6.79 and 6.15 coalesce at about −48° to a peak which appears at $\tau$ 6.47 in the high-temperature spectrum.

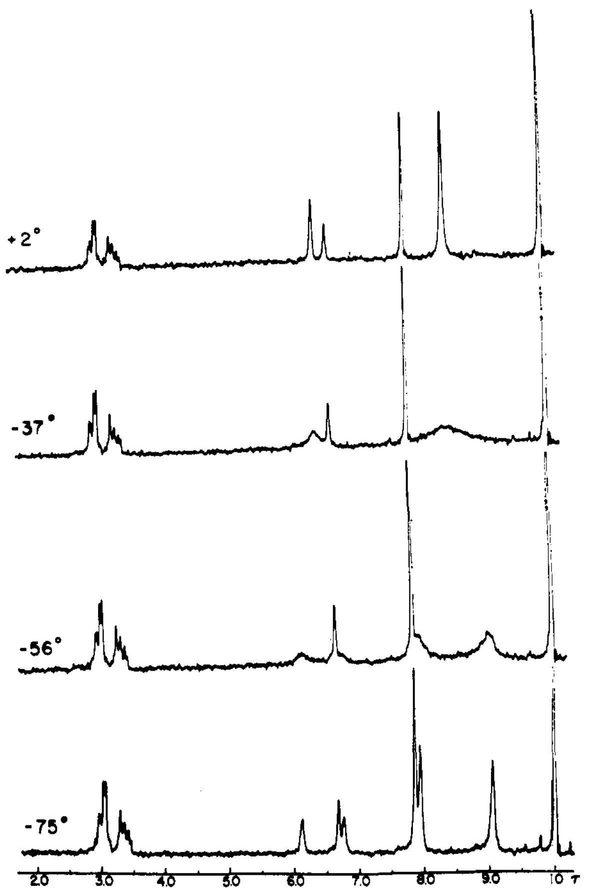


Figure 1. The 60-MHz $^1H$ nmr spectrum of bis(6-phenyl-1,3,5-trimethylcyclohexadienyl)iron(II) in $CS_2$ measured relative to TMS.

**Table I.** Nmr Spectrum of Bis(6-phenyl-1,3,5-trimethylcyclohexadienyl)iron(II) in Carbon Disulfide at −75°

| Position ($\tau$) | Rel area | Assignment |
|---|---|---|
| ~3.05 (multiplet) | 3 | 6-Phenyl (meta and para) |
| ~3.35 (multiplet) | 2 | 6-Phenyl (ortho) |
| 6.15 | 1 | 4-H |
| 6.71 | 1 | Endo 6-H |
| 6.79 | 1 | 2-H |
| 7.88 | 3 | 3-Methyl |
| 7.98 | 3 | 5-Methyl |
| 9.08 | 3 | 1-Methyl |

The limiting low-temperature spectrum of the di-*tert*-butyl adduct in $CS_2$ is attained near −38° and consists of seven sharp singlets. The peak assignments are given in Table II. The peaks at $\tau$ 6.35 and 6.95 coalesce at about 22° while those at $\tau$ 7.86 and 8.95 coalesce at about 37°.

The limiting high-temperature spectrum is attained near +100° (measured in deuteriotoluene) and consists of five sharp singlets.

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[1] Presented in part at the 159th National Meeting of the American Chemical Society, Houston, Tex., Feb 1970, Abstract ORGN-77.

[2] J. F. Helling and D. M. Braitsch, *J. Amer. Chem. Soc.*, **92**, 7207 (1970).

[3] A review of fluxional behavior is given by F. A. Cotton, *Accounts Chem. Res.*, **1**, 257 (1968).