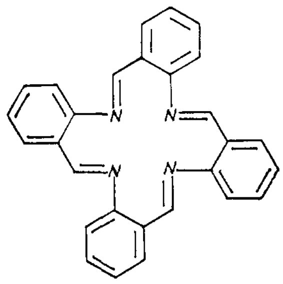

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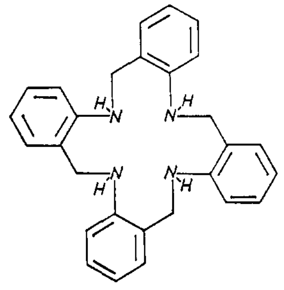
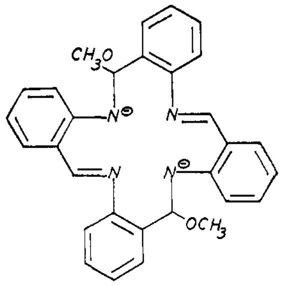


II



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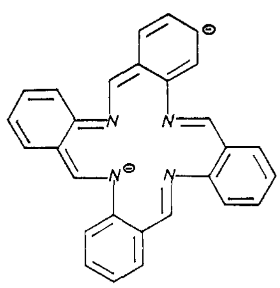

IV

rivative of TAAB, and TAAB(OMe)$_2$$^{2-}$, structure III, which has two azomethine linkages. The first complex gives a single two-electron wave at -0.970 V *vs.* sce, similar to waves observed for Ni(bipy)$_3$$^{2+}$.[5] No ligand reduction wave is observed in the region more negative than -1.000 V. By contrast, the first one-electron reduction wave of the methoxy derivative appears at -0.470 V *vs.* sce, very close to the first wave for Ni-TAAB^{2+}. No further reduction is observed until -1.500 V, where five electrons are transferred, enough to hydrogenate both double bonds (4) and to reduce the metal ion itself to Ni(0).

The position of the first reduction wave for a given dipositive metal ion also appears to reflect the degree of unsaturation of the ligand to which it is complexed. As the number of azomethine groups increases, the first electron addition becomes easier (more anodic). During addition of a second and third electron, when charge repulsion becomes a significant factor, the correlation of $E_{1/2}$ with degree of unsaturation is less clear. Except in the special case of complexes of TAAB itself, addition of a second electron is simultaneous with hydrogenation of the ligand. Obviously, the ligand TAAB has a special ability to stabilize the products of addition of two, three and, perhaps, even more electrons.

Ignoring changes in the ligand for the moment, the stepwise reductions lead formally to the following species, all of which have d^{10} configurations (number of electrons added is shown in parentheses): Cu$^+$ (1), Ni^0 (2), Co$^-$ (3). It is considered to be unlikely that the actual degree of oxidation of the metal ion is properly reflected by the formal oxidation state. It is known that the d^{10} configuration is unfavorable to planar coordination, and crystallographic studies[6] have confirmed earlier suggestions[4] that TAAB complexes tend toward square-planar coordination. It is more reasonable that the electrons are added to molecular orbitals that have significant ligand character. TAAB itself is an analog of the nonaromatic alternating hydrocarbon, tetrabenzo[16]annulene,[7] but the addition of two electrons would produce an analog (presumably planar) of the aromatic porphyrin dianion (one canonical form is given in structure IV). In this extreme model, the stabilized reduction products would be most simply described as d^8 ions (Cu^{3+}, Ni^{2+}, and Co$^+$) bound to the ligand dianion. The real situation must be intermediate, but the delocalization in the ligand–metal ion π orbitals must be such that charge density is decreased at the metal ion, thereby making the square-planar configuration energetically more favorable. However, electron density must remain sufficiently low at all points on the ligand to make hydrogen addition to the double bonds energetically and/or kinetically unfavorable.

These conclusions find some support in the contrasting chemical behavior of Cu(TAAB)$^{2+}$ and Ni(TAAB)$^{2+}$ when exposed to several atmospheres of hydrogen over PtO$_2$ in methanol. The copper complex is merely reduced to Cu(TAAB)$^+$, while the major product obtained from workup in the nickel(II) case is Ni(H$_8$-TAAB)$^{2+}$. The apparent combined stability of the reduced ligand–metal ion system, Cu(TAAB)$^+$, may result, then, from its energetically favored aromatic character combined with a relatively low electron density at all points on the pseudo-porphyrin ring. The unusual stabilities of the electronically saturated substrates, as well as the occurrence of multiple one-electron reduction sequences, may serve as models for the coinvolvement of ligand and metal ion in important naturally occurring redox systems containing such macrocycles as the porphyrin ring.

Acknowledgment. The support of the U. S. Public Health Service through Grant GM 10040 is gratefully acknowledged.

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The Reaction of Aryl and Vinyl Halides with Nickel(0) Complexes

Sir:

Recently, the importance of oxidative-addition reactions of low-valent transition metal complexes has been recognized, particularly in relationship to transition-metal catalysis.[1] Numerous examples of oxidative additions of organic halides to zerovalent d^{10} complexes of Pd and Pt affording products possessing stable carbon–metal σ bonds have been reported.[2] The corresponding reactions with nickel(0) complexes remain almost unexplored. The only example reported in which a stable carbon–metal σ bond is formed is the addition of tetrachloroethylene to (Et$_3$P)$_2$Ni(C$_2$H$_4$), affording

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(1) J. P. Collman, *Accounts Chem. Res.*, 1, 136 (1968).

(2) (a) C. D. Cook and G. S. Jauhal, *Can. J. Chem.*, 45, 301 (1967); (b) W. J. Bland and R. D. W. Kemmitt, *J. Chem. Soc., A*, 1278 (1968); (c) P. Fitton and J. E. McKeon, *Chem. Commun.*, 4 (1968); (d) P. Fitton, M. P. Johnson, and J. E. McKeon, *ibid.*, 6 (1968); (e) D. T. Rosevear and F. G. A. Stone, *J. Chem. Soc., A*, 164 (1968); (f) M. Green, R. B. L. Osborn, A. J. Rest, and F. G. A. Stone, *ibid.*, 2525 (1968).

Table I. Products Derived from the Oxidative Addition of Organohalides to $(R_3P)_2Ni(C_2H_4)$

Product	Mp, °C	Yield, %	ν_{Ni-P}, cm^{-1}	ν_{Ni-X}, cm^{-1}	Other absorptions between 200 and 450 cm^{-1}, cm^{-1}
$(Et_3P)_2Ni(C_6F_5)Br$	130–131 (lit.[a] 130–131)	11	422 (s)	307 (m)?	232 (w), 330 (m), 375 (m)
$(Ph_3P)_2Ni(C_6F_5)Br$	196–198 dec (lit.[a] 199–200 dec)	16	426 (vs)	308 (m)	231 (w), 256 (m), 276 (w)
$(Ph_3P)_2Ni(CF{=}CF_2)Cl$	120–123 dec	8	436 (m), 423 (sh)	384 (vs)	256 (s), 293 (s), 396 (w)
$(Et_3P)_2Ni(2,5\text{-}Cl_2C_6H_3)Cl$	101–102	6	415 (vs)	358 (s)	224 (m), 265 (vs), 332 (s), 375 (m)
$(Et_3P)_2Ni(2\text{-}ClC_6H_4)Cl$	91–92	19	416 (s)	330 (vs)?	230 (vs), 377 (m), 435 (w)
$(Et_3P)_2Ni(2\text{-}ClC_6H_4)Br$	108–109	9	416 (vs)		328 (m), 372 (w), 432 (w)

[a] J. R. Phillips, D. T. Rosevear, and F. G. A. Stone, *J. Organometal. Chem.*, **2**, 455 (1964).

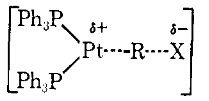
trans-chloro(trichlorovinyl)bis(triethylphosphine)nickel(II).[3] Stable π-allyl nickel halides have been formed in the reaction of allyl halides with either $(1,5\text{-COD})_2Ni(0)$[4] or $Ni(CO)_4$.[5] We have found that a variety of aryl and vinyl halides will react with $(R_3P)_2Ni(C_2H_4)$. Stable products were obtained from organic halides which yield *ortho*-substituted aryl nickel[6] or perhalovinyl nickel complexes.[3,7]

A typical reaction involved stirring 10 mmol of $Ni(acac)_2$, 20 mmol of R_3P, and 10 ml of 25% Et_2AlOEt in 50 ml of ether at −20–0° under an ethylene atmosphere. The mixture was gradually warmed to 25°, 15–20 mmol of the organohalide was added, and stirring was continued until gas evolution ceased.[8] The final products were isolated by column chromatography. The stable organonickel complexes obtained from bromopentafluorobenzene, chlorotrifluoroethylene, 1,2,4-trichlorobenzene, 1,2-dichlorobenzene, and 1-bromo-2-chlorobenzene are reported in Table I.[10]

In the 60-Mc nmr spectra of triethylphosphine complexes, the resonances exhibited by the methyl protons were insufficiently resolved to allow conclusions about their stereochemistry.[3,11] However, the stereochemistry about nickel can be assigned on the basis of far-ir data. In a study of tetrahedral, *cis*-square planar, and *trans*-square planar nickel(II) complexes, Boorman and Carty found a very strong absorption at 412–426 cm^{-1} only in *trans*-L_2NiX_2 (L = PEt_3, $PhPMe_2$, Ph_2PEt; X = Cl, Br, I), which they assigned as an asymmetric Ni–P stretching vibration.[12] In the far-ir spectra of the organonickel complexes reported in Table I, a single strong absorption is exhibited by all except the trifluorovinyl complex between 415 and 426 cm^{-1}, indicating a *trans*-square planar configuration about nickel.

Assignment of a Ni–X stretching vibration is difficult in the PEt_3 complexes since ligand absorptions occur in the same region. In the PPh_3 complexes, this interference is not so pronounced, so that there is a greater level of confidence in the ν_{Ni-X} assignments. The ν_{Ni-Cl} exhibited by the trifluorovinyl nickel complex is much higher than ν_{Ni-Cl} found in *cis*-square planar and tetrahedral complexes (340–300 cm^{-1}) and suggests a *trans*-square planar configuration about nickel.

Conclusions concerning the mechanism of this reaction were obtained from examination of product distributions obtained in the reactions with 1,2,4-trichlorobenzene and 1-bromo-2-chlorobenzene. Prior to this work, Cook and Jauhal have described $Pt(PPh_3)_2$, formed from dissociation of $Pt(PPh_3)_4$, as possessing nucleophilic character in its reactions with alkyl and aryl halides and have suggested the participation of the polar intermediate (or transition state?) shown below.[2a]



In the reaction of $(Et_3P)_2Ni(C_2H_4)$ with 1,2,4-trichlorobenzene, a substrate capable of forming three different isomeric products, the crude product mixture was dissolved in ether and saturated with anhydrous HCl until the protonation of all organonickel complexes was complete. Analysis of this product mixture by glpc revealed that three isomeric dichlorobenzenes were formed—*ortho* (7%), *meta* (6%), and *para* (87%). The protonation of pure *trans*-chloro(2,5-dichlorophenyl)bis(triethylphosphine)nickel(II) afforded only *p*-dichlorobenzene. Thus, substitution by nickel occurs preferentially at the 2-position of 1,2,4-trichlorobenzene, the *same* position at which nucleophilic substitution by methoxide ion occurs.[13,14]

If a SNAr mechanism is indeed operative, the reaction of 1-bromo-2-chlorobenzene with $(Et_3P)_2Ni(C_2H_4)$ would follow the paths illustrated below. The ligands on nickel are omitted for clarity. The

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(3) R. G. Miller, D. R. Fahey, and D. P. Kuhlman, *J. Amer. Chem. Soc.*, 90, 6248 (1968).

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(5) E. J. Corey and M. F. Semmelhack, *J. Amer. Chem. Soc.*, **89**, 2755 (1967).

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(8) In a separate experiment, we isolated $(Ph_3P)_2Ni(C_2H_4)$,[9] and after combining it with C_6F_5Br found that the reaction occurs very slowly at 0° but more rapidly as the temperature is increased.

(9) G. Wilke and G. Herrman, *Angew. Chem.*, 74, 693 (1962).

(10) Satisfactory elemental analyses were obtained for all new compounds. Others were characterized by comparison of their spectral data with those of authentic samples.

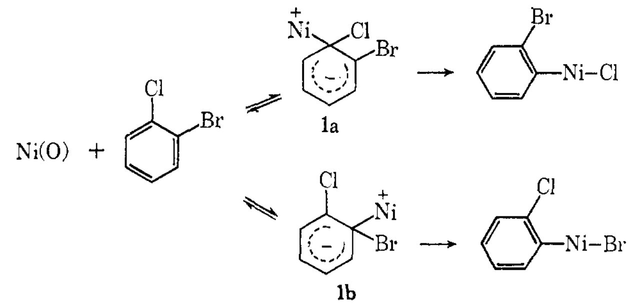
(11) H. C. Clark and W. S. Tsang, *J. Amer. Chem. Soc.*, **89**, 533 (1967).

(12) P. M. Boorman and A. J. Carty, *Inorg. Nucl. Chem. Lett.*, **4**, 101 (1968).

(13) G. M. Kraay, *Rec. Trav. Chim.*, **49**, 1082 (1930).

(14) We have also observed that a 2-chloro-4-nitrophenylpalladium complex is formed from the reaction of 1,2-dichloro-4-nitrobenzene and $Pd(PPh_3)_4$. Oxidative addition had occurred with the chloro group *para* to NO_2, the same one that is displaced in organic nucleophilic substitution reactions.

crude product from this reaction was protonated, and the relative yields of chlorobenzene and bromobenzene were determined by glpc. Since product formation in the oxidative addition is irreversible, the relative yields of products are directly proportional to their rates of formation, and therefore k_{Cl}/k_{Br} can be calculated to be 0.0030,[15] a value much lower than the k_{Cl}/k_{Br} = *ca.* 1–0.1 for most organic SNAr reactions.[16] The low value of k_{Cl}/k_{Br} indicates that the intermediate **1a**, and likely both **1a** and **1b**, revert to reactants much faster than they proceed to products. Interestingly, the low value of k_{Cl}/k_{Br} is within the range 0.0015–0.023 found for k_{Cl}/k_{Br} in the SN2 reactions of alkyl halides with vitamin B_{12s} and cobaloximes(I).[17]



[15] Although the competing halogens are not in identical environments, the activating powers of Cl and Br as *ortho* substituents in SNAr reactions are approximately the same.[16]

[16] J. F. Bunnett and Roland E. Zahler, *Chem. Rev.*, **49**, 273 (1951).

[17] G. N. Schrauzer and E. Deutsch, *J. Amer. Chem. Soc.*, **91**, 3341 (1969).

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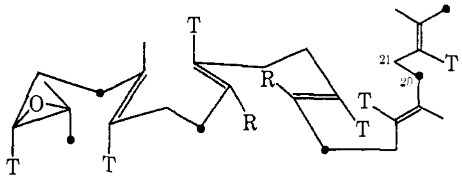
Mechanism of Squalene Cyclization. Biosynthesis of Fusidic Acid from (4*R*)-[2-^{14}C,4-^{3}H]Mevalonic Acid

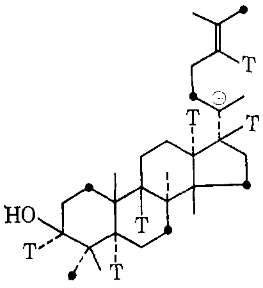
Sir:

Squalene obtained from (4*R*)-[4-^{3}H]MVA contains six tritium atoms,[1] and the derived 2,3-oxidosqualene[2] will therefore be labeled as indicated in **1a** (• denotes carbon atoms originating from C-2 of MVA; T ≡ ^{3}H). Enzymatic cyclization of 2,3-oxidosqualene to sterols and certain triterpenes is thought to proceed through the cation[3] **2** or its stabilized equivalent.[4] Cation **2** should retain six 4-*pro-R* protons (^{3}H) of MVA at C-3, 5, 9, 13, 17, and 24 and have the indicated stereochemistry.

In the sequence leading from **2** to sterols, four 1,2 migrations were postulated,[5] terminating in the elimination of a ^{3}H atom from C-9 to yield lanosterol. The transformation of lanosterol to cholesterol entails the loss of two more ^{3}H atoms[6] from C-3 and C-5. We have proved that cholesterol prepared from (4*R*)-[2-^{14}C,-4-^{3}H]MVA retained only three tritium atoms[6] at the 17α, 20,[7] and 24-*pro-R*[8] positions. The presence of isotopic hydrogens at C-17 and C-20 was taken as evidence in support of the intermediacy of cation **2** and of the rearrangements. Corey, *et al.*,[9,10] have shown that analogs **1b** and **1c** of 2,3-oxidosqualene undergo cyclization with rat liver enzymes to equivalents of cation **2**,



1a, R = CH_3
b, R = H (no tritium atoms)
c, R = CH_3; $\Delta^{20(21)}$ (no tritium atoms)



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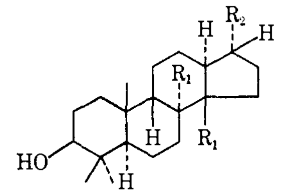
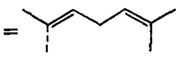
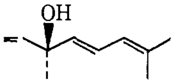
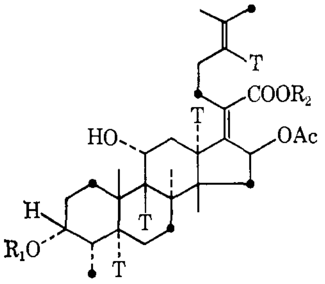


3, R_1 = H; R_2 =

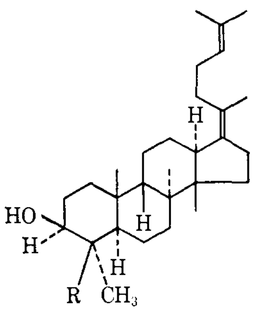


4, R_1 = CH_3; R_2 =

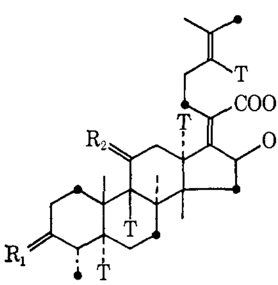




5a, R_1 = H; R_2 = H
b, R_1 = H; R_2 = CH_3
c, R_1 = Ac; R_2 = CH_3
d, R_1 = H; R_2 = H; no Δ^{24}
e, R_1 = H; R_2 = CH_3 no Δ^{24}



6a, R = CH_3
b, R = CH_2OH



7a, R_1 = 3α OAc; R_2 = O
b, R_1 = O; R_2 = O

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[2] E. J. Corey, W. E. Russey, and P. R. O. de Montellano, *J. Amer. Chem. Soc.*, **88**, 4750 (1966); E. E. van Tamelen, J. D. Willett, R. B. Clayton, and K. E. Lord, *ibid.*, **88**, 4752 (1966).

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