Evidence for a Novel Mechanism of the 1,2-Bond Shift Rearrangements catalysed by Coenzyme-B_{12}

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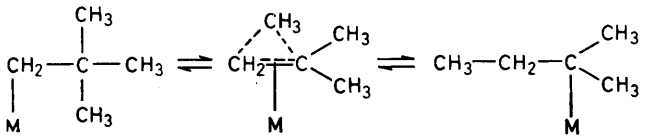
Summary The olefinic products arising from the oxidative addition at ambient temperatures of 2,2,6,6-tetramethylcyclohex-1-yl toluene-*p*-sulphonate to $(PPh_3)_2CoBr_2$, $(PPh_3)_2NiBr_2$, and hydroxo-cobalamin, all reduced with sodium borohydride, or to $(Me)_2CuLi$, provide firm evidence for a novel mechanism of the 1,2-bond shift rearrangements catalysed by vitamin B_{12} coenzyme.

DURING the last two decades there has been considerable interest in the mechanisms of skeletal rearrangements of hydrocarbons in an excess of hydrogen at elevated temperatures on heterogeneous transition metal catalysts, and in particular the 1,2-bond shift isomerization of neopentane.[1] By studying rearrangements of several model compounds we came to the conclusion[2-4] in the early seventies that alkyl groups covalently bonded to metal surfaces may isomerize in a manner akin to that of carbonium ions (Scheme 1). Since the half-reaction state of a free radical

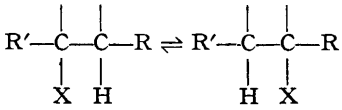


SCHEME 1

is anti-aromatic according to the $4n + 2$ rule ($n = 0$, and Walsh orbitals), a 1,2-bond shift should be highly improbable on energetic grounds. We therefore argued[2,3] that a key factor in significantly lowering the energy barrier is $d(\pi)$–

$p(\pi^*)$ bonding in the *bound* radical. A detailed molecular orbital description of this novel mechanism was given.[2,3]

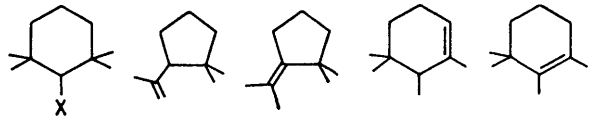
Contemporaneously but totally independently there have been extensive studies and discussions[5-7] of the vicinal interchange reactions catalysed by coenzyme B_{12} (equation 1), where X is hydroxy, amino, alkyl, or acyl, *etc.* There



(1)

are no known analogues so these reactions are regarded as unique.

In the mid-seventies we began to study certain types of organometallic reactions in order to find 1,2-bond-shift reactions analogous to those observed on metal surfaces. In particular compounds such as *O*-(2,2,6,6-tetramethylcyclohex-1-yl) *S*-methyl dithiocarbonate (**1a**) were oxidatively added at 100 °C, or above, to electron-rich noble metal compounds, *e.g.* $Pd(PPh_3)_4$.[8] The distribution of olefinic products obtained, (**2**)—(**5**), convinced us that the necessary bond



(1) (2) (3) (4) (5)

a; X = OCS_2Me

b; X = $OSO_2C_6H_4Me$-*p*

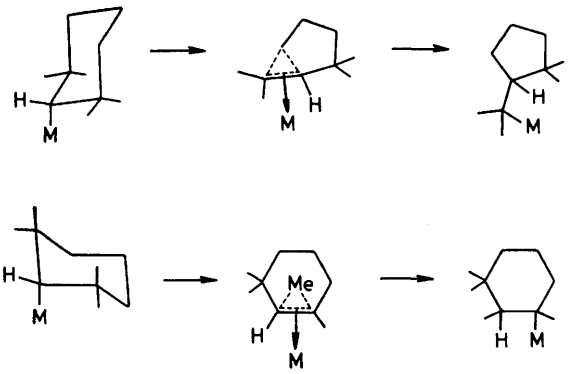
shifts involved in their formation are due to exactly the same type of mechanism as depicted in Scheme 1, and do not arise from carbonium ion or free radical intermediates. We concluded therefore that there is a distinct possibility that the same bond-shift mechanism applies in B_{12} catalysis, although a free radical theory is generally accepted for the vicinal interchanges (equation 1).

TABLE. Distributions of olefinic products.[a]

Complex	T/°C	(2)	(3)	(4)	(5)
A	20	38	14	34	14
B	60	35	14	39	12
B	20	38	14	37	11
C	60	37	12	37	13
C	20	38	12	38	11
D	−10	46	23	19	12

[a] With complexes A—C (see text) reactions were carried out as follows: 0·30—0·72 g of the complex and 0·05—0·15 g of toluene-*p*-sulphonate were added to ethanol under N_2. A large excess of sodium borohydride in wet ethanol was then added and the mixture stirred. Products were isolated after 1 to several hours at 60 °C, and after 1 to 2 days at 20 °C. Complex D was prepared, reactions with the toluene-*p*-sulphonate carried out, and the products isolated as previously described (ref. 10).

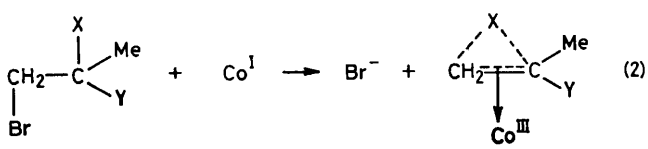
We now report conclusive evidence that our idea is correct. When 2,2,6,6-tetramethylcyclohex-1-yl toluene-*p*-sulphonate (**1b**) is oxidatively added at ambient temperatures to $(PPh_3)_2NiBr_2$ (A), $(PPh_3)_2CoBr_2$ (B), hydroxocobalamin (C), all reduced by an excess of sodium borohydride, or to $(Me)_2CuLi$ (D), olefins (**2**)—(**5**) are obtained in good yields (Table). Their distributions are very similar to those previously reported[8] and are certainly not due to free radical or carbonium ion intermediates The reaction systems containing sodium borohydride are highly basic and furthermore we had previously shown[8] that rearrangements of the 2,2,6,6-tetramethylcyclohexyl carbonium ion lead to very different ratios of olefins. In fact the distributions (Table) accord well with those expected from the antiperiplanar relationship required of the shifting group with respect to the metal (Schemes 1 and 2) and the probabilities of the alternatives for the final *cis*-β-H-elimination steps in the appropriate metal alkyls. A preponderance of (**2**) over (**3**), and of (**4**) over (**5**), is expected and found. Thus *sec*-alkylcobalamins decompose readily giving more terminal than internal olefins.[9]



SCHEME 2

Posner and Babiak[10] have also recently studied the reactions of several cycloalkyl tosylates with $(Me)_2CuLi$ at −10 °C and in some cases obtained olefins arising from 1,2-bond-shift rearrangements, but they were obviously puzzled as to the mechanism. On the other hand Salem *et al.*[11] recently arrived, solely on theoretical grounds, at the same mechanism that we have been advocating[8] for the B_{12} catalysis, but they were completely unaware that exactly the same theory, as applied to heterogeneous catalysis, had been described[2,3] several years earlier. Conversely, in extending our ideas to cobalamin catalysis[8] we were ignorant of the existence of the French paper.[11] We cite all this because it must now be stressed that the present results clearly confirm that 1,2-bond shifts such as those catalysed by B_{12} are not unique but occur widely in heterogeneous transition metal catalysis and in homogeneous organometallic reactions as well.

It is a moot point that the half-reaction state (π-complex in Scheme 1) may simultaneously develop in the act of oxidative addition and does not appear only in a separate consecutive event as implied by Scheme 2. The former possibility is theoretically feasible and indeed is supported by the invariance with time and temperature of the ratio (1/2) of the two products obtained by Scott *et al.*[12] in a study of a model reaction for methylmalonyl-CoA mutase. Reaction (2) is suggested by their results (X = COSEt;



(2)

Y = CO_2Et) but may only be possible for the one conformation out of three, *i.e.*, where X instead of Me or Y is antiperiplanar to the departing Br^- ion.

The 1/1 ratios of C_5/C_6-ring olefins (Table) obtained from (**1b**) for the Ni and Co complexes can also be explained on conformational grounds and on the basis that the appropriate π-complexes are directly involved in the oxidative addition step.

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