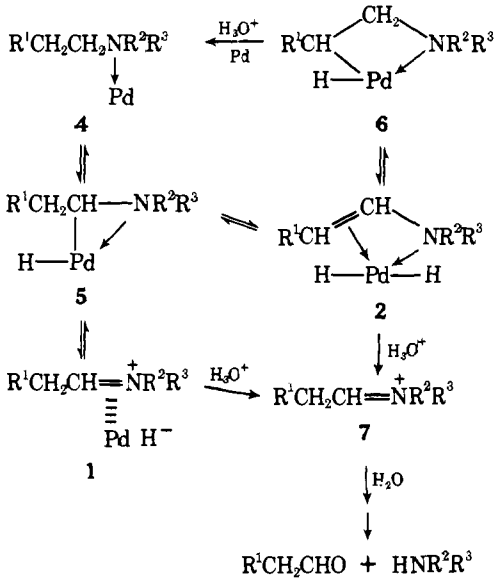
Scheme I



reaction pathway is a nucleophilic attack of the second molecule of the tertiary amine on the iminium ion complex **1**, resulting in the alkyl group exchange.[7] In contrast, under the hydrolysis condition, protonolysis of complexes **1** and **2** gives the non-metal-coordinated iminium ion **7**, which undergoes the usual acid-catalyzed hydrolysis steps of enamines to produce carbonyl compounds and secondary amines.[19] Protonolysis of intermediate **6** may cause the loss of the optical activity of recovered **3a** under the reaction conditions.

Recently Laine has reported that deuterium exchange of triethylamine by deuterium oxide takes place easily with the homogeneous $Rh_6(CO)_{16}$ catalyst[20] at the β position rather than the α position, suggesting a mechanism which involves simultaneous insertion of three rhodiums of $Rh_6(CO)_{16}$ into the α- and β-carbon–hydrogen bonds. This is in contrast to the results obtained with heterogeneous palladium catalysts where deuterium exchange at α position of tertiary amines exceeds that at the β position. When an equimolar mixture of tributylamine and deuterium oxide was treated with either palladium black or $Rh_6(CO)_{16}$ at 150 °C for 20 h, the relative ratio of the deuterium content of the α to β positions of the recovered tributylamine was 4:1 for palladium catalyst and 1:4 for $Rh_6(CO)_{16}$ catalyst.[21] With the catalytic hydrolysis of tertiary amines, at least, it is doubtful whether the homogeneous metal cluster catalyst can be used to model heterogeneous catalytic reactions.[22] Work is in progress to investigate the full scope of the present reaction and to apply our method to other systems.

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(9) In the absence of 2,4-dinitrophenylhydrazine, dibutylamine and *N,N*-dibutyl-2-butylamine, which are condensation products of dibutylamine and butanal, are obtained in 54 and 47% yield, respectively.

(10) Palladium catalyst gave the best result among the metals examined. Other palladium compounds such as $PdCl_2$ and $Pd(OAC)_2$ gave similar results. Alternatively, soluble ruthenium catalysts such as $RuCl_3$ can be used conveniently, giving similar results.

(11) The reaction of tertiary amines such as tributylamine with water in the presence of acid catalysts does not take place at 200 °C without palladium catalyst.

(12) The higher pK_a results in higher conversion of tertiary amines. The conversion of tributylamine increases in the order of $CH_3CO_2H < ClCH_2CO_2H < Cl_3CO_2H < NO_2C_6H_4SO_3H$. When 0.3 equiv of p-$NO_2C_6H_4SO_3H$ is used under the same reaction condition, the conversion reaches to 80%.

(13) 4-Methylamino-1-(3-pyridyl)butanone: IR (liquid film) 1655 cm^{-1} (C=O), 3100 (N—H); NMR ($CDCl_3$) δ 1.55 (br t, 2 H), 2.20 (s, 3 H), 2.35 (m, 4 H). Wada. E. *Arch. Biochem. Biophys.* **1957**, *72*, 145.

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(15) Deuterium exchange of tributylamine takes place only at the α and β positions upon treatment with D_2O at 190 °C for 40 h in the presence or absence of CH_3COOD. It is worthwhile to note that dibutylamine is deuterated only in the α position upon treatment with CH_3CO_2D–D_2O. (Murahashi, S.-I.; Watanabe, T., unpublished results.)

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(21) Under the same condition, rhodium black gave the similar α:β ratio (4:1) as palladium black.

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Retention of Stereochemistry during Multipositional Isomerization of an Olefin by Diiron Nonacarbonyl

Sir:

The preponderance of evidence indicates that olefins rearrange in the presence of iron carbonyl catalysts by a sequence of 1,3-hydrogen shifts. Numerous reports have dealt with this reaction,[1] and a few have provided convincing arguments regarding the detailed nature of the rearrangement. Casey and Cyr have established that during $Fe_3(CO)_{12}$ induced rearrangement of 3-ethyl-1-pentene-*3*-d_1 (**1**) to 3-ethyl-2-pentene, the deuterium label was scrambled randomly between the terminal methyl groups, as shown in **2**.[2] These results were interpreted in terms of rapidly equilibrating complex species, representatives of which are shown in Scheme I.

Only a small number of reports have concerned the stereochemistry of the hydrogen shift, and none have dealt with the stereochemistry of the hydrogen shift in purely hydrocarbon rearrangements. Ford and Strauss have shown that the rearrangement of the labeled *endo*-tricyclodecenol **3** proceeds stereospecifically to give the saturated ketone **4**, with the stereochemistry of the migrating deuterium as shown.[3] In another example, Green and Hughes found that the monoolefin-tetracarbonyliron complex **5** rearranged to the diene-tricarbonyliron complex **6**, with some of the optical activity of **5** remaining intact.[4]

Regarding the first example, it is difficult to envision another result, since it is essentially impossible for an iron species responsible for the hydrogen shift to approach the endo face of

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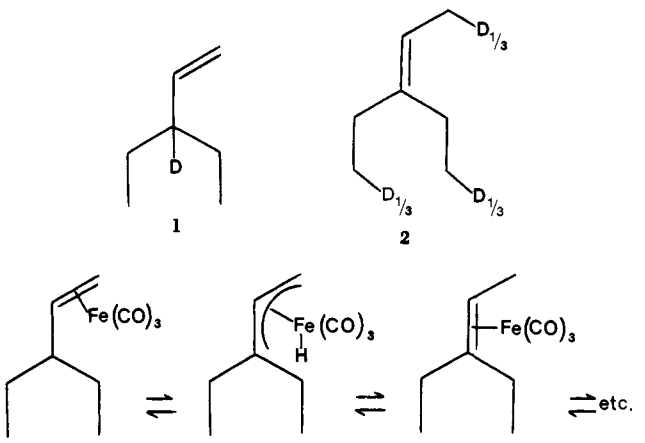
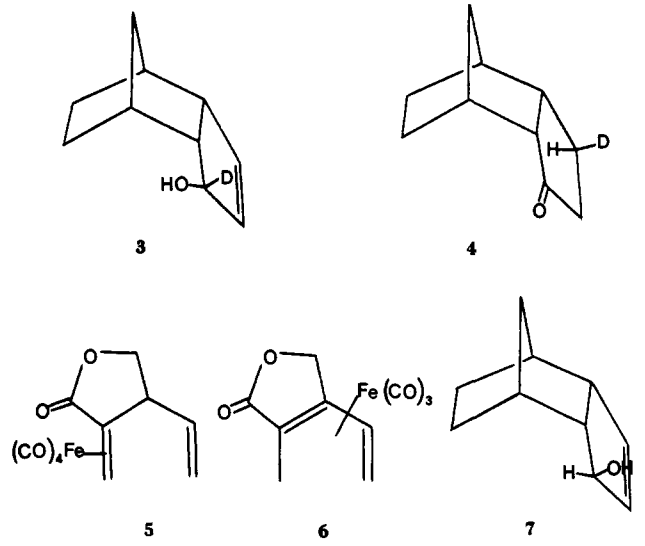
Scheme I



1 2

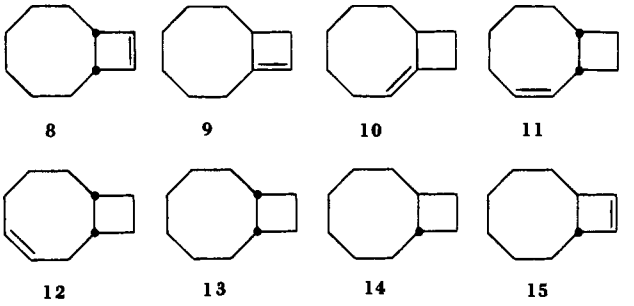
a molecule such as **3**. To illustrate, the *exo*-hydroxyl analogue **7** is stable to iron carbonyl induced rearrangement.[5] Both ex-



3 4 5 6 7

amples cited above involve a single 1,3-hydrogen shift. We report results in which stereochemistry is retained during multiple 1,3-hydrogen shifts induced by an iron carbonyl species in a simple hydrocarbon system.

When *cis*-bicyclo[6.2.0]dec-9-ene (**8**)[6] was treated in refluxing hexane with equimolar amounts of $Fe_2(CO)_9$, the starting material rapidly disappeared and was replaced by a mixture of bicyclodecenes **9–12**.[8] Catalytic hydrogenation of the product mixture provided *cis*-bicyclo[6.2.0]decane (**13**) contaminated with <3% *trans* isomer **14**. Bicyclo[6.2.0]dec-



8 9 10 11 12 13 14 15

8(9)-ene (**9**) also rearranged to the olefins **10–12** at a rate somewhat slower than that of the rearrangement of **8**.

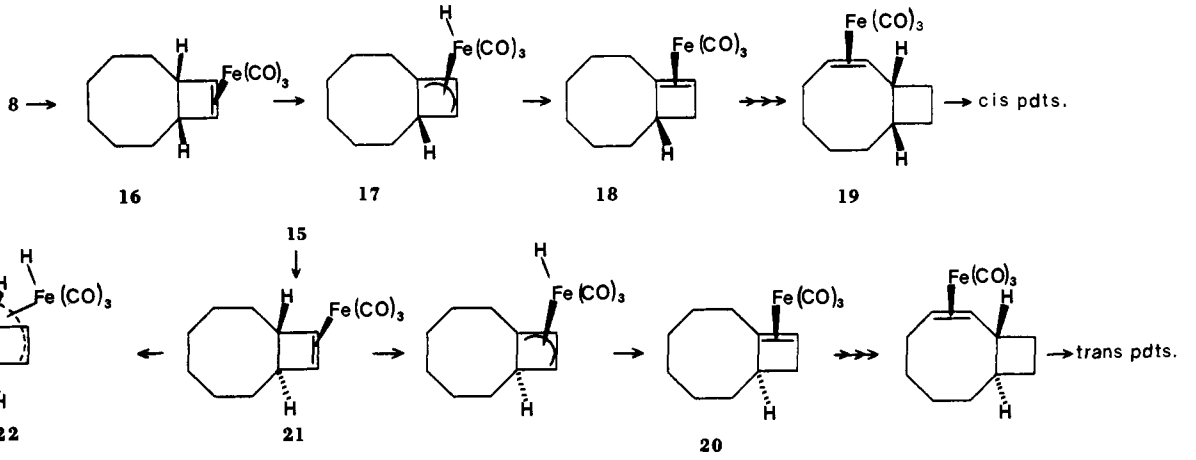
trans-Bicyclo[6.2.0]dec-9-ene (**15**)[9] rearranged in the presence of $Fe_2(CO)_9$ in refluxing hexane at a rate approximately equal to that of the rearrangement of the cis isomer **8**, to produce the hydrocarbon **9** and isomeric bicyclodecenes. Catalytic hydrogenation of the product mixture, however, showed the presence of both isomers **13** and **14**, in a percentage ratio of 62:38. After correction for the presence of **9** among the olefinic products (**9** yields 91% **13** and 9% **14** on hydrogenation), it was found that, of the hydrocarbons representing rearrangement beyond **9**, 45% of the product retained the original trans-fused stereochemistry of starting material **15**.

The stereochemical outcome of rearrangement was more pronounced at lower reaction temperatures. While **8** behaved essentially as it had at refluxing hexane temperature, the trans isomer **15** in refluxing pentane with $Fe_2(CO)_9$ failed to produce any isomer **9**. Catalytic hydrogenation of the product mixture yielded both **13** and **14**, but in this instance the trans isomer **14** predominated, making up 63% of the product mixture. Finally, at ambient temperature, the $Fe_2(CO)_9$–*trans*-bicyclo[6.2.0]dec-9-ene reaction yielded a product mixture in which 87% trans stereochemistry was retained. We believe this result to be the first demonstration that the iron carbonyl induced rearrangement of simple olefins can proceed stereoselectively during a multistep sequence.

The π-allylhydridoiron tricarbonyl mechanism,[10] an example of which appears in Scheme I, accounts reasonably well for our results. In order that stereochemistry be preserved during the isomerization of **8** to **11**, or especially of **15** to trans-fused analogues of **11**, a necessary requirement is that the original iron carbonyl species which brings about rearrangement remain attached throughout the sequence; such a prerequisite has been invoked previously.[2] These limitations are applied to our systems in Scheme II.

In hydrocarbon **8**, complexation must almost certainly take place on the exo face of the molecule to produce the complex **16**. Hydrogen abstraction to give the coordinatively saturated complex **17** seals the stereochemical fate of the rearrangement;

Scheme II



16 17 18 19 22 21 20

so long as decomplexation is not an important side reaction, the iron carbonyl moiety and the remaining bridgehead hydrogen will always bear a cis relationship to one another, and this relationship is carried through to products. In the penultimate step, a hydride is returned from the $-HFe(CO)_3$ moiety to the bridgehead to secure the cis fusion of the bicyclic hydrocarbon, as in **19.**

A similar argument can be applied to the trans isomer **15**; in all complex intermediates, the remaining bridgehead hydrogen bears a trans relationship to the attached iron species, and trans-fused products result. It is also possible to account for the temperature effect regarding **15** in terms of this mechanistic picture. At lower temperatures, complexes such as **20** possess sufficient stability to survive decomplexation; hence the hydrocarbon **9** is not produced. The limits of this stability are presumably exceeded at refluxing hexane temperature, and **9** is observed among rearrangement products. It is puzzling, in terms of such an argument, why **8** shows no such temperature effect. The complex **18** would be expected to be more stable than **20** because of steric effects; hence it should have more readily survived in the low-temperature case. Yet the hydrocarbon **9** was observed regardless of reaction temperature.

An intriguing alternative explanation for these results involves intermediate complexes which leave bridgehead hydrogen atoms intact. While such intermediates would be sterically difficult to attain from the cis complex **16,** similar problems are not present in **21**; hence a species such as **22** might be achievable. Nonallylic intermediates have been considered in iron carbonyl induced rearrangements of vinyl cyclopropanes.[11] We are actively pursuing labeling studies to distinguish between these alternative possibilities.

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(6) Prepared by the sequence *cis*-cyclooctene + ethyl diazoacetate → 9-carbethoxybicyclo[6.1.0]nonane → 9-hydroxymethylbicyclo[6.1.0]nonane → bicyclo[6.1.0]nonane-9-carboxaldehyde → tosylhydrazone → **8.** NMR and IR spectral data were consistent with structure **8,** and the chemistry of **8** agreed with that described by van Tamelen and co-workers.[7]
(7) Radlick, P.; Klem, R.; Spurlock, S.; Sims, J. J.; van Tamelen, E. E.; Whitesides, T. *Tetrahedron Lett.* **1968,** 5117–5121.
(8) The mixture of hydrocarbons was separated into its components most conveniently by column chromatography using $AgNO_3$–silica gel, monitored by GC. Compound **9** was identified from its ^1H NMR spectrum and thermal isomerization to 1-vinylcyclooct-1-ene, and **10** from its ^1H and ^{13}C NMR spectra. Compounds **11** and **12** could not be separated under any circumstances. A combination of ^1H and ^{13}C NMR spectra and catalytic hydrogenation to a single hydrocarbon, **13,** limited the possibilities to **11, 12,** bicyclo[6.2.0]dec-4-ene, and bicyclo[6.2.0]dec-1(8)-ene; the last two possibilities were eliminated by independent synthesis in the former case, and ^1H NMR spectra in the latter.
(9) Synthesized in low yield by the sequence *trans*-cyclooctene + dichloroketene → *trans*-10,10-dichlorobicyclo[6.2.0]decan-9-one → *trans*-bicyclo[6.2.0]decan-9-one → tosylhydrazone → **15** + **8** + **9,** followed by separation on $AgNO_3$–silica gel. Spectral data of **15** agree with those reported previously.[7]
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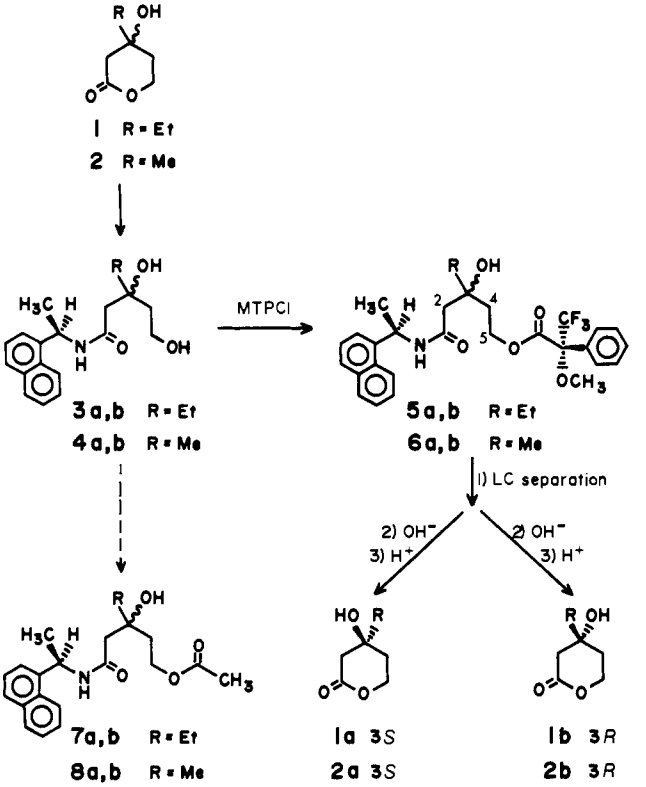
Absolute Configuration of Homomevalonate and 3-Hydroxy-3-ethylglutaryl and 3-Hydroxy-3-methylglutaryl Coenzyme A, Produced by Cell-Free Extracts of Insect Corpora Allata. A Cautionary Note on Prediction of Absolute Stereochemistry Based on Liquid Chromatographic Elution Order of Diastereomeric Derivatives

Sir:

Homomevalonate (HMev)[1] and 3-hydroxy-3-ethylglutarate (HEG)[2] have been implicated as probable intermediates in insect juvenile hormone (JH) biosynthesis. While the congeneric intermediate, mevalonate (Mev), has been shown to have the 3*R* configuration common to other organisms,[1b] no direct evidence has yet been presented for the absolute configuration of HMev or HEG (as its coenzyme A (CoA) ester). We report herein our findings with respect to the latter two compounds. We also confirm the 3*S* absolute stereochemistry of the Mev precursor 3-hydroxy-3-methylglutaryl CoA (HMG-CoA), whose prior assignment rested solely on enzymological conversions.[3]

Racemic homomevalonolactone[1a] (HMev>, **1**) was converted via Scheme I in 30–40% overall yield into the 1-amido-5 esters **5a,b** by (1) heating with neat 1-(+)-α-(1′-naphthyl)ethylamine, and (2) treatment with a pyridine solution of the acyl chloride of (+)-α-methoxy-α-trifluoromethylphenylacetic acid. These diastereomers were then separated by micropreparative liquid chromatography (LC) into stereoisomerically pure components.[4,5] Each diastereomer (4–6 mg) was then analyzed by 90-MHz ^1H NMR and spectra were compared with those obtained from the similarly prepared derivatives **6a,b** of (3*R*)- and (3*S*)-mevalonolactone (Mev>, **2**).[4-6] Strong correlations were observed between chemical shift of diagnostic NMR resonances (Table I) for each pair of HMev vs. Mev derivatives according to their elution order on LC. Each of these four derivatives was then converted into the parent lactone of high enantiomeric purity via base hydrolysis

Scheme I[a]



[a] For diastereomeric derivatives, **a** = fast eluting and **b** = slow-eluting on LC.

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