resin. Their formulation of the red complex as a monomeric rhodium(I) complex was supported in part by the isolation of $Rh(PPh_3)_3BF_4$ crystals from the solution reaction. Triphenylphosphine most likely functions as the reducing agent in the reaction as $POPh_3$ more recently has been shown to be the oxidation product obtained in the related reduction of Rh_2^{4+} to $Rh(PPh_3)_3(OCOCH_3)$ in presence of PPh_3 and $Li[OCOCH_3]$.[19]

$Rh(PPh_3)_x^+$ ions also can be introduced to the interlamellar surfaces of the mineral by direct exchange reaction between its Na^+ exchange form and a freshly prepared 8×10^{-3} *M* solution of the complex in methanol. This method of preparation affords a red mineral with an elemental composition that corresponds to $[(Rh(PPh_3)_{2.3}^+)_{0.12}, Na_{0.54}^+]$-hectorite. The observed PPh_3 to Rh ratio suggests the possible presence of two or more solvated $Rh(PPh_3)_x^+$ species, perhaps in dissociative equilibrium, on the mineral surfaces.

The addition of oxygen-free hydrogen to a suspension of $[(Rh_2^{4+})_{0.01}, H_{0.62}^+]$-hectorite in methanol at 25° results in the formation of a light yellow to colorless rhodium hydride complex which functions in the mineral environment as a catalyst for olefin hydrogenation. Analogous hydride formation and catalytic activity is observed for $[(Rh(PPh_3)_{2.3}^+)_{0.12}, Na_{0.54}^+]$-hectorite and for the $Rh(PPh_3)_x^+$-containing mineral prepared by addition of PPh_3 to $[(Rh_2^{4+})_{0.01}, H_{0.62}^+]$-hectorite. Catalytically active hydrides derived from the red rhodium(I)-triphenylphosphine complexes are known also to form in homogeneous methanol solution,[2] but Rh_2^{4+} in absence of phosphine ligand is reported to be inactive and does not react with hydrogen in methanol except at elevated temperatures when it is reduced to the metal.[2] Apparently, when the ion is present on the charged, intracrystal silicate surfaces, its reactivity toward metal hydride formation is enhanced greatly.

The hydrogenation rates obtained for 1.0 *M* 1-hexene in methanol are given in Table I. Hydrogen was allowed to bubble through the mineral–methanol mixtures at least 2 hr to ensure complete hydride formation, and then the olefin was added. After a brief induction period of ca. 15–20 min, linear hydrogen uptake occurred in each case. Included in the table are the rates for Rh_2^{4+} in the presence of PPh_3 ligand and at the exchange sites of a resin and in homogeneous solution at a PPh_3 to Rh ratio (2:1) which is known to provide an optimum rate.[2]

The mixed Rh_2^{4+}, H^+ exchange form of hectorite requires a PPh_3/Rh value greater than 6 to achieve an optimum rate of 22 ± 2 ml of H_2/min/mmol of Rh. Because the same rate is obtained at a much lower PPh_3 to Rh ratio in $[(Rh(PPh_3)_{2.3}^+)_{0.12}, Na_{0.54}^+]$-hectorite, the presence of hydrogen ion on the silicate surface apparently inhibits the formation or reactivity of the active hydride. Nonetheless, the hydrides derived from Rh_2^{4+} in the presence of PPh_3 are substantially more efficient as catalysts in the mineral environment than at the exchange sites of the resin.

The mineral-bound hydrides showed no activity toward hydrogenation of benzene in methanol at room temperature. This verifies that the activity toward olefin hydrogenation is due to metal hydride formation and not to trace amounts of metallic rhodium, which is an excellent catalyst for reduction of aromatic hydrocarbons as well as for olefins.[20] Moreover, all catalytic activity was lost when hydrogenated $[(Rh_2^{4+})_{0.01}, H_{0.62}^+]$-hectorite was washed with NaCl in methanol. This latter treatment would be expected to displace a cationic hydride complex from the silicate surface but not the free metal. No evidence for metal formation in the mineral environment was observed in the presence or absence of PPh_3 except at temperatures above 50° when the catalysts became gray and, finally, black.

Finally, the same type of metal hydride formation and catalytic activity observed above for hectorite has been achieved with montmorillonite. In this latter smectite, the negative charge on the silicate sheets arises mainly from isomorphous substitution of Mg^{2+} for Al^{3+} in two-thirds of the octahedral positions.

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References and Notes

(1) P. Legzdins, G. L. Rempel, and G. Wilkinson, *Chem. Commun.*, 825 (1969).
(2) P. Legzdins, R. W. Mitchell, G. L. Rempel, J. D. Ruddick, and G. Wilkinson, *J. Chem. Soc.*, 3322 (1970).
(3) *Mobil Oil*, Patent, U.S. No. 1,800,371 (1969).
(4) R. H. Grubbs and L. C. Kroll, *J. Am. Chem. Soc.*, **93**, 3062 (1971).
(5) J. Manassen, *Platinum Met. Rev.*, **15**, 142 (1971).
(6) J. P. Collman, L. S. Hegedus, M. P. Cooke, J. R. Norton, G. Dolcetti, and D. N. Marquardt, *J. Am. Chem. Soc.*, **94**, 1789 (1972).
(7) R. H. Grubbs, L. C. Kroll, and E. M. Sweet, *J. Macromol. Sci., Chem.*, **7**, 1047 (1973).
(8) R. H. Grubbs, C. Gibbons, L. C. Kroll, W. D. Bonds, Jr., and C. H. Brubaker, Jr., *J. Am. Chem. Soc.*, **95**, 2373 (1973).
(9) C. U. Pittman and G. O. Evans, *Chem. Tech.*, **3**, 560 (1973), and references therein.
(10) (a) L. J. Boucher, A. A. Oswald, and L. L. Murrel, Abstracts, 167th National Meeting of the American Chemical Society, Los Angeles, Calif., 1974, PETR-35; (b) J. P. Candlin and H. Thomas, *Adv. Chem. Ser.*, **No. 132**, 212 (1974).
(11) I. Dietzmann, D. Tomanova, and J. Hetflejs, *Collect. Czech. Chem. Commun.*, **39**, 123 (1974).
(12) M. Mejstrikova, R. Rericha, and M. Kraus, *Collect. Czech. Chem. Commun.*, **39**, 135 (1974).
(13) M. Capka and J. Hetflejs, *Collect. Czech. Chem. Commun.*, **39**, 155 (1974).
(14) J. C. Bailar, *Catal. Rev.-Sci. Eng.*, **10**, 17 (1974), and references therein.
(15) R. E. Grim, "Clay Mineralogy", 2nd ed, McGraw-Hill, New York, N.Y., 1968, pp 77–92, 188–200.
(16) D. M. Clementz, T. J. Pinnavaia, and M. M. Mortland, *J. Phys. Chem.*, **77**, 196 (1973).
(17) M. McBride, T. J. Pinnavaia, and M. M. Mortland, *Am. Mineral.*, **60**, 66 (1975).
(18) The fraction of exchange sites occupied by Rh_2^{4+} is comparable to the exchange capacity which can arise due to external SiO–H groups at the crystallite edges.[15] Because these exchange sites are very weakly acidic, they are not expected to be occupied to any appreciable extent by Rh_2^{4+} ions under the acidic conditions of the exchange reaction. To verify this, the same exchange reaction was carried out with microcrystalline samples of the structurally related but nonswelling layer lattice silicates biotite, talc, pyrophyllite, attapulgite, and kaolinite. In each case, no perceptible Rh_2^{4+} binding occurred.
(19) R. W. Mitchell, J. D. Ruddick, and G. Wilkinson, *J. Chem. Soc. A*, 3224 (1971).
(20) P. N. Rylander, "Catalytic Hydrogenation over Platinum Metal", Academic Press, New York, N.Y., p. 309.

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Biosynthesis of Sitosterol from (2*R*)- and (2*S*)-[2-^{3}H]Mevalonic Acid in the Pea. The Incorporation of a 15α-Tritium Atom Derived from (3*RS*, 2*R*)-[2-^{14}C,2-^{3}H]Mevalonic Acid

Sir:

The biosynthetic elaboration of sterols from lanosterol in rat livers [1]and yeast homogenates is thought to proceed via a $\Delta^{8,14}$-intermediate. The olefin is presumed to be formed in the course of the 14α-demethylation and involves the abstraction of a hydrogen derived from 2-pro *S* of mevalonic acid[2-4] (MVA) from C-15. Subsequently reduction of the Δ^{14} takes place through the acquisition of 14α-[5] and 15β-hydrogen[4,6] atoms. The overall sequence of reactions results in the inversion of the configuration[4,6] of the retained at C-15 hydrogen atom derived from 2-pro *R* of MVA from its 15β configuration, in protosterols[7] and lanosterol, to the

Table I. Specific Activities of ^{14}C and ^{3}H:^{14}C Ratios of Metabolites and Their Transformation Products (See Text)[a]

Entry and compound	Experiment A (3*RS*, 2*R*)-[2-^{14}C, 2-^{3}H]MVA			Experiment B (3*RS*, 2*S*)-[2-^{14}C, 2-^{3}H]MVA		
	^{14}C specific activity	^{3}H:^{14}C ratio		^{14}C specific activity	^{3}H:^{14}C ratio	
		Isotopic	Atomic		Isotopic	Atomic
1. MVA–amide		9.97	1.00:1		3.14	1.00:1
2. Squalene–6HCl		5.16	6.00:6		2.01	6.00:6
3. Sitosterol acetate (1)	3.26	5.15	4.99:5	2.94	1.26	3.13:5
4. 5α-Stigmastanol acetate (2)	3.22	5.18	5.03:5	2.90	1.22	3.03:5
5. 5α-Stigmast-14-en-3β-ol acetate (3)	3.22	4.54	4.40:5	2.89	1.17	2.91:5
6. 5α-Stigmasta-3β,14α, 15α-triol 3-acetate (4)	3.25	4.53	4.39:5	2.92	1.19	2.96:5
7. 5α-Stigmasta-3β,14α -diol-15-one 3-acetate (5)	3.23	4.49	4.35:5	2.90	1.16	2.89:5

[a] The results are the average of at least three crystallizations in which the ^{14}C specific activity and ^{3}H:^{14}C remained constant (±3%). Specific activity $\times 10^4$ dpm per mmol. The MVA and squalene were counted as benzhydrylamide and hexahydrochloride, respectively. The results are significant to ±3%. The atomic ratios are calculated on the basis the atomic ratio of squalene (6-^{3}H:6-^{14}C).

15α configuration in sterols biosynthesized in rat liver and yeast homogenates.

Recently results indicating the possible retention of both the 2-pro *R* and 2-pro *S* hydrogen atoms of MVA at C-15 of phytosterols biosynthesized in marigold flowers (*Calendula officinalis*) were reported.[8] This suggested that the 14α-demethylation in the biosynthesis of phytosterols in higher plants proceeds by a different mechanism,[9-11] e.g., via a $\Delta^{8(14)}$ rather than $\Delta^{8,14}$ intermediate. The feasibility of such a mechanism was enhanced by the isolation of 5α-stigmasta-8(14), 22-dien-3β-ol from rayless goldenrod (*Aplopappus heterophyllus*).[12]

In the broader sense the observations in marigold flowers could imply that the biosynthesis of sterols from cycloartenol, which is thought to be an intermediate in higher plants, proceeds by a different route than that from lanosterol. We have now obtained proof that a hydrogen (deuterium) atom from the water of the medium is incorporated at C-19 of sitosterol biosynthesized in the pea.[13] This is consistent with the hypothesis that cycloartenol (or a C-19 "anion") is a key intermediate in the biosynthesis of this phytosterol. Consequently we used peas to evaluate the events at C-15 in the biosynthesis of phytosterols.

Peas (45; Blue Bantam variety) were germinated in aqueous (3*RS*, 2*R*)-[2-^{14}C,2-^{3}H]MVA (10 μCi of ^{14}C; ^{3}H:^{14}C ratio 10.0). After 6 days the peas were processed and a nonsaponifiable residue was obtained (7.33×10^6 dpm of ^{14}C. An analogous experiment with (3*RS*, 2*S*)-[2-^{14}C,2-^{3}H]MVA (10 μCi of ^{14}C; ^{3}H:^{14}C ratio 3.14) gave a nonsaponifiable residue containing (1.07×10^7 dpm of ^{14}C). The "*R*" and "*S*" metabolites were extensively purified until homogenous squalene and sitosterol acetate were obtained[6,8] (Table I).

The photochemical dehydrogenation of cholestanol acetate in the presence of $C_6H_5I\,Cl_2$ gives among others 5α-cholest-14(15)-en-3β-ol acetate.[6,14] We have proven that the reaction is stereospecific and involves the overall abstraction of the 14α-and 15α-hydrogen atoms.[6] It can be accepted with certainty that an analogous dehydrogenation of 5α-stigmastanol acetate will also involve the removal of the 14α- and 15α-hydrogen atoms. We employed this reaction for the determination of the C-15 tritium content of the "*R*" and "*S*" sitosterol acetates. The sequence of transformations outlined in Scheme I was used. The results are summarized in Table I.

It is apparent that the sequence of reactions ("*S*"-**1**) → ("*S*"-**2**) → ("*S*"-**3**) → ("*S*"-**4**) → ("*S*"-**5**) proceeded without loss of tritium from C-15. (Table I, experiment B, entries 3-7). This indicates that the 2-pro *S* hydrogen (tritium) atom of MVA was abstracted from C-15 in the course of the biosynthesis of the "*S*"-sitosterol (**1**). In contrast the transformations ("*R*"-**1**) → ("*R*"-**2**) → ("*R*"-**3**) were accompanied by the loss of ca. 0.6 atom of tritium (Table I, experiment A, entries 3, 4, and 5). Subsequent transformation of ("*R*"-**3**) via ("*R*"-**4**) to ("*R*"-**5**) did not involve additional loss of tritium (Table I; experiment A, entries 6 and 7). It may thus be concluded that the "*R*"-sitosterol (**1**) retained tritium at the 15α-position.

Scheme I

sitosterol acetate (1) $\xrightarrow{i^a}$ 5α-stigmastanol acetate (2) $\xrightarrow{ii^a}$ 5α-stigmast-14-en-3β-ol acetate (3) $\xrightarrow{iii^a}$ 5α-stigmastane-3β,14α,15β-triol-3-acetate (4) $\xrightarrow{iv^a}$ 5α-stigmastane-3β,14α-diol-15-one 3 acetate (5)

[a] Key: i, EA, $HClO_4$, PtO_2, H_2; ii, C_6H_6, $C_6H_5ICl_2$, hν; iii, (1) $CHCl_3$, *m*-ClC_6H_4COOOH; (2) $(CH_3)_2CO$, H_2O, HJO_4; iv, CrO_3–pyridine.

Two observations require comment. It is apparent that the "*R*"-sitosterol acetate had only ca. 0.6 atom of tritium at the 15α-position. Also a significant loss of tritium occurred in the early stages of MVA metabolism as evidenced by the large drop of the ^{3}H:^{14}C ratio between MVA and squalene (Table I; entries 1 and 2). It is possible that the presence of less than an atom of tritium at the 15α-position of the "*R*"-sitosterol may be related to the loss of tritium in the initial metabolic stages. Alternatively this might be due to an uneven distribution of isotopes in the metabolite as previously noted for other polyprenoids.[15,16] The problem is currently being investigated.

Based on the above observations it is evident that the *end results* of events around C-14 and C-15 in the biosynthesis of sterols in rat liver homogenates, yeast homogenates, and in germinating peas are analogous. This leads to the conclusion that irrespective of whether lanosterol or cycloartenol is the key precursor, in the systems investigated so far, the overall outcome at C-14 and C-15 is the same. Although it is tempting to extend the mechanistic considerations on the 14α-demethylation from rat liver preparations to other systems (peas), the possibility of different pathways operating in higher plants cannot be excluded a priori, particularly in view of the isolation of 5α-stigmasta-8(14),15,24(28)-trien-3β-ol from the *Vernonia anthelminitica* plant.[17]

In view of the above observations, the results reported for Marigold flowers[8] are being reinvestigated.

References and Notes

(1) A. Fiecchi, L. Canonica, A. Scala, F. Cattabeni, E. Paoletti, and R. Paoletti, *Life Sci.*, **8**, part II, 629 (1969); A. Fiecchi, A. Scala, F. Cattabeni, and E. G. Paoletti, *Life Sci.*, **9**, part II, 1201 (1970); K. T. D. Alexander, M. Akhtar, R. B. Boar, J. F. McGhie, and D. M. R. Barton, *Chem. Commun.*, 1479 (1971).

(2) L. Canonica, A. Fiecchi, M. Galli Kienle, A. Scala, G. Galli, E. Paoletti, and R. Paoletti, *J. Am. Chem. Soc.*, **90**, 3597 (1968).
(3) G. F. Gibbons, L. J. Goad, and T. W. Goodwin, *Chem. Commun.*, 1458 (1968).
(4) E. Caspi, P. J. Ramm, and R. E. Gain, *J. Am. Chem. Soc.*, **91**, 4012 (1969); P. J. Ramm and E. Caspi, *J. Biol. Chem.*, **244**, 6064 (1969).
(5) M. Akhtar, J. A. Watkinson, A. D. Rahimtula, D. C. Wilton, and K. A. Munday, *Chem. Commun.*, 1406 (1968).
(6) E. Caspi, J. P. Moreau, and P. J. Ramm, *J. Am. Chem. Soc.*, **96**, 8107 (1974).
(7) E. Caspi, R. C. Ebersole, L. J. Mulheirn, W. O. Godtfredsen, and W. von Daehne, *J. Steroid Biochem.*, **4**, 433 (1973).
(8) J. Śliwowski, and Z. Kasprzyk, *Phytochemistry*, **13**, 1451 (1974).
(9) K. Bloch, *Science*, **150**, 19 (1965).
(10) J. Fried, A. Dudowitz, and J. W. Brown, *Biochem. Biophys. Res. Commun.*, **32**, 568 (1968).
(11) W. Lee and G. J. Schroepfer, Jr., *Biochem. Biophys. Res. Commun.*, **32**, 635 (1968); W. Lee, B. N. Lutsky, and G. J. Schroepfer, Jr., *J. Biol. Chem.*, **244**, 5440 (1969).
(12) L. H. Zalkow, G. A. Cabat, G. L. Chetty, M. Ghosal, and G. Keen, *Tetrahedron Lett.*, 5727 (1968).
(13) E. Caspi and J. K. Śliwowski, submitted for publication.
(14) R. Breslow, J. A. Dale, P. Kalicky, S. Y. Liu, and W. N. Washburn, *J. Am. Chem. Soc.*, **94**, 3278 (1972).
(15) R. Croteau and W. D. Loomis, *Phytochemistry*, **11**, 1055 (1972).
(16) M. Biollaz and D. Ariqoni, *Chem. Commun.*, 633 (1969).
(17) J. A. Fioriti, M. G. Kolor, and R. P. McNaught, *Tetrahedron Lett.*, 2971 (1970).
(18) This work was supported by National Institutes of Health Grant GM-HL 19882.
(19) Postdoctoral Fellow on leave from the Department of Biochemistry of Warsaw University, Poland.
(20) Undergraduate summer trainee supported in part by the A. T. and V. D. Fuller American Cancer Society Junior Research Fellowship and in part by National Science Foundation Grant GB 36201.

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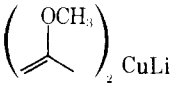
Preparation and Synthetic Applications of Lithium Di(α-methoxyvinyl)cuprate

Sir:

Acyl anion equivalents have been rigorously investigated within the last 5 years, as evidenced by the vast number of papers since 1969.[1] Baldwin and coworkers[1] have recently prepared α-methoxyvinyllithium (MVL) (**1**) and demonstrated its usefulness in 1,2-additions to various carbonyl moieties and alkylations with halides. We now wish to report the preparation of lithium di(α-methoxyvinyl)cuprate (**2**) from MVL and its synthetic utility in conjugate additions[2] and alkylations.

1



2

As shown in Scheme I, reaction of **2** with an α,β-unsaturated ketone **3** would result in a 3-(α-methoxyvinyl) ketone (**4**) which, when either hydrolyzed or ozonized, would produce a 1,4-diketone (**5**) or γ-ketoester (**6**), respectively.

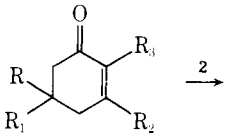
When purified cuprous iodide[3] was added to a stirred solution of MVL at −65°, the mixture gradually turned black, implying that the cuprate (**2**) had indeed formed (since the color of lithium divinylcuprate appears black[4]). However, this was not the case, as addition of 2-cyclohexen-1-one (**3a**) and work-up resulted in a nearly quantitative yield of 1,2-adduct, with no more than a few per cent of the conjugate addition product **4**. This problem was circumvented. Addition of MVL to a solution of cuprous iodide, dimethyl sulfide,[5] and freshly distilled THF at −40° initially produces a deep red-brown mixture which turns yellow near the end of the addition. After stirring for 30 min at −40°, the enone in THF is added and stirring continued at −40° for 10 min and then raised to −10 or −5°, where the red mixture is then stirred for 45–75 min, depending on the unsaturated ketone involved. Work-up is accomplished by quenching with 20% aqueous ammonium chloride, followed by routine ether extraction and isolation. The results are provided in Table I.

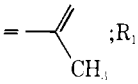
Table I. Reactions of Lithium Di(α-methoxyvinyl)cuprate (2) with α,β-Unsaturated Ketones

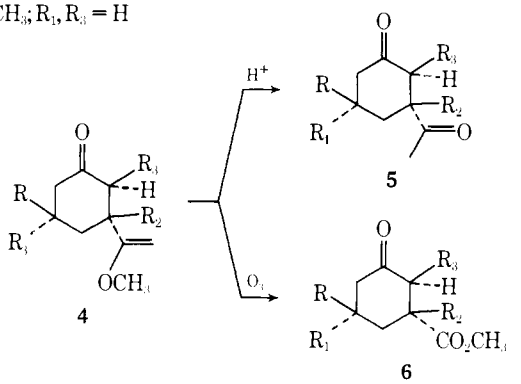
Electrophile	Adduct (% yield)
2-Cyclohexen-1-one (3a)[a]	4a (66)[d,h]
d-Carvone (96%) (3b)[b]	4b (50)[d,e,h]
5,5-Dimethyl-2-cyclohexen-1-one (3c)[c]	4c (67)[d,h]
Isophorone (3d)[c]	3d (80) + (4d + 1,2-adduct) (20)[f]
3,5-Dimethyl-2-cyclohexen-1-one (3e)[c]	3e (80) + (4e + 1,2-adduct) (20)[g]

[a] Stirred with 2 at −10° for 30 min. [b] Stirred with 2 at −10° for 30 min and −5° for 75 min. [c] Stirred with 2 at −10° for 45 min. [d] Distilled yield. [e] ^{1}H NMR reveals essentially one stereoisomer. [f] The crude recovery is quantitative and the per cent ratios are determined by ^{1}H NMR and ir analyses. [g] The crude recovery is quantitative, and the per cent ratios are determined by ^{1}H NMR, ir, and GLC analyses. [h] Satisfactory ^{1}H NMR, ir, and elemental analyses.

Scheme I



3a, R, R$_1$, R$_2$, R$_3$ = H
b, R =  ; R$_1$, R$_2$ = H; R$_3$ = −CH$_3$
c, R, R$_1$ = −CH$_3$; R$_2$, R$_3$ = H
d, R, R$_1$, R$_2$ = −CH$_3$; R$_3$ = H
e, R, R$_2$ = −CH$_3$; R$_1$, R$_3$ = H



The red mixture, formed on initial addition of MVL to the cuprous iodide–dimethyl sulfide complex and again after addition of the enone, is apparently the intermediate α-methoxyvinylcopper(I), and the yellow mixture is lithium di(α-methoxyvinyl)cuprate (**2**).[6]

Cuprate (**2**) is sensitive to the steric environment at the C-5 position of the cyclohexenones studied, as demonstrated with *d*-carvone (**3b**). The adduct (**4b**) is assumed to have the geometry shown, based on the fact that ^{1}H NMR reveals essentially one isomer and on the previous observation that 5-alkyl-2-cyclohexenones react with dialkylcuprates to give primarily trans products.[7] Conjugate addition appears to be inhibited by further alkyl substitution at the 3-position, but not at the 5-position (see the adducts of **3b** and **3c** in comparison to **3d** and **3e**).

The 1,4-addition products (**4a–c**) can be efficiently converted to diketones or ketoesters as demonstrated with **4c**. Hydrolysis of **4c** at room temperature for 30 min with di-