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RHODIUM CATALYZED HYDROACYLATION OF ETHYLENE WITH 4-PENTENALS. REACTIONS OF 4-HEXENAL-1-*d*

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Summary

A catalyst derived from 2,4-pentanedionatobis(ethylene)rhodium(I), I, promoted the addition of 4-pentenal to ethylene. The reaction was accompanied by the formation of double bond migration products derived from the 4-pentenal reactant and from the 6-hepten-3-one primary product. Compound I accomplished the addition of 4-hexenal to ethylene to afford high yields of 6-octen-3-one. The fate of the aldehyde hydrogen in this transformation has been determined in experiments employing 4-hexenal-1-*d* as reactant. Treatment of 4-hexenal-1-*d* with I in $CHCl_3$ and $CDCl_3$ afforded 6-octen-3-one possessing $>50\%$ d_0 molecules while the isotopic composition of recovered unexpended 4-hexenal remained $>96\%$ d_1. 6-Octen-3-one products with isotopic compositions of $>66\%$ d_0 were afforded when ethylene was introduced to reaction mixtures. The location of deuterium in 6-octen-3-one, derived from treatment of 4-hexenal-1-*d* with I in the absence of added C_2H_4, was determined to be distributed at C-1 and C-2 and at the C=C bond by analysis of the ^1H and ^2H NMR spectra. Unexpended ethylene was recovered and was found to contain a substantial amount of deuterium. Mechanistic implications of these results are discussed.

Introduction

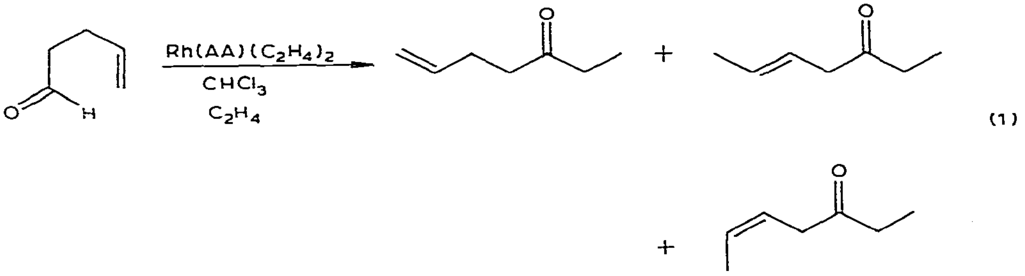
The activation of aldehyde C—H bonds by rhodium(I) in aldehyde decarbonylation [1—5] had led to a number of important synthetic applications [6—9] including stereoselective introduction of angular methyl groups in natural product syntheses [8,9] and preparations of specifically labeled deuterium-containing compounds [5]. Recently reported rhodium promoted hydroacylation reactions [10—11] have introduced a new area of transition metal mediated syntheses, the preparation of potential prostaglandin precursors via cyclization of highly substituted pentenal derivatives providing the first examples of reactions of this type [10].

On examination of reactions of the parent 4-pentenal, we have found that rhodium(I) complexes catalyze both intramolecular and intermolecular addition reactions, the course of the reaction being dictated by the nature of the rhodium catalyst employed [11a]. Results of our mechanistic study of the 4-pentenal to cyclopentanone conversion, accomplished by $RhCl(PPh_3)_3$, are reported elsewhere [12]. We report herein our findings related to intermolecular hydroacylation of ethylene by 4-pentenal derivatives, catalyzed by a species derived from 2,4-pentanedionatobis(ethylene)rhodium(I), I.

Results and discussion

Reaction of 4-pentenal with ethylene

Treatment of 4-pentenal with 2,4-pentanedionatobis(ethylene)rhodium(I), I, in ethylene-saturated $CHCl_3$ afforded the heptenones described in eq. 1, along with pentenal isomerization products. Yields of ca. 50% of C-7 ketones could be achieved at 100% conversion of 4-pentenal to products when an aldehyde : Rh mole ratio of 10 was employed. No aldehyde decarbonylation products were detected in the product mixtures. For example, during 16 h at 24—25°C, 6-hepten-3-one and *trans*- and *cis*-5-hepten-3-one were formed in 6, 39 and 2% yield, respectively. The remaining volatile products were derived from double bond migration in the 4-pentenal. *trans*-3-Pentenal, *cis*-3-pentenal and *trans*-2-pentenal were present in 15, 1, and 3% yields, respectively. A minor product with a GLC retention time identical with that of cyclopentanone was detected, its yield being a ca 1% by ^1H NMR analysis of its mixture with *trans*-5-hepten-3-one, isolated by GLC.



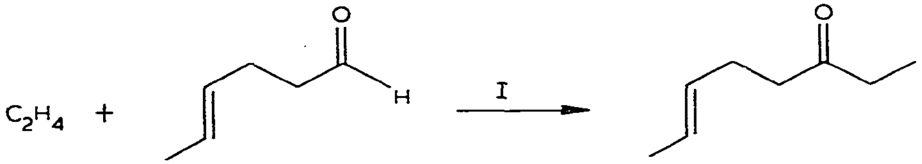
(1)

A parallel experiment conducted in the absence of added ethylene (aldehyde : Rh = 10) afforded the same heptenone and pentenal products, the yields of the former indicating that 75% of the ethylene available in I was consumed in the generation of heptenones.

Treatment of a mixture of 3-pentenals (*trans* : *cis* = 6) with I and C_2H_4 under the same conditions of solvent and temperature employed for the transformations described in eq. 1, afforded high yields of *trans*-2-pentenal as the only organic product detected (84% yield at 33% conversion during 19 h). This result supports the contention that the 5-hepten-3-ones are not derived from a Rh^I induced addition of the 3-pentenals to C_2H_4, but are generated by a

4-pentenal addition to C_2H_4, followed by double bond migration in the 6-hepten-3-one product.

The addition of hexanal to C_2H_4 was not promoted by I at room temperature in C_2H_4-saturated $CHCl_3$ during 80 h when a 10 : 1 aldehyde : Rh ratio was employed. Neither 3-octanone nor any decarbonylation product derived from hexanal could be detected in the mixture.



(2)

Reactions of 4-hexenal with ethylene

Yields of ketone adduct could be markedly increased when an aldehyde possessing an internal double bond was used as substrate. The catalyst promoted the addition of 4-hexenal to ethylene to give 6-octen-3-one, eq. 2, in high yield and we have examined this much cleaner reaction in a mechanistic study of the hydroacylation.

Treatment of 4-hexenal (90% *trans*) with I in C_2H_4-saturated $CHCl_3$ at 24—26° C has afforded 84—94% yields of predominantly *trans*-6-octen-3-one when 12.5 : 1 to 7.5 : 1 mole ratios of aldehyde to Rh were employed during a 28 h period. Optimum yields of 94% at 79% conversion (28 h) and 93% at 90% conversion (48 h) were achieved when a 7.5 : 1 aldehyde : Rh ratio was used. We have observed a maximum of 12 catalyst turnovers at an aldehyde : Rh ratio of 75 : 1.

Experiments conducted in the absence of added C_2H_4 afforded, in addition to 6-octen-3-one, products with GLC retention times corresponding to 1-pentene(minor) and *trans*- and *cis*-2-pentene decarbonylation products. As was the case in the presence of added C_2H_4, the 6-octen-3-one products possessed the same *trans* : *cis* composition as the 4-hexenal reactant. When a sample of *trans*-4-hexenal was treated with I in the absence of added C_2H_4 for 28 h

TABLE 1

ISOTOPIC COMPOSITIONS [a] OF RECOVERED 4-HEXENAL AND 6-OCTEN-3-ONE [b]

Medium	Time (h)	% Composition					
		Recovered 4-Hexenal			6-Octen-3-one		
		d_0	d_1	d_2	d_0	d_1	d_2
$CHCl_3$	56	1.9	98.1		54.4	45.6	
$CDCl_3$	56	3.5	96.2	0.2	58.6	41.4	
$CDCl_3$ [c]	48				64.8	34.9	0.3
$CHCl_3$—C_2H_4	49	1.7	93.7	4.6	66.7	33.1	
$CHCl_3$—C_2H_4	29	5.7	94.3		67.4	32.6	

[a] Determined by mass spectrometry using a duPont 21-491 instrument. [b] Reactant 4-hexenal (*trans* : *cis* = 9 : 1) was 1.6% d_0, 98.4% d_1 in each case. The experiments were conducted at room temperature and a 7.5 : 1 aldehyde : I ratio was employed. The precision in the determination of each composition value is estimated to be better than ±1 percentage point. [c] Conducted at 35°C employing a hexenal : Rh ratio of 11.5 : 1.

(aldehyde : Rh = 5.6), a 30% conversion of 4-hexenal to products was observed and 6-octen-3-one and pentene were formed in 60 and 20% yields respectively. No *cis*-4-hexenal was detected in the product mixture.

Reactions of 4-hexenal-1-d

In order to determine the fate of the aldehydic hydrogen as the aldehyde is transformed into the ketone product, we have synthesized high purity 4-hexenal-1-*d* and this compound has been treated with I. The isotopic compositions of the deuterio-4-hexenal reactant, recovered 4-hexenal and the 6-octen-3-one product from a series of experiments are given in Table 1. The deuterio-4-hexenal reacted more slowly with C_2H_4 than did its hydrido counterpart. The magnitude of the isotope effect has not yet been quantitatively determined. During 28 h at room temperature, only 40% of the 4-hexenal-1-*d* was converted to products in C_2H_4-saturated $CHCl_3$ when a 7.5 : 1 aldehyde : Rh ratio was employed. Under these conditions of slower octenone formation with accompanying lower octenone yield, some double bond migration ($<10\%$ of the aldehyde charged) in the hexenal reactant occurred and small amounts of pentenes were formed.

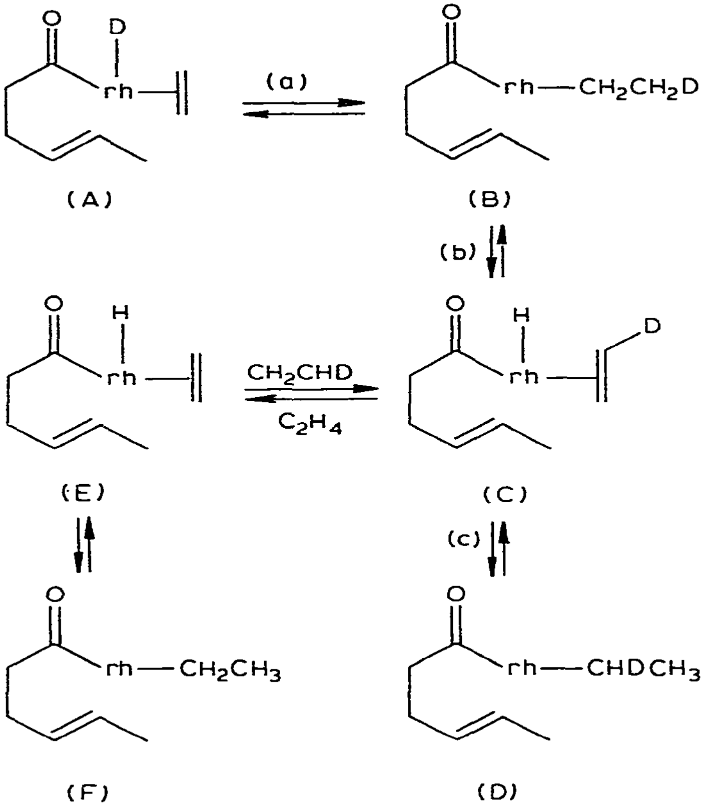
The data in Table 1 demonstrated that the recovered 4-hexenal that was not consumed in the hydroacylation reaction retained essentially all of its deuterium. Conversely, substantial amounts of d_0 octenone were generated in experiments conducted in both the presence and absence of added C_2H_4, the larger d_0 compositions being associated with experiments conducted in C_2H_4-saturated $CHCl_3$. Also noteworthy is the similarity of the isotopic compositions of products derived from experiments conducted in $CHCl_3$ vs $CDCl_3$.

The location of the deuterium in the deuteriooctenone product was unambiguously established by deuterium NMR analysis. A sample of 4-hexenal-1-*d* ($>99\%$ d_1) was treated with I in $CHCl_3$ in the absence of added C_2H_4 (aldehyde : Rh = 1.1) and the octenone product ($>50\%$ yield at 50% conversion during 60 h) was found to possess a 57.1% d_0, 39.1% d_1, 3.8% d_2 composition as determined by mass spectrometry. Integration of the deuterium NMR spectrum (C_6H_6 soln) gave the following values for the respective resonances relative to C_6D_6 taken as δ 7.15 ppm : δ 0.85, 1.82, 5.32, 5.41 ppm, rel. int. 1.18 : 1.00 : 1.45 : 0.54. Analysis of the PMR spectrum (C_6D_6) of 6-octen-3-one allowed the assignment of δ 0.85 ppm to the C-1 protons, 1.82 ppm to the C-2 protons and 5.32 ppm and 5.41 ppm to alkene protons. In C_6D_6 (90 MHz), the C-2 proton resonance is sufficiently separated from the C-4 and C-5 proton resonances to establish its identity as a quartet coupled to the C-1 CH_3 triplet, J = 7.3 Hz. Therefore, ca. half of the deuterium was divided almost equally between the two carbons of the ethyl group, and the remaining half resided at the carbon—carbon double bond. Unexpended ethylene in the product mixture derived from an analogous experiment was collected in a liquid nitrogen-cooled trap. Mass spectral analysis indicated its composition to be 79.2% d_0, 17.8% d_1, 3.1% d_2.

Mechanism of the aldehyde—alkene addition

These results are consistent with a mechanism involving the Rh^{III} intermediates described in Scheme 1. The rh represents the rhodium atom and its auxiliary

SCHEME 1



ligands. The mechanism would entail the formation of acylrhodium deuteride, A, which then rearranges to B, C and D. Reductive elimination of 6-octen-3-one-d_1 from B and D could regenerate the Rh^I catalyst. The formation of octenone-d_0 could occur either by displacement of coordinated CH_2CHD in C by C_2H_4, followed by rhodium hydride addition to generate F, or by addition of rhodium hydride in C to C_2H_4 already bound to Rh along with CH_2CHD.

Our observations that the octenone product is $>50\%$ d_0 and that the deuterium is equally distributed at C-1 and C-2 in the octenone-d_1, require that steps a, b and c and the formation of F be fast relative to the rate of reductive elimination in B, D, and F. They also eliminate from consideration the sole operation of a mechanism by which coordinated C_2H_4 inserts into the C—Rh bond in A, followed by carbon—deuterium coupling. This would generate an octenone with deuterium residing solely in the C-1 methyl group. We have not established whether the deuterium at the C=C bond in the octenone arises from intramolecular reactions of species such as A, Scheme 1 [12], or by addition of the Rh—D bond in A to the olefinic bond in another hexenal molecule followed by Rh—H elimination. Our finding that double bond migration in alkenes is accomplished in the presence of the catalyst is consistent with the latter. One might expect, however, to see the consistent formation of more octenone-d_2 in the product mixtures if this were occurring.

Precedent exists in organorhodium chemistry for each of the steps in Scheme 1. Oxidative addition of an aldehyde to rhodium(I) [13], Rh—H addition to coordinated alkene and elimination from alkylrhodium [2,14—16], rotation of C_2H_4 about the coordination bond [17,18], and reductive elimination via C—H [2,19] and C—C [13,20—22] coupling have been observed or proposed.

Experimental

All experiments employing organometallic compounds were conducted under argon or nitrogen. Solvents were purified by conventional means and were deoxygenated before use. 4-Pentenal and 3-pentenal were prepared by oxidation of 4-penten-1-ol and 3-penten-1-ol according to the procedure of Shiekh and Eadon [23] using a 6′ × 1/4″ 40/80 CuO GLC column at 250°C with a flow rate of ca 10 ml/min. The aldehyde products were collected on an XE-60 GLC column. 2-4-Pentanedionatobis(ethylene)rhodium(I), I, was prepared according to the procedure of Cramer [17]. The $LiAlD_4$ was purchased from Stohler Isotope Chemicals.

The ^1H NMR spectra were obtained using a Varian EM 390 spectrometer and the ^2H NMR spectra were recorded on a Bruker HX 270 instrument at 41.444 MHz in C_6H_6 solution employing a small amount of C_6D_6 (δ 7.15 ppm) as internal standard. Mass spectra were obtained on a duPont 21-491 instrument.

Yield and conversion data for 4-pentenal reactions were determined by GLC on 10′ × 1/4″ 20% Silicone XE-60 on 60/80 Chromosorb P and 10′ × 1/4″ 20% 1,2,3-tris(2-cyanoethoxy)propane (TCEP) on 60/80 Chromosorb W columns. The analogous data for 4-hexenal reactions were obtained using a 5′ × 1/8″ 15% Silicone XE-60 on Anakrom A 100/110 column employing a Varian Aerograph 1420 (temperature program) instrument. Dodecane was employed as an internal standard. Pentenes were analyzed on a 20′ × 3/8″ 20% B,B′-oxydipropionitrile (B,B′) on 60/80 firebrick column operated at 25°C. Standard mixtures of reactants and products were analyzed in order to determine the relationships between signal responses and molar ratios. Percent conversions are based on consumed aldehyde starting material and percent yields are defined as the percent of reacted starting material transformed into each product.

Reaction of 4-pentenal with I and C_2H_4

An ethylene-saturated $CHCl_3$ solution (9.3 ml) of 4-pentenal (0.15 ml, 1.5 mmol) was added to I (0.040 g, 0.15 mmol) at 25°C. Ethylene was then passed through the solution for 5 min. The stirred yellow solution turned darker in color during a 16 h period after which the reaction was terminated by exposure to air. During this period of time, 100% of the 4-pentenal was converted to products. The reaction was monitored by GLC analysis of aliquots. The heptenone and pentenal products were collected via preparative GLC and were identified by their PMR, infrared and mass spectra. The ketone products [24—26] possessed the following spectral properties. 6-Hepten-3-one: PMR (CCl_4), δ 5.9 (m, 1H), 4.9 and 5.1 (d, d, 1H each), 2.3 (m, 6H), 1.0 ppm (t, 3H); IR (neat), characteristic peaks at 920, 1000, 1640, 1715, 2800—2980, 3080 cm^{-1}; mass spectrum, parent ion at *m/e* 112 (70 ev). *trans*-5-Heptene-3-one: PMR (CCl_4), δ 5.6 (m, 2H), 3.0 (m, 2H, $J(CH_2{-}CH{=}C) = 4.0$ Hz), 2.5 (q, 2H), 1.8 (d, 3H, $J(CH_3\,CH{=}C)$ 3.5 Hz), 1.0 ppm (t, 3H); IR, 965, 1630, 1720, 2800—2980, 3020 cm^{-1}; mass spectrum, parent ion *m/e* 112 at 70 ev. *cis*-5-Hepten-3-one: the PMR spectrum was ca. the same as that of the *trans* isomer with the exception that resonances for the C-4 and C-7 protons were simple doublets, $J(CH_2{-}CH{=}C) = 5.0$ Hz and $J(CH_3{-}CH{=}C) = 6.4$ Hz; IR, 710, 1630, 1720, 2820—2980; 3040 cm^{-1}; mass spectrum parent ion, *m/e* = 112 (70 ev). Analysis of the product mixture on a B,B′ column indicated that no decarbonylation products were present.

Other experiments in which 4-pentenal or 3-pentenal were employed as reactants were conducted in a similar manner.

Synthesis of 4-hexenal and 4-hexenal-1-d

Lithium aluminum hydride, 1.50 g (0.0395 mol) was suspended in 50 ml of dry diethyl ether and 10.2 g (0.0718 mol) of ethyl 4-hexenoate was added at a rate that maintained the reaction mixture at a gentle reflux. The mixture was refluxed for 10 min after the addition was complete, after which a few ml of H_2O was added very carefully. The mixture was then poured into 100 ml of a 10% H_2SO_4 solution in ice water, the ether layer was separated, and the aqueous layer was extracted with two portions of ether, the ether portions were combined and dried, and the alcohol product was distilled at reduced pressure after removal of the ether.

The 4-hexenol product was then oxidized according to the procedure of Ratcliffe [27]. Chromium trioxide, 18 g, was added to 450 ml of CH_2Cl_2 which contained 28.5 g of pyridine at 5°C. The mixture was stirred for 5 minutes at 5°C then allowed to warm to 20°C during 1 h. A solution of 4-hexenal, 3.0 g, in CH_2Cl_2 was then added rapidly, the resulting mixture was stirred for 15 min after which the solution was decanted from an insoluble residue and the residue was washed with three 150 ml portions of ether. The ether extracts and the CH_2Cl_2 solution were then combined, washed with 5% NaOH, 5% HCl, 5% $NaHCO_3$ and saturated NaCl in that order. The organic phase was then dried over $MgSO_4$ and then distilled affording a 41% yield of 4-hexenal (*trans* : *cis* = 84 : 16).

This same procedure was employed in the synthesis of 4-hexenal-1-*d*, using $LiAlD_4$ as reagent.

Reaction of 4-hexenal with I and C_2H_4

Compound I, 0.021 g (0.086 mmol), was treated with 4-hexenal (*trans* : *cis* = 9 : 1), 0.064 g (0.65 mmol) in 1.15 ml of C_2H_4-saturated $CHCl_3$ containing dodecane standard. The resulting yellow solution was cooled to ca 5°C and C_2H_4 was slowly passed through the mixture for 5 minutes. The flask was then closed, and warmed to room temperature. The progress of the reaction was monitored by GLC. Products were isolated by preparative GLC after all volatiles were removed from the reaction flask and the products were concentrated. Other experiments using 4-hexenal and 4-hexenal-1-*d* were conducted in a similar manner.

The PMR spectrum of the 6-octen-3-one [28] in $CDCl_3$ exhibited a multiplet centered at δ 5.35 (2H), overlapping multiplets centered at 2.30 (6H), multiplet at 1.58 (3H), and a triplet at 1.03 ppm (3H) in 2 : 6 : 3 : 3 ratio. The corresponding resonances in C_6D_6 relative to TMS were centered at δ 5.36 (2H), 2.18 (4H), 1.92 (2H), 1.55 (3H), 0.89 ppm (3H). The mass spectrum showed a parent ion, *m/e* 126 (70 ev).

Acknowledgements

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