net absorption from the solvent in the mixed solution but leaving unchanged other absorptions which might have been obscured by the solvent peak.

It would be advantageous to be able to distinguish single nuclei by this method as this would in principle allow the fate of every single nucleus in the reactant to be traced to the product. This may be achieved by saturation of a single peak in the homogeneous part of the dc field at the receiver coil, followed by immediate mixing and return through this region for observation. This and other extensions and optimizations of these techniques and their application to the investigation of reaction mechanisms are currently under study in our laboratory.

Acknowledgment. The authors would like to thank the National Research Council of Canada for a grant in aid of research (C.A.F.). Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. They would also like to acknowledge the technical assistance of R. D. Kendrick and D. Sproat.

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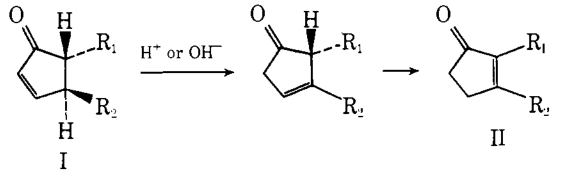
Remote Double Bond Migration via Rhodium Catalysis: A Novel Enone Transposition

Sir:

Δ^2-Cyclopentenones of type I are versatile intermediates in organic synthesis because of their ready ability to equilibrate to cyclopentenones of type II (eq 1). Isomerization of I to the more stable cyclopentenone II can be effected by heating in the presence of acid[1] or base.[2] Unlike the cyclopentenone rearrangement (eq 1) there is no analogy in cyclohexenone chemistry (e.g., III → IV (n = 1)). *In fact, there is no recorded equilibrium of cycloalkenones of type III with their corresponding (more stable) α,β-unsaturated cycloalkenones (e.g., IV) via migration of the double bond about the ring.*[3] We now report the smooth conversion of cycloalkenone III to its more stable isomer IV via rhodium catalysis which constitutes a synthetically useful new enone transposition and complements existing methods.[5]



(1)

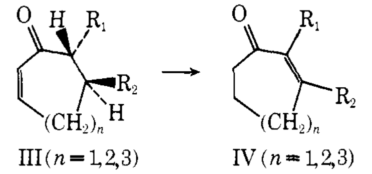
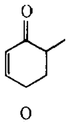
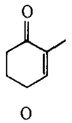
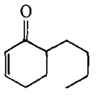
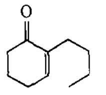
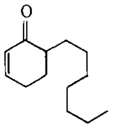
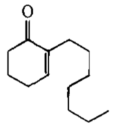
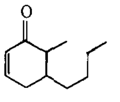
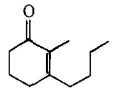
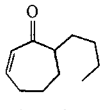
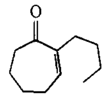
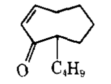
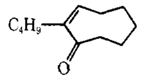
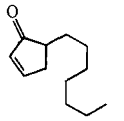
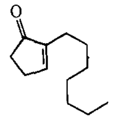
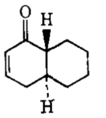
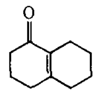
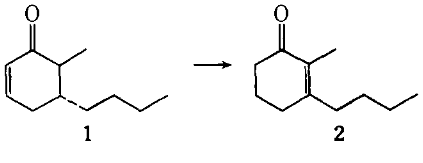


Table I. Enone Transposition via $RhCl_3 \cdot 3H_2O$ Catalysis[a]

Starting enone	Product	Time, h	Yield (%)[b]
		24	95[c]
		3 24	95 95
		3 24	94 91[d]
		3 24	95 91[e]
		24	80
		3 36	88 80
		12	62[f]
		24	85

[a] All reactions were carried out in a sealed tube at 100 °C containing 0.02–0.03 equiv of $RhCl_3 \cdot 3H_2O$ in absolute ethanol. [b] All yields are for isolated chromatographically pure substances. [c] Yield determined by GLC analysis. [d] Ca. 4% of the saturated ketone was isolated. [e] Ca. 6% of the saturated ketone was isolated. [f] Ca. 31% of the saturated ketone was isolated.

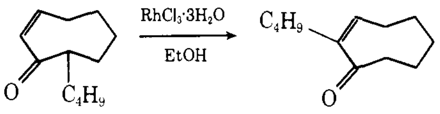
In the case of 2-methyl-3-butyl-Δ^5-cyclohexenone (**1**), isomerization to the thermodynamically more stable 2-methyl-3-butyl-Δ^2-cyclohexenone (**2**) can be carried out over



1 2

a 3-h period in absolute ethanol containing a catalytic amount (0.02 equiv) of $RhCl_3 \cdot 3H_2O$ at 100 °C in a sealed tube. Analysis (NMR)[6] of the reaction product (95%) indicates the complete absence of olefinic protons attributable to the starting enone and the presence of a singlet at 1.70 (olefinic methyl). In the case of enone **1** there is not appreciable isomerization in the presence of catalyst after 24 h at room temperature or after 4 h at 55 °C. After 24 h at 100 °C, enone **1** gives in addition to a 91% yield of **2**, 6% of the corresponding saturated ketone, 2-methyl-3-butylcyclohexanone. In some cases where the temperature was maintained at 100 °C for >24 h, we have isolated (Table I) the corresponding saturated ketones as minor products. In general, however, the isomerization of the less stable cyclohexenone to the more stable system can be performed in high yield (Table I).

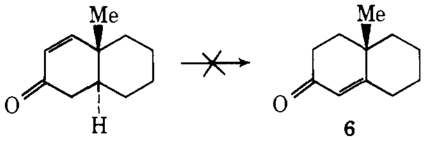
We have also observed in larger ring systems (e.g., III, n = 2, 3) a similar isomerization to the more stable α,β-unsaturated enone. For example, similar treatment of 2-butyl-Δ^7-cyclooctenone (**3**) resulted in an 80% isolated yield of 2-butyl-Δ^2-cyclooctenone (**4**). Likewise, 2-butyl-Δ^6-cycloheptenone was smoothly converted to its more stable isomer.



3 **4**

The following procedure illustrates the simplicity of the method. A solution of pure 2-heptyl-Δ^5-cyclohexenone (178 mg, 0.92 mmol) dissolved in absolute ethanol (180 μl) was treated with $RhCl_3 \cdot 3H_2O$ (4.6 mg, 0.017 mmol) at 100 °C in a sealed tube for 3 h under an atmosphere of nitrogen. Chromatography of the reaction mixture on silica gel (elution with pentane-ether (8:1)) gave the rearranged enone, 2-heptyl-Δ^2-cyclohexenone in 94% yield.

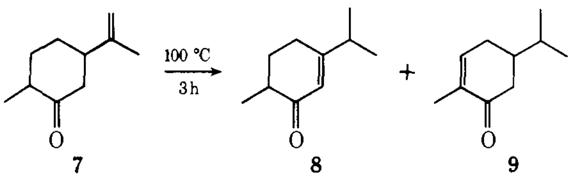
That the double bond migrates about the ring was strongly suggested by our initial observation that the $\Delta^{1,2}$-octalone **5** did not undergo isomerization to the $\Delta^{4,5}$-octalone **6**. Further support that the double bond migrates about the ring was obtained by treatment of cyclohexenone **1** with $RhCl_3 \cdot 3H_2O$ in CH_3OD at 100 °C. The product as indicated by ^1H NMR and mass spectral analysis (0% d_{1-5}, 14% d_6, 55% d_7, 31% d_8) revealed at least 31% of all ring protons had undergone complete exchange.[7]



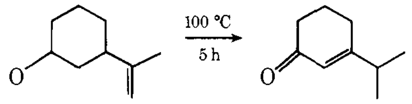
5 **6**

We have also found that the double bond need not be part of a cyclic framework. In a preliminary experiment, dihydrocarvone (eq 2) smoothly isomerized to a 7:1 mixture of **8** and **9**, respectively, in 90% yield. The remote double bond of 3-isopropenyl cyclohexanone (**10**) likewise isomerized to 3-isopropyl-Δ^2-cyclohexenone (eq 3) in 95% yield. Utilization of anhydrous $RhCl_3$ for the transformation **10** → **11** (eq 3) resulted in recovery of starting olefin **10** with no indication of any formation of enone **11**. The amount of $RhCl_3 \cdot 3H_2O$ required for the conversion of **7** and **10** into their respective enones was on the order of 0.08 equiv. Less than this amount results in incomplete isomerization and recovery of substantial amounts of starting material. For example, treatment of dihydrocarvone with only 0.03 equiv of catalyst under the above conditions resulted in recovery of 38% starting material even after prolonged heating.

Transition metal reagents have been employed as catalysts for olefin isomerization previously.[8] More recently tristri-



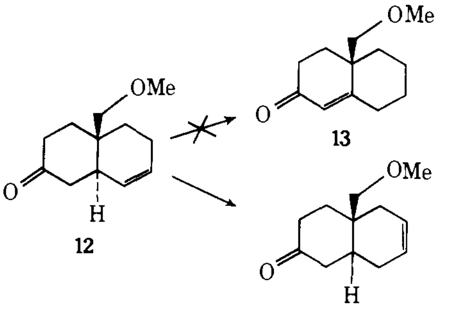
7 **8** **9** (2)



10 **11** (3)

phenylphosphinerhodium chloride has been used by Birch for the conjugation of 1,4-dienes to 1,3-dienes[9] and by Corey for the isomerization of allyl ethers to 1-propenyl ethers.[10] Under the conditions reported by Birch (refluxing $CHCl_3$) and Corey (refluxing 10% aqueous ethanol) employing $(Ph_3P)_3RhCl$, 3-isopropenylcyclohexanone did not undergo to any appreciable extent (<5%) isomerization to enone **11**.

In an extension of the above work, we attempted the isomerization of the γ,δ-unsaturated enone **12** to the more stable α,β-unsaturated octalone **13**. Treatment of **12** with 0.08 equiv of $RhCl_3 \cdot 3H_2O$ in absolute ethanol at 100 °C for 5 h gave none of the anticipated octalone **13**. We isolated the δ,ϵ-unsaturated enone **14** in 90% yield.[11]



12 **13** **14**

Further studies are in progress to examine the potential of this new enone transposition and the ability to migrate remote double bonds to their "more stable position" with the possibility of bringing about "remote epimerizations".

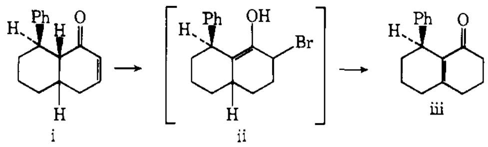
Acknowledgment. We are indebted to Glen Herman for mass spectral data. We thank Professor S. Danishefsky for a generous sample of 2-methyl-Δ^2-cyclohexenone. This investigation was supported in part by grant CA 13689-04 from the National Cancer Institute, DHEW.

References and Notes

(1) Cf. G. W. Cavrel, B. S. Goodrich, and D. G. Laing, *Aust. J. Chem.*, **23**, 83 (1970).

(2) Cf. G. Stork, G. L. Nelson, F. Rouessac, and O. Gringore, *J. Am. Chem. Soc.*, **93**, 3091 (1971).

(3) House[4] has previously reported the slow isomerization of the less substituted enone i to the more stable isomer iii with hydrogen bromide in acetic acid which presumably proceeds via the enol bromide ii.



(4) H. O. House and R. W. Bashe, III, *J. Org. Chem.*, **30**, 2942 (1965).

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(6) All spectra were recorded at 60 MHz in carbon tetrachloride. Chemical shifts are reported in parts per million (δ) relative to tetramethylsilane as an internal standard.

(7) After treatment of **2** with CH_3OD at 100 °C for 24 h, the acidic protons in the recovered enone had undergone appreciable deuterium exchange as indicated by ^1H NMR and mass spectral analysis (<0.5% $d_{1,2}$, 5% d_3, 33%

d_4, 42% d_5, 19% d_6).

(8) R. Cramer, *J. Am. Chem. Soc.*, **88**, 2272 (1966), and references cited therein.

(9) A. J. Birch and G. S. R. Subba Rao, *Tetrahedron Lett.*, 3797 (1968).

(10) E. J. Corey and J. W. Suggs, *J. Org. Chem.*, **38**, 3224 (1973).

(11) It is of interest to note that octalone **14** is thermodynamically favored over the starting octalone.

(12) Fellow of the Alfred P. Sloan Foundation, 1974–1976.

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Received July 26, 1976

The Reaction of Tertiary Ethynyl Alcohols with Formamide Acetals: Formation of Dienamines and Enamine Orthoformates

Sir:

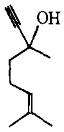
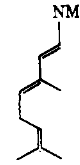
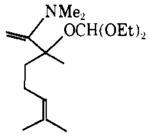
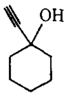
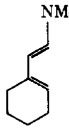
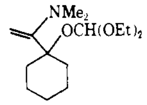
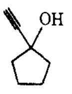
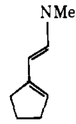
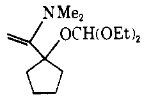
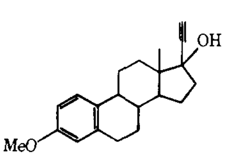
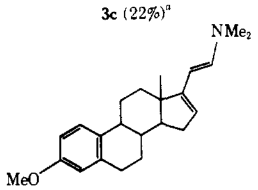
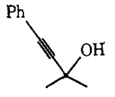
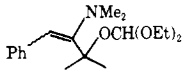
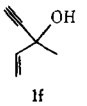
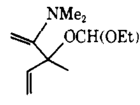
The addition of nucleophiles to unactivated acetylenic bonds has been effected in the presence of strong base and by transition metal/Lewis acid catalysis. Neither of these methods, however, provides an efficient synthesis of enamines.[1] We have previously observed that tertiary ethynyl carbinols may be converted by *N,N*-dimethylacetamide diethyl acetal to enamines with rearranged skeletons.[2,3] We now report that with *N,N*-dimethylformamide acetals (**2**), these carbinols (**1**) afford dienamines **3** and/or enamine orthoformates **4** (see Table I), formally the products of addition of dimethylamine to the acetylene bond.

The conversion involves heating the alcohol, **1**, with excess amide acetal. Maximum total yields were obtained when ethanol and a trace of pivalic acid were added. The enamine product(s) may be isolated directly by distillation or the total reaction mixture may be hydrolyzed and the corresponding carbonyl compounds isolated.

The ratio of enamine orthoformate to dienamine appears to be a function of the structure of the alcohol. Carbinols **1a–c** afford good yields of mixtures of the enamine orthoformate and dienamine products. In the case of 17α-ethynyl 17β-sterols (e.g., **1d**), the dienamine containing no detectable amount of enamine orthoformate is formed; hydrolysis of the steroidal dienamines (by elution through wet silica gel with chloroform) affords the $\Delta^{17(20)}$-en-21-al derivatives, key intermediates in the synthesis of corticosteroids.[4]

Tertiary propargyl alcohols in which the acetylene is substituted with an alkyl group do not undergo either of these

Table I

Alcohol 1	Dienamine 3 (yield)	Enamine orthoformate 4 (yield)	2, MeCCO$_2$H, EtOH (mmol, mg, ml/mmol of 1)	T, t (°C, h)
 **1a**	 **3a** (24%)[a]	 **4a** (40%)	3.5, 3.8, 0.20	125, 38
 **1b**	 **3b** (42%)[a]	 **4b** (47%)[b]	3.7, 2.5, 0.13	120, 40
 **1c**	 **3c** (22%)[a]	 **4c** (46%)[b]	3.5, 2.2, 0.12	120, 40
 **1d**	 **3d**[c]		18, 0.6, 0.31	120, 4
 **1e**		 **4e** (55%)[d]	3.6, 1.6, 0.16	145, 90
 **1f**		 **4f** (50%)	1.8, 0.8, 0.16	125, 36

[a] Hydrolysis on wet silica afforded the corresponding aldehydes. [b] Hydrolysis on wet silica afforded the corresponding keto orthoformate. [c] Crude dienamine **3d** could be isolated by removing all volatile materials from the reaction mixture under reduced pressure. Preparation of the corresponding aldehyde was most efficiently accomplished, however, by hydrolyzing the entire reaction mixture on wet silica. This procedure afforded consistently high yields (>90% based on alcohol **1d**) of *trans*-3-methoxyestra-1,3,5,17 (20)-tetraen-21-al, mp 164–168 °C.[6] [d] Some starting alcohol, contaminated with **4e** and possibly traces of dienamine product, was recovered.