Title
REARRANGEMENTS OF 4-ALKYNYL-4-HYDROXY-3-METHYLENECYCLOBUTENE 4-ALKENYL-4-
HYDROXY-3-METHYLENECYCLOBUTENE AND 4-ALKYL-4-HYDROXY-3-
METHYLENECYCLOBUTENES

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Publication Date
1992-04-05

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Figure 1.

The catalytic activity of this Rh/Cu system. Such a broad range of chemoselectivity in hydrogenation reactions is remarkable.\(^5\)\(^6\)

The functionalities that cannot be tolerated under the reaction conditions are (1) aryl iodides because they deactivate the catalyst toward reaction with an alkene, (2) terminal alkynes which also deactivate the catalyst, (3) 1-(trimethylsilyl)-1-alkynes which do not reduce cleanly to the alkene, and (4) terminal alkenes or propargylic alcohols because they undergo regioisomerization.

Several reaction conditions were studied to see the effect of using silanes in the absence of water so that no silicon sol or gel formation would occur. When the triethoxysilane reaction was executed on 7-tetradecyne (1 mol % RhCl\(_3\), and 15 mol % Cu(NO\(_3\))\(_2\) in THF) in the absence of water, approximately 50% of the alkyn was hydrosilylated and 35% was converted to 7-tetradecene (4.8:1 Z/E ratio) after 24 h. Then, addition of water to the reaction mixture caused protodesilylation of the alkenytriethoxysilane to afford a total of 71% yield of 7-tetradecene (3.5:1 Z/E ratio). If we used triethylsilane in place of triethoxysilane (1 mol % RhCl\(_3\), and 15 mol % Cu(NO\(_3\))\(_2\) in THF\(^7\)) in the absence of water, approximately 50% of the alkyn was hydrosilylated and 30% was converted to 7-tetradecene (3.8:1 Z/E ratio) after 24 h. Then, addition of water to the reaction mixture caused protodesilylation of the alkenytriethylsilane to afford a total of 60% yield of 7-tetradecene (3.6:1 Z/E ratio). In the absence of triethoxysilane, a mixture of RhCl\(_3\) and Cu(NO\(_3\))\(_2\) in THF and water does not respond as a hydrogenation catalyst with exogenous H\(_2\); thus, the silane is essential and the use of triethoxysilane under our standard reaction conditions proved to afford the highest yields and stereoselectivities.

We also screened other metal salts [Al(NO\(_3\))\(_3\), Ti(OEt)\(_4\), Zr(OEt)\(_4\), Zr(O)(NO\(_3\))\(_2\), Ni(NO\(_3\))\(_2\), Cu(OAc)\(_2\), Cu(SO\(_4\))\(_2\)] with RhCl\(_3\) and noted that all of these metal salts dramatically changed the activity and the stereoselectivity of the reduction process; however, the RhCl\(_3\)/Cu(NO\(_3\))\(_2\) combination was optimal.

It is clear from powder X-ray diffraction (XRD) analysis of the xerogel (solvent free gel) that Cu(0) is present in the material. However, we were not able to detect any Rh(0) species even with more concentrated Rh samples; thus, we cannot presently determine whether this catalyst system is homo- or heterogeneous.\(^8\)\(^9\) A bimetallic system is indeed necessary since the reduction does not occur in the absence of either one of the two metals. Scanning electron micrographs (SEM) of the xerogel show only amorphous material. It was intriguing that while the Pd-containing xerogel\(^1\) had an unusually large surface area (BET using N\(_2\) adsorption at 77 K) of 852 m\(^2\)/g and a specific pore volume (N\(_2\) pore volume filling) of 3.33 cc/g, the Rh/Cu material had a very small surface area of only 2.8 m\(^2\)/g and an undetectably low specific pore volume. Moreover, when resuspended in an aqueous THF solvent, the Rh/Cu xerogel was not an active hydrogenation catalyst in the presence of H\(_2\).

Acknowledgment. This research was funded by the donors of the Petroleum Research Fund, administered by the American Chemical Society, the Department of the Navy, Office of the Chief of Naval Research, Young Investigator Award Program (1989–92), the National Science Foundation (RII-8922165, DMR-9158315, DMR-9101539), and generous industrial contributors to the NSF Presidential Young Investigator Award (1991–96) for J.M.T.: Hercules Incorporated, IBM Corporation, Ethyl Corporation, and the Shell Development Co. The SEM was purchased with a grant from the National Science Foundation (BIR-8805143). We thank Molecular Design Ltd. for the use of their synthetic database.

Supplementary Material Available: Detailed reduction procedures and spectroscopic data for the compounds listed in Table I (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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Rearrangements of 4-Alkynyl-, 4-Alkenyl-, and 4-Alkyl-4-hydroxy-3-methylenecyclobutenes

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Received May 4, 1992 (Revised Manuscript Received June 21, 1992)

Summary: Reported here are the thermal rearrangements of the 4-alkynyl- (1), 4-alkenyl- (7), and 4-alkyl-4-hydroxy-2-methyl-1-phenyl-3-benzylidene cyclobutenes (11) to, respectively, the phenol 5, derived from the p-quino nemethide 4, the benzylidene cyclohex enone 10, and the acyclic dienone 14.

Generation of quinonemethides from methylenecyclobutenes, as represented by the transformation of 1 to 4, is unprecedented. However, a number of related transformations have appeared that suggest this to be a reasonable process. For example, many simple acyclic (Z)-1,2,4-heptatrien-6-ynes (enynylalenes) have been shown to undergo facile cycloaromatization to produce products formally derived from α,3-dehydrotoluene biradical intermediates.\(^1\)\(^2\) Similar allenic and biradical intermediates are envisaged to be involved in the rearrangement presented here. Another related analogy is the facile ring formation of the 4-alkynyl- (1), 4-alkenyl- (7), and 4-alkyl-4-hydroxy-3-methylenecyclobutenes (11) to, respectively, the phenol 5, derived from the p-quino nemethide 4, the benzylidene cyclohex enone 10, and the acyclic dienone 14.

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with their spectral and analytical data.


Finally, it was observed that the E isomer of 11 gives 3(Z,5(E))-4-methyl-3,6-diphenylhexa-3,5-dien-2-one (14) in 38% isolated yield when subjected to thermolysis in refluxing p-xylene for 38 h. This product presumably arises from the penultimate common allene precursor, 12, which suffers a 1,5-hydrogen shift (ene reaction) to give the ultimate precursor to 14 (Scheme III).

The E stereochemistry of the 5-alkene moiety in 14 was disclosed by the coupling constant of the alkene protons (J = 16.2 Hz). The stereochemistry of the 3-alkene was not established but assigned as Z based upon the assumption that this site did not suffer stereochemical change during the thermolysis.

The required alkylidenecyclobutenones 1, 7, and 11 were synthesized from 3-methoxy-4-phenylcyclobutenedione (15) as outlined in Scheme IV. As a representative case, 3-methoxy-4-phenylcyclobutenedione (15) was converted to the 4-benzylidenecyclobutenones 16a and 16b (60-85%, 1:1.7 mixture of the E and Z isomers) upon treatment with the ylide derived from benzyltriphenylphosphonium chloride in anhydrous ether at ambient temperature. These benzylidenecyclobutenones were further function-

(3) The assigned structures of all new compounds are in agreement with their spectral and analytical data.

ring-closed carbocyclic products. To this end, the E isomer of 7 was subjected to thermolysis in refluxing p-xylene. After 30 min, the reaction was complete and a mixture of the E and Z isomers (1:2:2) of 4-benzylidene-3-methyl-2-phenylcyclohex-2-en-1-one (10) was realized in 65-81% isolated yield (Scheme II). This transformation is envisaged to involve ring opening of 7 to the conjugated allene intermediate 8 which undergoes electrocyclic ring closure to 9 followed by tautomerization to the cyclohexenones 10. It is of interest that the product is isolated as the benzyllidene cyclohexenone rather than the tautomeric phenol. Further studies are needed in order to reveal the generality of this unusual transformation.

Finally, it was observed that the E isomer of 11 gives 3(Z,5(E))-4-methyl-3,6-diphenylhexa-3,5-dien-2-one (14) in 38% isolated yield when subjected to thermolysis in refluxing p-xylene for 38 h. This product presumably arises from the penultimate common allene precursor, 12, which suffers a 1,5-hydrogen shift (ene reaction) to give the ultimate precursor to 14 (Scheme III).

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(7) This was obtained in 60% overall yield upon treatment of 2,3-dimethoxycyclonobutenediones (dimethyl sulfate) with phenyllithium followed by trifluoroacetic anhydride.
(8) The product of ylide attack on the vinylogous ester carbonyl group to give the regiosomer of 16 was previously reported. This product (17%) was not detected in our reaction. Its reported spectral data (1H NMR and IR) are slightly different than those observed for either 16a or 16b. See: Knorr, H.; Ried, W.; Knorr, U.; Pustosefek, P.; Orszegk, G. Liebigs Ann. Chem. 1977, 545. Ried, W.; Knorr, H.; Knorr, U. Chem. Ber. 1978, 109, 1006.
alized by addition of methylolithium (THF, -78 °C) followed by hydrolysis (trifluoroacetic anhydride) to produce a diastereomeric mixture (1.5:1) of 17 (75-91%). This mixture served as the precursors to the isomeric mixtures of 1 (45%), 7 (61-66%), and 11 (70%) upon addition of hexynyllithium, vinylolithium, and methylithium, respectively. It was noticed that the Z isomers of 1, 7, and 11 were much less thermally stable than their E counterparts, and thus the E isomers were employed for the thermolysis studies reported here.

Acknowledgment. The authors thank the National Institutes of Health (GM-36312) for financial support of this work. We are also grateful to Catherine A. Moore for technical assistance in obtaining high resolution mass spectral data.

Supplementary Material Available: Experimental procedures and data for all compounds (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

A New Strategy for the Synthesis of Nucleoside Analogues Based on Enzyme-Catalyzed Aldol Reactions
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Summary: A new synthetic approach to nucleoside analogs based on enzyme-catalyzed aldol condensations has been demonstrated in the synthesis of 6-adenyl-6-deoxy-D-fructose and 6-adenyl-6-deoxy-L-sorbos. Nucleoside analogues with modifications at the carbohydrate or base portion have been used extensively as antibiotics and as biological probes.1-7 Nucleosides are traditionally synthesized by chemical methods.3 Enzymatic synthesis of nucleosides based on nucleoside phos-