and requires no comment except that the homoallylic tosylate provided the corresponding alkene without complication (entry 6), as noted earlier. The aldehyde and ketone (*vide infra*) were reduced readily to the corresponding hydroxy compounds and again no incorporation of the n-C_4H_9 group into the product is rather surprising. The ester group resisted reduction (entries 8 and 9) and in fact survived completely in both inter- and intramolecular competitive experiments (entries 12–15).

The selectivity evidently enhances the synthetic utility of the reagent.[10] Similar competition reactions with the earlier Cu(I) reagent[1] were erratic presumably due to incomplete formation of the Cu(I) ate complex, a small but variable amount of $LiAlH(OCH_3)_3$ remaining in the reaction medium.

Reduction of α,β-Unsaturated Ketones to Saturated Ketones.[11] Although aldehydic and ketonic compounds (Table II, entries 10, 11) are readily reduced with the ate complexes, the carbonyl groups may survive as enolates, if 1,4- rather than 1,2-addition to the α,β-unsaturated carbonyl systems proceeds.[12] The resulting enolate then would be utilized directly for further reactions such as alkylation and Michael addition.[13] An extensive search for the optimal reaction conditions to achieve the conversion of cyclohex-2-enone to cyclohexanone has been pursued in a manner similar to that described earlier. In short, the reactivity of LiCuHR as well as the yield of product decreases in the order of $R = n\text{-}C_4H_9 > C{\equiv}C\text{-}t\text{-}C_4H_9 > C{\equiv}C\text{-}n\text{-}C_3H_7$, hydrogen being the only ligand transferred (no observable formation of 3-butylcyclohexanone with $LiCuH(n\text{-}C_4H_9)$). Because of the higher susceptibility of the α,β-unsaturated carbonyl system to this reduction than halo and mesyloxy groups, the reaction is complete within 0.5 hr at −40° with $LiCuH(n\text{-}C_4H_9)$ (4 equiv) (entry 16), and even with reagents with R = alkynyl (4 equiv) it proceeded to provide an acceptable yield of product, although somewhat higher temperatures were required. However, use of 6 molar equiv of the latter reagents (alkynyl) in ether improves the yield of cyclohexanone. Thus, the product was formed in 50 and 90% yields in 1 hr using $LiCuH(C{\equiv}C\text{-}t\text{-}C_4H_9)$ at −40° and 0°, and in 30 and 90% yields under the same conditions with $LiCuH(C{\equiv}C\text{-}n\text{-}C_3H_7)$.[14] Tetrahydrofuran does not offer any advantages over ether and appears to retard the reaction and induces side reactions in the case of $R = n\text{-}C_4H_9$. We conclude that 4 molar equiv of $LiCuH(n\text{-}C_4H_9)$ in ether at −40° represents optimal conditions for the reduction of α,β-unsaturated ketones, achieving efficient, high yield conversion under mild conditions and with operational simplicity.

According to the Whitesides procedure,[3c] 6.0 mmol of CuH was prepared under argon at −50° in a 50-ml round-bottomed flask, equipped with a magnetic stirrer and sealed with a rubber septum. After the CuH was washed with four 20-ml portions of cold (−50°) ether, 15 ml of cold (−40°) ether was added with stirring and then 6.0 mmol of cold n-BuLi in hexane (Foote Mineral Co.) was syringed into the flask over 1 min. The resulting dark brown solution (reagent partially insoluble) was stirred for 10 min. After addition of 610 mg (1.5 mmol) of ethyl 12-mesyloxystearate in 1 ml of ether, the cooling bath was removed and stirring was continued for 2 hr at room temperature. The reaction mixture was poured into aqueous saturated ammonium chloride solution, the ethereal layer was decanted and the aqueous layer was washed with 50 ml of ether. The combined ether extracts were processed in the usual manner to provide 400 mg (85%) of ethyl stearate (silicic acid chromatography). The same procedure was applied to 246 mg (1.5 mmol) of 6-methylbicyclo[4.4.0]dec-1-en-3-one, except that the reaction temperature was maintained at −40°. The products weighed 246 mg (98%), consisting of 6-methylbicyclo[4.4.0]decan-3-ones (85%) and starting material (15%) (Table II, entry 18).

Acknowledgment. The authors thank the Defense Research Board of Canada and Hoffmann-La Roche Inc., for financial support.

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[10] Compare this selectivity with that observed or expected for the methods quoted in ref 8.

[11] For recent reviews on related subjects, see (a) G. H. Posner, *Org. React.*, **19**, 1 (1972); (b) J. F. Normant, *Synthesis*, 63 (1972).

[12] A recent view on the mechanistic aspect of cuprate reactions, see H. O. House and M. J. Umen, *J. Org. Chem.*, **38**, 3893 (1973), and references cited therein.

[13] *E.g.*, ref 11b, p 79; J. E. Dubois, C. Lion, and C. Moulineau, *Tetrahedron Lett.*, 177 (1971); C. Wakselman and M. Mondon, *ibid.*, 4285 (1973); G. H. Posner and J. J. Sterling, *J. Amer. Chem. Soc.*, **95**, 3076 (1973); R. K. Boeckman, Jr., *ibid.*, **95**, 6867 (1973).

[14] For the use of a so-called nontransferable group as one of the cuprate ligands, see E. J. Corey and D. J. Beames, *J. Amer. Chem. Soc.*, **94**, 7210 (1972), and ref 2b.

[15] 1967 National Research Council (Canada) Science Scholarship Awardee.

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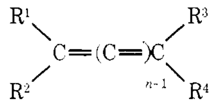
A Stereoselective Synthesis of Partially Substituted 1,2,3-Butatriene Derivatives *via* Hydroboration

Sir:

We wish to report the first stereoselective synthesis of 1,2,3-butatriene derivatives. Almost a century ago van't Hoff[1] made a well-accepted prediction that cumulenes (**1**) with odd numbers of double bonds should



1

be capable of exhibiting cis–trans isomerism. Recent studies, both experimental[2] and theoretical,[3] have indicated that although the energy barrier to the cis–trans isomerization of hexapentaenes ($n = 5$) is too low to permit separation of the two stereoisomers at ambient temperatures, separation of tetrasubstituted *cis*- and *trans*-1,2,3-butatrienes is feasible. To date, however, no methods appear to have been available for the stereoselective synthesis of 1,2,3-butatriene derivatives.[4]

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[1] J. H. van't Hoff, "Die Lagerung der Atome in Raume," Verlag F. Vieweg und Sohn, Braunschweig, 1877, p 14.

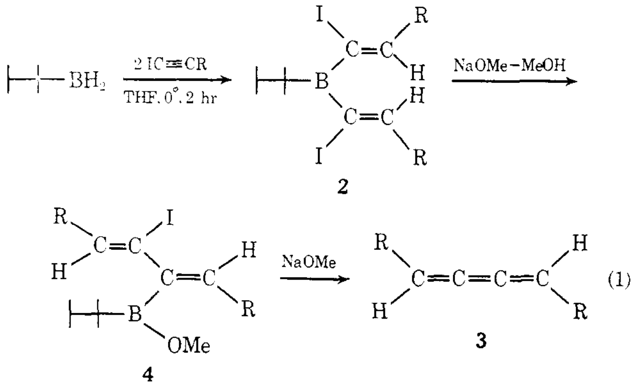
[2] (a) R. Kuhn and K. L. Scholler, *Chem. Ber.*, **87**, 598 (1954); (b) R. Kuhn and D. Blum, *ibid.*, **92**, 1483 (1959); (c) R. Kuhn and B. Schulz, *ibid.*, **98**, 3218 (1965); (d) R. Kuhn, B. Schulz, and J. C. Jochims, *Angew. Chem., Int. Ed. Engl.*, **5**, 420 (1966).

[3] M. J. S. Dewar and E. Haselback, *J. Amer. Chem. Soc.*, **92**, 590 (1970).

[4] For an extensive review, see H. Fischer in "The Chemistry of Alkenes," S. Patai, Ed., Interscience, New York, N. Y., 1964, pp 1025–1159.

The relatively unstable nature of partially substituted 1,2,3-butatrienes,[4] coupled with the difficulty associated with the separation of stereoisomers, makes it highly desirable to develop stereoselective, low temperature procedures for the preparation of these theoretically intriguing compounds as isomerically pure samples.

We have found that the reaction of thexylborane (2,3-dimethyl-2-butylborane) with 2 molar equiv of 1-iodo-1-alkynes at 0° proceeds to near completion (88% for 1-iodo-1-hexyne) to form, presumably, the fully substituted organoborane **2**. On the other hand, the corresponding reaction with either 1-chloro- or 1-bromo-1-alkyne becomes quite sluggish beyond the formation of the thexyl-1-halo-1-alkenylborane.[5] Treatment of the product derived from thexylborane and 1-iodo-1-hexyne with 2 molar equiv of sodium methoxide at 0° readily produces *trans*-1,4-di-*n*-butyl-1,2,3-butatriene (**3a**) in 47% yield by glpc (eq 1).



2

4

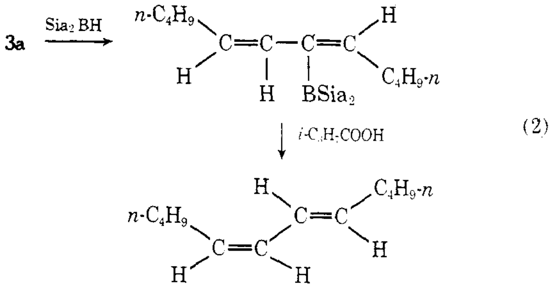
3

a, R = n-C_4H_9–
b, R = c-C_6H_{11}

In each case the product is stable in solution (hexane, benzene, or tetrahydrofuran) for at least 72 hr at 25° (glpc examination). On evaporation of the solvent, however, an initially clear oil gradually turns gelatinous.[6] The gelatinous substance does not redissolve in any of the organic solvents tested, including those mentioned above. This peculiarity has precluded purification of the product by distillation or preparative glpc. Fortunately, highly pure samples of **3** were obtained by column chromatography as described in detail for the preparation of **3a**. Thexylbis(1-iodo-1-*n*-hexenyl)borane (**2a**) (25 mmol, prepared from 14 ml of 1.79 *M* thexylborane and 50 mmol of freshly distilled 1-iodohexyne[7] in 25 ml of THF at 0°) was treated with 2.7 g (50 mmol) of sodium methoxide dissolved in 50 ml of methanol (10 min at 0° then 3 hr at room temperature). The resultant mixture was condensed to *ca.* 20 ml by evaporation and extracted with petroleum ether (total 80 ml) to remove most of the methanol. The extract was condensed to *ca.* 40 ml and passed through a column packed with 50 g of Florisil[8] (F-101, 100–200 mesh, Fisher) using petroleum ether as eluent. The first compound eluted was essentially pure **3a** (~99% by glpc). Although the elemental analysis has not been performed, **3a** has been well identified immediately following evaporation of the solvent: mass spectrum (35 eV) *m/e* (relative intensity) 164 (100), 165 (12.4), 166 (0.6); pmr ($CDCl_3$, TMS) δ 0.92 (t, 6 H), 1.1–1.8 (m, 8 H), 1.9–2.5 (m, 4 H), and 5.54 (t, $J = 5$ Hz, 2 H) ppm; ir (neat) 3000(s), 2900(s), 1660(w), 1480(m), 1390(m), 825(m) cm^{-1}; uv_{max} (hexane) 255 (ϵ 28,600), 226 (ϵ 11,700) nm; $n^{26.5}\mathrm{D}$ 1.4972.

Glpc examination (2 ft SE-30, column temperature 100°) of a reaction mixture containing **3a** at the injection block temperature of 125° reveals only a single sharp peak in the region expected for the C_{12}-hydrocarbons. At the injection block temperature of $\geq 200°$ a doublet consisting of the original peak and a new peak with a slightly shorter retention time was observed, indicating a rapid isomerization of **3a**.[9] We have found that the isomerization is markedly catalyzed by a trace amount of iodine. Thus, when 0.3 mol % of iodine was added to **3a**, a nearly 1:1 mixture of **3a** and the new product was obtained within 10 min at 25°. The new peak does not correspond to either *cis*- or *trans*-5,7-dodecenyne.[10,11] That the new product is the cis isomer of **3a** has been established by the pmr spectrum of the 1:1 mixture which was virtually identical with that of **3a**. This, in turn, has firmly established that **3a** which exhibits a sharp single glpc peak is indeed isomerically pure (>99%).

The trans geometry of **3a** has been established by its conversion into essentially pure *cis,trans*-5,7-dodecadiene in 71% yield by the hydroboration with disiamylborane followed by protonolysis with isobutyric acid.[12] The results are in agreement with the exclusive cis addition of the B–H bond to the central double bond of **3a** followed by protonolysis which proceeds with retention of configuration[13] (eq 2).



The preparation and structural determination of **3b** was performed in an analogous manner: yield by glpc, 29%; pmr (CCl_4, TMS) δ 1.0–2.5 (m, 22 H); 5.45 (d, $J = 4$ Hz, 2 H) ppm; ir (neat) 2900(s), 2850(s), 1630(w), 1440(s), 827(m) cm^{-1}; $n^{25}\mathrm{D}$ 1.5440. We are inclined to assign the strong ir band of **3** at ~825 cm^{-1} to the out-of-plane C–H bending vibration of the

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(5) E. Negishi and T. Yoshida, *J. Chem. Soc., Chem. Commun.*, 606 (1973).

(6) Various attempts to prevent the formation of the gelatinous substance, including (a) addition of antioxidants, such as hydroquinone and 4-methyl-2,6-di-*tert*-butylphenol, and (b) exclusion of oxygen and light, have been frustrated. Similar behaviors of other strained olefinic substances have been reported. See, for a recent example, W. S. Trahanovsky and M. G. Park, *J. Amer. Chem. Soc.*, **95**, 5412 (1973).

(7) 1-Iodo-1-hexyne must not contain any trace of iodine (*vide infra*).

(8) When aluminum oxide (Woelm, basic, activity grade 1) was used as a packing material, an extensive isomerization was observed.

(9) When the injection block temperature was 400°, the two peaks were comparable in size.

(10) G. Zweifel and N. L. Polston, *J. Amer. Chem. Soc.*, **92**, 4068 (1970).

(11) E. Negishi, G. Lew, and T. Yoshida, *J. Chem. Soc., Chem. Commun.*, 874 (1973).

(12) The hydroboration–protonolysis of the cis isomer is expected to produce a mixture of *cis,cis*- and *trans,trans*-5,7-dodecadienes. Indeed, the 1:1 mixture of **3a** and its stereoisomer yielded, in addition to the cis,trans isomer, the cis,cis and/or trans,trans isomers (These two isomers have essentially the same glpc retention times under various glpc conditions).

(13) H. C. Brown, "Boranes in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1972.

trans butatriene moiety, although this point remains to be established. Finally, the exclusive formation of the trans isomer **3** is in agreement with the formation of **4** as an intermediate and its base-assisted anti elimination reaction.[14] We are currently trying to achieve (a) a stereospecific transformation of **3** into their cis isomers and (b) a synthesis of unsymmetrically 1,4-disubstituted analogs for observation of the pmr coupling constants for the two vinylic protons.[15]

Acknowledgment. Financial support by Syracuse University is gratefully acknowledged.

[14] For related transformations, see (a) G. Köbrich and M. R. Merkle, *Angew. Chem., Int. Ed. Engl.*, **6**, 74 (1967); (b) G. Zweifel, H. Arzoumanian, and C. C. Whitney *J. Amer. Chem. Soc.*, **89**, 3652 (1967); (c) G. Zweifel and H. Arzoumanian, *ibid.*, **89**, 5086 (1967); (d) E. Negishi, J. J. Katz, and H. C. Brown, *Synthesis*, 555 (1972).

[15] A value of 7.8 Hz has been predicted: M. Karplus, *J. Amer. Chem. Soc.*, **82**, 4431 (1960).

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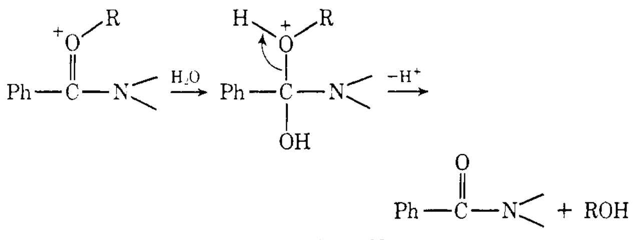
Alkyl Carbon–Oxygen Bond Cleavage in the Hydrolysis of Imidate Esters to Amides in Acid Solution

Sir:

The hydrolysis of imidate esters has seen considerable investigation, particularly since this reaction offers an alternative approach to the study of the type of tetrahedral addition intermediate implicated in many acyl transfer reactions. In general the hydrolysis produces ester and amine at low pH with a change over to amide and alcohol at high pH,[1,2] although exceptions to this behavior have been observed.[2,3]

Recently a study of the sulfuric acid catalyzed hydrolysis of a series of methyl benzimidates was reported.[4] In 5% H_2SO_4 only the expected ester product was obtained, but in 65% H_2SO_4 considerable amide was formed, the relative amount increasing with the degree *N*-methyl substitution. This result was interpreted in terms of acidity dependence of the breakdown of the tetrahedral intermediate. The suggestion then followed that the analogous benzamides could not be hydrolyzing *via* similar tetrahedral intermediates, since these reactions show no detectable ^{18}O exchange during hydrolysis at these or any other acidities. That is, if the tetrahedral intermediate obtained in an acid-catalyzed imidate hydrolysis can expel alcohol to give amide, the analogous tetrahedral intermediate for an acid-catalyzed amide hydrolysis could expel water, a process which (assuming rapid proton transfers) would result in ^{18}O exchange.

An alternative explanation is that the pathway by which the imidates hydrolyze to give amide does not involve a tetrahedral intermediate. Study was therefore initiated into the nature of this reaction. The following results present evidence concerning the position of bond cleavage. Amide products would arise from cleavage of either the acyl carbon–oxygen bond or the alkyl carbon–oxygen bond;[5] a tetrahedral intermediate requires the former (see above equation).



imidate, R = CH_3
amide, R = H

N,O-Dimethylbenzimidate-^{18}*O* (Ia), *N,O*-dimethylbenzimidatonium-^{18}*O* fluoroborate (Ib), and *N,N,O*-trimethylbenzimidatonium-^{18}*O* fluoroborate (II) were prepared by methylation[4] of labeled benzamides,[4] and the ^{18}O content of the amide product isolated from hydrolysis in 65% H_2SO_4 was determined. For comparison purposes a similar study was carried out on the hydrolysis of compound I in dilute base, where amide is also formed. The results are reported in Table I.

Table I. ^{18}O Content of Amides Obtained from Hydrolysis of Labeled Imidates

Substrate[a]	Solvent	Time (hr)	Temp, (°C)	% ^{18}O in amide[c]	Mode of cleavage
Ia	65% H_2SO_4	55	85	1.52	O–CH_3
Ib	65% H_2SO_4	50	85	1.61	O–CH_3
II	65% H_2SO_4	110	85	1.59	O–CH_3
Ia	0.01 *N* NaOH	6	25	0.19[d]	O-acyl
Ib	0.01 *N* NaOH[b]	6	25	0.25[d]	O-acyl

[a] 1.60% ^{18}O. [b] Corrected for deprotonation of Ib. [c] Amides were purified by recrystallization or distillation and analyzed on an AEI Model Ms 902 mass spectrometer, error ±0.05. [d] Labeled amide showed no loss of ^{18}O under identical conditions.

In the basic hydrolysis the results are consistent with a tetrahedral intermediate; unlabeled amide is obtained, implying acyl carbon–oxygen cleavage. This is reassuring since to date all studies of imidate hydrolysis in the pH range have dealt with the results in terms of tetrahedral intermediates in various forms.[1-3]

However, in 65% H_2SO_4, the amides retain the label of the imidates, demonstrating alkyl carbon–oxygen cleavage. Thus a tetrahedral intermediate must be ruled out as the precursor. Consequently arguments relating to a comparison of imidate and amide hydrolysis in concentrated acids cannot hold, since an analogous hydrolysis reaction cannot occur for amides. In particular the problem of explaining the lack of ^{18}O exchange during amide hydrolysis in the light of the imidate results is resolved. It is the imidate hydrolysis (to amide) that does not involve a tetrahedral intermediate. The question of the mechanism of amide hydrolysis is still open.[6]

The reaction responsible for the amide products is an interesting one. From the negative entropies of

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[1] G. L. Schmir and B. A. Cunningham, *J. Amer. Chem. Soc.*, **87**, 5692 (1965); G. M. Blackburn and W. P. Jencks, *ibid.*, **90**, 2638 (1968); R. K. Chaturvedi and G. L. Schmir, *ibid.*, **90**, 4413 (1968); T. C. Pletcher, S. Koehler, and E. H. Cordes, *ibid.*, **90**, 7072 (1968).

[2] T. Okuyama, T. C. Pletcher, D. J. Sahn, and G. L. Schmir, *J. Amer. Chem. Soc.*, **95**, 1253 (1973).

[3] P. Deslongchamps, C. Lebreux, and R. Taillefer, *Can. J. Chem.*, **51**, 1666 (1973).

[4] C. R. Smith and K. Yates, *J. Amer. Chem. Soc.*, **94**, 8811 (1972).

[5] The terms acyl and alkyl carbon are used in analogy with normal carboxylate esters.

[6] See, for example, ref 4 and the following: C. A. Bunton, S. J. Farber, A. J. G. Milbank, C. J. O'Connor, and T. A. Turney, *J. Chem. Soc., Perkin Trans. 2*, 1869 (1972); C. R. Smith and K. Yates, *J. Amer. Chem. Soc.*, **93**, 6578 (1971); *Can. J. Chem.*, **50**, 771 (1972); M. Liler, *J. Chem. Soc. B*, 334 (1971).