enzyme, the absorption maximum of the O-cinnamoyl group is essentially nonexistent.

The thiol-subtilisin synthesized here is an active enzyme, catalyzing the hydrolysis of N-*trans*-cinnamoylimidazole, *p*-nitrophenyl acetate, and *p*-nitrophenyl N-benzyloxycarbonylglycinate, one of the more specific substrates of subtilisin. These catalyses are due to the synthetic thiol-subtilisin since: (1) the intermediate cinnamoyl-enzyme in the hydrolysis of N-*trans*-cinnamoylimidazole has the spectral characteristics of a thiol enzyme (see above); (2) the *p*-nitrophenyl acetate hydrolysis follows Michaelis–Menten kinetics; (3) the hydrolyses of *p*-nitrophenyl acetate and *p*-nitrophenyl N-benzyloxycarbonylglycinate are inhibited to the extent of 95 and 70%,[9] respectively, by *p*-chloromercuribenzoate, whereas the subtilisin catalyses of these hydrolyses are not; (4) the rate of deacylation of cinnamoyl-thiol-subtilisin and the k_{cat} of the *p*-nitrophenyl acetate hydrolysis are dependent on a basic group of *ca.* pK_a 7.5.[10]

The kinetic properties of thiol-subtilisin are now being investigated in two ways: (1) comparison with subtilisin; this comparison involves two enzymes of common basic group but different nucleophilic entity; (2) comparison with papain; this comparison involves two enzymes with the same nucleophilic entity but different basic group.

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[9] This 70% inhibition means that a small amount of another enzymatic activity highly active toward the glycine substrate is still present in the thiol-subtilisin preparation. Theoretically ~10% of subtilisin could still be present since titration of the subtilisin with phenylmethanesulfonyl fluoride to complete inactivity required 0.9 equiv of inhibitor while only 0.8 equiv of thiol group was found in thiol-subtilisin. However, the extraneous enzymatic activity unaffected by *p*-chloromercuribenzoate is also unaffected by phenylmethanesulfonyl fluoride and thus cannot be regenerated subtilisin.

[10] K. E. Neet and D. E. Koshland, Jr., personal communication, have prepared a thiol-subtilisin. Both they and we have found no significant activity toward aromatic amino acid alkyl ester substrates (ethyl N-acetyl-L-tyrosinate and methyl N-acetyl-L-tryptophanate, respectively) (their suggestion). This apparent inactivity could be due to either a specificity of thiol-subtilisin for powerful acylating agents or because the rate of deacylation of acyl-thiol-subtilisins is much slower than that of acyl-subtilisins, as we have in fact found.

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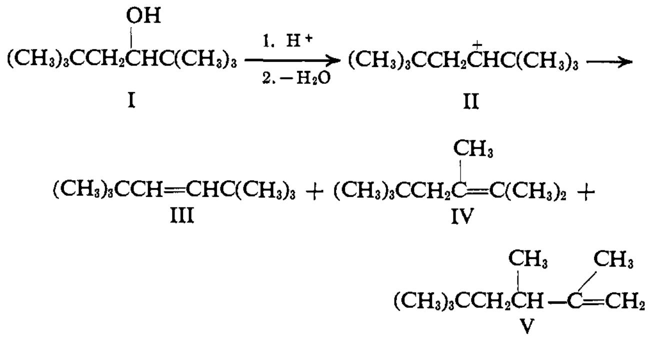
Dehydration, without Rearrangement, of a Neopentyl-Type Secondary Alcohol

Sir:

The dehydration of a secondary alcohol, such as 2,2,5,5-tetramethyl-3-hexanol (I), has been shown to produce a mixture of olefins (III–V) which results from the intermediate carbonium ion (II) by the well-known Whitmore or Wagner–Meerwein type of rearrangement.[1,2]

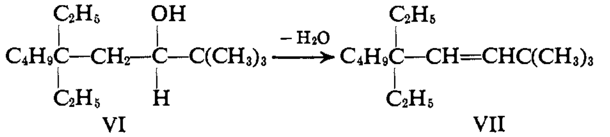
We wish to report what appears to be the first example of the dehydration of an alcohol, similar to I, which affords only a single olefin uncontaminated with skeletal rearrangement products.



$$\underset{\text{I}}{(CH_3)_3CCH_2\overset{\overset{OH}{|}}{C}HC(CH_3)_3} \xrightarrow[2.\,-H_2O]{1.\ H^+} \underset{\text{II}}{(CH_3)_3CCH_2\overset{+}{C}HC(CH_3)_3} \longrightarrow$$

$$\underset{\text{III}}{(CH_3)_3CCH{=}CHC(CH_3)_3} + \underset{\text{IV}}{(CH_3)_3CCH_2\overset{\overset{CH_3}{|}}{C}{=}C(CH_3)_2} + \underset{\text{V}}{(CH_3)_3CCH_2\overset{\overset{CH_3}{|}}{C}H{-}\overset{\overset{CH_3}{\diagup}}{C}{=}CH_2}$$

When 5,5-diethyl-2,2-dimethyl-3-nonanol (VI), bp 93–94° (1.4 mm), $n^{25}\text{D}$ 1.4528 (*Anal.* Calcd for $C_{15}H_{32}O$: C, 78.87; H, 14.12; Found: C, 79.17; H, 13.98), was heated with potassium hydrogen sulfate at 170–180° for 20 hr, there was obtained 5,5-diethyl-2,2-dimethyl-3-nonene (VII), bp 120–121° (40 mm), $n^{25}\text{D}$ 1.4394, in 81% yield. *Anal.* Calcd for $C_{15}H_{30}$: C, 85.63; H, 14.37. Found: C, 85.70; H, 14.40.



$$\underset{\text{VI}}{C_4H_9\underset{\underset{C_2H_5}{|}}{\overset{\overset{C_2H_5}{|}}{C}}{-}CH_2{-}\underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{C}}{-}C(CH_3)_3} \xrightarrow{-H_2O} \underset{\text{VII}}{C_4H_9\underset{\underset{C_2H_5}{|}}{\overset{\overset{C_2H_5}{|}}{C}}{-}CH{=}CHC(CH_3)_3}$$

Analysis of the dehydration product by vapor phase chromatography, 10-ft Carbowax (15%) on Chromosorb W column at 170°, indicated the presence of only one olefin. The infrared spectrum of VII shows absorptions at 3040 and 970 cm^{-1} characteristic of a *trans*-olefin. The nmr spectrum has an AB absorption pattern centered at τ 4.8, with a coupling constant of 16 cps, representative of a *trans* structure. Although assignments cannot be made for all of the methyl and methylene absorptions of VII, they essentially are superimposable on those of 3,3-diethylheptanonitrile which had been converted to alcohol VI by treatment with *t*-butyllithium, followed by hydrolysis and reduction of the intermediate ketone with lithium aluminum hydride. The only additional absorption is a singlet at τ 9 which is attributed to the *t*-butyl group.

In order to substantiate the structure of VII further, 3-deuteroxy-5,5-diethyl-2,2-dimethylnonane-3,4,4-d_3, bp 125–126° (9 mm), $n^{25}\text{D}$ 1.4512, was prepared from the corresponding ketone by deuteration with deuterium oxide followed by reduction with lithium aluminum deuteride and treatment with deuterium oxide and base. *Anal.* Calcd for $C_{15}H_{28}D_4O$: C, 77.51; H + D, 15.61. Found: C, 77.41; H + D, 15.48. Removal of deuterium oxide from this deuteroxy compound by heating with potassium hydrogen sulfate gave 5,5-diethyl-2,2-dimethyl-3-nonene-3,4-d_2 in 74% yield, bp 133–134° (80 mm), $n^{25}\text{D}$ 1.4365. *Anal.* Calcd for $C_{15}H_{28}D_2$: C, 84.81; H + D, 15.19. Found: C, 84.61; H + D, 14.97. The nmr spectrum of the latter is devoid of vinyl proton absorption, but is identical otherwise with that of the olefin VII.

Treatment of I with potassium hydrogen sulfate under the conditions used for VI led to a mixture of three isomeric olefins as shown by gas chromatographic analysis.

Molecular models of II and the corresponding carbonium ion from VI indicate that crowding is far more serious in the latter. In addition, the hindrance appears to be still greater in the expected carbonium ions which might arise from the rearrangement of intermediates from VI. This suggests that steric factors

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[1] F. C. Whitmore and P. L. Meunier, *J. Am. Chem. Soc.*, **55**, 3721 (1933).

[2] F. L. Howard, T. W. Mears, A. Fookson, and P. Pomerantz, *ibid.*, **68**, 2121 (1946).

control the formation of the single olefin, VII, from the dehydration of VI.

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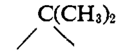
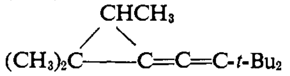
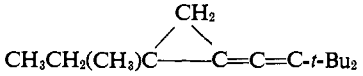
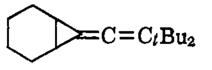
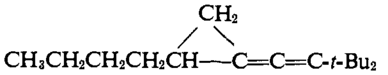
Dimerization and Cycloadditions of Tetra-*t*-butylhexapentaene

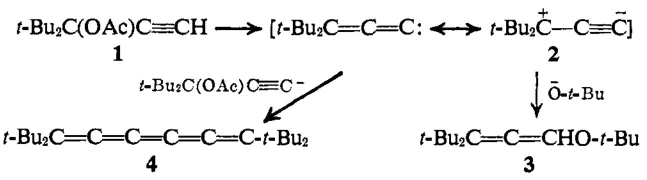
Sir:

Di-*t*-butylpropargyl acetate (**1**) was prepared as a possible generator of di-*t*-butylvinylidenecarbene (**2**) by γ-elimination reactions.[1] Such a carbene would be expected to react with nucleophiles at the terminal carbon atom.[2] The ester **1** was prepared from the alcohol[3] by reaction with methyllithium followed by acetic anhydride.

Reactions of **1** with potassium *t*-butoxide and olefins gave moderate yields of di-*t*-butylvinylidenecyclopropanes[4] (Table I). In the absence of olefins, **1** was allowed to react with potassium *t*-butoxide to give the allenic ether **3** and the hexapentaene **4** in yields of 19 and 20%. The products probably arose from reactions of **2** with the alkoxide and acetylide ions, respectively, rather than SN2′ displacements on **1** because **3** and **4** were essentially absent in the reactions of **1** in the presence of olefins.

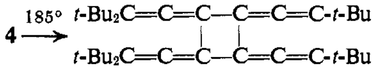
Table I. Di-*t*-butylvinylidenecyclopropanes

Olefin	Product	Bp, °C (mm)	Yield, %
$(CH_3)_2C{=}C(CH_3)_2$		Mp 69–70°	52
$(CH_3)_2C{=}CHCH_3$		48 (0.4)	10
$CH_3CH_2(CH_3)C{=}CH_2$		54 (0.5)	10
		89 (0.35)	22
$CH_3CH_2CH_2CH_2CH{=}CH_2$		75 (0.5)	22



The ether **3** had infrared absorption at 1935 and 1955 cm^{-1}, indicating the presence of the allenic system. The nmr spectrum of **3** showed absorption at δ 6.25 (vinyl hydrogen), 8.74 (alkoxy methyls), and 8.80 (*t*-butyl methyls). The intensity ratio of vinyl to methyl hydrogens was 1:28. The hexapentaene **4** had electronic absorption maxima at 237 (ϵ 185,000), 308 (28,900), and 336 mμ (33,000), in agreement with previously synthesized aliphatic hexapentaenes.[5,6] In addition, there was a weak (ϵ 870) absorption at 417 mμ which was present after repeated crystallizations and sublimations. The nmr spectrum of **4** showed a single unsplit resonance at δ 1.28. The infrared spectrum of **4** showed absorption at 2020 and 1990 cm^{-1} which may be attributed to stretching of the double bonds of the cumulative system.

The cumulene **4** was inert to oxygen at room temperature and showed no tendency to polymerize. Upon melting (185°), however, **4** dimerized in 95% yield to tetrakis(di-*t*-butylvinylidene)cyclobutane (**5**). The symmetry of the dimer was deduced from the single, unsplit nmr signal (δ 1.20). Structure **5** is also consistent with the infrared allene absorption at 1950 and 1925 cm^{-1} the absence of isolated or conjugated double bond absorptions, and the electronic absorption maxima at 316 (ϵ 2040), 298 (1720), 268 (13,200), 258 (16,300), and 250 mμ (15,800). The spectrum is very similar to that reported for tetramethylenecyclobutane.[7] The dimer **5** melted without decomposition at 361°. Unlike the photodimer of tetraphenylbutatriene,[8] dimer **5** has shown no tendency to revert to monomer.



5

The dimerization **4** → **5** occurred to only a slight extent in solution in decahydronaphthalene at 200°, even though **4** was completely consumed. The major product was the bisallene formed by the addition of hydrogen to the central bond of **4**. This material was not obtained analytically pure. A possible explanation for the reactions of **4** is that **4** is thermally converted to a triplet which can react with solvent or with **4** to give dimer. Such a species should be reactive in other cycloaddition reactions.

At 200°, **4** added tetrafluoroethylene to give **6** in

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(1) H. D. Hartzler, *J. Am. Chem. Soc.*, **83**, 4990 (1961).

(2) Evidence has recently been presented to demonstrate that the position of attack by nucleophiles on vinylidene carbenes is markedly influenced by steric effects: G. F. Hennion and C. V. DiGiovanna, *J. Org. Chem.*, 30, 3696 (1965).

(3) W. J. Hickenbottom, A. A. Hyatt, and M. B. Sparke, *J. Chem. Soc.*, 2529 (1954).

(4) Accurate analytical data were obtained for all new compounds.

(5) F. Bohlmann and K. Kieslich, *Ber.*, **87**, 1363 (1954).

(6) L. Skattebøl, *Tetrahedron*, **21**, 1357 (1965).

(7) G. W. Griffin and L. I. Peterson, *J. Am. Chem. Soc.*, **85**, 2268 (1963).

(8) R. O. Uhler, H. Shechter, and G. V. D. Tiers, *ibid.*, **84**, 3397 (1962); K. Brand, *Ber.*, **54**, 1947 (1921).