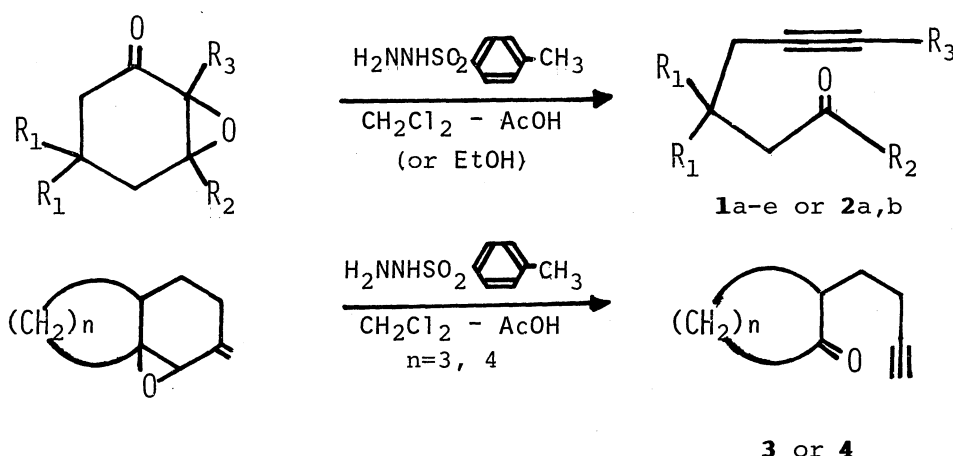


REDUCTIVE CYCLIZATION OF NONCONJUGATED
ACETYLENIC KETONES TO 2-METHYLENECYCLOPENTANOLS¹⁾

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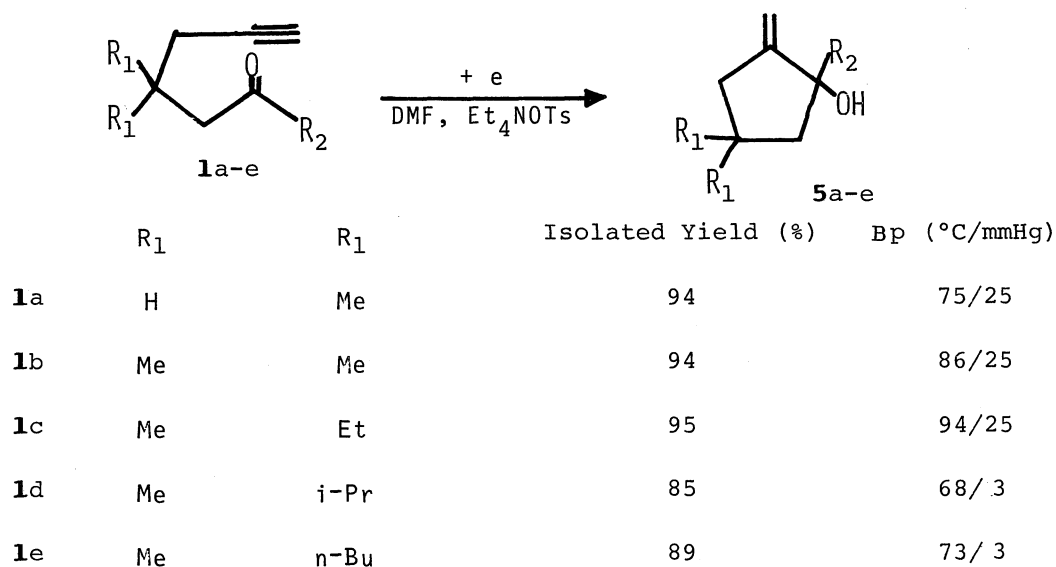
Electroreduction of a series of γ -ethynyl ketones in dimethylformamide gave the cyclization products, 2-methylene-cyclopentanol, as the sole product in excellent yields. Furthermore, this electrochemical technique was applied to a new synthesis of bicyclic alcohols with an exocyclic double bond adjacent to a bridgehead hydroxyl group.

It was demonstrated in our recent study^{2),3)} that cis-1,2-dialkylcyclopentanol were obtained in excellent yields from electroreductive cyclization of hept-6-en-2-one derivatives. The remarkable stereo- and regioselectivities and high yields³⁾ in this cyclization reaction prompted us to examine the electroreduction of γ -ethynyl ketones to 2-methylenecyclopentanol, of which structure is found in a certain natural product such as steviol⁴⁾ or gibberellic acid.⁵⁾ The starting nonconjugated acetylenic ketones **1-4** were prepared from the corresponding α,β -epoxyketones in 58-74% yields by the modified Eschmoser procedure.⁶⁾

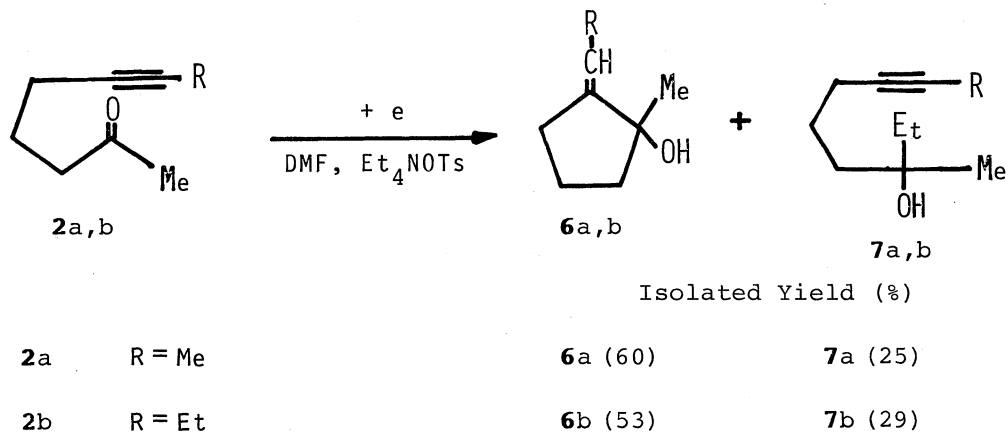


The electroreduction of **1a-e** was carried out using carbon rod electrode at room temperature in anhydrous dimethylformamide containing tetraethylammonium p-toluenesulfonate as a supporting electrolyte. A ceramic cyclinder was used as a diaphragm and the electrolysis was continued until 4F/mole of electricity was passed. The reduction gave 2-methylene-1-alkylcyclopentanol **5a-e**⁷⁾ as the sole

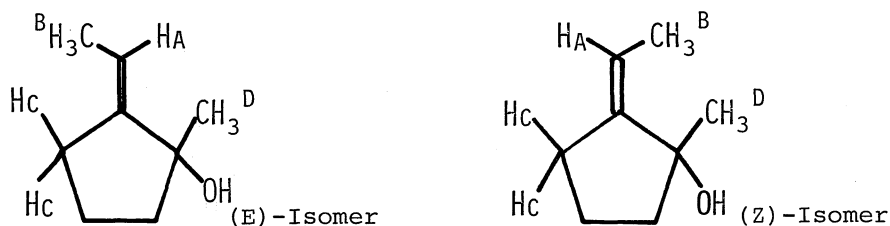
product in good yields.



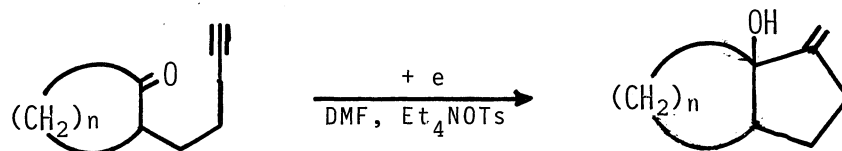
The introduction of an alkyl group on the terminal carbon atom of the triple bond of acetylenic ketone **1** brought about the formation of a by-product and the decrease in the yield of the cyclized product. For example, the reduction of **2a,b** gave the cyclopentanol **6a,b** and the acetylenic alcohol **7a,b**⁸⁾ in the ratio of ca. 2:1.



Comparison of the NMR spectrum of the product **6a** with that of the authentic sample of (E)-2-ethylidene-1-methylcyclopentanol, prepared from the Grignard reaction of (E)-2-ethylidenecyclopentanone,⁹⁾ indicated obviously that the product **6a** consists of the mixture of (E)- and (Z)-ethylidene-1-methylcyclopentanol¹⁰⁾ in the ratio of approximately 1:2.



The preferential formation of the (Z)-isomer in the electroreduction of **2a** is noteworthy in contrast with the reverse stereoselectivity in the reductive cyclization of steroidal acetylenic ketones with naphthalene anion radical.¹¹⁾ Furthermore, this electroreductive reaction was applied to a novel synthesis of bicyclic alcohols possessing an exocyclic methylene group adjacent to a bridgehead hydroxyl group such as **8** or **9**.



3 (n=3)

4 (n=4)

8 (n=3): Y = 75%, bp 58°C/3mm

9 (n=4): Y = 63%, bp 64°C/3mm

In comparison with the hitherto known reductive cyclization of a certain γ -ethynyl ketone with naphthalene anion radical¹¹⁾ or lithium in liquid ammonia,¹²⁾ this electrochemical reduction may possess quite high potentiality as a new synthetic method of 2-methylenecyclopentanol from the viewpoint of the wide generality, the excellent yield and the simplicity of the procedure.

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 Bp(°C/mmHg): **1a**(70/25), ^{6c)} **1b**(78/25), ^{6b), 6c)} **1c**(90/25), **1d**(60/3), **1e**(69/3), **2a**(70/20), **2b**(75/20), **3**(71/5), **4**(78/5). ^{6b)}
- 7) Satisfactory spectroscopic and elemental analyses were obtained for all new compounds described in this communication: the exo-methylene group of **5a-e**; NMR (in CCl₄, δ-ppm), 4.82-4.87 (triplet of doublet, 2H); IR (neat, cm⁻¹), 3080-3070, 1655-1660, 890-900.
- 8) The noncyclized ethylated alcohol **7a,b** may probably be formed through the nucleophilic interaction of the generated anion species of **2a,b** with tetraethylammonium tosylate. Bp(°C/mmHg); **6a**(76/20), **6b**(82/20), **7a**(98/20), **7b**(104/20).
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- 10) The NMR spectra of (E)- and (Z)-2-ethylidene-1-methylcyclopentanol may be assigned as follows (in CCl₄).

	(Z)-Isomer (δ-ppm)	(E)-Isomer (δ-ppm)
H _A	5.31 (triplet of quartet) J _{AB} =7.3Hz, J _{AC} =2.2Hz	5.44 (triplet of quartet) J _{AB} =6.5Hz, J _{AC} =2.5Hz
H _B	1.78 (triplet of doublet) J _{BC} =2.0Hz	1.27 (triplet of doublet) J _{BC} =1.5Hz
H _D	1.37 (singlet)	1.24 (singlet)

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