Tetrahedron Letters,Vol.25,No.40,pp 4549-4552,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

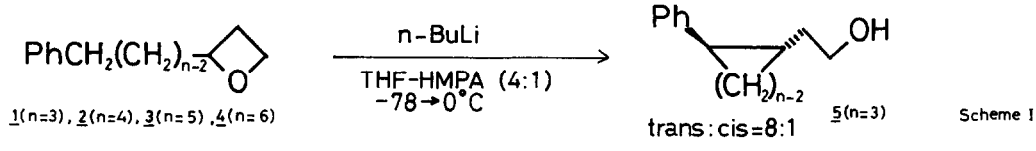
AN INTRAMOLECULAR NUCLEOPHILIC SUBSTITUTION OF OXETANES

Masahiko Yamaguchi* and Ichiro Hirao
Department of Industrial Chemistry, Kyushu Institute of Technology,
Sensui-cho, Tobata, Kitakyushu 804, JAPAN

Abstract: The intramolecular attack of carbanions to oxetanes were examined and several three, five, and six membered carbocyclic compounds were synthesized.

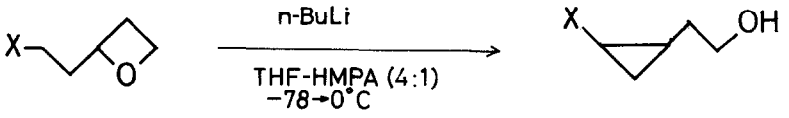
The intramolecular attack of carbanions on epoxides[1), 2)] is a well known method for the ring formation, and several types of compounds were employed for this purpose. They include epoxynitriles[2a)], epoxysulfones[2b)], and epoxyalkenes[2c)]. To our knowledge, the use of oxetanes, a strained four membered cyclic ether, has not appeared in this type of cyclization reaction. In this communication, we wish to describe the results of the investigation on the synthesis of carbocyclic compounds utilizing the intramolecular attack of carbanions on oxetanes.

Initially, the reaction of benzyl anions were carried out. Several 2-(ω-phenylalkyl)oxetanes (1, 2, 3, 4), synthesized from the corresponding 1,3-diols[3)], were treated with n-butyllithium at -78°C in THF-HMPA (4:1), and the reaction temperature was slowly raised to 0°C (Method A). The length of carbon chain played an important role in the cyclization reaction. And, empolying the Method A, only 2-(2-phenethyl)oxetane (1) gave the expected product, 1-phenyl-2-(2-hydroxyethyl)cyclopropane (5) in 82 % yield with trans-configuration predominantly (trans : cis = 8 : 1) (Scheme I). The trans-configuration was confirmed by the comparison of ^{1}H- and ^{13}C-NMR spectra with the authentic sample, which was prepared from trans-1-hydroxymethyl-2-phenylcyclopropane[2d)] by one-carbon homologation.



1(n=3), 2(n=4), 3(n=5), 4(n=6) 5(n=3) Scheme I

Similarly, the intramolecular attack of tolyl, allyl, and propargyl anions to oxetanes were examined to give cyclopropane derivatives (Scheme II and Table I). In case of 2-[2-(o-tolyl)ethyl]oxetane (7), the three membered ring formation, by the attack of the secondary benzylic carbanion, occurred exclusively, and no cyclohexane, formed by the reaction of the primary benzylic carbanion,



Scheme II

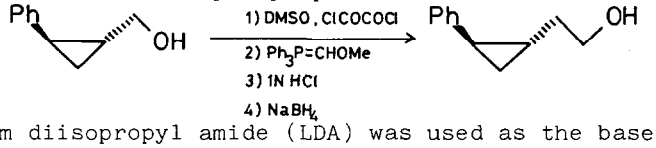
Table I. Synthesis of Cyclopropane Derivatives.

X	yield of cyclopropanes (%) [a]	trans : cis [b]
C_6H_5-	82	8 : 1 [c]
o-$CH_3C_6H_4$-	84, quant. [d]	9 : 1
(E)-C_6H_5CH=CH-	67	2 : 1 [e], [f]
(Z)-C_6H_5CH=CH-	40	1 : 1 [e], [f]
$C_6H_5C\equiv C$-	50	3 : 1 [e]

a) All the products gave satisfactory spectral data (^{1}H- and ^{13}C-NMR, IR) and elemental analyses by high resolution mass spectroscopy.

b) The ratio was determined by ^{13}C-NMR.

c) The configuration was determined by the comparison of the spectral data (^{1}H- and ^{13}C-NMR) of the authentic sample, which was prepared from the known trans-cyclopropane[2d] as follows.



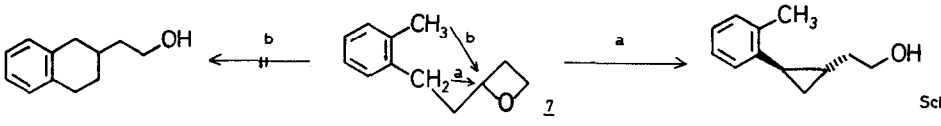
d) Lithium diisopropyl amide (LDA) was used as the base.

e) The configuration was determined tentatively.

f) (E)-Olefine was obtained.

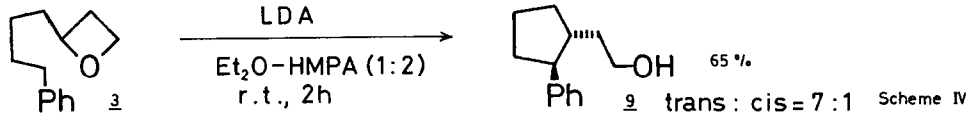
was detectable (Scheme III). The cyclopropane formation was also favored in the reaction of (E)- and (Z)-2-(4-phenyl-3-butenyl)oxetane (8) rather than five membered ring. Notably, (E)- or (Z)-8 gave the olefinic cyclopropane with (E)-configuration concerning the carbon-carbon double bond.

The oxetane (3), which failed to give cyclization product by the Method A, was transformed to cyclopentane (9) under a rather forced reaction condition —— using LDA as the base at r. t. in ether : HMPA (1:2) for 2 h (Method B) ——



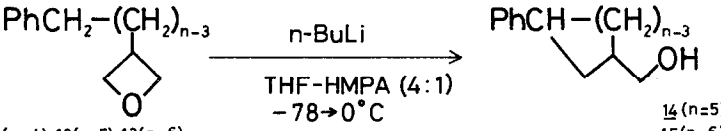
Scheme III

in 65 % yield (Scheme IV). Preference of the trans-isomer (trans : cis = 7 : 1) was also observed, which was determined by the high field chemical shift in ^{13}C-NMR spectra of α-methylene carbon of the minor isomer (δ 53.2 for the major isomer and δ 48.8 for the minor isomer).[4] Four and six membered ring formation under this reaction conditions, however, failed.



Scheme IV

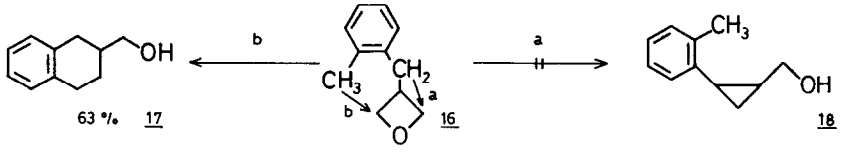
Next, the cyclization of 3-substituted oxetanes were performed. The proper length of the carbon chain was crucial for the ring closure process. Thus, three and four membered ring formation did not take place either by the Method A or B. Cyclopentane (14)[5] and cyclohexane (15)[6] derivatives, in contrast, were readily synthesized utilizing the Method A in good yield. Notably, 1-phenyl-3-hydroxymethylcyclohexane (15) was obtained as a single isomer, determined by ^{13}C-NMR (Scheme V). The ineffectiveness in the formation of cyclopropane



Scheme V

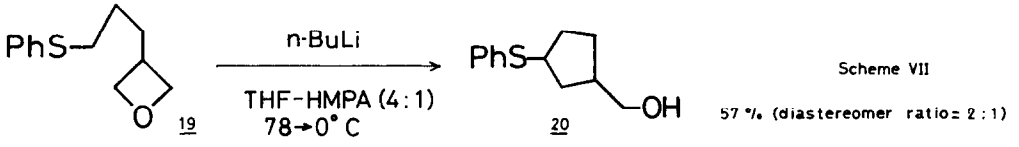
in 3-substituted oxetane might be explained by the difficulties of the system to achieve the proper collinear arrangement for displacement at the oxetane carbon.

Additional examples of the carbocyclic ring formation of the carbanions generated at the side chain of 3-position of oxetane are also described. Thus, 3-(o-tolylmethyl)oxetane (16) was treated with n-butyllithium in THF-HMPA (4:1) at -78°C to 0°C and the corresponding tetrahydronaphtalene (17) was obtained in 63 % yield. Contrasted with the 2-substituted oxetane, dipicted above, six membered ring formation occurred exclusively by the intramolecular attack of the primary carbanion, and no cyclopropane (18) was isolated (Scheme VI).



Scheme VI

Sulfur stabilized carbanion was also employed in the cyclization reaction and



Scheme VII

3-(3-phenylthiopropyl)oxetane (19) was reacted by the Method A to give the expected phenylthiocyclopentane (20), which was obtained as a 2:1 mixture of diastereomers (Scheme VII).

A typical procedure is described for the synthesis of 1-phenyl-2-(2-hydroxyethyl)cyclopropane (5) by the Method A: Under a nitrogen atomosphere, to a THF-HMPA solution (2+0.5 ml) of 2-(2-phenethyl)oxetane (78 mg, 0.5 mmol) was added a hexane solution of n-butyllithium (0.4 ml, 0.6 mmol) at -78°C. The reaction temperature was raised to 0°C for 2 h, and the reaction was quenched by adding saturated aqueous ammonium chloride. After a usual work-up, 1-phenyl-2-(2-hydroxyethyl)cyclopropane (64 mg, 82 %) was obtained by thin layer chromatography on silica gel with ethyl acetate : hexane (1:3) as the eluent. ^{1}H-NMR ($CDCl_3$) δ 0.6-1.4 (3H,m), 1.4-1.8 (3H,m), 2.45 (1H,s), 3.66 (2H,t,J=5.5Hz), 6.8-7.4 (5H,m). ^{13}C-NMR ($CDCl_3$) δ 15.6, 20.2, 22.8, 37.3, 62.5, 125.3, 125.6, 128.2, 143.4 for the major isomer; 20.5, 31.7, 127.9, 128.9 for the minor isomer. The ratio was estimated to be 8:1. IR (neat) 3300, 1605, 1500, 1050, 750, 700 cm^{-1}. Exact mass calcd for $C_{11}H_{14}O$: 162.1044. Found: 162.1042.

References and Notes

1) For a review, C. J. M. Stirling, Chem. Rev., 78, 517 (1978).

2) a) G. Stork, L. D. Cama, and D. R. Coulson, J. Am. Chem. Soc., 96, 5268 (1974); G. Stork and J. F. Cohen, ibid, 96, 5270 (1974). b) Y. Gaoni, Tetrahedron Lett., 1976, 503; idem, J. Org. Chem., 47, 2564 (1982); J. M. Decesare, B. Corbel, and T. Durst, Can. J. Chem., 59, 1415 (1981). c) M. Apparu and M. Barrelle, Tetrahedron, 34, 1691 (1978). d) J. H. Babler and A. J. Tortorello, J. Org. Chem., 41, 885 (1976); N. J. Barnes, A. H. Davidson, L. R. Hughes, G. Procter, and V. Rajcoomar, Tetrahedron Lett., 22, 1751 (1981).

3) P. Picard, D. Leclercq, J.-P. Bats, and J. Moulines, Synthesis, 1981, 550.

4) ^{1}H-NMR ($CDCl_3$) δ 1.0-2.8 (11H,m), 3.49 (2H,t,J=6.5Hz), 7.21 (5H,s). ^{13}C-NMR ($CDCl_3$) δ 24.1, 32.5, 35.5, 37.5, 44.8, 53.2, 62.0, 125.9, 127.4, 128.3, 145.2 (The major isomer); 23.7, 30.5, 30.9, 34.0, 40.6, 48.8, 125.7, 127.9 (The minor isomer). IR (neat) 3350, 755, 700 cm^{-1}. Exact mass calcd for $C_{13}H_{18}O$: 190.1357. Found: 190.1349.

5) ^{1}H-NMR ($CDCl_3$) δ 1.1-2.7 (8H,m), 2.7-3.3 (1H,m), 3.59 (2H,d,J=6Hz), 7.23 (5H,s). ^{13}C-NMR ($CDCl_3$) δ 28.4, 33.3, 38.2, 42.0, 45.9, 67.4, 125.8, 126.9, 128.2, 145.4 (The major isomer); 29.3, 34.7, 36.9, 41.4, 44.6 (The minor isomer). IR (neat) 3300, 750, 700 cm^{-1}. Exact mass calcd for $C_{12}H_{16}O$: 176.1201. Found: 176.1206.

6) ^{1}H-NMR ($CDCl_3$) δ 0.8-2.2 (10H,m), 2.2-2.8 (1H,m), 3.47 (1H,d,J=5Hz), 7.22 (5H,s). ^{13}C-NMR ($CDCl_3$) δ 26.1, 34.3, 37.4, 40.9, 43.9, 68.5, 125.9, 126.7, 128.3, 147.4. IR (neat) 3300, 750, 700 cm^{-1}. Exact mass calcd for $C_{13}H_{18}O$: 190.1358. Found: 190.1408.

(Received in Japan 18 June 1984)