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INTRAMOLECULAR CYCLIZATION OF ACETYLENIC HOMOALLYLIC KETONES MEDIATED BY THE ADDITION OF STANNYL RADICALS ; A SHORT FACILE PATHWAY TO α-METHYLENE-β-SUBSTITUTED CYCLOPENTANONES

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Abstract : α-(Stannyl)methylenecyclopentanones are obtained by tributylstannane addition reactions of acetylenic homoallylic ketones. α-Methylenecyclopentanones are produced upon destannylation.

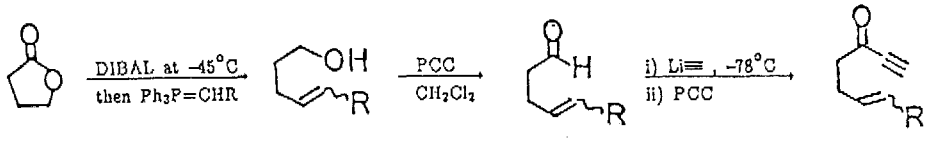
Since the isolation of sarkomycin[1], xanthocidin[2] and methylenomycin[3], α-methylene-cyclopentanone synthesis commanded considerable attention from synthetic chemists. The key steps of the reported synthetic routes in the construction of α-methylenecyclopentanones involve retro Diels-Alder reactions[4], palladium catalyzed cyclizations[5] and intramolecular carbenoid cyclization reactions with rhodium(II) catalyst[6].

We now wish to report a new method for the synthesis of α-methylenecyclopentanones utilizing intramolecular radical cyclization reactions initiated by addition of stannyl radicals to acetylenic homoallylic ketones.

Triple bonds have been used as radical trapping groups in many intramolecular cyclization reactions, but recently much attention was directed to the use of vinyl radicals generated by the addition of stannyl radicals to triple bonds. We have already shown that the cyclization reaction of vinyl radicals generated from allylic propiolates represent a novel synthetic route to α-methylene-γ-butyrolactones[7], and we were intrigued by the possibility of using the analogous radical cyclization reactions for the synthesis of carbocyclic ring systems.

Substrate acetylenic homoallylic ketones were prepared from γ-butyrolactone in four steps.

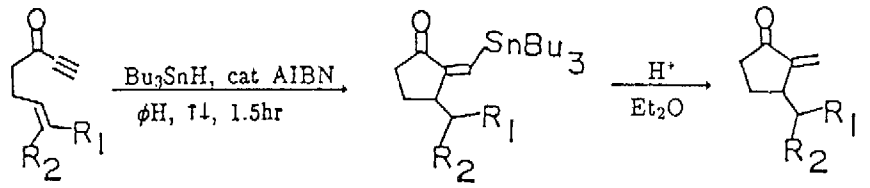
< SCHEME 1 >



R= Ph: E/Z= 3.5/ 1
R= COOEt : exclusively E isomer

Three acetylenic homoallylic ketones (1a~1c) were reacted separately with tributylstannane(1.2eq) in benzene (0.025M solution) under reflux in the presence of cat. AIBN for 1.5hrs, and cyclization products(2a~2c) were isolated in good yields (88~92%).

< SCHEME 2 >



1a : R_1=Me, R_2=Me
1b : R_1=Ph, R_2=H
1c : R_1=COOEt, R_2=H

2a : 91%
2b : 92%
2c : 88%

3a : 88%
3b : 92%
3c : 82%
Homosarkomycin ethyl ester

It was apparent that the formation of carbocyclic ring system is much more favorable than the lactone formation from allylic propiolates.

The cyclization products were easily transformed to α-methylenecyclopentanones (3a~3c) under the usual destannylation conditions. For example, destannylation of 2c (R_1=COOEt, R_2=H) resulted in the formation of homosarkomycin ethyl ester[8,9] (3c) in 82% yield.

Further examples of these intramolecular cyclization reactions of vinyl radicals in natural product synthesis will be reported in due course.

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8. Selected spectroscopic data : IR(NaCl) 3200~2560(br s), 1700~1770(br s), 1640(s), 1210~1160(br s), 1100(s). ^{1}H-NMR(80MHz,$CDCl_3$) : δ1.28(t,3H), 1.40~1.80(m,1H), 2.10~2.70(m,5H), 2.90~3.50(m,1H), 4.18(q,2H), 5.29(d,1H), 6.07(d,1H). Mass spectrum, m/e 182
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