

Strain Assisted Carbon-Carbon Bond Cleavage via Carbon Centred Radical. A Facile Route to Bridged Eight Membered Rings

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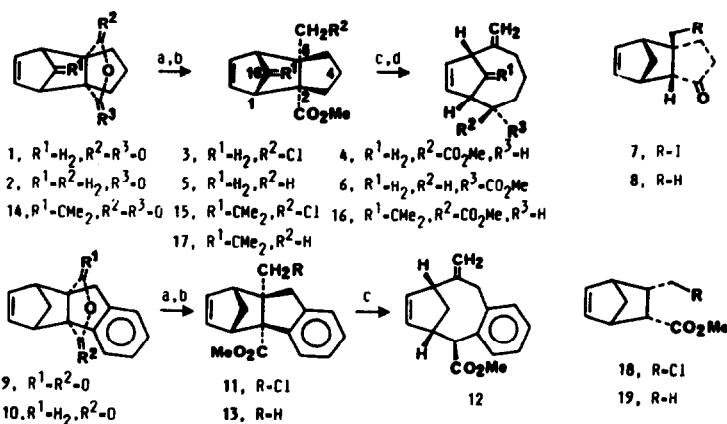
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Abstract : Tributyltin hydride reaction of the tricyclo[5.2.1.0^{2,6}]decenes 3, 11, 15 bearing the 1,4-halo carbonyl system has been shown to involve C-C bond cleavage as the major reaction path leading to bridged eight membered rings in contrast to reduction of the carbon-halogen bond in 7.

In recent years a wide variety of useful synthetic transformations involving carbon-carbon bond formation¹ and fragmentation^{2,3} has been achieved through tributyltin hydride (TBTH) based radical reactions. While transformations involving C-C bond fragmentation via alkoxy and iminyl radicals² have been well studied, those involving carbon centred radicals have received little attention³ and have been successful only in cyclopropane and cyclobutane derivatives. Ring systems⁴ other than these including a tricyclo[5.2.1.0^{2,6}]decene⁵ undergo only reduction. We now demonstrate that cleavage⁶ of the C₂-C₆ bonds of tricyclo[5.2.1.0^{2,6}]decenes can be achieved efficiently via carbon centred radicals providing a convenient and completely stereoselective route to the bridged eight membered rings present in taxanes.⁷

In a representative sequence, the anhydride 1⁸ was reduced with NaBH₄ in THF to afford the lactone 2⁹ (81%), mp 179°C, which on refluxing with freshly distilled SOCl₂ in MeOH gave the chloro-ester 3 in 63% yield. When a benzene solution of 3 was refluxed for 6-7 h with 1.6 equivalent of TBTH in presence of AIBN, it underwent smooth fragmentation to produce the diene 4 in 87% yield. The appearance of a two proton multiplet at δ 4.62 in addition to an olefinic singlet at δ 5.76 (C₈, C₉ protons) is indicative of the structure 4. The unambiguous structural and stereochemical assignment of 4 follows from comparison of the chemical shift of the C₉-olefinic proton of 4 (δ 5.76) with that of 6 (δ 5.96) obtained by epimerisation of 4 with NaOMe - MeOH. A trace of the reduced product 5 could also be detected by ¹H NMR.

The ring cleavage observed during TBTH reaction of 3 to produce 4 is in contrast to the exclusive reduction⁵ of the structurally analogous iodo ketone 7 to 8. The difference in reactivity pattern between 3 and 7 is possibly the result of the strain associated with 3 arising from a nonbonding interaction between the hydrogens at C₁₀ and CH₂'s of the 5-membered ring syn to C₁₀. To determine the importance of non-bonding interaction on the reaction course, the chloro-esters 11 and 15 from where the



Reagents : a, NaBH₄, THF, 0°C to rt, 51-81%; b, SOCl₂-MeOH, reflux, 2-3 h, 61-70%;
 c, TBTH, AIBN, C₆H₆, reflux, 6-12 h, 66-88%; d, NaOMe-MeOH, reflux, 65%.

C₃-C₄ and C₁₀ hydrogens respectively have been removed by strategic placement of sp² carbons, were chosen. As expected TBTH reaction of 11, prepared from the anhydride 9⁸ through 10 gave a 1:1 mixture of 12 (25%) and 13 (31%) even though the tertiary radical formed in this case after C-C bond cleavage was expected to be stabilised more than its debenzo analogue arising from 3. Similarly the chloro-ester 15 prepared from 14¹⁰ produced in 66% yield ca 70:30 mixture of 16 and 17. Finally, the strain free chloro-ester 18 afforded predominantly the reduced product 19. Thus, tricyclo[5.2.1.0^{2,6}]decenes may be made to undergo radical induced C-C bond cleavage assisted by the strain arising through non bonded interaction.

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