VINYLCYCLOPROPANES AS SYNTHONS FOR MACROCYCLES

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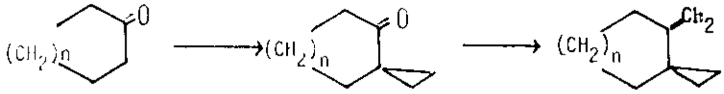
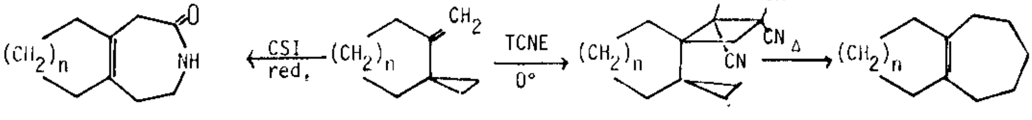
Nature utilizes isoprenoids as C_5-building units for the formation of small, medium and large-sized cyclic terpenoids. For obvious reasons only four of the carbon-chain in isoprene could be embodied in the chain back-bone of the cyclic terpenoids. Our studies of the tendency of properly activated vinylcyclopropanes to undergo 1,5-conjugative additions with electrophilic olefins[1-4] indicated that the vinylcyclopropane system can be utilized as a new C_5-building unit for macrocycles. Unlike isoprenoids, the C_5-unit of the _spiro_-vinylcyclopropane will be shown to provide new synthon for the expansion of a cyclic system by a 5-carbon chain. This entails a multi-stage process involving first the introduction of a spiranic cyclopropane ring in a cyclic ketone at a position α to the carbonyl followed by Wittig reaction to form 4-methylene_spiro_[2.x]alkane (I) as outlined below.[2]



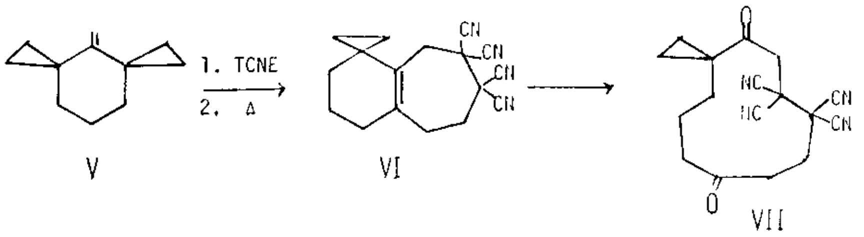
(I)

The reaction of (I) with electrophilic olefins such as TCNE or CSI leads to formation of a bicyclic system containing new seven-membered rings (III or IV), as depicted below.[2]

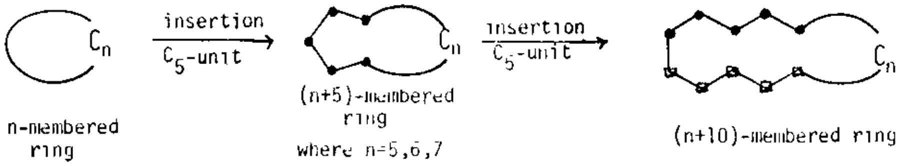


IV I II III

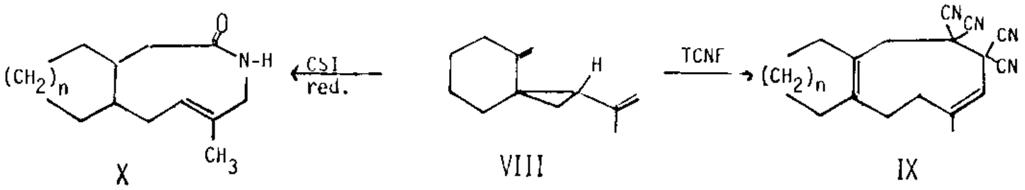
Ruthenium-tetroxide oxidation of III led to 10-, 11-, and 12-membered ring diketones. The reaction of 4-methylene-_dispiro_[2.1.2.x]alkanes (V) similarly with TCNE led to bicyclic system (VI) which upon oxidation gave the 11-membered ring spiro-diketone (VII).[5]



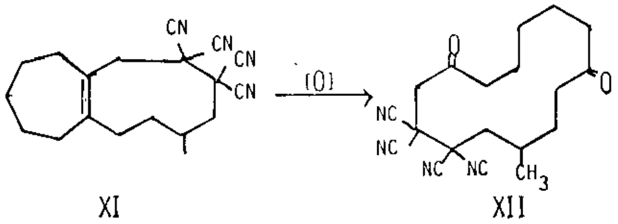
Selective protection of the unconjugated carbonyl followed by Wittig reaction of the conjugated ketone provides a new vinylcyclopropane synthon which could give rise to a 16-membered ring tri-ketone. Essentially, this is a demonstration of a stepwise expansion of the cyclic system in (V) by a chain of 5-carbon atoms at a time as outlined below.



This basic approach could in fact be expanded to include divinylcyclopropanes (VIII) which were shown lately to react rather efficiently with both TCNE and CSI[7,8] to form bicyclic systems containing 9-membered rings (IX and X).



Adduct (IX, n=3) could be selectively reduced to the dihydro-adduct (XI) which on oxidation yields the 14-membered ring diketone (XII) as illustrated below.[5]



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