Spiro-Annulation *via* Ring Closing Metathesis Reaction♣

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Abstract: Various spiro cyclic systems are prepared from β-di-carbonyl compounds and active methylene substrates *via* palladium catalyzed allylation and ring-closing metathesis (RCM) reaction as key steps.

Key words: allylation, metathesis, cyclopentane, spiro compounds, annulation

Spiro-annulation has considerable synthetic value because the spiro-linkage[1] is present in many natural products such as acoranes, chamigrenes,[2] angularly fused cyclopentanoids (e.g., isocomene, laurenene)[3] and fredericamycin **1**.[4] Among the non-natural products [5.5.5.5]fenestrane **2**[5] and spiranes[6] posses the spiro-linkage as fundamental unit. Spiro compounds having mutually perpendicular π-electron systems ("spiro-polyene") exhibit new kind of homoconjugation called "spiro conjugation". Apart from these theoretical aspects, spiro-polyenes are also of industrial interest. Some hetero-spirenes act as photochromic systems which can undergo reversible photochemical ring opening and find their utility in silver-free imaging systems and as memories in data display devices.[7] Construction of spirocyclics is usually achieved by intramolecular alkylation, cycloaddition reaction, ring closure in a preformed geminally substituted derivative or by rearrangements.[8] Most of these methods are restricted to a single substitution pattern.

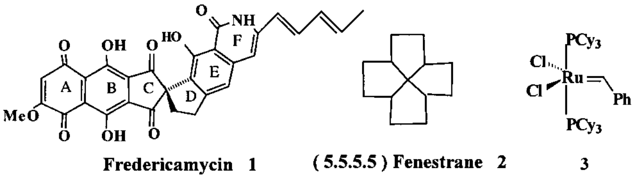
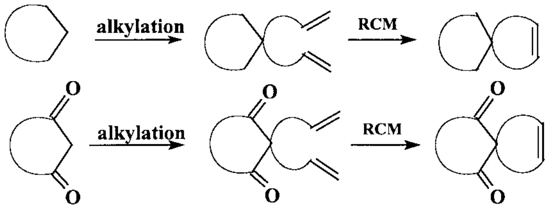


Figure 1

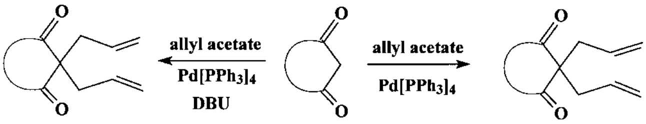
In this communication we wish to report a simple but effective methodology involving two-step catalytic procedure for the synthesis of a variety of spiro systems using ruthenium-based alkylidene complex **3** for key C-C bond formation reaction.[9]

Two independent routes for the construction of spiro-linkage starting from carbonyl compounds and active methylene substrates are displayed in equations **1-2**. In these routes active methylene compound(s) and /or carbonyl derivative(s) is/are bis-alkylated at the reactive position with suitable electrophiles and then the resulting alkylated derivative is subjected to RCM reaction to generate the spiro system (eq **1-2**).



Equation 1 and 2

The preparation of the cyclization precursors were achieved by palladium-catalyzed allylation of the corresponding 1,3-dicarbonyl compounds. Substrates **4**, **6**, and **8** were prepared by treatment of corresponding diones with allylacetate in presence of Pd $(PPh_3)_4$.[10] Compounds **10** and **14** were prepared by the above said procedure in presence of base such as DBU.[11] (Scheme 1).



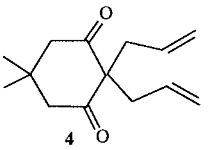
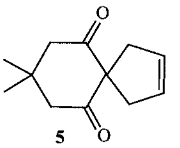
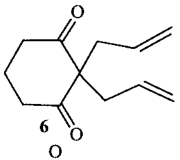
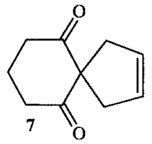
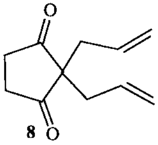
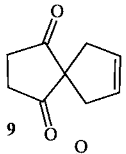
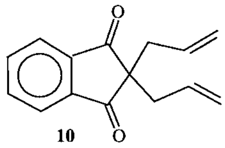
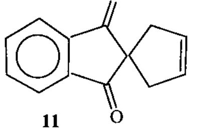
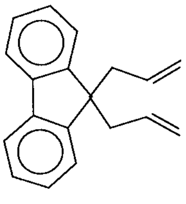
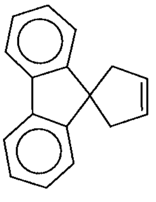
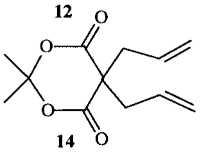
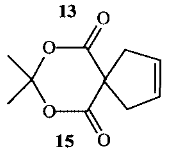
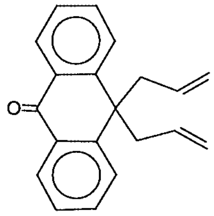
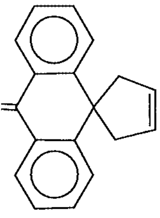
Scheme 1

9,9-Diallylfluorene **12** was obtained by reaction of fluorene with allylbromide in presence of potassium metal in dioxane.[12] The progress of the reaction was monitored with the aid of silica gel TLC plates impregnated with silver nitrate. RCM reaction of various diallylated substrates were accomplished by treatment of the corresponding derivatives with catalytic quantities of **3** (5-10 mole %) in either CH_2Cl_2/RT or at toluene reflux.[13] All the RCM products gave consistent spectral and analytical data.

Some of the RCM products deserve special mention. For example, substrates **9** and **11** constitutes CD and BCD ring of fredericamycin **1** structure. Since Meldrum's acid[14] has many interesting applications in heterocyclic chemistry, substrate **15** may find useful applications in organic synthesis. Similarly, many of the RCM products reported in the Table are potential precursors to various unknown fenestrane ring systems.

In conclusion, for the first time we have succeeded in developing a general and versatile method for the synthesis

Table

S.No	Diallyl product	Yield %	RCM Product #	M.P °C	Yield %
1	 **4**	53	 **5**	95 - 96	95
2	 **6**	76	 **7**	64 - 65	93
3	 **8**	88	 **9**	89 - 90	77
4	 **10**	49	 **11**	162 - 163	80
5	 **12**	76	 **13**	87 - 88	87
6	 **14**	52	 **15**	85 - 86	73
7	 **16**[15]	58	 **17**	104 - 105	92

of several spiro-carbocyclic systems using commercially available (or easily prepared) β-diketones as starting materials. Since RCM method developed here offers very mild reaction conditions for the formation of spiro-compounds with additional double bond for further synthetic manipulation; this procedure may find interesting applications in natural and non-natural product synthesis.

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References and Notes

^{13}C NMR data [$CDCl_3$, 75.0 MHz] for selected compounds: (**7**) δ 207.1, 127.1, 70.9, 39.1, 37.6, 17.5. (**9**) δ 213.4, 127.4, 61.0, 41.0, 34.8. (**11**) δ 203.0, 141.9, 135.5, 128.3,123.6, 57.6, 41.7. (**13**) δ 154.3, 139.4, 130.3, 127.7, 127.0, 122.4, 119.7, 55.4, 46.2. (**15**) δ 170.0, 127.1, 104.6, 51.1, 46.6, 28.7. (**17**) ^{13}C NMR data [$CDCl_3$, 50.0 MHz] δ 153.0, 134.2, 130.1, 129.3, 126.6, 126.3, 56.0, 45.7, 29.7.

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(13) **Typical experimental procedure**: A mixture of diallyl compound **4** (25 mg, 0.114 mmol) and Grubbs's catalyst **3** (5 mg, 5.4 mol%) in dry CH_2Cl_2 (4 ml) was stirred at RT for 12 h under N_2 atmosphere. The reaction mixture was charged on a silica gel column and eluted with ethyl acetate-pet ether (60-80^{o}C) mixture (3:97) to give the product **5** (21 mg, 95%) m.p 95-96 ^{0}C. ^{1}H NMR: [$CDCl_3$, 300 MHz] δ 5.54 (s, 2H), 2.86 (s, 4H), 2.64 (s, 2H), 1.00 (s, 6H); ^{13}C NMR: [$CDCl_3$, 75.0 MHz] δ 205.9, 127.0, 69.7, 51.4, 38.9, 30.3, 28.4. In case of substrates **4**, **6**, **8**, **14** and **16** the RCM reaction was conducted in CH_2Cl_2 solution at RT, while with the substrates **10** and **12** the reaction was carried out in refluxing toluene solution.

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