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Design and synthesis of spiro-heterocycles by ring-closing metathesis

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Synthesis of diverse spiro-heterocyclic compounds *via* the ring-closing (RCM) metathesis approach is described. Specifically, synthesis of various derivatives of barbituric acid, Meldrum′s acid, tetronic acid and thiotetronic acid are described by RCM approach.

Keywords: Metathesis, spirocycles, 1,3-dicarbonyl compound, spiro-annulation, Meldrum′s acid, barbituric acid, tetronic acid, pyrazolone

Recently, ring-closing metathesis (RCM) has been used as a reliable tool for the construction of various carbo- and heterocycles. In this respect, a well-defined ruthenium-based carbene complexes **GI** and **GII** are useful (**Figure 1**, ref.1). Metathesis has been utilized as a key step in this strategy to prepare various spirocyclic β-dicarbonyl compounds.

The recent efforts using metathesis catalyzed by ruthenium carbene complexes led to useful methodologies for the preparation of polycyclics and unusual amino acid derivatives[2]. Herein, full details of RCM methodology to prepare various β-dicarbonyl compounds containing a hetero atom is reported[3].

Spiro-annulation has a significant value in organic synthesis because several natural and non-natural products contain spiro-linkage as a key structural element. Among the natural products, fredericamycin **1** and laurenene **2** and several non-natural products such as [5.5.5.5] fenestrane **3** and [4,5] coronane **4** (ref. 4a), have the spiro-linkage as a basic structural unit (**Figure 2** and **Figure 3**). Although, several synthetic methodologies are available for design of spirocycles, most of these routes rely on reactive intermediates and they are restricted to a single substitution pattern. Moreover, the end products are devoid of any additional functional groups for further synthetic manipulation. It seems that a general methods for generation of spirocycles is important for designing complex natural and non-natural products containing spiro-linkage.

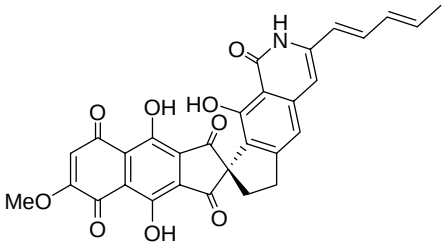


Figure 2 — Examples of complex natural products containing spiro-linkage

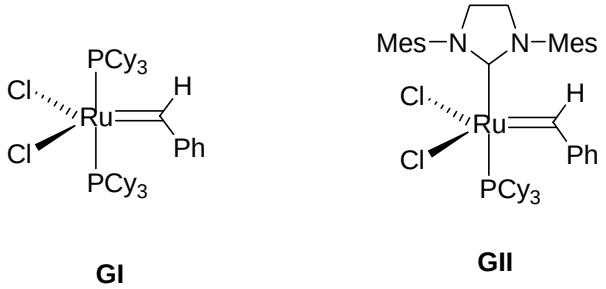


Figure 1 — 1st and 2nd generation Grubbs catalysts

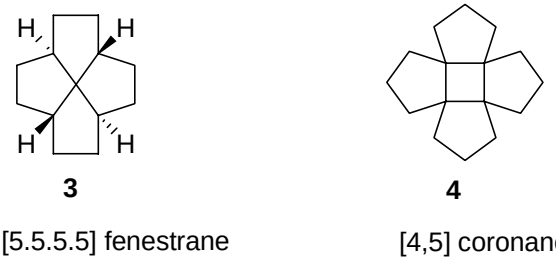
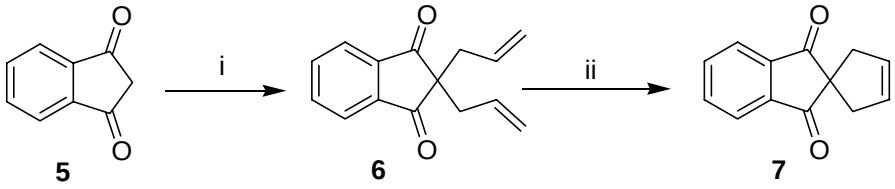


Figure 3 — Examples of non-natural products containing spiro-linkage



(i) [$Pd(PPh_3)_4$], DBU, allyl acetate, THF (ii) GI

Scheme I

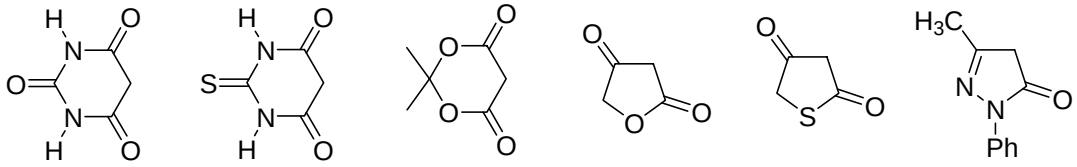


Figure 4

Recently, Hudlicky pointed out that creation of a quarternary centre is the most difficult task among various other synthetic transformations[4b]. Therefore, it was sought to investigate a conceptually new approach based on the RCM as a key step. Towards the realization of RCM approach, initially, β-dicarbonyl compounds as useful precursors have been identified. To this end, the indanedione **5** was treated with allyl acetate in presence of $Pd(PPh_3)_3$/DBU to deliver diallylated product **6** (**Scheme I**, ref.2b). RCM of **6** gave spirocyclic compound **7** and this methodology has been generalized with various carbocyclic β-dicarbonyl compounds.

As a logical extension of this methodology it is planned to study several other β-dicarbonyl derivatives containing heterocyclic systems. In this regard, biologically relevant heterocycles **8**-**13** (**Figure 4**) are chosen as starting materials for spiro-annulation. Several barbituric acid derivatives have found interesting application in medicinal and supramolecular chemistry. Therefore, the application of RCM strategy can generate useful derivatives of these compounds and worthy of systematic investigation. Moreover, barbituric acid **8**, has widely been used in the manufacturing of plastics, textiles, polymers and pharmaceuticals. Pharmacologically active barbituric acid derivatives are either mono- or di-C-alkylated derivatives. The first intravenous barbituric acid was a combination, in equal parts, of barbital and dial (or diallylbarbituric acid, **Figure 5**).

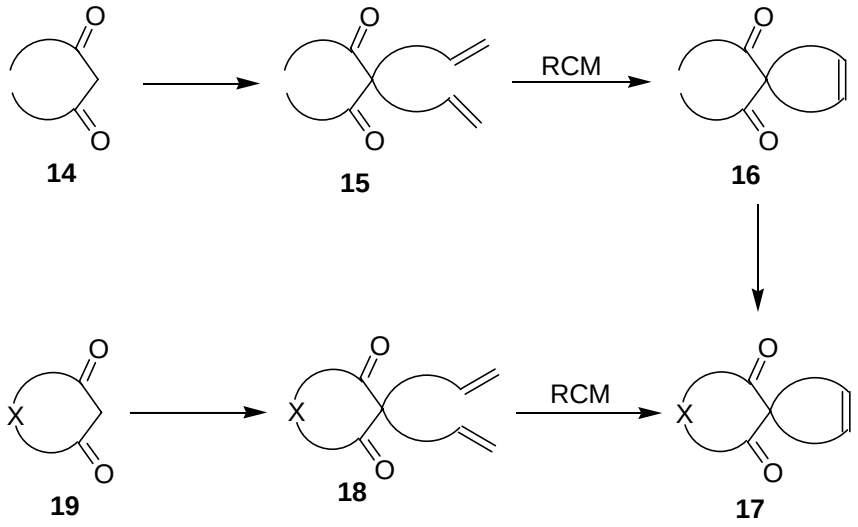
Figure 5 — First examples of pharmaceutically important intravenous barbiturates

Since then, several important drug molecules based on 5,5-dialkylated barbituric acid were discovered[5]. In addition to their pharmaceutical applications, they are also useful building blocks in assembling supramolecular structures *via* noncovalent interactions[6]. In this respect, recently Fenniri *et al.* have devised helical nanotubes[7].

Results and Discussion

As part of a major programme directed towards the application of metathesis in organic synthesis[2f], RCM is envisioned as a useful protocol for designing new barbituric acid derivatives[8]. Therefore, the readily available β-dicarbonyl compounds **8**-**12** were selected as starting substrates (**Figure 4**).

Meldrum′s acid (MA) is a useful synthon for the synthesis of heterocyclic and carbocyclic frame works[9]. Also, it is a useful precursor for cyclic AAA derivatives[10-12]. Towards spiro-annulation of these heterocycles, two strategies based on RCM are conceived. The first strategy (**Scheme II**) involves the



Scheme II

RCM of dialkylated malonate precursor embodying methylene moiety tether both terminal olefinic groups (**14→15→16→17**). Condensation of alkenylated malonate precursor with acetone before or after metathesis sequence can generate MA derivatives. Alternatively, condensation of the intermediate malonate precursor with various substituted urea derivatives, in principle, can deliver annulated barbituric acid derivatives.

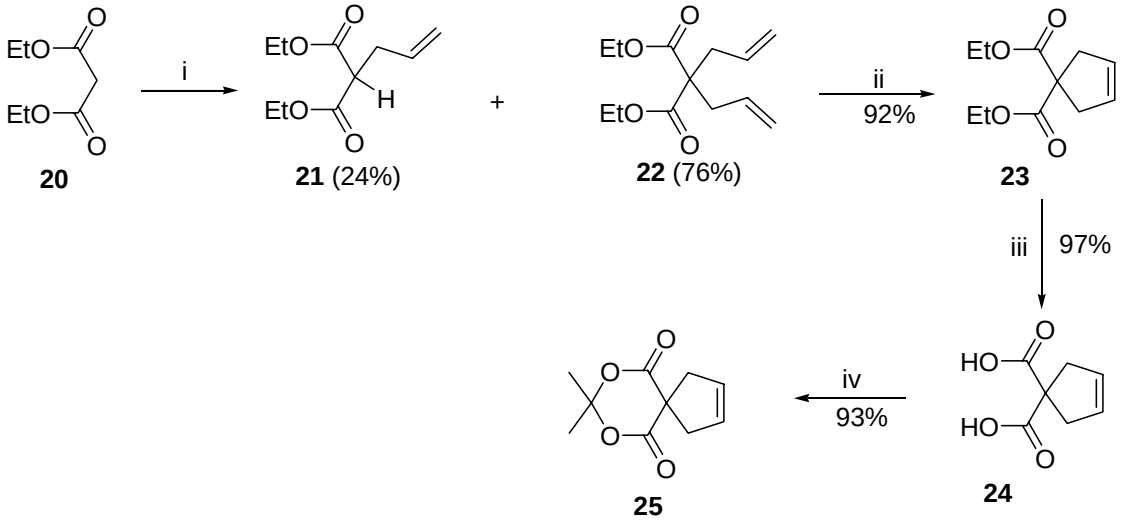
The second strategy (**19→18→17**) involves alkenylation of active methylene group present in cyclic active methylene compound **19** by various alkenyl electrophiles containing terminal olefin. The RCM of these dialkenylated derivative generates spiro-annulated compound **17** (**19→18→17**). By varying the length of electrophiles containing terminal olefin, it is possible to generate a library of annulated MA derivatives.

To realize the first strategy**,** diethyl malonate **20** was treated with allyl bromide in presence of phase-transfer catalyst (PTC) such as benzyltriethyl-ammonium chloride (BTEAC) and potassium carbonate in chloroform to generate diallyl derivative **22** in 76% yield. ^{1}H NMR spectral data of **22** indicated the presence of olefinic protons at δ 5.04-5.12 and 5.33-5.67 and the disappearance of OC-CH_2-CO peak suggested that the alkylation had occurred at the active methylene position. The ^{13}C NMR (seven signals, δ 13.9, 36.6, 57.1, 61.1, 118.9, 132.2, 170.6.) spectral data indicated the presence of the C_2 symmetry element present in the molecule. Then, the RCM of **22** using first generation Grubbs catalyst **GI** in dichloromethane gave cyclized product **23** in 92% isolated yield after column chromatography. The structure of the compound **23** has been established on the basis of ^{1}H NMR and ^{13}C NMR spectral data. For example, ^{1}H NMR spectral data showed the disappearance of allylic peaks (δ 5.06-5.12 as double doublet and δ 5.61-5.70 as multiplet) and the appearance of ring olefinic protons at δ 5.63 as a singlet. The appearance of six signals in the ^{13}C NMR spectrum indicated the presence of the C_2 symmetry present in the molecule.

Later on, the spirodiester **23** was converted into diacid **24** by treatment with ethanolic KOH at 70°C in 97% yield. Condensation of diacid **24** with acetone gave the spiro-annulated Meldrum′s acid derivative **25** (**Scheme III**). The structure of **25** was in agreement with its spectral data.

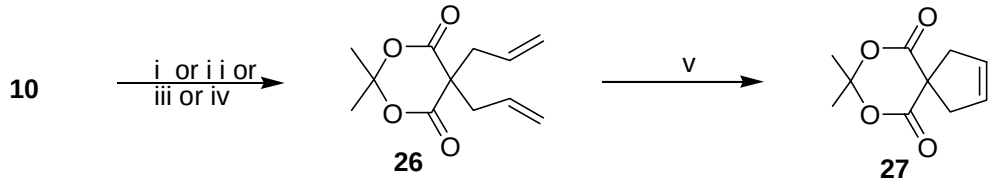
Thereafter, the alternate strategy involving alkenylation of the preformed Meldrum′s acid was attempted. In this respect, the known diallylated Meldrum′s acid **26** (ref.13) was prepared by reacting with allyl bromide in presence of KF/celite in acetonitrile at 85°C. It is found that the other reaction conditions are also useful to effect the diallylation. Among the different conditions (**Scheme IV**) used for the diallylation, the PTC condition using K_2CO_3/ BTEAC/ $CHCl_3$ was also found to be applicable with electrophiles containing 4-6 carbon atoms.

Treatment of the diallyl Meldrum′s acid **26** with **GI** at RT in dichloromethane gave the expected product



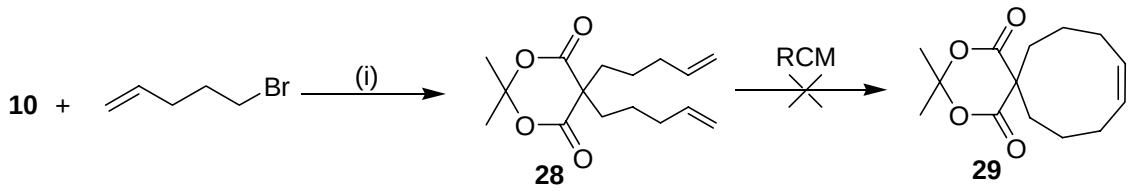
(i) allyl bromide, NaH-THF (ii) GI (iii) KOH,-C_2H_5OH, 70 °C (iv) acetone, acetic anhydride-H_2SO_4

Scheme III



(i) allyl bromide/ DBU / $Pd(PPh_3)_3$ / THF, 52%, (ii) allyl bromide/ K_2CO_3 / DMF, 93%
(iii) allyl bromide/ K_2CO_3 / BTEAC/ $CHCl_3$, 95%, (iv) allyl bromide/ KF /celite/ CH_3CN, 96%
(v) GI, dichloromethane, RT, 86%

Scheme IV

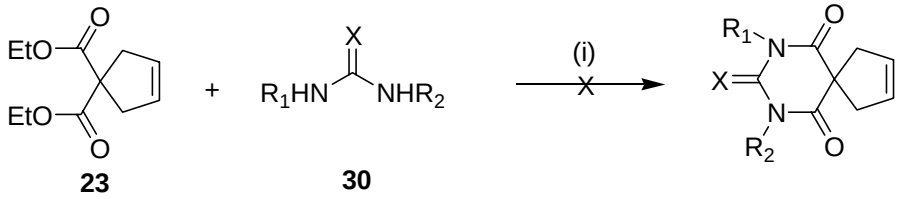


(i) KF/ celite/ CH_3CN, 85 °C, 9 hr, 51%

Scheme V

27 in 86% yield (**Scheme IV**). The ^{1}H NMR spectral data of this compound obtained by this route is identical to that of the product obtained from the earlier route. Subsequently, attempts were directed to generalize this methodology. In this context, the Meldrum′s acid **10** was reacted with 5-bromo-1-pentene to deliver the dialkenylated derivative **28** (**Scheme V**). The structure of the dipentenyl Meldrum′s acid derivative **28**, was firmly established on the basis of ^{1}H NMR (300 MHz) spectral data. Various attempts to generate the corresponding nine membered Meldrum′s acid derivative **29** by the RCM were unsuccessful.

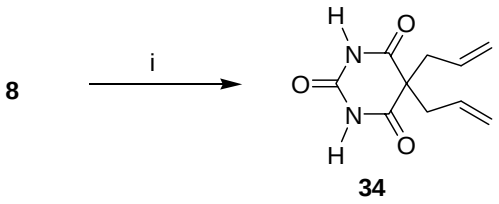
Since the malonate ester **23** was obtained in good yield, attempts were made to condense it with various urea derivatives **30** and it was found that the



(i) Na/ C_2H_5OH/ 80 °C/ 40 hr

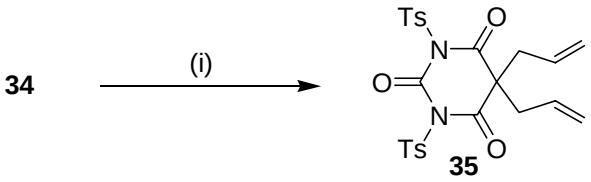
31: $R_1=R_2$=H, X=O
32: $R_1=R_2$=H, X=S
33: $R_1=R_2$=Ph, X=S

Scheme VI



(i) allyl bromide, K_2CO_3, BTEAC, $CHCl_3$, 57%

Scheme VII



(i) Et_3N, CH_2Cl_2, TsCl, RT, 4 days, 10%

Scheme VIII

recovered starting material could be obtained in all instances (**Scheme VI**).

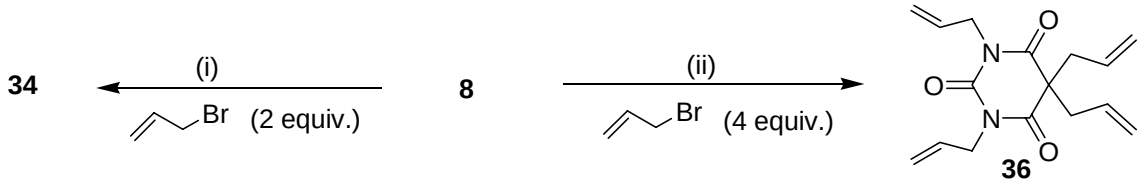
Although simple malonate esters were condensed with various urea derivatives to generate barbituric acid analogues, the malonate ester derivative **23** in the present study is highly hindered and the nucleophilic substitution reaction (S_N^2 type) may not be facile with such a highly hindered substrate.

In view of the above observation, the other alternate route was attempted where allylated barbituric acid may be subjected to the RCM reaction. In this respect, barbituric acid **8** was diallylated using allyl bromide and potassium carbonate in presence of PTC such as BTEAC in chloroform to generate the known diallyl barbituric acid **34** in 57% yield (**Scheme VII**). Unfortunately, diallyl barbituric acid **34** was found to be insoluble in most of the common organic solvents and, therefore, efforts have been made to generate various barbituric acid derivatives which are soluble. A survey of the literature indicates that several barbituric acid derivatives form supra molecular structures through hydrogen bonding network[14]. Therefore, it is reasoned that by disrupting the hydrogen bonding pattern, it may be possible to produce suitable barbituric acid derivatives that are soluble in common organic solvents. It appears that replacing the hydrogen atom present on nitrogen of barbituric acid by a suitable protecting group is a reasonable proposition to achieve this goal. Towards this end, barbituric acid **34** was treated with tosyl chloride to generate the corresponding tosyl derivatives. In this regard, only 10% of the required product was formed and even under forcing reaction conditions there was no improvement of the yield (**Scheme VIII**).

On several occasions allyl groups are used for *N*-protection and therefore it was decided to treat the barbituric acid **8** with the excess amount of allyl bromide. Accordingly, barbituric acid **8** was treated with four equivalents of allyl bromide in presence of potassium carbonate under PTC conditions using BTEAC. Tetra-allylated barbituric acid **36** was formed in 52% yield and was found to be liquid at RT and also soluble in most of the organic solvents (**Scheme IX**).

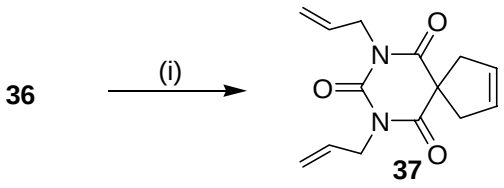
With the availability of **36** in sufficient quantity, the next step, *i.e.* the RCM has been realized with the first generation Grubbs catalyst in toluene at 80ºC to generate the spiro-annulated barbituric acid **37** in 95% yield (**Scheme X**). In this reaction it is noted that the allyl groups present on *N*-atom are intact during the RCM sequence. It is known in the literature[15] that several *N*-allyl derivatives undergo de-allylation reaction during the RCM sequence.

Later on the attention was turned to prepare various *N*-protected barbituric acid derivatives (**Table I**). The RCM of these barbituric acid derivatives proceeded



(i) K_2CO_3, BTEAC, $CHCl_3$, RT, 52%, m.p. 177°C (ii) K_2CO_3, BTEAC, $CHCl_3$, RT, 52%, liquid

Scheme IX



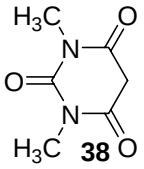
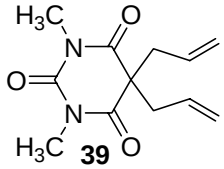
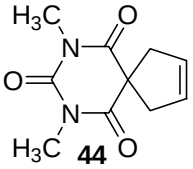
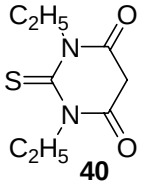
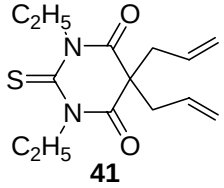
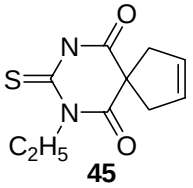
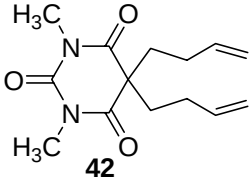
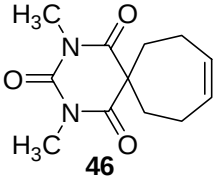
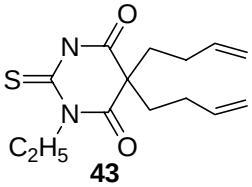
(i) RCM, 95%, GI

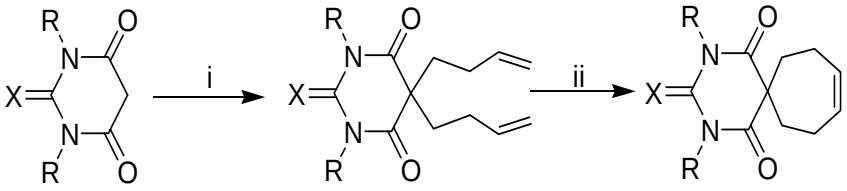
Scheme X

smoothly to generate the corresponding spiro derivatives (**Table I**, entries 2-5).

It is planned to extend this methodology to higher membered systems such as seven-membered spiro-barbituric acid derivatives. In this regard, 1,3-dimethyl barbituric acid was alkylated with 4-bromo-1-butene under PTC conditions (K_2CO_3, BTEAC, $CHCl_3$) at RT to generate the compound **42** in 35% yield (**Scheme XI**). The ^{1}H NMR spectral data indicated the characteristic *N*-CH_3 signal at δ 3.29 and

Table I — Dialkenylated and RCM products of barbituric acid derivatives

Entry No	Substrate	Dialkenylated Products	Yield (%)	RCM Product	Yield (%)
1	**8**	**34**	57	—	—
2	**8**	**36**	52	**37**	95
3	 **38**	 **39**	81	 **44**	88
4	 **40**	 **41**	85	 **45**	92
5	**38**	 **42**	35	 **46**	81
6	**40**	 **43**	32	—	—



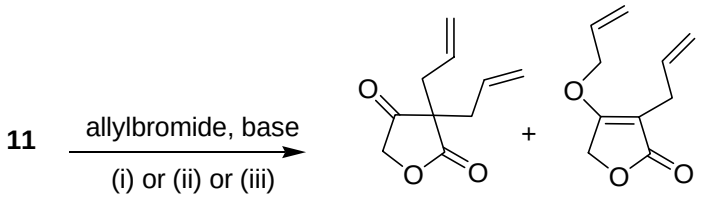
38: X=O, R=CH_3
40: X=S, R=C_2H_5

42: X=O, R=CH_3, 35%
43: X=S, R=C_2H_5, 32%

46: X=O, R=CH_3, 81%

(i) 4-bromo-1-butene, K_2CO_3, BTEAC, $CHCl_3$, RT
(ii) GI, toluene, 90 °C

Scheme XI



(i) *n*-Bu_4NF, H_2O, THF, RT	25%	55%
(ii) K_2CO_3, TBAHS, $CHCl_3$, RT	30%	50%
(iii) K_2CO_3, BTEAC, $CHCl_3$, 0-15 °C	55%	35%

Scheme XII

the peaks corresponding to terminal olefin at 4.91 and 5.60-5.66 as multiplets. Further, the ^{13}C NMR (eight signals, δ 28.8, 36.5, 39.3, 55.7, 115.8, 135.7, 150.3, 171.8) spectral data indicated the presence of the C_2 symmetry element present in the molecule. The 5,5-dibutenyl barbituric acid derivative **42** was then subjected to the RCM to generate the seven-membered spiro-annulated barbituric acid derivative **46** in 81% yield. The ^1H NMR spectral data indicated the absence of allyl moiety (absence of signals at δ 4.91 and δ 5.60-5.66) and the presence of olefinic peak at δ 5.65. Moreover, the ^{13}C NMR spectral data (seven signals, δ 25.1, 34.8, 39.4, 53.9, 130.1, 141.5, 172.9) indicated the presence of the C_2 symmetry element present in the molecule.

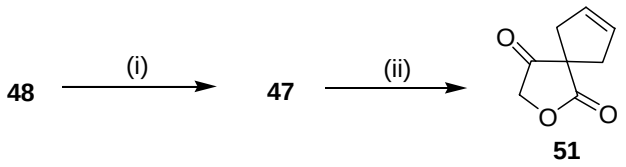
Since thiobarbituric acid derivatives have paved the way for modern intravenous anesthesia and affords a series of sedative hypnotic agents that tend to show both faster and shorter duration of action than their oxygenated analogues, it is planned to extend the methodology to this system. Although the thio-derivative **43** was prepared, the corresponding RCM product could not be obtained in the pure form.

Having obtained the spiro-annulated derivatives of Meldrum's acid and barbituric acid, it is decided to extend this methodology to other highly acidic β-dicarbonyl systems. Tetronic acid **11** and thio-tetronic acid **12** seem to be potential candidates in this respect.

One of the nagging problems associated with alkylation of these β-dicarbonyl systems is unwanted O-alkylation (**Scheme XII**). The conditions established in case of Meldrum′s acid and barbituric acid proved to be handy at this point. Various conditions to obtain the C-diallylated tetronic acid are outlined in **Scheme XII**.

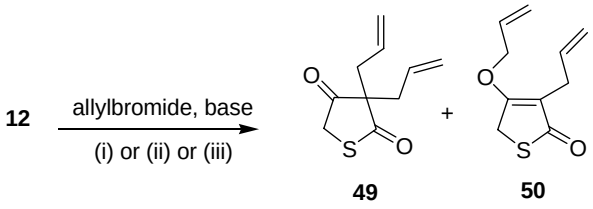
Conducting the allylation reaction at low temperature seems to be useful. However, unwanted O-alkylated isomer is unavoidable. Later on, it is found that the O-allylated isomer **48** can be easily converted to the desired product **47** by microwave assisted Claisen rearrangement supported by silica gel (**Scheme XIII**, ref.16).

After successful diallylation of tetronic acid **11**, the diallylated product **47** was subjected to the RCM by using **GI** (5-10 mole%) in DCM at RT to deliver the



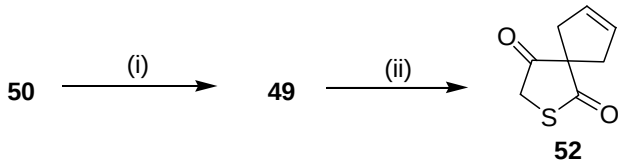
(i) Claisen rearrangement, silica gel support, 75%
(ii) GI, CH_2Cl_2, RT, 60%

Scheme XIII



(i) *n*-Bu_4NF, H_2O, THF, RT	20%	60%
(ii) K_2CO_3, TBAHS, $CHCl_3$, RT	30%	60%
(iii) K_2CO_3, BTEAC, $CHCl_3$, 0-15 °C	60%	30%

Scheme XIV



(i) Claisen rearrangement, silica gel support, 65%
(ii) GI, CH_2Cl_2, RT, 79%

Scheme XV

desired spiro-annulated tetronic acid **51** in 69% yield (**Table II**). The product **51** was characterized by ^{1}H and ^{13}C NMR spectral data. The ^{1}H NMR spectral data indicated the disappearance of allylic signals at δ 5.13-5.20 and δ 5.59-5.65 as multiplets and the appearance of cyclopentene proton signal at δ 5.68 (s, 2H). Further, the ^{13}C NMR signals confirmed the formation the desired product which displayed six different carbon signals (δ 35.2, 42.3, 66.3, 127.3, 197.1, 209.1).

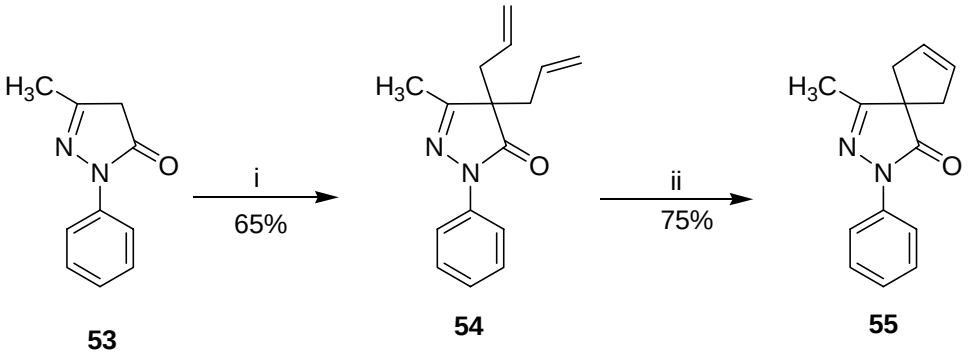
Next, along the similar lines thiotetronic acid **12** was alkylated to give O- and C-alkylated products (**Scheme XIV**). Here also the O-allylated compound was obtained as a major product under fluoride mediated allylation conditions. To improve the yield of C-diallylated thiotetronic acid **49**, various other conditions were tried (**Scheme XIV)**.

When the reaction-mixture was stirred at RT in presence of potassium carbonate and PTC such as tetrabutylammonium hydrogensulphate (TBAHS) in chloroform, a slightly improved yield of the desired product was achieved. However, when the reaction temperature was maintained between 0-15°C under BTEAC conditions, the desired C-diallylated product **49** was obtained in 60% yield. The unwanted O-allylated isomer **50** obtained here was converted to the desired C-diallylated product **49** by microwave-assisted Claisen rearrangement supported by silica gel (**Scheme XV**). The desired product **49** indicated the absence of O-CH_2 signal at δ 3.95 and the presence of allyl peak at δ 5.08-5.12 (m, 4H) and δ 5.54-5.65 (m, 2H) in ^{1}H NMR spectral data. Further, the seven ^{13}C NMR signals supported the formation of desired product **49**.

When the diallylated thiotetronic acid **49** was subjected to the RCM with first generation Grubbs catalyst (5-10 mole%) in dichloromethane at RT the desired spiro-annulated thiotetronic acid **52** was formed in 79% yield (**Scheme XV**). The ^{1}H NMR spectral data of **52** clearly exhibited the disappearance of allyl moiety and the appearance of cyclopentene protons at δ 5.62 (s, 2H). Further, six-line ^{13}C NMR spectrum (δ 39.3, 42.3, 60.1, 127.3, 201.9, 205.0) indicated structure **52**. The mass spectral data (*m/z*, 168) further supported its structure.

Pyrazolone derivative (3-methyl-1-phenyl-2-pyrazolin-5-one) **53** is an important biologically active substrate useful in the prevention of and/or treatments for hypoxic ischemic brain disorders, especially those of newborns caused by labour[17]. Therefore, efforts are made to test whether this strategy can be extended to substrate **53**.

Accordingly, the 3-methyl-1-phenyl-2-pyrazolin-5-one **53** was diallylated by using potassium carbonate and BTEAC in chloroform at RT to deliver the desired diallylated pyrazolone derivative **54** in 65% yield (**Scheme XVI**). After successful diallylation of this simple carbonyl system, the diallylated pyrazolone **54** was subjected to RCM reaction by using (5-10 mole%) the first generation Grubbs catalyst in toluene to yield the spiro-annulated pyrazolone derivative **55** in 75% yield. The ^{1}H NMR spectral data indicated the absence of allylic protons (at δ 4.98-5.15 as double doublet and 5.4-5.6 as a multiplet) and the presence of olefin protons (cyclopentene) at δ 5.77 (s, 2H). Further, the ten line ^{13}C NMR spectrum supported the formation of the product **55**.



53 **54** **55**

(i) allyl bromide, K_2CO_3, BTEAC, $CHCl_3$, RT
(ii) GI, toluene, 90 °C

Scheme XVI

Table II — Dialkenylated and RCM products of various β-dicarbonyl compounds

Entry No	Substrate	Dialkenylated product	Yield (%)	RCM product	Yield (%)
1	**11**	**47**	55	**51**	69
2	**12**	**49**	60	**52**	79
3	**53**	**54**	65	**55**	75
4	**10**	**26**	96	**27**	78
5	**10**	**28**	47	—	—
6	**20**	**22**	76	**23**	92

The different dialkenylated products derived from hetero β-dicarbonyl compounds and a choice of carbocyclic compounds studied are listed in **Table II**. Also, in **Table II** the corresponding RCM products of hetero β-dicarbonyl compounds and carbocyclic compounds are included respectively.

Conclusion

It is demonstrated that various heterocyclic β-dicarbonyl systems can be dialkenylated and later on they were subjected to RCM reaction to generate spiro-annulated systems. After considerable amount of experimentation suitable reaction conditions were found. In view of various applications of these heterocyclic systems in organic synthesis and medicinal chemistry this methodology may find useful applications[18].

Experimental Section

All the reactions were monitored by employing TLC technique using appropriate solvent system for development. Reactions involving oxygen sensitive reagents or catalysts were performed in degassed solvents. Melting points were recorded on Labhosp or Veego melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Nicolet Impact-400 FT-IR spectrometer. The ^{1}H NMR spectra were generally recorded on Bruker (200, 500 or 600 MHz) spectrometers. Mass spectral measurements were carried out on GCD 1800 Hewlett-Packerd GS-MS spectrometer. The high-resolution mass measurements were carried out using JEOL JMS-DX 303 GC-MS instrument. Elemental analysis was performed on Carlo-Erba MOD 1106 CHN analyzer.

Allylation of Meldrum's acid (5,5-diallyl-2,2-dimethyl-1,3-dioxane-4,6-dione) 26 (ref. 19,20)

To a suspension of Meldrum's acid **10 (**72 mg, 0.5 mmole) in chloroform (10 mL), powdered potassium carbonate (414 mg, 3 mmole) and BTEAC (2 85 mg, 1.25 mmole) were added. The reaction-mixture was cooled to 0°C and allyl bromide (212 mg, 1.75 mmole) was added dropwise. Then, the reaction-mixture was stirred at RT for 16 hr and quenched with water (10 mL). The aqueous layer was extracted with chloroform (3 × 20 mL). The combined organic layer was washed with water, brine and dried

over anhyd. $MgSO_4$. The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 2% ethyl acetate-petroleum ether as an eluent to give **26** (107 mg, 95%) as a thick colourless liquid.

R_f: 0.8 (10% Ethyl acetate-petroleum ether); IR ($CHCl_3$): 1755 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.68 (s, 6H), 2.70 (d, *J*=6, 4H), 5.25 (dd, *J*=4.5; 1.5, 4H), 5.65 (m, 2H).

Preparation of 5-[2-cyclopentene]-2,2-dimethyl-1,3-dioxane-4,6-dione, 27

To a solution of diallyl Meldrum′s acid **26** (124 mg, 5.54 mmole) in dichloromethane (10 mL), first generation Grubbs catalyst (32 mg, 38.9 mmole) was added and the reaction-mixture was stirred at RT for 56 hr under nitrogen. The solvent was removed and the crude product was purified by silica gel column chromatography using 5% ethyl acetate-petroleum ether as eluent to give **27** (93.3 mg, 86%) as a white crystalline solid, m.p. 85-87°C; R_f: 0.6 (10% ethyl acetate-petroleum ether); IR (KBr): 1753 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.75 (s, 6H), 3.12 (s, 4H), 5.69 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.7, 46.6, 51.2, 104.7, 127.2, 170.6.

Preparation of 5,5-di[pent-4-ene]-2,2-dimethyl-1,3-dioxane-4,6-dione, 28

To a solution of Meldrum′s acid **10** (72 mg, 0.5 mmole) and KF/celite (295 mg, 50 mmole) in acetonitrile (5 mL), 5-bromo-1-pentene (225 mg, 1.5 mmole) was added at RT. The reaction-mixture was stirred at 85°C for 9 hr. The reaction-mixture was cooled to RT and was filtered. Then the solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 5% ethyl acetate-petroleum ether as eluent to give **28** (72 mg, 51%) as a white crystalline solid, m.p. 53-55°C; R_f: 0.6 (10% ethyl acetate-petroleum ether); IR (neat): 1745 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.33 (m, 4H); 1.71 (s, 6H); 2.0 (m, 8H); 4.89 (m, 4H); 5.63 (m, 2H).

Preparation of 2,2-diallyl-diethyl malonates, 22

To a suspension of sodium hydride (0.66 g, 27.5 mmole) in THF (20 mL), diethyl malonate **20** (2 g, 12.5 mmole) was added at 0°C under nitrogen and stirred for 15 min. A slight excess of allyl bromide (3.33 g, 27.5 mmole) was added to the corresponding malonate anion. The reaction-mixture was stirred for 4 hr at 0-25°C and then at RT for 10 hr. Then, the reaction-mixture was filtered through a sintered funnel and the solvent was removed. The residual mass was dissolved in minimum amount of water and was extracted with ethyl acetate. The crude product was purified by silica gel column chromatography using 0.5% ethyl acetate-petroleum ether as eluent to give **22** (940 mg, 76%) and **21** (299 mg, 24%) as thick liquid.

R_f **22**: 0.8 (5% ethyl acetate-petroleum ether); IR (neat) **22**: 1762 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): **22** δ 1.24 (t, *J*=7, 7.5, 6H), 2.63 (d, *J*=7, 4H), 4.17 (q, O-CH2, *J*=7, 7.5, 7, 4H), 5.09 (m, 4H), 5.61-5.69 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): **22** δ 13.9, 36.6, 57.1, 61.1, 118.9, 132.2, 170.6; R_f **21**: 0.75 (5% ethyl acetate-petroleum ether); IR (neat) **21**: 1761 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): **21** δ 1.24 (t, *J*=7, 6H), 2.62 (dd, *J*=7& 6.5, 2H), 3.41 (t, *J*=7.5, 1H), 4.17 (q, O-CH_2, *J*=2.5, 4H), 5.08 (m, 2H), 5.61-5.69 (m, 1H).

Preparation of cyclopent-3-ene-1,1-dicarboxylic acid diethyl ester, 23 (ref.21)

To a solution of diallyl-malonate **22** (100 mg, 4.17 mmole) in dichloromethane (20 mL), first generation Grubbs catalyst (27 mg, 0.33 mmole) was added and stirred at RT for 20 hr under nitrogen. The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 2% ethyl acetate-petroleum ether as an eluent to give **23** (81 mg, 92%) as a thick liquid.

R_f: 0.6 (5% ethyl acetate-petroleum ether); IR (neat): 1758 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.27 (t, *J*=6, 6H), 3.03 (s, 4H), 4.21 (q, O-CH_2, *J*=6, 4H), 5.63 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 40.6, 58.6, 61.3, 127.6, 172.0.

Allylation of barbituric acid, 36

To a suspension of barbituric acid **8** (200 mg, 1.56 mmole) in chloroform (10 mL), powdered potassium carbonate (1.29 g, 9.37 mmole) and BTEAC (889 mg, 3.9 mmole) were added. The reaction-mixture was cooled to 0°C and allyl bromide (850 mg, 7.03 mmole) was added drop-wise. After 18 hr at RT, the reaction-mixture was quenched with water (10 mL) and the aqueous layer was extracted with chloroform (3 × 20 mL). The combined organic layer was washed with water, brine and dried over anhyd. $MgSO_4$. The solvent was removed and the crude product was purified by silica gel column

chromatography using 5% ethyl acetate-petroleum ether to give **36** (234 mg, 52%) as a colourless thick liquid.

R_f: 0.8 (20% ethyl acetate-petroleum ether); IR (neat): 1686, 1654 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.69 (d, *J*=7.4 Hz, 4H), 4.42 (d, *J*=5.9 Hz, 4H), 5.03 (t, *J*=6.9 Hz, 2H), 5.12 (br s, 2H), 5.24 (d, *J*=1.2 Hz, 2H), 5.17 (br s, 2H), 5.37-5.58 (m, 2H), 66-5.85 (m, 2H); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 43.1, 43.8, 56.6, 118.4, 120.8, 130.4, .2, 149.8, 170.2. MS: *m/z* 311.2025 (M+Na).

Preparation of tosylated diallyl barbituric acid, 35

To a suspension of diallyl barbituric acid **34** (180 mg, 0.87 mmole) in dichloromethane, triethylamine (350 mg, 3.15 mmole) was added followed by tosyl chloride (420 mg, 2.16 mmole). The reaction-mixture was stirred at RT for 4 days. The reaction-mixture was quenched with water and was extracted with ethyl acetate (2 × 50 mL). The organic layer was washed with 2*N* HCl, water, brine and dried over anhyd. $MgSO_4$. The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 10% ethyl acetate-petroleum ether as an eluent to give **35** (48 mg, 10%) as a colourless crystalline solid, m.p. 114-15°C; R_f: 0.6 (20% ethyl acetate-petroleum ether); IR (KBr): 1697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)**:** δ 2.4 (s, 6H), 2.72 (d, *J*=6.3, 4H), 5.10-5.18 (m, 4H), 5.5-5.7 (m, 2H), 7.3-7.4 (d, *J*=5.5, 4H), 8.1-8.2 (d, *J*=5.5, 4H); ^{13}C NMR (75 MHz, $CDCl_3$)**:** δ 21.9, 41.5, 59.5, 121.8, 128.6, 129.4, 129.8, 131.8, 134.8, 145.6, 146.6, 168.8, 180.6.

Preparation of 3,3-diallyl furan-2,4-dione, 47

To a solution of tetronic acid **11** (150 mg, 1.5 mmole) in THF (5 mL) a solution of *n*-Bu_4NF (TBAF) in H_2O (75% w/w, 945 mg, 3.3 mmole of *n*-Bu_4NF in 1.26 g of H_2O) was added and the reaction-mixture was stirred at RT for 1 hr. During this period the reaction-mixture became homogeneous. Then, allyl bromide (425 mg, 3.5 mmole) was added and the reaction-mixture was stirred at RT for 24 hr. The reaction-mixture was concentrated by distilling off the solvent and diluted with water (10 mL) and the residue was extracted with ethyl acetate (4 × 25 mL). The organic layer was washed with water, brine and dried over anhyd. $MgSO_4$ The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 1% ethyl acetate-petroleum ether as an eluent to give **47** (45 mg, 25%) and **48** (99 mg, 55%) as colourless liquid. R_f: 0.9 (10% ethyl acetate-petroleum ether); IR (neat): 3021, 2928, 1731(C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)**:** δ 2.50 (d, *J*=6.3, 4H), 4.39 (s, 2H), 5.13-5.20 (m, 4H), 5.59-5.65 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$)**:** δ 39.1, 54.1, 121.2, 130.2, 203.8, 209.8; GC-MS: *m/z* 180 (M^+).

Preparation of 3,3-diallyl thiophene-2,4-dione, 49

To a solution of thiotetronic acid **12** (150 mg, 1.29 mmole) in THF (5 mL) a solution of *n*-Bu_4NF in H_2O (75% w/w, 945 mg, 3.3 mmole of *n*-Bu_4NF in 1.26 g of H_2O) was added and the reaction-mixture was stirred at RT for 1 hr until it becomes homogeneous. Then, allyl bromide (470 mg, 3.88 mmole) was added and the reaction-mixture was stirred at RT for 24 hr. The reaction-mixture was concentrated by distilling off the solvent. Water (10 mL) was added to the residue and was extracted with ethyl acetate (4 × 25 mL). The organic layer was washed with water, brine and dried over anhyd. $MgSO_4$ The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 1% ethyl acetate-petroleum ether as an eluent to give **49** (39 mg, 20%) and continued elution gave **50** (117 mg, 60%) as colourless thick liquid. R_f: 0.8 (10% ethyl acetate-petroleum ether); IR (neat): 3077, 2923, 1695(C=O), 1423 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)**:** **49** δ 2.42 (m, 4H), 3.75 (s, 2H), 5.08-5.12 (m, 4H), 5.65-5.54 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$)**:** δ 40.9, 41.2, 60.6, 120.7, 130.5, 203.5, 207.7; GC-MS: *m/z* 196 (M^+); ^1H NMR (300 MHz, $CDCl_3$): **50** δ 2.99 (d, *J*=6.5, 2H), 3.95 (s, OCH_2, 2H), 4.68 (d, *J*=5, 2H), 5.35-5.47 (m, 4H), 5.92-5.99 (m, 2H).

Preparation of 2-oxa-spiro[4,4]non-7-ene-1,4-dione, 51

To a solution of diallyltetronic acid **47** (40 mg, 0.22 mmole) in dichloromethane (10 mL), first generation Grubbs catalyst (18 mg, 10 mole%) was added and stirred at RT for 56 hr under nitrogen. The solvent was removed and the crude product was purified by silica gel column chromatography using 5% ethyl acetate-petroleum ether as an eluent to give **51** (30 mg, 60%) as a colourless low boiling liquid. R_f: 0.6 (10% ethyl acetate-petroleum ether); IR (neat): 1719(C=O), cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.63(d, *J*=8, 4H), 4.32 (s, 2H), 5.68(s, 2H);

^{13}C NMR (75 MHz, $CDCl_3$): δ 35.2, 42.3, 66.3, 127.3, 197.1, 209.1; GC-MS: *m/z* 152 (M^+).

Preparation of 2-thia-spiro[4,4]non-7-ene-1,4-dione, 52

To a solution of diallylthiotetronic acid **49** (65 mg, 0.33 mmole) in dichloromethane (15 mL), first generation Grubbs catalyst (27.2 mg, 10 mole%) was added and the reaction-mixture was stirred at RT for 52 hr under nitrogen. The solvent was removed and the crude product was purified by silica gel column chromatography using 5% ethyl acetate-petroleum ether as an eluent to give **52** (35 mg, 79%) as a colourless liquid. R_f: 0.5 (10% ethyl acetate-petroleum ether); IR (neat): 2933, 1683(C=O), 1433 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.77(s, 4H), 4.02 (s, 2H), 5.62(s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.38, 42.3, 60.1, 127.3, 201.9., 205.01; GC-MS: *m/z* 168(M^+).

Preparation of 4,4-diallyl-5-methyl-2-phenyl-2,4-dihydro-pyrazol-3-one, 54

To a suspension of 3-methyl-1-phenyl-2-pyrazoline-5-one **53** (300 mg, 1.72 mmole) in chloroform (10 mL), powdered potassium carbonate (1.42 g, 10.3 mmole) and BTEAC (980 mg, 4.3 mmole) were added. The reaction-mixture was cooled to 0°C and to this ice-cooled solution, allyl bromide (625 mg, 5.16 mmole) was added dropwise and the reaction-mixture was stirred at 0°C for 1 hr. Then, the reaction-mixture was stirred at RT for 24 hr. At the conclusion of the reaction (TLC monitoring), the reaction-mixture was quenched with water (10 mL). The organic layer was separated and the aqueous layer was extracted with chloroform (3 × 20 mL). The combined organic layer was washed with water, brine and dried over anhyd. $MgSO_4$. The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 5% ethyl acetate-petroleum ether as an eluent to give **54** (284 mg, 65%) as colourless liquid. R_f: 0.7 (15% ethyl acetate-petroleum ether); IR (neat): 1713 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.04 (s, 3H), 2.29 (sextet, *J*=15.4, 2H), 2.59 (q, *J*=7, 2H), 4.98-5.15 (dd, *J*=16, 10, 4H), 5.4-5.6 (m, 2H), 7.13 (t, *J*=7.5, 1H), 7.36 (t, *J*=8, 2H), 7.9 (d, *J*=8.5, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.2, 38.8, 59.1, 118.7, 119.5, 124.8, 128.7, 130.8, 137.8, 161.7 (C=N), 174.5 (C=O).

General procedure for the microwave assisted Claisen rearrangement of 48/50

O-Allylated substrate **48**/**50** was mixed homogeneously with pre-activated silica gel [(100-200 mesh), activated under microwave for 5 min before use], in a beaker and irradiated in microwave oven (Ken star, OM-992E), for 7 min. The resulting mixture was purified by flash silica gel chromatography. Elution with 2% ethyl acetate-petroleum ether gave the required product as a colourless liquid.

3,3-Diallyl furan-2,4-dione, 47

O-Allylated tetronic acid **48** (70 mg, 0.389 mmole) was irradiated under microwave oven in presence of silica gel (400 mg) according to the general procedure for 7 min to furnish **47** (53 mg, yield* 75%) as colourless liquid. The spectral data of the compound obtained by this method is identical to that of the compound reported earlier.

3,3-Diallyl thiophene-2,4-dione, 49

O-Allylated thiotetronic acid **50** (40 mg, 0.204 mmole) was irradiated under microwave irradiation in presence of silica gel (400 mg) according the general procedure for 7 min to furnish **49** (26 mg, 65%) as a colourless liquid. The spectral data of the compound obtained by this method is identical to the compound reported earlier.

Preparation of 5,5-diallyl-1,3-dimethyl-pyrimidine-2,4,6-trione, 39

To a suspension of 1,3-dimethyl barbituric acid **38** (150 mg, 0.962 mmole) in chloroform (10 mL), powdered potassium carbonate (796 mg, 5.77 mmole) and BTEAC (548 mg, 2.41 mmole) were added. The reaction-mixture was cooled to 0°C and to this ice-cooled stirred solution, allyl bromide (407 mg, 3.37 mmole) was added dropwise and the reaction-mixture was stirred at 0°C for 1 hr. Subsequently, the reaction-mixture was stirred at RT for 24 hr. At the conclusion of the reaction (TLC monitoring), the reaction-mixture was quenched with addition of water (10 mL). The organic layer was separated and the aqueous layer was extracted with chloroform (3 × 20 mL). The combined organic layer was washed with water, brine and dried over anhyd. $MgSO_4$. The

*Yield calculated on the basis of GC.

solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 3% ethyl acetate-petroleum ether as an eluent to give **39** (227 mg, 81%) as a colourless solid; m.p. 58-59°C; R_f: 0.8 (10% ethyl acetate-petroleum ether); IR (neat): 2960, 1677 (C=O), 1439 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.69 (d, *J*=7.4, 4H), 3.26 (s, 6H), 5.02-5.11 (m, 4H), 5.45-5.54 (m, 2H); ^{13}C NMR (50.38 MHz, $CDCl_3$): δ 27.9 (N-CH_3), 42.7, 56.9, 119.9, 130.8, 150.8 (-NCON-), 170.5 (C=O); GC-MS: *m/z* 236 (M^+).

Anal. ($C_{12}H_{16}N_2O_3$): Calcd C, 61.04; H, 7.35; N, 11.85. Found: C, 61.00; H, 6.82; N,11.56%.

Preparation of 5,5-diallyl-1,3-diethyl-2-thioxo-dihydro-pyrimidine-4,6-dione, 41

To a suspension of 1,3-diethyl-2-thio barbituric acid **40** (200 mg, 1 mmole) in chloroform (10 mL), powdered potassium carbonate (828 mg, 6 mmole) and BTEAC (570 mg, 2.5 mmole) were added. The reaction-mixture was cooled to 0°C and to this ice-cooled solution, allyl bromide (424 mg, 3.5 mmole) was added dropwise and the reaction-mixture was stirred at 0°C for 1 hr. Then the reaction-mixture was stirred at RT for 24 hr. At the conclusion of the reaction (TLC monitoring), the reaction-mixture was quenched with of water (10 mL). The organic layer was separated and the aqueous layer was extracted with chloroform (3 × 20 mL). The combined organic layer was washed with water, brine and dried over anhyd. $MgSO_4$. The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 2% ethyl acetate-petroleum ether as an eluent to give **41** (214 mg, 85%) as a colourless thick liquid. R_f: 0.8 (10% ethyl acetate-petroleum ether); IR (neat): 1760, 1679 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.15 (t, *J*=7, 6H), 2.67 (d, *J*=7.4, 4H), 4.36 (q, *J*=7, 4H), 4.97-5.97 (dd, *J*=10.3, 6.9, 4H), 5.36-5.56 (m, 2H); ^{13}C NMR (50.38 MHz, $CDCl_3$): δ 12.2 (ethyl-CH_3), 43.3 (N-CH_2), 56.7, 120.6, 130.4, 168.8 (NC=O), 178.8 (C=S); GC-MS: *m/z* 280 (M^+).

Preparation of 5,5-di-but-3 enyl-1,3-dimethyl-pyrimidine-2,4,6-trione, 42

To a suspension of 1,3-dimethyl barbituric acid **38** (100 mg, 0.641 mmole) in chloroform (10 mL), powdered potassium carbonate (531 mg, 3.85 mmole) and BTEAC (365 mg, 1.603 mmole) were added. The reaction-mixture was cooled to 0°C and to this ice-cooled solution, 4-bromo-1-butene (303 mg, 2.24 mmole) was added dropwise and the reaction-mixture was stirred at 0°C for 1 hr. Then the reaction-mixture was stirred at RT for 24 hr. At the conclusion of the reaction (TLC monitoring), the reaction-mixture was quenched by addition of water (10 mL). The organic layer was separated and the aqueous layer was extracted with chloroform (3 × 20 mL). The combined organic layer was washed with water, brine and dried over anhyd. $MgSO_4$. The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 4% ethyl acetate-petroleum ether as an eluent to give **42** (60 mg, 35%) as a colourless thick liquid. R_f: 0.7 (10% ethyl acetate-petroleum ether); IR (neat): 1753, 1692 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.92 (q, *J*=7, 7.5, 4H), 2.13 (t, *J*=7.5, 4H), 3.29 (d, *J*=5, 6H), 4.91 (dd, *J*=10.5, 6.5, 4H), 5.60-5.66 (m, 2H); ^{13}C NMR (50.38 MHz, $CDCl_3$): δ 28.8, 36.5, 39.3 (N-CH_3), 55.7, 115.8, 135.7, 150.3 (NC=O), 171.8 (C=O).

Preparation of 5,5-di-but-3-enyl-1,3-diethyl-2-thioxo-dihydro-pyrimidine-4,6-dione, 43

To a suspension of 1,3-diethyl-2-thiobarbituric acid **40** (150 mg, 0.75 mmole) in chloroform (10 mL), powdered potassium carbonate (1 g, 7.25 mmole) and BTEAC (900 mg, 3.95 mmole) were added. The reaction-mixture was cooled to 0°C and to this ice-cooled solution, 4-bromo-1-butene (512 mg, 3.79 mmole) was added dropwise and the reaction-mixture was stirred at 0°C for 1 hr. Then, the reaction-mixture was stirred at RT for 24 hr. At the conclusion of the reaction (TLC monitoring), the reaction-mixture was quenched with water (10 mL). The organic layer was separated and the aqueous layer was extracted with chloroform (3 × 20 mL). The combined organic layer was washed with water, brine and dried over anhyd. $MgSO_4$. The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 5% ethyl acetate-petroleum ether as an eluent to give **43** (65 mg, 32%) as a colourless thick liquid. R_f: 0.6 (10% ethyl acetate-petroleum ether); IR (neat):1726, 1646 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.24 (t, *J*=7, 6H), 1.90 (q, *J*=7., 4H), 2.23 (t, *J*=7.5, 4H), 4.32 (q, *J*=7, 4H), 4.93 (m, 4H), 5.62-5.69 (m, 2H); ^{13}C NMR (50.38 MHz, $CDCl_3$): δ 12.3, 28.3, 36.5, 39.3 (N-CH_3), 55.7, 116.6, 136.5, 167.2 (C=O), 171.8 (C=S).

Preparation of 7,9-dimethyl-7,9-diaza-spiro[4,5]-dec-2-ene-6,8,10-trione, 44

To a suspension of 5,5-diallyl-1,3-dimethyl barbituric acid **39** (70 mg, 0.297 mmole) in toluene (5 mL), first generation Grubbs catalyst (24.4 mg, 10 mole%) was added and the reaction-mixture was stirred at 90°C for 30 hr under nitrogen. Then, the solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 5% ethyl acetate-petroleum ether as an eluent to give **44** (54 mg, 88%) as a white solid; m.p. 136-38°C; R_f: 0.6 (10% ethyl acetate-petroleum ether); IR (neat): 1686 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.00 (s, 4H), 3.30 (s, 6H), 5.66 (s, 2H); ^{13}C NMR (50.38 MHz, $CDCl_3$): δ 28.8, 45.3, 54.8, 127.2, 151.3 (NC=O), 172.3 (C=O); GC-MS: *m/z* 208 (M^+). Anal. ($C_{16}H_{12}N_2O_3$): Calcd C, 57.68; H, 5.80; N, 13.45. Found: C, 58.23; H, 6.32; N, 13.0%.

Preparation of 7,9-diallyl-7,9-diaza-spiro[4,5]dec-2-ene-6,8,10-trione, 37

To a suspension of tetraallyl barbituric acid **36** (90 mg, 0.313 mmole) in toluene (10 mL), first generation Grubbs catalyst (25.7 mg, 10 mole%) was added and stirred at 90°C for 26 hr under nitrogen. The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 5% ethyl acetate-petroleum ether as an eluent to give **37** (86 mg, 95%) as a faint yellow solid; m.p. 52-53°C; R_f: 0.5 (10% ethyl acetate-petroleum ether); IR ($CHCl_3$): 1692, 1646 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.99 (s, 4H), 4.45 (d, *J*=5.8, 4H), 5.22 (t, *J*=9.5, 4H), 5.64 (s, 2H), 5.72-5.89 (m, 2H); ^{13}C NMR (50.38 MHz, $CDCl_3$): δ 44.1, 44.9, 54.8, 118.8, 127.2, 131.1, 150.3 (NC=O), 171.5 (C=O).

Preparation of 7,9-diethyl-8-thioxo-7,9-diaza-spiro[4,5]dec-2-ene-6,10-dione, 45

To a suspension of 5,5-diallyl-1,3-diethyl thiobarbituric acid **41** (70 mg, 0.25 mmole) in toluene (5 mL), first generation Grubbs catalyst (21 mg, 10 mole%) was added and stirred at 90°C for 30 hr under nitrogen. The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 5% ethyl acetate-petroleum ether as eluent to give **45** (58 mg, 92%) as a white solid; m.p. 88-89°C.

R_f: 0.6 (10% ethyl acetate-petroleum ether); IR (KBr): 1745, 1701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.22 (t, *J*=7, 6H), 2.99 (s, 4H), 4.41 (q, *J*=7, 4H), 5.63 (s, 2H); ^{13}C NMR (50.38 MHz, $CDCl_3$): δ 12.1, 43.6, 44.1, 55.8, 126.9, 169.8 (C=O), 179.4 (C=S). MS: *m/z* 253.1436 (M+1).

Preparation of 2,4-dimethyl-2,4-diaza-spiro[5,6]dodec-9-ene-1,3,5-trione, 46

To a suspension of 5,5-dibutenyl-1,3-dimethyl barbituric acid **42** (35 mg, 0.133 mmole) in toluene (5 mL), first generation Grubbs catalyst (11 mg, 10 mole%) was added and stirred at 90°C for 30 hr under nitrogen. The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 6% ethyl acetate-petroleum ether as an eluent to give **46** (25 mg, 81%) as a white solid; m.p. 125-26°C; R_f: 0.6 (15% ethyl acetate-petroleum ether); IR (KBr): 1697, 1687 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.27 (m, 4H), 2.46 (m, 4H), 3.29 (bs, 6H), 5.65 (t, *J*=3.2, 2H); ^{13}C NMR (50.38 MHz, $CDCl_3$): δ 25.1, 34.8, 39.4, 53.9, 130.1, 141.5 (NC=O), 172.9 (C=O).

Preparation of 4-methyl-2-phenyl-2,3-diaza-spiro[4,4]nona-3,7-dien-1-one, 55

To a suspension of diallyl pyrazolone **54** (120 mg, 0.444 mmole) in toluene (15 mL), first generation Grubbs catalyst (36 mg, 10 mole%) was added and stirred at 90°C for 36 hr under nitrogen. The solvent was removed under vacuum and the crude product was purified by silica gel column chromatography using 8% ethyl acetate-petroleum ether as an eluent to give **55** (75.3 mg, 75%) as a light brown solid; m.p. 111-12°C; R_f: 0.7 (15% ethyl acetate-petroleum ether); IR (KBr): 1715 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.05 (s,3H), 2.59 (d, *J*=14.9, 2H), 2.90 (d, *J*=15.2, 2H), 5.77 (s, 2H), 7.15 (t, *J*=7.4, 1H), 7.38 (t, *J*=7.5, 2H), 7.92 (d, *J*=8.4, 2H); ^{13}C NMR (50.38 MHz, $CDCl_3$): δ 13.1, 41.1, 57.4, 118.5, 124.7, 128.4, 128.7, 138.1, 164.2 (C=N), 176.9 (C=O). MS: *m/z* 227.0880 (M+1).

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