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Synthesis of 5-Dienyl Pyrimidinones and Tandem [1,5] Shifts in [4+2] Cycloadditions of 1,3-Diazabuta-1,3-Dienes with Butadienylketene#

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Abstract: The reactions of 1-aryl-2-phenyl-4-methylthio-4-secondaryamino / 4-*N*-allyl-*N*-aryl amino-1,3-diazabuta-1,3-dienes **1** with butadienylketene leading to a mixture of 5-dienyl pyrimidinones **4** and 5-butenyl pyrimidinones **6** are reported. Tandem [1,5]H and [1,5]SMe shifts are invoked to explain the formation of pyrimidinones **6**.

Because of the well documented synthetic potential and highly exceptional regio, stereo and facial selectivity of 1,3-dienes in Diels-Alder cycloadditions, the synthesis of suitably functionallised 1,3-dienes continues to attract the increasing attention of synthetic community.[1] The synthesis of heteroatom and carbocyclic/heterocyclic ring substituted 1,3-dienes is of particular interest because of their existence as intermediates in the synthesis and in the structure of various natural products.[2,3] However, most of the reported methods invariably suffer from multiplicity of the steps involved, cumbersome experimental procedures and low isolated yields. It was felt that carbocyclic/heterocyclic ring substituted 1,3-dienes can easily be prepared by the cycloaddition reactions of suitably substituted substrates with butadienylketene. The formation of butadienylketene as an intermediate has been detected in the thermolysis of appropriately substituted cyclobutenones[4] and in the photolysis of substituted phenols *via* transient cyclohexa-2,4-dienone intermediates.[5] However, the butadienylketene so generated, undergoes facile intramolecular processes and hence limits its utility towards intermolecular cycloadditions. Recently, we reported a convenient route for the generation of butadienylketene and utilised it successfully in [2+2] cycloaddition reactions with imines leading to α-dienyl β-lactams.[6] As part of the ongoing studies on azadiene-ketene cycloaddition reactions,[7,8] we report herein, a simple protocol for the synthesis of dienyl pyrimidinones involving [4+2] cycloadditions of 1,3-diazabuta-1,3 dienes with butadienylketene and novel [1,5] H and [1,5] SMe shifts accompanying such cycloadditions.

The reactions of various 1-aryl-2-phenyl-4-methylthio-4-secondary amino-1,3-diazabuta-1,3-dienes **1** ***a-d***

Dedicated to Professor Harjit Singh on the occasion of his 60th Birthday

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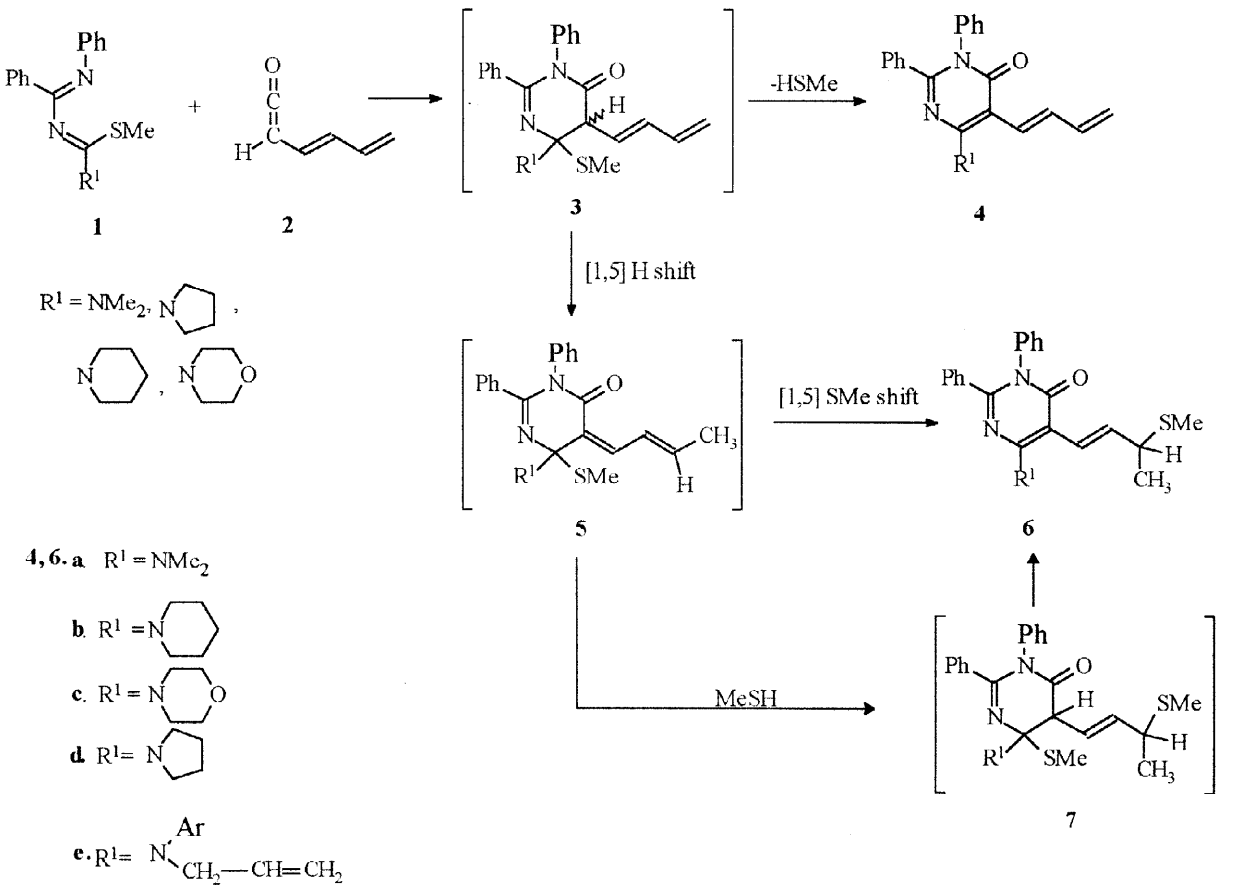
with butadienylketene **2**, generated *in situ* from sorbyl chloride and triethylamine in dry methylene chloride, resulted in a mixture (~1:1) of 5-(1',3'-butadienyl)pyrimidinones **4** and 5-(1'-butenyl)pyrimidinones **6**. (Scheme 1). The separation of this mixture of **4** and **6** having close R_f values, was accomplished by a careful silica gel column chromatography with natural loss of yields. The structures **4** and **6** were assigned to these products on the basis of their analytical and spectral data.[9]

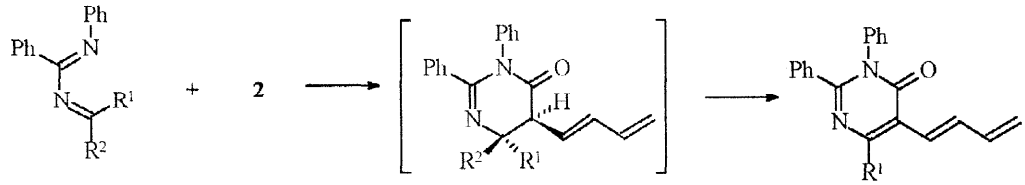


Scheme 1

The plausible mechanism for the formation of these pyrimidinones is outlined in Scheme-1. In this scheme it is assumed that the reactions of 1,3-diazabuta-1,3-dienes **1** with butadienylketene **2** leads to the initial formation of intermediate **3**, presumably consisting of a stereoisomeric mixture having H-5 being *cis* / *trans* to the methylthio at C-6. The *trans* stereomer undergoes facile elimination of methylmercaptan to yield pyrimidinones **4**. Whereas, the *cis* stereoisomer prefers suprafacial [1,5] H shift over its equilibration to *trans* stereomer yielding another intermediate **5**, which in turn undergoes [1,5] SMe shift to yield pyrimidinone **6**. It is also possible that the nucleophlic addition of the methylmercaptan eliminated during the formation of pyrimidinone **4**, to the activated diene of intermediate **5** may form another intermideate **7** which on elimination of methylmercaptan then yields pyrimidinone **6**. The later mechanistic

possibility is discounted on the basis crossover experiment performed in presence of propanethiol, wherein no addition product corresponding to the incorporation of propanethiol was isolated. similarly the reactions of 1-aryl-2-phenyl-4-*N*-allyl-*N*-arylamino-4-methylthio-1,3-diazabuta-1,3-denes **1e** with butadienylketene (**2**) gave a mixture of pyrimidinone **4e** and **6e**. A similar, but acid catalysed 1,5-sulfenyl shift, has recently been reported in case of simple dienes.[10]

In order to further establish the exclusive migration of methylthio function in formation of **6**, it was thought worthwhile to investigate the reactions of butadienylketene with 1,3-diazabuta-1,3-dienes **7** and **8** having one and two secondary amino functions at 4-position, respectively. The reactions of both **7** and **8** resulted in the exclusive isolation of pyrimidinones **10** and **4c,d**, respectively, formed presumably *via* the elimination of secondary amine from the initially formed intermediate **9** (Scheme 2).

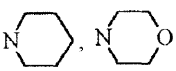


7 / 8

9

10 / 4 b,c

7. $R^1 = H, CH_3$; $R^2 = NMe_2$

8. $R^1 = R^2 =$ 

10. $R^1 = H, CH_3$

Scheme 2

In conclusion, the cycloaddition reactions of 1,3-diazabuta-1,3-dienes with butadienylketene have resulted in a novel and convenient route for the synthesis of pyrimidinone substituted 1,3-dienes. The cycloadditions of carefully chosen substrates with butadienylketene,may lead to a general method for the synthesis of various of carbocyclic/heterocyclic ring substituted 1,3-dienes. Tandem double [1,5] shifts i.e [1,5] H shift followed by [1,5] SMe shift, observed in case of the reactions of 1,3-diazabuta-1,3-dienes **1** are unusual and interesting. The detailed investigations concerning such tandem [1,5] shifts in reactions of azadienes with butadienylketene are underway.

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9. **5-(1',3'-Butadienyl)-2,3-diphenyl-6-morpholinopyrimidin-4(3*H*)-one 4c.** Yield 30%; mp 133-134 °C; ν_{max}/cm^{-1} (KBr) 1661 (C=O), 1541, 1504 and 1484; δ_H (300 MHz) 3.59-3.62 (m, 4H, CH_2NCH_2), 3.80-3.83 (m, 4H, CH_2OCH_2), 5.07 (d, *J* 10.0, 1H, H-4'), 5.25 (d, *J* 16.9, 1H, H-4'), 6.33 (d, *J* 15.6, 1H, H-1'), 6.48 (ddd, *J* 16.9, 10.7 and 10.0, 1H, H-3'), 7.12-7.33 (m, 10H, ArH) and 7.46 (dd, *J* 15.6 and 10.7, 1H, H-2'); δ_C (75.5 MHz) 49.4 (CH_2NCH_2), 67.1 (CH_2OCH_2), 99.6 (C-5), 116.5 (C-4'), 125.5 (C-2'), 127.8, 128.3, 128.8, 129.0, 129.3, 129.6, 132.2 (C-1'), 134.8, 137.6, 138.8 (C-3'), 154.2 (C-6), 160.6 (C-2) and 162.5 (C-4); *m/z* 385 (M^+). Anal. Calcd for $C_{24}H_{23}N_3O_2$: C, 74.78; H, 6.01; N, 10.90. Found: C, 75.02; H, 6.09; N, 10.65.

2,3-Diphenyl-5-(3'-methylthiobut-1'-en-yl)-6-morpholinopyrimidin-4(3*H*)-one 6c. Yield 33%; mp 116-117.5 °C; ν_{max}/cm^{-1} (KBr) 1660 (C=O), 1548, 1507 and 1487; δ_H (300 MHz) 1.42 (d, *J* 6.9, 3H, CH_3), 2.05 (s, 3H, CH_3), 3.34-3.45 (m, 1H, H-3'), 3.57-3.60 (m, 4H, CH_2NCH_2), 3.79-3.82 (m, 4H, CH_2OCH_2), 6.26 (d, *J* 15.8, 1H, H-1'), 6.66 (dd, *J* 15.8 and 8.5, 1H, H-2') and 7.11-7.33 (m, 10H, ArH); δ_C (75.5 MHz) 14.1 (SCH_3), 20.7 (CH_3), 45.2 (C-3'), 49 2 (CH_2NCH_2), 67.0 (CH_2OCH_2), 99.8 (C-5), 122.0 (C-2'), 127.8, 128.2, 128.8, 129.0, 129.2, 129.6, 134.6 (C-1'), 134.8, 137.7, 154.7 (C-6), 160.4 (C-2) and 162.7 (C-4); *m/z* 433 (M^+, 6%), 386 (98%), 358 (22%), 344 (10%), 326 (5%), 298 (6%), 225 (5%), 180 (100%) and 77 (88%). Anal. Calcd for $C_{25}H_{27}N_3O_2S$: C, 69.26; H, 6.28; N, 9.69. Found: C, 69.41; H, 6.14; N, 9.87.
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