

SYNTHESIS AND DIELS-ALDER REACTION OF STABLE ARYL FREE 1,3-DIAZABUTADIENE

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SUMMARY : The Diels-Alder reactions of 1-methoxycarbonyl-4-dimethylamino-2-thiomethyl-1,3-diazabutadiene with dimethyl acetylenedicarboxylate (DMAD) and monophenyl ketene give pyrimidines in one pot.

The hetero Diels-Alder reaction is a versatile route for the synthesis of functionalized heteroaromatic systems difficult to assemble by alternative methodology¹⁻³. However, owing to the difficulty in the preparation of stable dienes having two nitrogen atoms in the 1,3 positions, little is known about their reactions⁴. A select number of 1,3-diazadienes prefer heterocumulenes⁵ and a few electron deficient⁶ and electron rich⁷ dienophiles as 2π partners in Diels-Alder reactions.

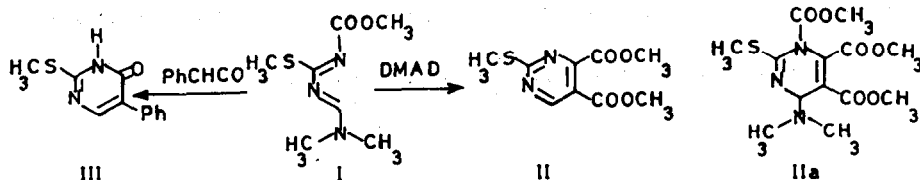
A careful literature survey reveals the notable drawback associated with the majority of the available 1,3-diazadienes, namely that they are substituted with phenyl groups in various positions, including on the nitrogen atoms. As a consequence, the cycloadducts with these substituents, which on account of the poor leaving ability of the phenyl group, effectively prohibit the aromatization of the system. This limits the synthetic applicability of these dienes used as 4π components in the construction of various naturally occurring pyrimidine moieties, which are aromatic and not substituted with aryl groups⁸.

In the light of these limitations we are prompted to communicate the synthesis of the stable acyclic diene, 1-methoxycarbonyl-4-dimethylamino-2-thiomethyl-1,3-diazabutadiene (I) which possesses synthetic potential because of the absence of the aryl group, and is designed in such a way that the substituents are readily eliminated from the cycloadduct in order to facilitate aromatization without the influence of any added reagent. This diene successfully undergoes a [4+2] cycloaddition reaction with dimethyl acetylenedicarboxylate leading to the formation of a functionalized heteroaromatic compound (II) - dimethyl 2-thiomethylpyrimidine-5,6-dicarboxylate in 72% yield. The reaction gains importance, because this is the first report of one pot synthesis of a heteroaromatic system from acyclic 1,3-diazadiene via a Diels-Alder reaction.

The scope of this process was then extended using monophenyl ketene as a 2π component, and the resulting cycloadduct, after the elimination of $-\text{COOCH}_3$ and $-\text{N}(\text{CH}_3)_2$, led to the formation of 2-thiomethyl-5-phenyl-6-pyrimidone (III) in 96% yield.

The diene (I) was prepared from methyl N-methoxycarbonylcarbamido thioate and N,N-DMF diacetal. The cycloaddition of (I) with DMAD was carried out at refluxing in

in benzene. When the reaction was carried out at a lower temperature (50°C) for a



longer time (24 hrs), traces of the intermediate (IIa) were also isolated, in addition to (II). The reaction with phenylketene (generated in situ), was carried out in benzene at 0-5°C.

The exploration of the synthetic utility of this diene as a 4π component in Diels-Alder reactions for the synthesis of naturally occurring heteroaromatic moieties are underway.

References

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9. Spectral data : Compound(I) (mp. 60-1°C); IR(KBr) : 2920, 1700, 1640, 1570 cm^{-1} ; $\delta_{\text{H}}(\text{CDCl}_3)$: 8.34(s,1H), 3.77(s,3H,-OCH₃), 3.17, 3.10(s singlets, 6H, -N(CH₃)₂), 2.46(s,3H, S-CH₃)ppm; $\delta_{\text{C}}(\text{CDCl}_3)$: 178.35(s,CO), 162.46(s,C₂), 155.24(d,C₄), 52.75(q, -OCH₃), 41.29, 35.20(2, quartets, -N(CH₃)₂), 15.44(q,-SCH₃)ppm; Mass : m/z 203(M⁺).
Compound(II) (mp.87-8°C); IR(KBr) : 2950, 1750, 1720, 1560, 1530 cm^{-1} ; $\delta_{\text{H}}(\text{CDCl}_3)$: 9.04(s,1H), 4.00, 3.92(2 singlets, 6H, 2COOCH₃), 2.62(s,3H,-SCH₃)ppm; $\delta_{\text{C}}(\text{CDCl}_3)$: 177.35(s,CO), 164.92(s,CO), 163.22(s,C₂), 159.17(s,C₆), 158.77(d,C₄), 115.54(s,C₅), 53.02(q,OCH₃), 52.64(q,OCH₃), 14.31(q,SCH₃)ppm; Mass : m/z 242(M⁺).
Compound(IIa) (mp. 107-8°C), IR(KBr) : 2920, 1740, 1710, 1680, 1600, 1550; $\delta_{\text{H}}(\text{CDCl}_3)$: 6.35(s,1H), 3.90, 3.81, 3.60(s, all COOCH₃), 3.35(s,N(CH₃)₂), 2.60(s,CH₃); $\delta_{\text{C}}(\text{CDCl}_3)$: 184.05, 173.51, 168.21, 167.50, 163.41, 153.42, 96.22, 53.39, 52.35, 49.97, 41.54, 13.41; Mass : m/z 345(M⁺).
Compound(III) (mp. 240-1°C); IR(KBr) : 3480, 3000, 1640, 1550; $\delta_{\text{H}}(\text{DMSO-d}_6)$: 8.10(s,1H), 7.74-7.34(m,5H), 2.55(s,3H); $\delta_{\text{C}}(\text{DMSO-d}_6)$: 161.40(s,CO), 161.05(s,C₂), 150.55(d-C₄), 133.00(s,C₅); 128.00, 127.94, 127.44, 121.86 (all aromatic signals), 12.89(q,S-CH₃); Mass : m/z 218(M⁺).

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