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Novel Chemistry Of The IMDA Adducts Of The Amides Derived From Dichloromaleic Anhydride And β-Aminomethylstyrenes

Janet R. Dawson and John M. Mellor*

Department of Chemistry, Southampton University, Southampton SO17 1BJ

Abstract: Reaction of amides derived from dichloromaleic anhydride and β -aminomethylstyrenes affords unstable Diels Alder adducts, which give via competing processes a number of products including pyrrolidinones by a novel sequence of dehydrochlorination and subsequent ring-opening of a cyclohexadiene.

The use of halo-substituted dienophiles in the Diels Alder reaction has been an important method of introducing unsaturation into the Diels Alder adducts by a later dehydrohalogenation. Such dienophiles have been used both in intermolecular¹ and intramolecular² examples of the Diels Alder reaction. In intermolecular cases dechlorodecarboxylation¹ can introduce unsaturation. In the case of intramolecular Diels Alder (IMDA) reactions of trienes derived from dichloro- and bromomaleic anhydride, we have shown³ that the halo functionality can be used to introduce double bonds into the adducts by either dehydrohalogenation or by dechlorodecarboxylation. In these earlier studies the trienes were limited to acyclic examples. The IMDA reaction has been used very effectively in synthesis⁴ in the creation of tricyclic systems by cyclisation of substrates derived from β -aminomethylstyrenes (Scheme 1).



The use of dienophilic moieties derived from dichloromaleic anhydride offers the possibility of a similar sequence whereby the initial Diels Alder substrate (1) might undergo cyclisation to the intermediate (2) and then by aromatisation afford the tricycle (3). However it occurred to us that the intermediate (2) shown in Scheme 2 might be able to react further by dehydrochlorination and hence lead to novel chemistry. In this paper we describe an unprecedented sequence leading the substrates (1), via Diels Alder addition to the triene intermediates (2), dehydrochlorination to the non-aromatic tetraenes (4), and finally electrocyclic ring-opening

to give the unusual unsaturated pyrrolidinones (5).

The required substrates (1a-1d) were obtained by reaction of (Z)-3-carbomethoxy-2,3-dichloroacryloyl chloride with the readily available amines, prepared either by condensation of cinnamaldehyde with aniline or benzylamine, followed by reduction of the intermediate imines, or by the reported route⁵ of Mannich reaction of a substituted acetophenone, with later reduction and dehydration. In all cases, and in agreement with earlier studies³ the configurationally stable Z-isomers were obtained. The amides (1a-1d) were heated under reflux in benzene, toluene or xylene as shown in Table 1.



a) $R_1 = H$; $R_2 = Ph$; **b**) $R_1 = H$; $R_2 = CH_2Ph$; **c**) $R_1 = Me$; $R_2 = CH_2Ph$; **d**) $R_1 = Cl$; $R_2 = CH_2Ph$

Scheme 2

The major products are the unsaturated pyrrolidinones (5) isolated from reaction in xylene in 40-80% yields. Two series of pyrrolidinones were observed. The pyrrolidinones (5a-Z), (5b-Z) and (5d-Z) were found to undergo isomerisation on heating in xylene to give respectively the pyrrolidinones (5a-E), (5b-E) and (5d-E).

Microanalytical data confirmed the isomeric nature of the two series of compounds, and the assigned structures are fully in agreement with the ¹-H, and ¹³-C n.m.r. spectra, and i.r. and u.v. spectra. In particular observation of bands (λ_{max} . 326nm and 324nm) in the u.v. spectra of (**5a-Z**) and (**5a-E**) is in excellent accord with bands observed⁶ at 330nm in the structurally closely related fulgides. The relative assignment of structure to the pyrrolidinones (**5a-Z**) and (**5a-E**) can be made by observation of a resonance in the ¹-H n.m.r. spectrum at 7.9 ppm in pyrrolidinone (**5a-E**) and at 6.9 ppm in pyrrolidinone (**5a-Z**), and relation to analogous data⁷ reported elsewhere. In most reactions shown in Table 1 a number of minor products were isolated. From the amides (**1a-1d**) a series of naphthalenes (**6a-6d**) were obtained in low yield. The microanalytical data showing the absence of chlorine and the observation of the naphthalene chromophore were important steps in assigning structures to (**6a-6d**). From (**1a**) and (**1b**) the minor products (**3a**) and (**3b**) respectively were isolated. Again

the combination of microanalytical and spectroscopic data permitted structural assignments. The *cis*-ring fusion is assigned by comparison of coupling constant data with literature analogies.^{2,8}

Table 1

Products of Intramolecular Diels Alder Reactions

Starting Amide	Reaction Conditions	Products and Yields (%)
1a	Benzene reflux 11h	5a-Z (15)
1a	Toluene reflux 19h	5a-Z (39), 5a-E (30), 6a (8)
1a	Xylene reflux 6h	5a-E (40), 3a (10), 6a (13)
1 b	Benzene reflux 6h	5b-Z (51)
1 b	Toluene reflux	5b-Z (45), 5b-E (31), 6b (4)
1 b	Xylene reflux 4h	5b-E (49), 3b (12), 6b (9)
1 c	Xylene reflux 4h	5c-E (81), 6c (10)
1 d	Xylene reflux 4h	5d-Z (29), 5d-E (50), 6d (12),

The results shown in Table 1 establish that following the cyclisation of the amides (1a-1d) to give the tricyclic lactam intermediates (2 cis or trans ring fusion) the major reaction pathway is formation of the pyrrolidinones (5) and pathways leading to the naphthalenes (6a-6d), or to the aromatic tricycles (3a) and (3b) without loss of HCl are minor. The dominant formation of the pyrrolidinones (5) is readily explained. The IMDA reaction can lead to either cis or trans fused lactams (2). The formation of a trans fused adduct is to be expected on the basis of our studies³ and of an earlier example.⁴ The minor reaction pathway is likely to afford cis fused lactams. The highly strained trans lactams have the favourable trans anti-periplanar relation permitting loss of HCl to give the tetraenes (4). In the case of the cis lactams loss of HCl to give a tetraene will be slower. Hence the minor cis fused lactam (2) may undergo an effective 1,3-hydrogen shift to give the aromatic products (3). From the intermediate tetraenes (4) electrocyclic ring opening, which has good precedent, 9 gives the major reaction products, the pyrrolidinones (5). A minor pathway from the tetraenes (4) is formation of the naphthalenes (6), by loss of further HCl. Confirmation of part of Scheme 2 is found in the observation that the pyrrolidinones (5) on heating slowly afford the naphthalenes (6). A thermal equilibrium between the intermediates (4) and the pyrrolidinones (5) has close analogy with the behaviour of the well known fulgide photochromics,9 and suggests the merit of a more detailed study of the behaviour of the pyrrolidinones (5) and compounds available from these novel heterocycles.



The results presented in Table 1 and rationalised in Scheme 2 establish an important new avenue in the chemistry of Diels Alder adducts derived from halo-substituted dienophilic moieties. The pyrrolidinone products e.g. (5-E) are an interesting addition to the bismethylene chromophores, including the fulgides (7) and fulgimides (8), first explored¹⁰ and developed extensively¹¹ by Heller *et al*, and recently extended to the fulgenates (9)¹² and fulgenolides (10),¹³ which are attracting attention, because of their photochromic properties, in areas such as optical storage¹⁴ and holography.¹⁵

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