"IONIC" DIELS-ALDER REACTION OF HETARYLDIENAMINES

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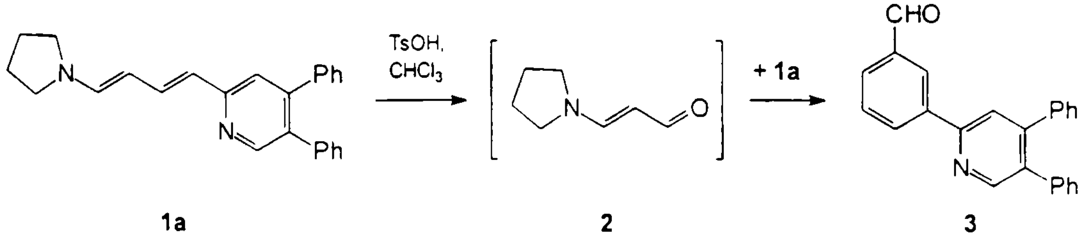
Abstract: Hetaryldienamines 1 were found to undergo "ionic" Diels-Alder reaction with α,β-unsaturated carbonyl compounds 4 and 6 in the presence of catalytic amounts of *p*-toluenesulfonic acid. Depending on the structure of the carbonyl compound employed either cyclohexadiene 5 or benzene derivatives 7 are obtained.

Introduction

In recent years we have developed a convenient method for the large scale preparation of hetaryldienamines (1-3). These dienamines are electron-rich dienes and were found to undergo Diels-Alder and related cycloaddition reactions (4). Although dienes 1 proved to be fairly stable compounds, both in the solid state and in organic solutions, they rapidly decompose under acidic conditions - due to the enamine function - and turn into tarry mixtures.

Results and Discussion

The investigation of the decomposition mixture obtained from acid treatment of 2-[4-(1-pyrrolidinyl)-1,3-butadienyl]-4,5-diphenylpyridine 1a afforded a product in moderate yield (5) which was identified as 3-[4-4,5-diphenylpyrid-2-yl]benzaldehyde 3.

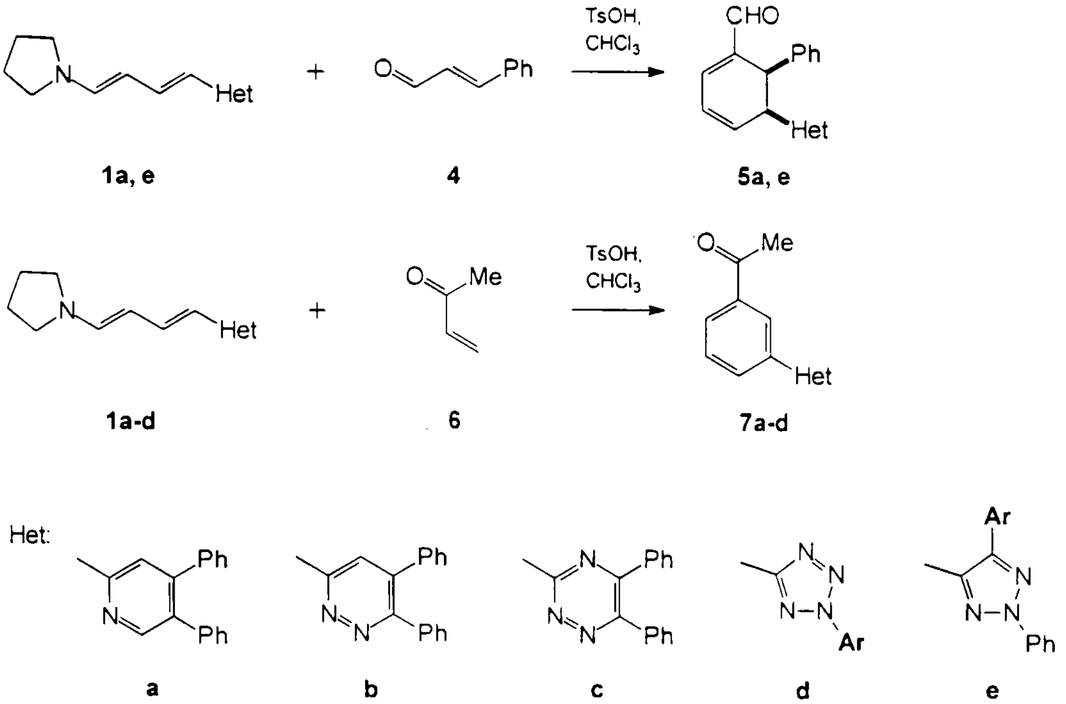


The formation of compound 3 is rationalized by assuming aerial oxidation of the dienamine 1a under the reaction conditions to furnish the unsaturated aldehyde 2 (6); a subsequent "ionic Diels-Alder" reaction (7) of this intermediate 2 as a dienophile with an other molecule of 1a as a diene followed by the elimination of two molecules of pyrrolidine to give the isolated product 3.

Although α,β-unsaturated carbonyl compounds have been known to undergo Diels-Alder reaction with electron rich dienes (*e.g.* dienamines) (8) for a long time, a new application of this reaction has recently been studied extensively:(7) α,β-unsaturated carbonyl compounds and their acetals were found to react smoothly with a variety of dienes in the presence of Bronsted or Lewis acids. Because of the ionic character of the suggested oxocarbenium intermediates these reactions were dubbed "ionic" Diels-Alder reactions (7).

In order to demonstrate that this type of reaction is involved in the formation of the unexpected product 3, a detailed investigation of the acid-catalysed reaction of hetaryldieneamines 1 with α,β-unsaturated carbonyl compounds has been carried out.

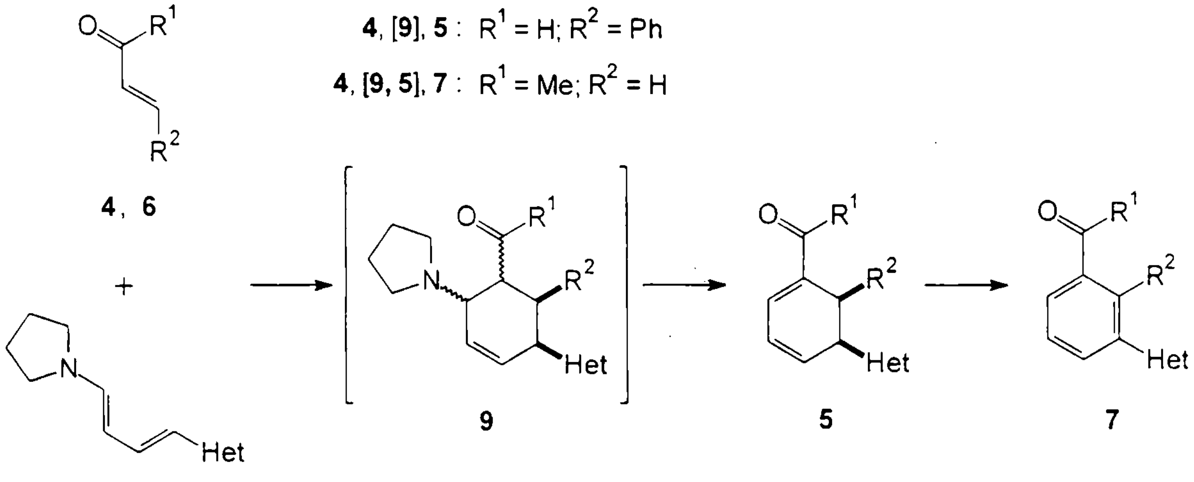
As model α,β-unsaturated carbonyl compounds (*E*)-cinnamaldehyde 4 and methyl vinyl ketone 6 were selected, and a series of hetaryl-dienamines 1a-e was employed as electron-rich dienes. Owing to the facile decomposition of dienamines when treated with acid, suitable conditions had to be established for the cycloaddition reaction of 1 in the presence of acid. It was found that the reaction of the 2-pyridyldienamine 1a and cinnamaldehyde 4 in chloroform was markedly accelerated by the addition of catalytic amounts of a Bronsted or Lewis acid. Among the various catalysts tried (including boron trifluoride diethyletherate, lithium perchlorate, titanium tetrachloride, trifluoroacetic acid) *p*-toluenesulfonic acid monohydrate (0.2 equivalent) proved most efficient.



The series of dienamines 1a-e was subjected to the reaction with (*E*)-cinnamaldehyde 4 under established conditions; only compounds 1a and 1e afforded identifiable products which proved to be the 1-formyl-5-hetaryl-6-phenyl-1,3-cyclohexadiene derivatives 5a and 5e. The formation of these products is rationalised by assuming the [4+2] cycloaddition reaction to be followed by a spontaneous elimination of pyrrolidine. The lack of isolable products from the reactions of the other dienamines we attribute to their greater acid sensitivity.

By contrast, the products obtained in good to moderate yields from the reaction of dienamines 1a-d with methyl vinyl ketone 6 were identified as 3-hetarylacetophenones 7a-d. The aromatic nature of these products is considered to provide both the driving force for their formation and also the compound stability to give isolable products. However, the isolated yields of the products vary within a wide range, presumably due to the differing sensitivities of the dienamines 1a-d towards acid.

The fact that only a single regioisomer was isolated from these reactions suggests that the reaction proceeds in a regioselective manner. The selectivity is in accordance with the charge distribution along the olefin chains as the more electron-deficient β-position of the oxo compound is attached to the relatively electron-rich position 1 of the diene, while the less positive α-position is connected to the less negative C-4 atom. Furthermore, the *cis* geometry of the substituents in the cyclohexadiene products 5a and 5e (9) ($J_{5,6}$ = 1.7 Hz) shows that the reactions are diastereoselective.



These findings permit the conclusion that the first reaction step is the regioselective (with R^2 = Ph also diastereoselective) "ionic" Diels-Alder reaction of the dienamine 1 and the carbonyl compound 4 or 6 leading to the asymmetric intermediate 9. Probably, the diastereoselectivity giving rise to the *cis* geometry of 9 (R^2 = Ph) is due to the attractive dispersion interaction between the heteroaromatic and phenyl substituents (10). Cycloadducts 9 undergo spontaneous elimination of pyrrolidine to furnish cyclohexadienes 5, which in particular cases (*e.g.*, R^1 = Me, R^2 = H) upon aerial oxidation are transformed into benzaldehydes **7**. Aromatization is prevented in the cyclohexadienes **5a**, **5e** (R^1 = H, R^2 = Ph) for steric reasons, the bulky groups (4-hetaryl and 5-Ph) being unable to accommodate a coplanar geometry in the conceivable aromatic oxidation product.

Acknowledgment

Thanks are due to Dr. Eszter Gács-Baitz for recording the NMR spectra. This work was supported by the funds OTKA 014865 and TéT A48.

References and Notes

All new compounds have fully been characterised by means of IR, UV, high resolution NMR and MS spectroscopy.

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(4) A. Messmer, Gy. Hajós, and G. Timári, *Monatsh. Chem.* **119**, 1113 (1988)

(5) A solution of **1a** (351 mg, 1 mmol) and *p*-toluenesulfonic acid monohydrate (40 mg, 0.2 mmol) in dichloromethane (5 ml) was left at room temperature for a week. Column chromatography on aluminium oxide with hexane/ethyl acetate yielded **3** mp 85-88°C (94 mg, 28%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.13 (s, 1H), 8.75 (s, 1H), 8.59 (t, *J* = 2.0 Hz, 1H), 8.52 (s, 1H), 8.39 (dt, *J* = 9.0, 2.0 Hz, 1H), 7.96 (dt, *J* = 9.0, 2.0 Hz, 1H), 7.85 (s, 1H), 7.32-7.19 (m, 10H)

(6) The oxidation of related dienes to α,β-unsaturated aldehydes has been reported: A. Gelléri and A. Messmer, *Tetrahedron Lett.* **14**, 4295 (1973), R. Taylor, *J. Chem. Res. (S)*, **1987**, 178

(7) D. B. Gorman and P. G. Gassman, *J. Org. Chem.* **60**, 977 (1995), and references cited therein

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(9) General procedure: A solution of **1** (1 mmol), the carbonyl compound **4** or **6** (4 mmol), and *p*-toluenesulphonic acid monohydrate (40 mg, 0.2 mmol) in chloroform (5 ml) was left in an open flask for 2 days. After neutralization the solvent was evaporated and the product purified by column chromatography (aluminium oxide; hexane/ethyl acetate). Yields (mp): **5a**: 72% (131-3°C); **5e**: 68% (154-6°C): **7a**: 56% (116-9°C): **7b**: 26% (126-9°C); **7c**: 17% (128-31°C): **7d**: 37% (120-2°C); ^{1}H NMR (400 MHz, $CDCl_3$) of **5a**: δ 9.52 (s, 1H), 8.62 (s, 1H), 7.43-7.06 (m, 16H), 6.60 (dd, *J* = 9.4, 6.2 Hz, 1H), 6.46 (dd, *J* = 9.4, 6.0 Hz, 1H), 4.50 (d, *J* = 1.7 Hz, 1H), 4.11 (dd, *J* = 6.0, 1.7 Hz, 1H). ^{1}H NMR (400 MHz, $CDCl_3$) of **7a**: δ 8.75 (s, 1H), 8.66 (t, *J* = 2.2 Hz, 1H), 8.31 (dt, *J* = 7.9, 2.2 Hz, 1H), 8.04 (dt, *J* = 7.9, 2.2 Hz, 1H), 7.84 (s, 1H), 7.61 (t, *J* = 7.9 Hz, 1H), 7.33-7.18 (m, 10H), 2.81 (s, 3H).

(10) For an analogous case *see*, J. Cioslowski, J. Sauer, J. Hetzenegger, T. Karcher, and T. Hierstetter, *J. Am. Chem. Soc.* **115**, 1353 (1993)

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