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Steric Control of Chemoselectivity in the Reaction of Ynamine Esters with Heterodienes

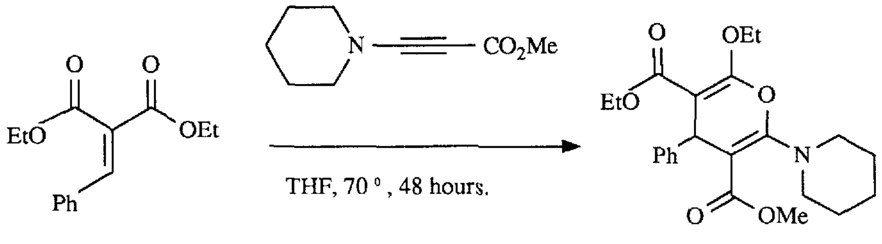
Colin P. Dell

Lilly Research Centre, Erl Wood Manor, Windlesham,
Surrey, GU20 6PH, U.K.

Key Words: Regioselective; chemoselective; hetero-Diels-Alder reaction; ynamine; pyran.

Abstract: Ynamine esters undergo regioselective formal hetero-Diels-Alder reactions with α,β-unsaturated-1,3-dicarbonyl compounds yielding functionalised pyrans. The chemoselectivity of the reaction appears to be governed by steric factors.

We recently reported[1] the use of a formal hetero-Diels-Alder reaction between 2-arylidene-1,3-indanediones and ynamines[2] bearing electron-withdrawing groups as a useful method for the preparation of multiply functionalised indeno[1,2-*b*]pyrans. As an extension to this chemistry, we have examined the use of other heterodienes in which the 4π component does not form part of a ring. In an initial experiment, we found that diethyl benzylidenemalonate reacted smoothly with methyl 3-(1-piperidino)prop-2-ynoate yielding a mixture of the pyran **1** (60%) and the dienamide **2** (20%). The former is the expected formal hetero-Diels-Alder product whilst the latter is probably a result of [2+2] addition of the ynamine to the ester carbonyl followed by ring-opening of the oxete in the opposite sense. Such products have been observed by Ficini[3] in the reactions of unsaturated aldehydes with ynamines, but never previously from esters which instead yield cyclobutenes as secondary products[4].



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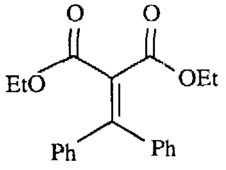

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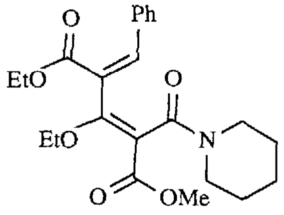

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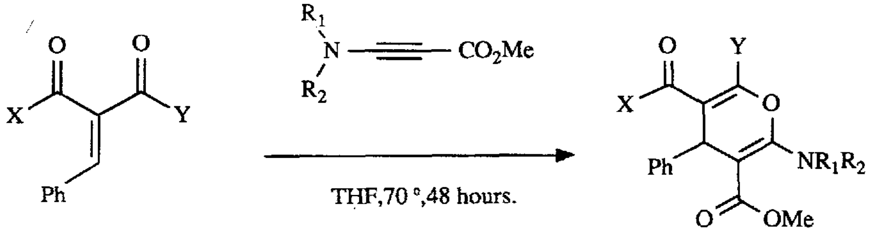
The logical extension to this result was to examine the reactions of ynamine esters with heterodienes bearing two different carbonyl groups. These results are summarised below (Table) and clearly demonstrate that not only is the reaction regioselective[5], but also chemoselective[5] in that only addition across the 4π component bearing the carbonyl group *trans* to the bulky phenyl substituent is observed. The steric origin of this phenomenon is suggested by the failure of the more hindered heterodiene **3** to undergo the reaction, even under more forcing conditions. Although enol ethers have been demonstrated to undergo regio- and chemoselective hetero-Diels-Alder reactions with 2-methylene-1,3-dicarbonyl compounds[6] and some evidence also exists in the work of Tietze[7] that selectivity is possible,this work represents the first example of the use of functionalised ynamines in the preparation of diversely functionalised 4-phenylpyrans in a regio- and chemoselectively unambiguous fashion.



Table

R_1 - R_2	X	Y	Yield*(%)
-[CH_2]$_5$-	OEt	Me	90
-[CH_2]$_5$-	OEt	Ph	62
-[CH_2]$_5$-	Me	Ph	28
-[CH_2]$_4$-	Me	Ph	15

* Isolated yields of pure material

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REFERENCES AND NOTES

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2. For a review of the synthetic utility of ynamines see: Ficini, J.; *Tetrahedron*, **1976**, *32*, 1449-1486.
3. Ficini, J.; Krief, A.; *Tetrahedron Lett.*, **1969**, 1427-1430.
4. Ficini, J.; Krief, A.; *Tetrahedron Lett.*, **1970**, 885-888.
5. Only the indicated isomer was detectable in the crude reaction mixture. Isomer assignments were based on ^{13}C n.m.r. data and where appropriate by ^1H n.m.r. nuclear Overhauser effect experiments. All new compounds possessed spectral and analytical parameters fully consistent with the depicted structures.
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