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A Convenient Route to Polyfunctionalised Indeno[1,2 - b]pyran Derivatives

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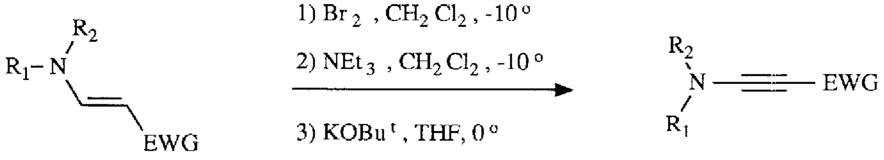
Key Words: Regioselective hetero-Diels-Alder reaction; ynamine; indeno[1,2-*b*]pyran.

Abstract: ***2-Arylidene-1,3-indanediones undergo facile formal hetero-Diels-Alder cycloadditions with ynamines bearing electron-withdrawing groups yielding polyfunctionalised indeno[1,2-b]pyrans.***

Although the use of enol ethers and even simple alkenes as partners to 1-oxa-1,3-dienes in hetero-Diels-Alder approaches to dihydropyran ring systems is well documented[1], ynamines[2] have received relatively little attention as the 2π components in such schemes[3]. Indeed, ynamines bearing useful functional groups do not appear to have been utilised in pyran synthesis at all. In this communication, we report the synthesis of diversely funtionalised indeno[1,2-*b*]pyrans by a formal hetero-Diels-Alder reaction of 2-arylidene-1,3-indanediones[4,5] with ynamine esters and nitriles.

The desired ynamine esters (**1**, EWG = CO_2Me) were prepared by a route analogous to that described for methyl 3-dimethylaminoprop-2-ynoate[6] (scheme 1).

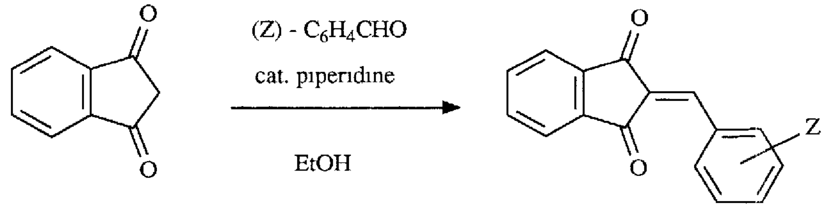


1

R_1, R_2, EWG - see table

Scheme 1

With the failure in our hands of existing routes[7,8] to ynamine nitriles, this bromination/dehydrobromination chemistry[6] was extended to encompass for the first time ynamine nitrile synthesis[9]. Whilst the esters (**1**, EWG = CO_2Me) were relatively stable, isolable compounds, it proved necessary to generate the nitriles (**1**, EWG = CN) at low temperature and use them without purification[10] The 2-arylidene-1,3-indanediones **2** were prepared by established procedures[4] (scheme 2).

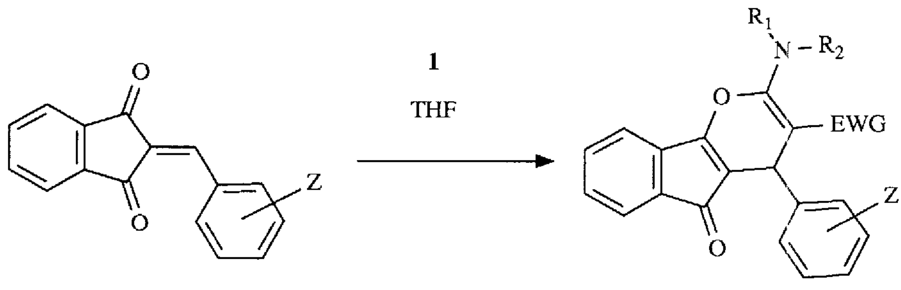


2

Z - see table

Scheme 2

The key reaction[11] proceeded as envisaged (scheme 3) providing multiply functionalised indeno[1,2-*b*]pyrans[12] **3**, generally in moderate yields (table). Furthermore, in common with related chemistry[3,5], the formal [4+2] cycloaddition was regioselective, producing only the depicted 2-dialkylaminopyran isomer[13]. This regiochemistry was unambiguously demonstrated by a series of ^1H n.m.r. nuclear Overhauser difference experiments on **3b**, showing the close spatial proximity of the pyran 4H, the ester CO_2Me and the *ortho* protons of the *para*-nitrophenyl group



2 **3**

R_1 , R_2 , EWG, Z - see table

Scheme 3

Table

R_1 - R_2	EWG	Z	Compound (Yield*,%)
-$[CH_2]_4$-	CO_2Me	3-NO_2	**3a** (43)
-$[CH_2]_4$-	CO_2Me	4-NO_2	**3b** (32)
-$[CH_2]_5$-	CO_2Me	3-NO_2	**3c** (50)
-$[CH_2]_5$-	CO_2Me	4-NO_2	**3d** (37)
-$[CH_2]_5$-	CO_2Me	3-CF_3	**3e** (28)
-$[CH_2]_2O[CH_2]_2$-	CO_2Me	4-NO_2	**3f** (39)
-$[CH_2]_2O[CH_2]_2$-	CN	4-NO_2	**3g** (11)
-$[CH_2]_2O[CH_2]_2$-	CN	3-CF_3	**3h** (10)

* Isolated yields of pure material

Mechanistically, it is interesting to speculate whether the reaction is a true concerted [4+2] process or a stepwise one[2], proceeding *via* nucleophilic attack of the highly polarised ynamine **1** on the electron deficient arylidene indanedione **2**. At present we have no evidence to be able to distinguish between these pathways.

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10. In our hands neither 3-(4-morpholino)- nor 3-(dimethylamino)-propynenitrile were isolable by distillation. Typically, for ynamine nitrile synthesis, we carried out the potassium *tert*-butoxide step at -60°, allowed the crude reaction mixture to warm to -20° and then added **2** directly to the mixture.

11. Typical procedure: to a stirred suspension of 2-(4-nitrobenzylidene)-1,3-indanedione (7.15g, 25.6mmol) in dry THF (125 cm^3) at room temperature was added dropwise over five minutes methyl 3-(1-pyrrolidino)prop-2-ynoate (6.85g, 44.7mmol). There was a slight exotherm and the bulk of the arylidene indanedione dissolved. After two hours, a further portion of the arylidene indanedione (3.60g, 12.9mmol) was added. Fifteen hours later, the brown-black solution was concentrated to dryness. The viscous gum was triturated with dichloromethane and this solution then concentrated. Addition of 2:1 hexane/ether to the resulting gum caused solidification. The solid was then stirred with methanol to remove traces of impurities, filtered off, dried *in vacuo*, providing **3b** as a yellow powder (5.33g, 32%).

12. All new compounds possessed spectral and microanalytical parameters which were fully consistent with the depicted structures.

13 The other regioisomer was not present in the crude reaction mixture.

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