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Vinylketene-Enamine Cyclocondensation: a New Access to Functionalized Phenols

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Abstract: The cyclocondensation between vinylketenes **2**, generated by rhodium acetate catalysed Wolff rearrangement of diazo compounds **1**, and enamines **3** led to functionalized phenolic derivatives **5** in moderate to good yields.

Ketenes are specially prone to [2+2] cycloadditions, therefore the use of vinylketenes as diene components has been limited.[1] However it has been shown by Danheiser *et al.* that (trimethylsilyl)vinylketene participated in Diels-Alder reactions when exposed to the action of electron-deficient olefinic or acetylenic dienophiles.[2] More recently Barbaro *et al.* have reported that the reaction between methylvinylketene and very electrophilic reactants gave an unique isomer from a 1,4-cycloaddition while, with electron-rich species, such as enolethers or ynamines, only 1,2-cycloadducts were formed.[3] Finally, it was found that the reaction between some enamines and vinylketene, or its 2-methyl or 2-bromo derivatives, generated *in situ* from the corresponding α,β-unsaturated acid chlorides, gave rise either to mixtures of cyclobutanones and cyclohexenones or solely to the latter compounds depending on both the structure of the vinylketene and the solvent used.[4]

As part of our continuing interest in the preparation of highly substituted phenolic derivatives[5] we now describe that the reaction between vinylketenes bearing an electron-withdrawing group on the ketene moiety and β-monosubstituted enamines gives rise to functionalized phenols.[6]

The vinylketenes **2** were generated by exploiting the rhodium acetate catalysed Wolff rearrangement[5c,7] of diazo compounds **1** readily obtained from α,β-unsaturated acid derivatives precursors.[8] When exposed to enamine **3a**, vinylketenes **2a-d** led to phenols **5a-d** in good yields.[9] These compounds result from the formation of the intermediate [4+2] cycloadducts **4** followed by the spontaneous elimination of pyrrolidine.

The indanic derivative **5e** was obtained, somewhat less efficiently, from the reaction between **1c** and enamine **3b**. The method proved to be also applicable with functionalized enamines as demonstrated by the reaction between diazo ester **1b** and enaminoester **3c** which gave rise to phenol **5f** in 64% yield.

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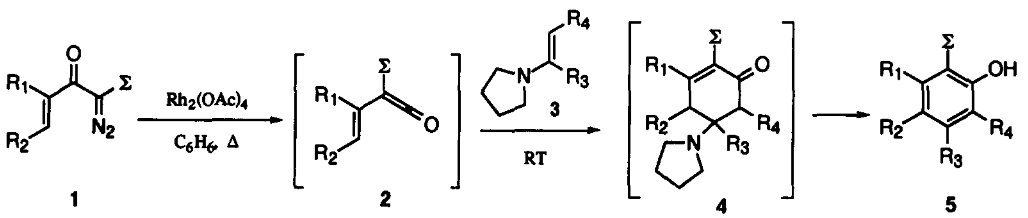
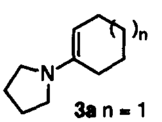
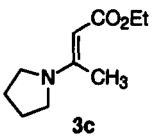


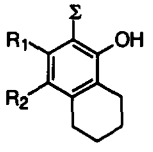
1a $R_1 = H$, $R_2 = Ph$, $\Sigma = PO(OMe)_2$
1b $R_1 = H$, $R_2 = Ph$, $\Sigma = CO_2Et$
1c $R_1 = H$, $R_2 = CH_3$, $\Sigma = CO_2Et$
1d $R_1 = CH_3$, $R_2 = H$, $\Sigma = CO_2Et$



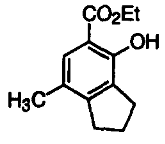
3a n = 1
3b n = 0



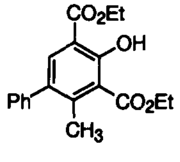
3c



5a (84%)
5b (73%)
5c (64%)
5d (75%)



5e (47%)



5f (64%)

In conclusion we describe here a convergent access to functionalized phenolic derivatives in moderate to good yields. We are currently exploring the further synthetic possibilities of this method for the preparation of more elaborate phenols.

References and notes

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8. The E stereochemistry of diazo compounds **1a,b** or **1c** is required in order to avoid either competitive electrocyclic ring closure of intermediate vinylketenes or rhodium-carbenoid insertion reaction.
9. All new compounds gave spectral and analytical data in full agreement with proposed structures. General procedure: diazo compound **1** was refluxed in benzene (or dichloromethane in the case of **1d**) in the presence of a catalytic amount (3% mol) of rhodium acetate until complete disappearance of starting material (5 to 20 mn). The reaction mixture was then cooled to room temperature and after the addition of a solution of enamine **3** (1.2 eq.) in the same solvent, stirred overnight. After solvent evaporation the crude product was purified by flash column chromatography on silicagel.

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