Carbonyl Ylide Formation from the Rhodium(II) Acetate Catalysed Reaction of Keto α-Diazoacetate Derivatives

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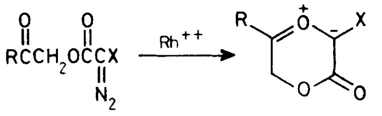
Formation of carbonyl ylides from the reaction of keto α-diazoacetates with rhodium(II) acetate has been found to be dependent on the electrophilicity of the intermediate rhodium carbenoid.

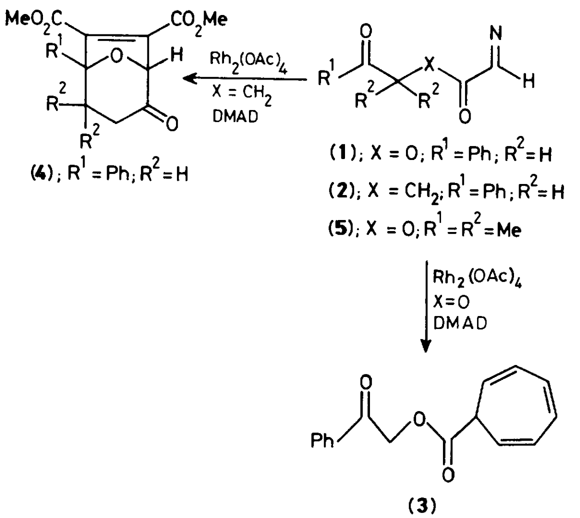
A major challenge in organic synthesis today is to devise reactions that can form several carbon–carbon bonds in one operation leading to the construction of polycyclic structures with proper regio- and stereo-chemical control. Recently, a tandem cyclization–cycloaddition reaction was developed in our laboratories as a method for synthesizing oxapolycyclic ring systems.[1] It involves a rhodium(II) acetate induced diazoketone cyclization onto a neighbouring carbonyl group followed by a 1,3-dipolar cycloaddition.[2—4] In trying to extend the reaction to the synthesis of more complex ring systems, we have investigated the feasibility of incorporating an additional heteroatom into the 1-diazo-2-pentanedione backbone. In this communication we report that rhodium induced carbonyl ylide formation of α-diazoacetate derivatives can be accomplished but that the process is highly dependent upon the electronic nature of the substituent attached to the diazo carbon atom (Scheme 1).



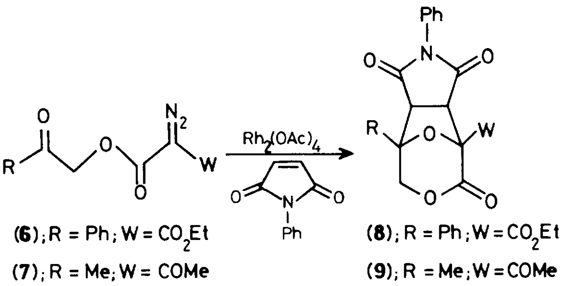
X = COMe or CO$_2$Et

Scheme 1

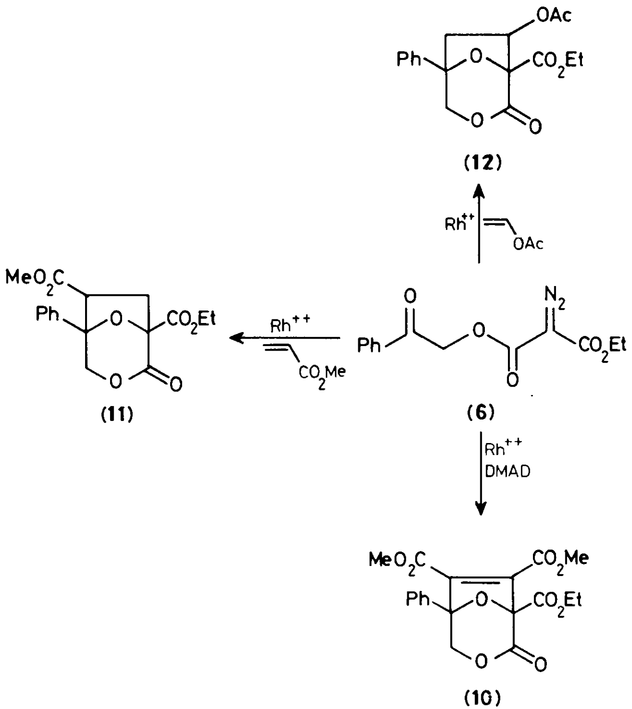
The 5-keto-1-diazoacetates (**1**) and (**5**) were prepared by acylation of the corresponding α-hydroxyketones with the toluene-*p*-sulphonyl hydrazone of glyoxylic acid chloride.[5] Treatment of (**1**) with a catalytic amount of rhodium(II) acetate at 25 °C in benzene with dimethyl acetylenedicarboxylate (DMAD) afforded cycloheptatriene (**3**), the consequence of carbenoid insertion into benzene. This result stands in sharp contrast to the corresponding 1-diazo-2,5-pentanedione system (**2**) which smoothly undergoes the tandem cyclization–cycloaddition reaction under identical conditions (Scheme 2). Attempts to take advantage of the Thorpe–Ingold effect[6] by utilization of the 4-*gem*-dimethyl analogue (**5**) also met with a similar lack of success.



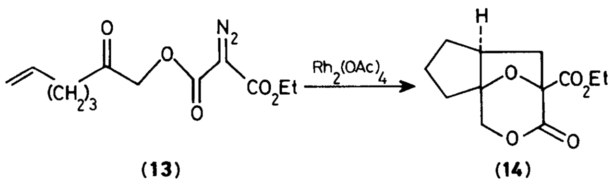
Scheme 2



Scheme 3



Scheme 4



Scheme 5

One possible explanation for the differing reactivity of the α-diazoacetate system is the inherent decrease in electrophilic character conferred upon the intermediate rhodium carbenoid when the diazoketone is replaced by a diazoacetate functionality. This decrease in electrophilicity may attenuate the rate of carbenoid attack on the remote carbonyl group to the point where an alternative reaction path can occur. In order to compensate for this diminished electrophilicity, we elected to substitute the hydrogen of the diazo carbon atom with an electron withdrawing group. Toward this end, the mixed diazomalonate (**6**) and diazoacetoacetate (**7**) were synthesized *via* the diazo transfer reaction of the corresponding 1,3-dicarbonyl compound.[7] Reaction with rhodium(II) acetate at 80 °C in the presence of *N*-phenyl maleimide afforded cycloadducts (**8**) and (**9**) in 75—85% yield (Scheme 3). Cycloaddition of the carbonyl ylide derived from (**6**) was also carried out in the presence of DMAD, methyl acrylate, and vinyl acetate to give cycloadducts (**10**)—(**12**), respectively (Scheme 4). The regio- and stereo-chemistry of the cycloadducts was assigned on the basis of their spectral properties and by FMO considerations.[8] For carbonyl ylides, the HOMO of the dipole is dominant for reactions with electron-deficient dipolarophiles such as methyl acrylate, while the LUMO becomes important for cycloaddition to more electron rich species such as vinyl acetate.

Having established the validity of increasing the electrophilicity of the intermediate rhodium carbenoid to allow for carbonyl ylide formation, we next explored the intramolecular cycloaddition reaction of a mixed diazomalonate containing a suitably positioned C–C double bond. To this end, ethyl diazomalonate (**13**) was prepared and treated with $Rh_2(OAc)_4$ at 80 °C to give the tricyclic lactone (**14**) in 65% yield† (Scheme 5).

In conclusion, complex oxapolycyclic lactones can be readily synthesized by the rhodium(II) acetate catalysed reaction of 1-acyl-1-diazoacetates. Incorporation of the lactone functionality into the resulting cycloadduct instills additional chemical versatility which should allow for subsequent synthetic manipulations.

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† All compounds gave satisfactory analyses. Complete spectroscopic and degradative details will be given in our full publication.