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Amino alcohol-mediated enantioselective syntheses of α-substituted indanones and tetralones, ammonium enolates as key intermediates

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ABSTRACT

Optically active 2-substituted-1-indanones or 2-substituted-1-tetralones are isolated from amino alcohol-mediated asymmetric domino reactions of α-disubstituted ketones, β-ketoesters, enol carbonates, α,β-unsaturated ketones, a silyl enol ether, or a β-ketoacid, with some of these reactions occurring under UV-light irradiation or Pd catalysis. The absence of a relationship between the nature of the substrate and the absolute configuration of the ketone produced is due to the protonation of a common ammonium enolate as the key enantioselective step. The enantioselectivity depends on various factors, which indicates the occurrence of side pathways.

Contents

1. Introduction

Over the past few years, the enantioselective protonation of prochiral enolic species has emerged as a powerful method for the synthesis of optically active ketones and esters. This reaction is, conceptually, particularly simple.[1] Various procedures have been developed, but the nature of the key intermediate and the factors governing the differentiation of its enantiotopic faces often remain a matter of debate.[1,2] Our contribution to this topic concerns enantioselective syntheses mediated by unichiral aminoalcohols **AH***,[3] of 2-substituted-1-indanones **K-5** and 2-substituted-1-tetralones **K-6** from; (i) the photochemical reaction of α-disubstituted ketones **αK**,[4] (ii) the Pd-catalyzed reaction of β-ketoesters ^{Al}**KE** and ^{Bn}**KE**,[5–7] enol carbonates ^{Al}**EC** and ^{Bn}**EC**,[6–8] α,β-unsaturated ketones **UK**,[9] trimethylsilyl enolate **ES-5$_{Me}$**;[10] or (iii) the decarboxylation of β-ketoacids **KA**[11] (Scheme 1). Baiker and co-workers have reinvestigated these enantioselective stereoablative[12] reactions of ^{Bn}**KE** and **KA-6$_{Me}$**.[13,14]

Herein our aim is to discuss the mechanisms and to point out the similarities in the intermediates leading to enantioenriched **K-5** and **K-6** from these different substrates and experimental conditions.

2. The photochemical approach

Irradiation of ketones such as **αK** at λ = 366 nm leads to Norrish type II reactions, that is, the cleavage of the C—C(*i*-Pr) bond, to afford **K** via an enol as intermediate (Scheme 2).[15]

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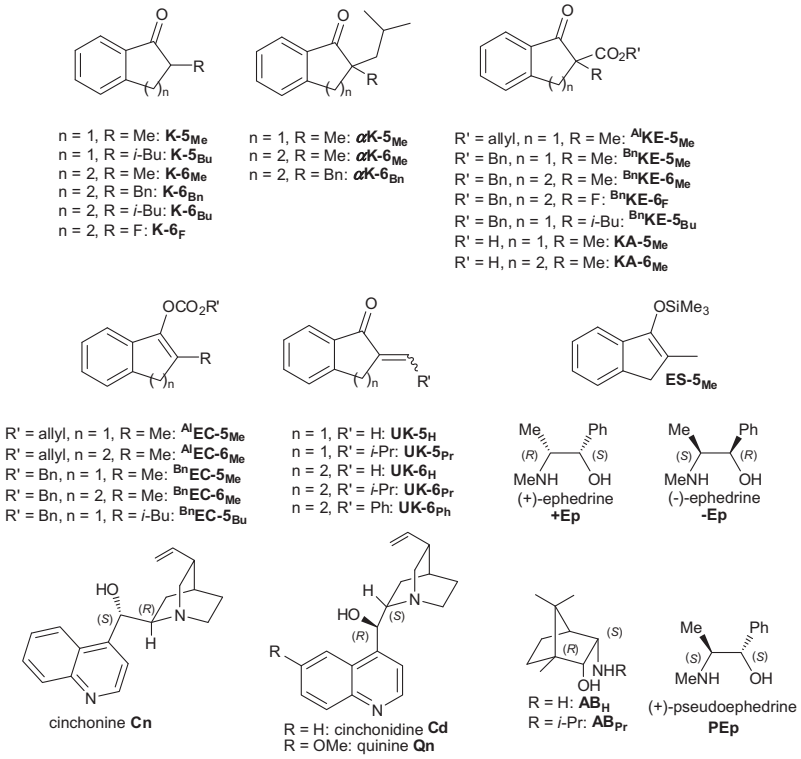
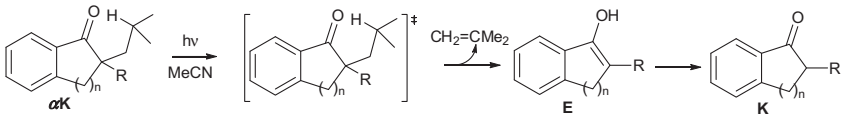
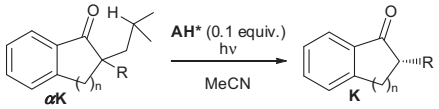


Scheme 1. Main compounds contained within this report.



Scheme 2. Norrish-type II reaction of **αK**.

Carried out in the presence of catalytic amounts of **AH***, such a photolysis of **αK-5$_{Me}$**, **αK-6$_{Me}$**, and **αK-6$_{Bn}$** leads to **K-5$_{Me}$**, **K-6$_{Me}$**, and **K-6$_{Bn}$**, respectively, with enantiomeric excesses (ee's) of up to 89% (Eq. 1).[4] One important drawback of this photochemical synthesis is the Norrish type I photoreactivity of **K**, that is, the homolytic cleavage of the CO—CR bond. Since **αK** and **K** have similar UV spectra, the possibility for this reversible photocleavage that causes the racemization of **K**, increases with the conversion of **αK**. Consequently, moderate conversions of **αK** are required to obtain fair ee's.

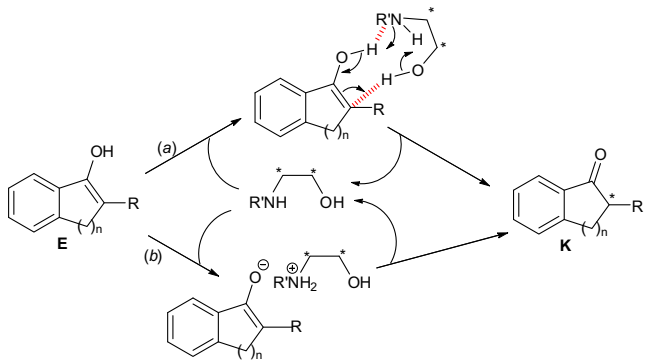


(1)

n = 1, R = Me, **AH*** = **- Ep**, rt: 70% conversion, (*R*)-**K-5$_{Me}$**, 45% e.e.
n = 2, R = Me, **AH*** = **- Ep**, rt: 69% conversion, (*R*)-**K-6$_{Me}$**, 41% e.e.
n = 2, R = Me, **AH*** = **AB$_{H}$**, rt: 86% conversion, (*R*)-**K-6$_{Me}$**, 63% e.e.
n = 2, R = Me, **AH*** = **AB$_{Pr}$**,- 40 °C: 60% conversion, (*R*)-**K-6$_{Me}$**, 89% e.e.
n = 2, R = Bn, **AH*** = **AB$_{Pr}$**,- 40 °C: 55% conversion, (*S*)-**K-6$_{Bn}$**, 23% e.e.

Monitoring the photolysis of **αK-5$_{Me}$** by ^{1}H NMR and UV spectroscopy, in the absence of **AH***, has led to the characterization of enol **E-5$_{Me}$** (δ = 1.96 (Me) and 3.16 (CH_2) ppm; λ_{max} = 265–270 nm)[4a,16] and the observation of its quantitative conversion into **K-5$_{Me}$** by the addition of **–Ep**.[4a] Since the solution obtained after this addition gave circular dichroism signals identical to those obtained from the irradiation of a mixture of **αK-5$_{Me}$** and **–Ep**,[4a] the involvement of the enol in the interactions with **AH*** giving rise to an asymmetric pathway was established. The asymmetric transformation of **αK** only requires organocatalytic conditions since the **E** → **K** reaction is more rapid than the **αK** → **E** reaction, hence an **AH***/**E** ratio superior to 1 throughout the photolysis.

Given initial studies on photodienols,[17] we first suspected an **E** → **K** reaction occurring via a nine-membered ring intermediate formed by polar interactions between the enol and the two functionalities of **AH*** (Scheme 3, path *a*);[4b] however literature reports[18] and subsequent studies[19] led us to propose the participation of an ammonium enolate (Scheme 3, path *b*).



Scheme 3. Plausible enantioselective pathways from **E**.