Tetrahedron: Asymmetry Vol. 3, No. 9, pp. 1161-1164, 1992
Printed in Great Britain

0957-4166/92 $5.00+.00
Pergamon Press Ltd

Palladium-Catalyzed Cleavage of Prochiral Enol Carbonates: Enantioselective Ketonisation of Resulting Enols*

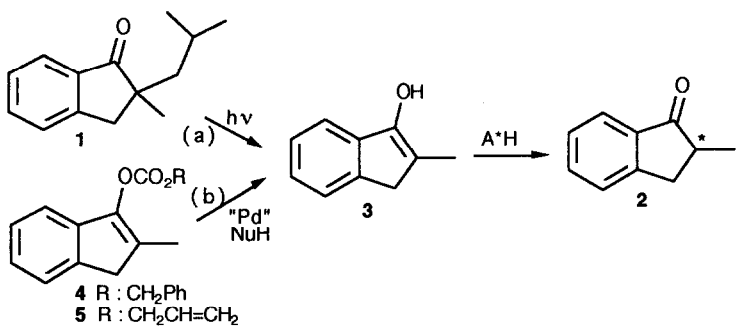
Françoise Hénin, Jacques Muzart
Unité "Réarrangements Thermiques et Photochimiques" Associée au CNRS
Université de Reims Champagne-Ardenne, B.P. 347, 51062 Reims Cedex, France

(*Received* 11 *August* 1992)

Summary: The palladium-catalyzed deprotection of (2-methyl-1-indenyl) benzyl carbonate and (2-methyl-1-indenyl) allyl carbonate in the presence of (+) or (-)ephedrine has led to 2-methyl-1-indanone with enantiomeric excesses of up to 40%.

For a few years, we have been involved in the asymmetric protonation of photoenols[1,2] and recently, we have described the Norrish type II reaction of 2-methyl-2-isobutyl-1-indanone **1** in the presence of (-) ephedrine which afforded *(R)*-2-methyl-1-indanone **2** through asymmetric tautomerisation of the intermediate enol **3** (Scheme 1, path a).[3] This work exhibited one of the rare examples of asymmetric protonation of a simple enol.[4-7]

Scheme 1

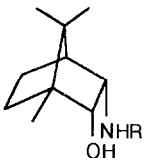


We have now envisaged obtaining **3** from enol carbonates **4** and **5**. The palladium-catalyzed cleavage/decarboxylation of allyl- or benzyl carbonates has been largely used in organic synthesis[8] and we suspected that the benzyl- and allyl enol carbonates **4** and **5** would lead to **3** as transient species under literature conditions. Thus, we decided to perform these reactions in the presence of chiral protic sources (Scheme 1, path b) and we report here the results (Tables 1 and 2).

The deprotection of **4** has been carried out at room temperature in acetonitrile in the presence of palladium on charcoal, chiral protic species, and continuous bubbling of hydrogen. The comparison of the results assembled in Table 1 depicts that a) it is necessary to use a chiral aminoalcohol (runs 1 to 3) rather than a chiral alcohol, amine, or acid (runs 4 to 6) to observe fair enantiomeric excesses (e.e.), b)*(R)*-**2** was the major enantiomer obtained when using (-)ephedrine. Such observations, already made for the asymmetric protonation of photochemically produced **3**,[3] would be due to a synergic effect of the amino and hydroxy groups allowing

* Part of this work has been presented as poster at the GECOM XX, Reims, May, 11-15, 1992.

the tautomerisation step to go through a nine-membered cyclic transition state.[9]



6a R : H
6b R : *i*-Pr

Table 1: Deprotection of **4**.

Run	Chiral protic species (equiv.)	Time h	**2** Yield %	e.e. %[a]
1	(-)ephedrine (0.5)	1.5	93	*(R)*, 32
2	**6a** (0.30)	1.5	99	*(R)*, 40
3	**6b** (0.34)	1	99	*(R)*, 30
4	methyl (*S*)-lactate (0.95)	3	82	0
5	cis-4-hydroxy-D-proline[10] (0.34)	5	96	*(R)*, 3
6	*(R)*-α-methylbenzylamine (excess)	1	b	0

[a]Configuration in brackets of the main enantiomer determined from $[\alpha]_D$ comparisons;[11] e.e. (± 3%) determined by $[\alpha]_D$ comparisons[11] and CPV on a 25 m fused silica coated with CP-cyclodextrin-β-2,3,6,-M-19 glass capillary column (sold by Chrompack). [b]not calculated.

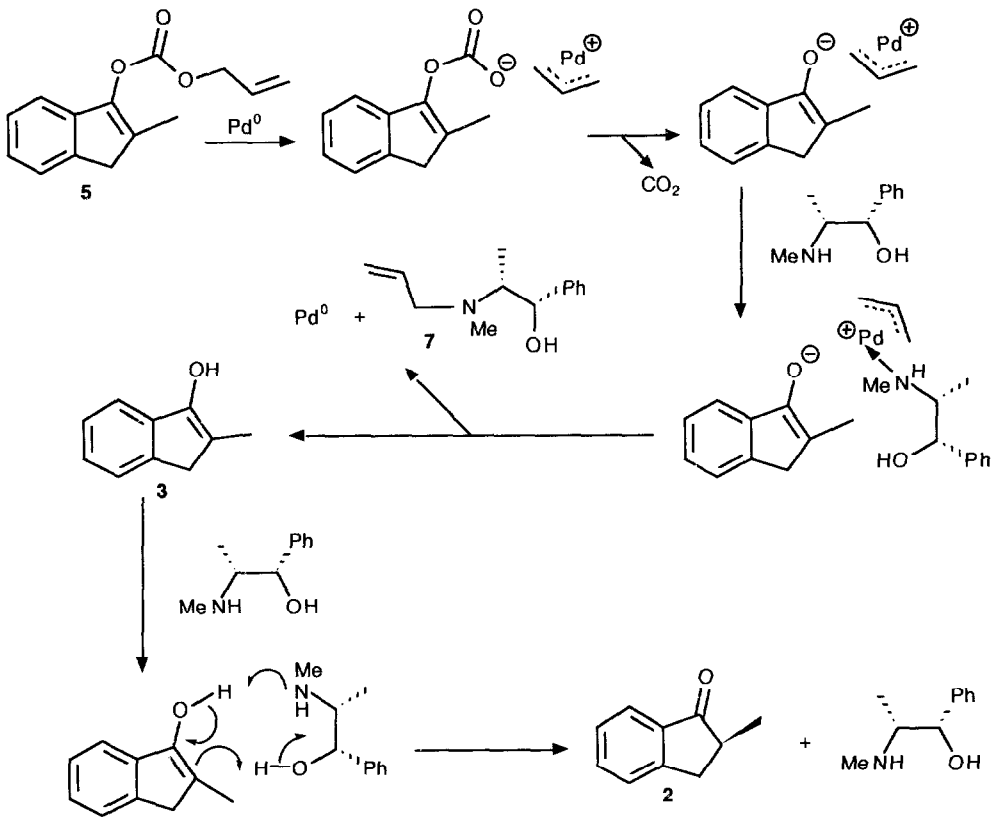
Table 2: Deprotection of **5**.[a]

Run	Pd catalyst (equiv.)	PPh_3 equiv.	Time h	ephedrine, equiv.	**2**[b] Yield %	e.e. %[c]
7	$Pd(OAc)_2$ (0.04)	0.16	15.5	(+), 0.25	27[d]	≈ 0
8	$Pd(OAc)_2$ (0.05)	0.12	6	(-), 1	80	*(R)*, 27
9	$Pd(OAc)_2$ (0.08)	0.12	48	(+), 1	99	*(S)*, 21
10	$Pd(OAc)_2$ (0.09)	0.16	4.5	(+), 3.28	92	*(S)*, 25
11	$Pd_2(dba)_3CHCl_3$ (0.06)	0.14	3	(+), 2.99	68[e]	*(S)*, 16
12[f]	$Pd(OAc)_2$ (0.06)	0.12	24	(-), 1.56	90	*(R)*, 38
13[g]	$Pd(OAc)_2$ (0.06)	0.10	47	(+), 1	99	*(S)*, 4
14[h]	$Pd(OAc)_2$ (0.06)	0.11	4	(-), 0.2	89	0

*[a]Reaction carried out at room temperature except for run 12. [b](+) or (-)ephedrine in brackets. [c]see note (a) in table 1. [d]34% of **5** has been recovered. [e]5% of **5** has been recovered. [f]Reaction carried out at 0°C. [g]Reaction carried out in the presence of HCO_2NH_4 (1.8 equiv). [h]Reaction carried out in the presence of dimedone (1.5 equiv).*

The palladium-catalyzed deprotection of **5** has been accomplished in acetonitrile in the presence of ammonium formate or dimedone and/or chiral ephedrine. From the main results listed in Table 2, it appears that a) $Pd(OAc)_2/PPh_3$ as catalyst led to a better yield and e.e. than $Pd_2(dba)_3CHCl_3/PPh_3$ (runs 10 and 11) b) ammonium formate and dimedone compete with ephedrine in the tautomerisation step and the e.e. diminishes (runs 13 and 14), c) **2** seems to be slighty racemised by the palladium catalyst since the e. e. is reduced when the work-up is carried out later (runs 8 and 9),[12] d) a large excess of the quantity of ephedrine did not allow a better e.e. (run 10), e) in the absence of HCO_2NH_4 or dimedone, the use of less than 1 equiv. of ephedrine did not allow the full conversion of **5**, and furthermore led to a very low e.e. (run 7), f) chilling the reaction mixture from room temperature to 0°C slowed the reaction rate and increased the e.e. (run 12).

Scheme 2



From palladium-literature data[8,13] and preceeding results concerning tautomerisation of photoenols,[3,9] we envisaged the mechanism indicated in scheme 2 to rationalise the results obtained with **5** as starting compound and (+)ephedrine as stoichiometric reagent. Ephedrine would play two roles: firstly, it would act as nucleophile[13] towards the *in-situ* produced η^3-allylpalladium complex; secondly, it would catalyze the enantioselective tautomerisation of the intermediate enol.[3,9,14] This scheme rationalizes the necessity of the presence of at least 1 equiv. of the amine to reach full conversion of **5** under these conditions and supposes the formation of the adduct **7**. Indeed, the polar product recovered at the end of the reaction (93% yield) presents a

negative rotation ($[\alpha]_D$: -2) and corresponds to **7** according to its 250 MHz NMR spectrum ($CDCl_3$, d: 0.89, d, *J* 6.9 Hz, $CHC\underline{H}_3$; 2.30, s, $NC\underline{H}_3$; 2.87, qq, *J* 6.9, 3.8,$C\underline{H}CH_3$; 3.16, d, *J* 6.9, $C\underline{H}_2CH{=}CH_2$; 3.84, O$\underline{H}$; 4.88, d, *J* 3.8, $C\underline{H}OH$; 5.18, m, $C\underline{H}_2{=}CH$; 5.83, m, $C\underline{H}{=}CH_2$; 7.1-7.8, $C_6\underline{H}_5$).

Preliminary experiments have shown that a similar cleavage / decarboxylation / enantioselective ketonisation can be carried out from a β-ketoester. We are also carrying out investigations in the area of enols produced by metal-catalyzed isomerisation of allyl alcohols.[15]

Acknowledgment: We are grateful to Pr H. Rau (Hohenheim University, Stuttgart) for kind hospitality in his laboratory where experiments have been followed by CD spectroscopy. We thank DRCI for travel facilities.

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[7]In contrast, intensive research work is currently devoted to the asymmetric protonation of enolates, see a) ref. cited in[3], b) K. Matsumoto, H. Ohta *Tetrahedron Lett.* 1991, **32**, 4729, c) C. Fehr *Chimia* 1991, **45**, 253, d) *"The Chemistry of Enols"* Z. Rappoport, Ed., J. Wiley: Chichester, 1990.

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[12]Indeed, optically active **2** (e.e. 38%) submitted to the experimental conditions has been partially racemized: S. Jamal, unpublished results. This racemization could involve the formation of a palladium enolate of **2** as intermediate.

[13]a) A. Groult, A. Guy *Tetrahedron* 1983, **39**, 1543, b) T. Tsuda, T. Kiyoi, T. Saegusa *J. Org. Chem.* 1990, **55**, 3388.

[14]A referee has envisaged the liberation of the enolate of **2** during the catalytic cycle and that this enolate would be the real species interacting with ephedrine. Two experiments respectively reported in the note[9] of a preceeding study[3] and in the note[12] of the present paper lead us to consider rather a chiral tautomerisation of **3**.

[15]For a different approach involving an enantioselective tautomerisation due to a chiral rhodium complex, see[4].