

## Rhodium Catalysed Decarbonylation of Optically Active Campholenal Analogues

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**Abstract:** Campholenal analogues (+)-1a-d were decarbonylated with a catalytic amount of Rh/Al<sub>2</sub>O<sub>3</sub> with only slight racemization. Experiments with other catalysts showed that racemization increases with the ability of the metal to form a  $\pi$ -allyl complex and to catalyse the hydrogenation of the  $\beta$ -elimination side product. (Ph<sub>3</sub>P)<sub>3</sub>RhCl gave the best results.

Decarbonylation of campholenal ((+)-1a) [1] using Pd/C [2] has recently been shown to proceed with practically complete racemization [3]. Requiring the optically active olefins 3a-d (see table 2) in both antipodal forms as chiral building blocks for the preparation and olfactive evaluation of precious flowery and woody natural [4] and synthetic [5] fragrances, we decided to study the mechanism of racemization and to examine alternative catalysts which might prevent it.

As the enantiomers of 1a were inseparable on diverse chiral GC or SCF-HPLC [6] columns, its optical purity was determined by integration of the aldehydic signal using <sup>1</sup>H-NMR analysis in the presence of Eu(hfbc)<sub>3</sub> ((+)-1a,  $\alpha_D^{20} = +8.8$  neat, 90% e.c.[7]; (-)-1a,  $\alpha_D^{20} = -9.6$  neat, 96% e.c.). Distillation of (+)-1a at 190°C in the presence of Pd/C 5% (6% by weight), afforded practically racemic 3a [8] in 77% yield (entry 1, table 1).

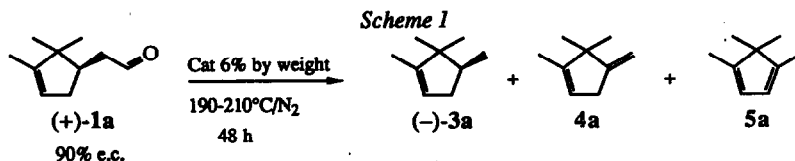


Table 1

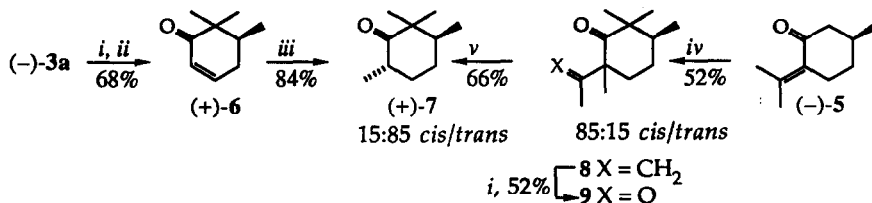
Entry	Catalyst	Yield% <sup>a</sup>	(-)-3a%	4a%	5a%	e.c.% <sup>b</sup>
1	Pd/C 5%	77	>96	<2	<2	55 (59) <sup>c</sup>
2	Ni/Al <sub>2</sub> O <sub>3</sub> 5%	12	76	5	19	80
3	Pt/C 5%	30	71	15	14	83
4	Rh/Al <sub>2</sub> O <sub>3</sub> 5%	80	51	36	13	88
5	Rh/Al <sub>2</sub> O <sub>3</sub> 5%	78 <sup>d</sup>	50	26	24	85
6	(Ph <sub>3</sub> P) <sub>3</sub> Rh(H)(CO)	23	55	37	8	85
7	(Ph <sub>3</sub> P) <sub>3</sub> RhCl	70	>94	<1	<5	88 (94) <sup>c</sup>

a) distilled material after 48 h, higher yields were obtained after prolonged periods. (-)-3a, 4a and 5a are only partially separable by GC, the ratio was determined by integration of the olefinic protons in the <sup>1</sup>H-NMR analysis; b) calculated using Europium III-tris(3-(heptafluorobutyl)-d-camphorate); c) starting from (-)-1a; d) under 1.1 atm of H<sub>2</sub> instead of N<sub>2</sub>.

Ni/Al<sub>2</sub>O<sub>3</sub> 5% [9] and Pt/C 5% [10] were less active (entries 2 and 3, table 1) and furthermore gave mixtures of (-)-3a, 4a and 5a [11]. The partial racemization could not be directly determined on chiral GC columns or by <sup>1</sup>H-NMR analysis due to inefficient separation [6]. Consequently (-)-3a was subjected to ozonolysis, followed by

intramolecular aldol condensation [1] to give the enone (+)-6 ( $\alpha_D^{20} = +64$  neat, 88% e.c.; (-)-6,  $\alpha_D^{20} = -68$  neat, 94% e.c.) which was analysed by  $^1\text{H-NMR}$  in the presence of  $\text{Eu}(\text{hfbc})_3$ .

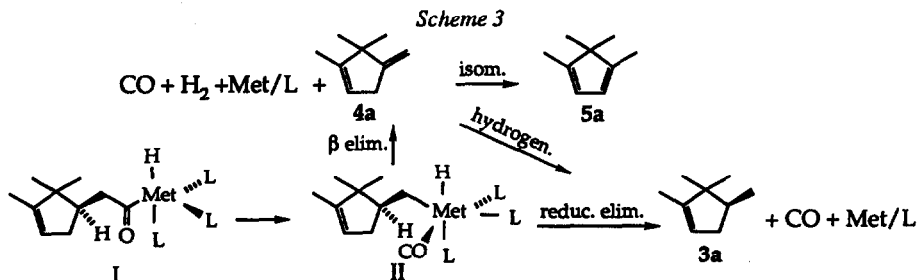
Scheme 2



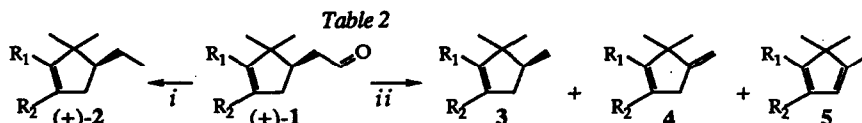
i)  $\text{O}_3$ ,  $\text{CH}_2\text{Cl}_2$ ,  $\text{DMS}$ ; ii)  $p\text{TsOH}$ , cyclohexane; iii)  $\text{NH}_3/\text{Li}$ ,  $\text{MeI}/\text{THF}$ ; iv)  $\text{KH}$ ,  $\text{MeI}$ ,  $\text{THF}$ ; v)  $\text{KOH}$ ,  $\text{EtOH}$   $\updownarrow$

During the preparation of (+)-1a and (+)-1c (table 2) and their precursors, several inconsistent reports [12], indicating inverse optical properties for the same absolute configuration, persuaded us to correlate (+)-6 with (-)-S-pulegone ((-)-5)[13]. Accordingly, permethylation of (-)-5 [14], [15] gave a 85:15 mixture of (+)-cis/trans-8, whose ozonolysis followed by reduction ( $\text{DMS}$ ) and basic treatment [16] afforded the equilibrated 15:85 (-)-cis / (+)-trans ketone 7 [5] of the same absolute configuration as that obtained by monomethylation [17] of (+)-6. The optically pure ketone (-)-trans-7 ( $\alpha_D^{20} = -50.7$  neat) was similarly obtained from (+)-R-pulegone ( $\alpha_D^{20} = +24.1$  neat). An attempted direct hydrolytic ( $\text{H}_2\text{SO}_4 : \text{H}_2\text{O}$ ) retro-aldol [18] on cis/trans-8 was unsuccessful.

Having confirmed the correct absolute configuration [12a] we then investigated the use of  $\text{Rh}/\text{Al}_2\text{O}_3$  5% [19] as catalyst, which resulted in a rapid decarbonylation with only slight racemization (entry 4, table 1). Subsequently, the best results in terms of chemical and optical purity were obtained under homogeneous conditions by employing a catalytic amount of Wilkinson catalyst, already successfully used by Walborsky and Allen [20] for the decarbonylation of optically active  $\alpha$ -substituted aldehydes (entry 7, table 1). The accepted mechanism [21] is illustrated in the following scheme.



Thus, the metal complex II may give rise to either (-)-3a by reductive elimination or 4a by  $\beta$ -elimination, further isomerisation leads to 5a. Formally, racemization may occur by hydrogenation of 4a in the presence of nascent hydrogen produced from the  $\beta$ -elimination pathway or by displacement of the double bond in 3a via a  $\pi$ -allyl complex. Decarbonylation performed under  $\text{H}_2$  (entry 5, table 1) does not displace the equilibrium towards reductive elimination and resulted in partial racemization. Alternatively, when the aldehyde (+)-1b [1] (table 2) was decarbonylated at  $190^\circ\text{C}$  with  $\text{Pd}/\text{C}$  5%, a 3 : 4 mixture of rac 2a : 3b distilled in 75% yield. When pure (+)-2a [22] was refluxed with  $\text{Pd}/\text{C}$  at  $190^\circ\text{C}$  for 6 hrs, a 2 : 1 mixture corresponding to the thermodynamic ratio of 2a (12.01 kcal/mol [23]) and 3b (12.36 kcal/mol) was formed. These two experiments clearly indicate migration of the double bond via a  $\pi$ -allyl complex. Decarbonylation using metallic rhodium was also extended to aldehydes (+)-1c [24] and (+)-1d [25] (both 95% e.c.) without noticeable racemization.



Entry	R <sub>1</sub>	R <sub>2</sub>	Yield % (for i)	Yield % (for ii)	Product distribution %		
					α 3	4	5
a	Me	H	94	80	(-) 51	36	13
b	Et	H	72	78	(-) 50	29	21
c	H	Me	83	61	(+) 49	41	10
d	H	Et	72	58	(+) 59	41	0
e	(CH <sub>2</sub> ) <sub>2</sub> OH	H	85				
f	(CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> Me	H	76 <sup>iii</sup>				

i) NH<sub>2</sub>NH<sub>2</sub>, KOH, ethyleneglycol; ii) Rh/Al<sub>2</sub>O<sub>3</sub> 5%, 6% by weight 190°C/N<sub>2</sub>, 48 h; iii) after esterification, MeOH, cat. H<sub>2</sub>SO<sub>4</sub>.

The olefins (+)-2a-d, (-)-3a,b and (+)-3c,d are important precursors for the preparation of optically active cyclohexenones, naturally occurring in iris concrete [26]. The alcohol (+)-2e and the methyl ester (+)-2f obtained by *Wolff-Kishner* reduction of (+)-1e and (+)-1f respectively [1] are also potential chirons in the context of a systematic study of the lipophilic part of sandalwood-like alcohols derived from campholenal analogues [1]. Further synthetic transformation of these olefins will be presented in due course.

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25. Obtained similarly to (+)-1c [12a] from (-)-ethyl apopinene [1]. Exp. generalities, see [1]. (+)-1d : 0.83(s, 3H); 1.01(t, 7, 3H); 1.06(s, 3H); 2.0(m, 3H); 2.25-2.55(m, 4H); 5.15(brs, 1H); 9.81(t, 2, 1H); 12.2q, 22.5q, 24.1t, 28.1q, 40.4t, 43.5d, 45.2t, 45.9s, 133.6d, 142.8s, 202.9d; 166(M<sup>t</sup>, 6), 122(50), 107(100), 91(37), 81(28), 67(21),  $\alpha_D^{20} = +33.6$ ; (+)-2a: 12.6q, 13.3q, 19.7q, 22.9t, 26.1q, 35.5t, 46.9s, 52.7d, 121.8d, 148.8s,  $\alpha_D^{20} = +2.9$ ; (+)-2b: 0.75(s, 3H), 0.92(t, 7, 3H); 0.98(s, 3H), 1.07(t, 7, 3H); 1.24(m, 1H); 1.45-1.70(m, 2H); 1.80(m, 1H); 1.94(m, 2H); 2.35(m, 1H); 12.2q, 13.3q, 19.7t, 20.2q, 22.7t, 26.1q, 35.4t, 47.1s, 52.9d, 119.3d, 155.0s, 152(M<sup>t</sup>, 17), 137(100), 123(33), 95(45), 81(45),  $\alpha_D^{20} = +2.5$ ; (+)-2c: 0.79(s, 3H), 0.92(t, 7, 3H); 1.01(s, 3H); 1.20(m, 1H); 1.46(m, 1H); 1.67(s, 3H); 1.70(m, 1H); 1.92(dd, 10, 14, 1H); 2.28(dd, 7, 15, 1H); 5.32(brs, 1H), 13.5q, 16.8q, 22.1q, 22.9t, 28.5q, 42.1t, 46.1s, 52.0d, 136.7d, s; 138(M<sup>t</sup>, 6), 123(100), 109(19), 81(67), 67(21),  $\alpha_D^{20} = +27.9$ ; (+)-2d: 0.78(s, 3H); 0.92(t, 7, 3H); 1.01(t, 7, 3H); 1.03(s, 3H); 1.20(m, 1H); 1.48(m, 1H); 1.67(m, 1H), 1.90(m, 1H); 2.00(m, 2H); 2.30(m, 1H); 5.13(brs, 1H); 12.3q, 13.6q, 22.1q, 22.8t, 24.3t, 28.5q, 40.2t, 45.6s, 51.6d, 134.3d, 142.8s; 152(M<sup>t</sup>, 5), 137(100), 123(19), 95(60), 81(46),  $\alpha_D^{20} = +30.6$ ; (+)-2e: 0.77(s, 3H), 0.93(t, 7, 3H); 1.00(s, 3H); 1.23(m, 1H); 1.48(m, 1H); 1.60(m, 1H); 1.65(m, 1H); 1.82(m, 1H); 2.23(m, 2H); 2.37(m, 1H); 3.76(m, 2H); 5.36(brs, 1H); 13.3q, 20.3q, 22.6t, 26.1q, 30.3t, 35.6t, 47.4s, 52.4d, 61.3t, 122.5d, 149.3s; 168(M<sup>t</sup>, 5), 153(23), 135(15), 123(27), 109(100), 93(40), 79(21), 67(20), 55(19);  $\alpha_D^{20} = +4.3$ ; (+)-2f: 0.76(s, 3H); 0.92(t, 7, 3H); 0.97(s, 3H); 1.22(m, 1H); 1.46(m, 1H); 1.63(m, 1H); 1.81(m, 3H); 1.94(m, 2H); 2.29(m, 1H); 2.35(t, 7, 2H); 3.67(s, 3H); 5.27(brs, 1H); 13.3q, 20.2q, 22.6t, 23.3t, 26.1q, 26.3t, 34.0t, 35.5t, 47.2s, 51.4q, 52.7d, 120.9d, 152.0s, 174.1s, 224(M<sup>t</sup>, 8), 209(47), 177(32), 135(100), 123(56), 93(52), 55(36),  $\alpha_D^{20} = +5.6$ ; (-)-3a: see [3],  $\alpha_D^{20} = -5.1$ ; (-)-3b: 0.75(s, 3H), 0.94(d, 7, 3H); 0.95(s, 3H); 1.07(t, 3H); 1.84(m, 2H); 1.95(m, 2H); 2.27(m, 1H); 5.23(brs, 1H); 138(M<sup>t</sup>, 17), 123(100), 109(25), 95(18), 81(57), 67(25),  $\alpha_D^{20} = -9.2$ ; (+)-3c: 0.78(s, 3H); 0.92(d, 7, 3H); 0.98(s, 3H); 1.66(s, 3H); 1.90(m, 2H); 2.25(m, 1H); 5.13(brs, 1H); 124(M<sup>t</sup>, 11), 109(100), 81(20), 67(55),  $\alpha_D^{20} = +17.2$ ; (+)-3d: 0.78(s, 3H); 0.92(d, 7, 3H); 1.00(s, 3H); 1.01(t, 7, 3H); 1.90(m, 1H); 2.00(m, 3H); 2.26(m, 1H); 5.12(brs, 1H); 138(M<sup>t</sup>, 10); 123(100); 121(48), 93(27), 81(57), 67(19),  $\alpha_D^{20} = +1.4$ ; (+)-cis-8: 0.90(d, 7, 3H); 0.97(s, 3H); 1.14(s, 3H); 1.15(s, 3H); 1.43(m, 1H); 1.64(m, 1H); 1.69(s, 3H); 1.98(m, 2H); 2.15(m, 1H); 4.86(s, 2H); 16.1q, 20.1q, 21.9q; 25.9t, 26.0q, 26.1q, 31.2t, 37.8d, 48.4s, 53.3s, 110.6t, 147.6s, 218.6s; 194(M<sup>t</sup>, 5); 137(13); 123(72); 107(26), 96(31), 82(100), 67(50), 55(24),  $\alpha_D^{20} = +97.2$ ; (+)-cis-9: 0.91(d, 7, 3H); 1.02(s, 3H); 1.10(s, 3H); 1.25(s, 3H); 1.45(m, 1H); 1.54(m, 1H); 1.81(m, 1H); 2.07(s, 3H); 2.08(m, 1H); 2.40(dt, 4, 12, 1H); 16.2q, 22.2q, 23.0q, 25.5t, q, 25.7q, 30.1t, 40.1d, 49.6s, 62.6s, 205.9s, 215.6s; 196(M<sup>t</sup>, 4); 154(86), 139(70), 125(21), 96(36), 84(100), 69(91), 43(74),  $\alpha_D^{20} = +212$  (c = 2.0, CHCl<sub>3</sub>).
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