"Synthetic Enzymes". Highly Stereoselective Epoxidation of Chalcone in a Triphasic Toluene-Water-Poly[(S)-alanine] System *(reprint)*

By Sebastián Juliá, Jaume Masana, and Juan Carlos Vega

thus obtainable only as a chloroform solution with 2—4% of *(2)* and 10—15% of *tert*-butyl alcohol.

Although the hydrocarbon *(1)* is a highly reactive compound, which polymerizes in condensed phase even at −78 °C, its solution in chloroform containing a small amount of hydroquinone can be kept several days at −30 °C. Its spectroscopic data[5] resemble those of cyclopropane and cyclopropene. In particular the ^{13}C-H spin-spin coupling constants (158 and 225 Hz) compared to the coupling constants observed for cyclopropane and 3,3-dimethylcyclopropene (respectively 161 and 220 Hz)[6], suggest no difference in the states of hybridization of the corresponding C—H bonds. This would indicate that *(1)* is a normal spiro compound, and that the interaction between the cyclopropane Walsh orbitals and the cyclopropene π orbitals (pseudoconjugation)[7], if at all present, is not important. Confirmation by UV and PE spectroscopy has so far been precluded by the impurities present in *(1)*.

The high strain of *(1)* is revealed by its unusual chemical reactivity compared with that of 3,3-disubstituted cyclopropenes. As expected, the cyclopropene double bond is very
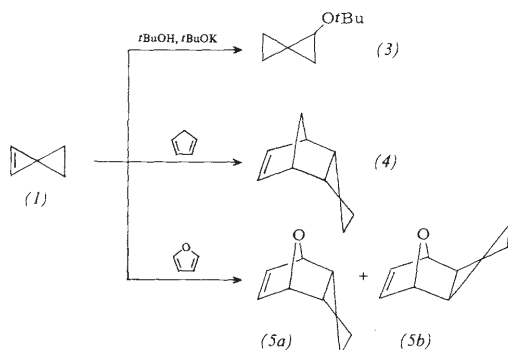
reactive toward nucleophiles; for example, *(1)* adds readily *tert*-butanol in the presence of *tert*-BuOK to give the spiro compound *(3)*[5]. Unlike 3,3-dimethylcyclopropene[8], spiropentene reacts rapidly and quantitatively, even at 0 °C, with cyclopentadiene and furan, respectively giving almost exclusively[9] the *endo* adduct *(4)*[5] and two adducts *(5a)*[5] and *(5b)* (1:3)[10]. Assignment of the configurations is based on the ^{1}H-NMR spectra. In particular, the bridgehead protons show neat coupling to the vicinal cyclopropyl hydrogens only for the *endo* configuration[10]. It appears also to be general that the olefinic protons of the endo-adducts are more shielded than the vinyl protons of the *exo* adducts.
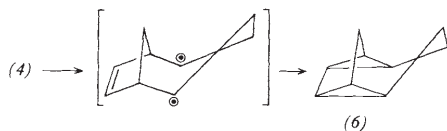
Heating of the compounds *(4)* or *(5)* does not regenerate *(1)* (retro Diels-Alder rupture). *(5)* leads to several unidentified products, while *(4)* affords a unique compound *(6)* both in the vapor phase at 500 °C and in the condensed phase at 180 °C. The mass spectral data show that *(6)* is an isomer of the starting material *(4)*. The NMR spectrum has multiplets between $\delta = 0.1$ and $\delta = 2.0$, but no more absorption in the olefinic proton region. Such rearrangements *via* stabilized 1,3-diradicals, have been already observed in analogous systems[11].

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[5] Spectroscopic data of the new compounds: *(1)*: IR (CDCl$_3$) 3060, 1635, 1010 cm^{-1}; ^{1}H-NMR (CDCl$_3$): $\delta = 7.10$ (br. q, 2H, $J = 1.5$ Hz), 0.58 (br. t, 4H, $J = 1.5$ Hz); ^{13}C-NMR (CDCl$_3$): $\delta = 114.7$ (C2, C1), 16.8 (C3), 4.1 (C4, C5). *(3)*: ^{1}H-NMR (CCl$_4$): $\delta = 3.32$ (m, 1H), 1.18 (s, 9H); 0.72—1.05 (m, 6H). *(4)*: ^{1}H-NMR (CCl$_4$): $\delta = 5.83$ (t, 2H), 2.78 (m, 2H), 1.6—1.9 (m, 4H), 0.1—0.9 (m, 4H). *(5a)*: ^{1}H-NMR (CCl$_4$): $\delta = 6.05$ (br. s, 2H), 4.76 (m, 2H), 2.12 (m, 2H), 0.35—1.05 (m, 4H). *(5b)*: ^{1}H-NMR (CCl$_4$): $\delta = 6.46$ (br. s, 2H), 4.58 (br. s, 2H), 1.38 (s, 2H), 0.35—1.05 (m, 4H).
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[9] Less than 5% of a second adduct was present but could not be separated. However, the chemical shift of the olefinic protons ($\delta = 6.35$) is in good agreement with the shift expected for the *exo* adduct.
[10] Cyclopropene itself gives two adducts with furan in the ration of 1:1, see *R. W. La Rochelle, B. M. Trost*, J. Chem. Soc. Chem. Commun. *1970*, 1353.
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"Synthetic Enzymes". Highly Stereoselective Epoxidation of Chalcone in a Triphasic Toluene-Water-Poly[(S)-alanine] System[**]

By *Sebastián Juliá, Jaume Masana*, and *Juan Carlos Vega*[*]

The use of synthetic peptides as stereoselective catalysts in organic reactions is an attractive alternative to the use of enzymes[1]. However, many of the examples reported[2] have considerable disadvantages: optical yields may be too low[2a]; reaction times too long[2b], or the amounts of protein required too large[2c, d]. To our knowledge we report here the first example of a nearly stereospecific reaction by means of a triphase catalysis using readily available synthetic chiral polypeptides, which does not suffer from any of the drawbacks of the methods just mentioned. Thus, we have achieved the epoxidation of chalcone *(1)* to levorotatory *(2)* in optical yields higher than 90% and satisfactory chemical yields with poly[(S)-alanine] *(5a)*, poly[5-benzyl-(S)-glutamate] *(5b)*, and poly[5-butyl-(S)-glutamate] *(5c)* as catalysts.
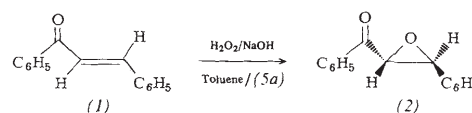

Previously, epoxychalcone *(2)* was obtained in 34% optical yield by a phase-transfer method using benzylquininium chloride as catalyst[3]. Its absolute configuration has recently been determined[3]. The polypeptides were synthesized according to Scheme 1, method *A* being used for the preparation of polyalanine, and method *B* being preferred for the synthesis of polyglutamates[4].

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The polymerization of the *N*-carboxy anhydrides *(4)*, was performed with *n*-butylamine (molar ratio 10:1). This assumes that the polymers contain an avarage of ten amino acids. IR data show both extended and helicoidal conformations to be present[5].

a, R = CH₃; *b*, R = (CH₂)₂COOCH₂C₆H₅;
c, R = (CH₂)₂COO(CH₂)₃CH₃
m = 10

Scheme 1
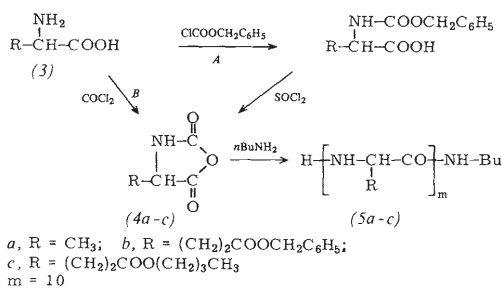
Experimental

Poly[(*S*)-alanine] *(5a)*: (*S*)-Alanine *N*-carboxyanhydride[4b] (11.39 g, 0.1 mol) is dissolved in acetonitrile (400 ml) (dried over P₂O₅). *n*-Butylamine (0.728 g, 0.01 mol) is added and the mixture is stirred for 4 d at room temperature. A white solid appears. The solvent is removed *in vacuo*, and the polymer is washed with diethyl ether. The polymer is dried *in vacuo*. Yield 7.5 g; m.p. >300 °C; IR (KBr): 3370, 3060, 1655, 1630, 1540 cm⁻¹; ¹H-NMR (CF₃COOH): $\delta = 7.3$ (--N*H*), 4.2 (--NH--C*H*--CO), 3.0 (--C*H₂*--R), 1.1 (CH₂--C*H₂*--C*H₂*--CH₃, and NH--CH(C*H₃*)CO), 0.5 (CH₂)₃--C*H₃*); $[\alpha]_{589}^{20} = -120.5$ ($c = 0.996$, CF₃COOH).

(−)-1,3-Diphenyl-2(*R*),3(*S*)-epoxypropan-1-one *(2)* (Table 1, exp. 3): To a solution of *(1)* (1.00 g, 4.8 mmol) in toluene (6.00 g) is added poly[(*S*)-alanine] (400 mg, 0.5 mmol; approx. mol. weight 783). The mixture is stirred for 30 min and a solution of NaOH in 30% H₂O₂ (0.08 g/ml) is slowly added dropwise. The mixture is stirred at room temperature for 48 h. The catalyst is filtered and washed with CH₂Cl₂ (50

Table 1. Epoxidation of chalcone *(1)* in the presence of polypeptides *(5)*. Levorotatory epoxide *(2)* was formed in all cases *(2)* [a].

Exp.	Poly-peptide	*(1)* [g]	NaOH/H₂O₂ [b] [ml]	Toluene [g]	*(5)* [g]	*(5)*:*(1)*	*t* [h]	Chem. yield [c] [%]	Opt. yield [d] [%]
1		1	4.4	6	—	—	48	0	—
2	*(5a)*	1	4.4	6	0.2	0.2:1	48	76	86
3	*(5a)*	1	4.4	6	0.4	0.4:1	48	70	86
4	*(5a)*	1	4.4	6	0.8	0.8:1	48	26	97
5	*(5a)*	0.5	4.4	6	0.4	0.8:1	24	85	93
6	*(5a)*	0.5	8.8	6	0.4	0.8:1	48	80	93
7 [e]	*(5a)*	0.5	4.4	6	0.4	0.8:1	48	36	72
8	*(5b)*	1	4.4	6	1.3	1.3:1	48	6	57
9	*(5b)*	1	8.8	13	0.65	0.65:1	144	12	11
10	*(5b)*	1	8.8	26	1.3	1.3:1	144	8	11
11	*(5c)*	1	4.4	6	0.98	0.98:1	48	10	28

[a] For conditions of the reaction, see *Experimental*. [b] Solid NaOH in H₂O₂ 30% (0.08 g/ml). [c] Product isolated by silica-gel chromatography. [d] $100 \times [\alpha]_{578}^{20}$ 214; maximum value $[\alpha]_{578}^{20} = -214$ ($c = 1.6$ in CCl₂H₂). [e] Polymer recovered after one experiment.

Our experiments are summarized in Table 1. From the results, the following inferences can be made:

a) Use of polyglutamates *(5b)* and *(5c)* instead of polyalanine *(5a)* lowers both the optical and the chemical yield significantly (exp. 8—11).

b) The polyalanine *(5a)* is necessary both for reaction to occur as well as for stereoselectivity to be observed. This implies that reaction takes place at the chiral interface (exp. 1).

c) The change in weight ratio chalcone *(1)*:polymer *(5)* does not seem to influence significantly the stereoselectivity (exp. 2, 3, 5 and 9,10), even though, optical yields higher than 90% were only obtained at a weight ratio of 1:0.8 (exp. 4—6, but not 7).

d) Polyalanine *(5a)* recovered from the reaction can be recycled[6] (exp. 7), giving rise to a decrease in chemical yield and optical purity, although the latter is still substantial.

e) The relative proportions in the liquid/solid/liquid phases seems to be important. For example, exp. 4 which gave a much lower chemical yield than exp. 3, used the same weight of aqueous phase and toluene while the weight of polymer was double. An increase in the proportion of toluene (compare exps. 8 and 10) resulted in a decrease in optical purity. The amount of aqueous solution does not appear to be crucial.

These results show that the use of simple polypeptides as "synthetic enzymes" may be a valuable tool for performing stereoselective organic reactions.

ml). The organic phase is washed three times with water, dried over MgSO₄, and the solvent evaporated. The residue is purified by column chromatography, using 100 g of silica gel (Merck 0.2—3.0, 200 mm) and toluene as eluant. Yield 0.754 g (70%); $[\alpha]_{578}^{20} = -184$ ($c = 2.717$ in Cl₂CH₂), m.p. 59—61 °C. Spectroscopic data: IR, ¹H-NMR were satisfactory and in agreement with the literature[7]. Crystallization of this epoxide from *n*-hexane gave a product with $[\alpha]_{578}^{20} = -214$ °C, m.p. 63—65 °C. The m.p. and rotation remained unchanged after a second crystallization. The crude extract obtained in experiment 6 is divided into two parts before chromatography. One of them was chromatographed as described, yielding an epoxide of 93% o.p. The other one was directly crystallized from *n*-hexane yielding a product of 96% o.p. and m.p. 63—65 °C.

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Upright Unsymmetrical Coordination in a Cyclopropenylnickel Complex: Synthesis and Structure of [(C₃Ph₃)Ni(PPh₃)₂]PF₆

By *Carlo Mealli, Stefano Midollini, Simonetta Moneti, and Luigi Sacconi*[*]

Unsymmetrical coordination of the cyclopropenylium ion has been found only in the complex [(C₃Ph₃)Pt(PPh₃)₂]PF₆[1]. Here the $C_3Ph_3^{\oplus}$ triangle has an isosceles shape with one large (1.58 Å) and two short (1.39 Å) sides. The PtP₂ fragment is displaced towards the base which lies approximately in the plane of the PtP₂ unit ("in-plane" conformation).

We have succeeded in preparing the analogous nickel complex [(C₃Ph₃)Ni(PPh₃)₂]PF₆ *(1)*, whose X-ray structure analysis shows that the $C_3Ph_3^{\oplus}$ unit is coordinated to the metal in an unprecedented unsymmetrical fashion (Fig. 1)[2].
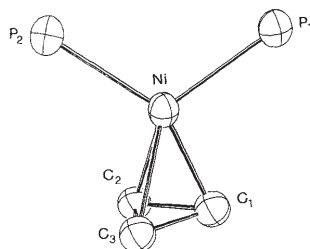
Fig. 1. ORTEP diagram of the skeleton of the complex cation in *(1)*. Important distances [Å] and angles [°] are: Ni—P1 = 2.242(4), Ni—P2 = 2.234(4), Ni—C1 = 1.91(1), Ni—C2 = 2.02(1), Ni—C3 = 2.07(1), C1—C2 = 1.46(2), C1—C3 = 1.44(2), C2—C3 = 1.34(2), P1—Ni—P2 = 107.4(2), C1—Ni—C2 = 43.7(5), C1—Ni—C3 = 42.1(5), C2—Ni—C3 = 38.4(4), C1—C2—C3 = 61.4(8), C1—C3—C2 = 63.4(9), C2—C1—C3 = 55.2(8).

Also in this complex the cyclopropenylium ion has an isosceles shape but the base (1.35 Å) is shorter than the two other sides (1.43 Å). The nickel atom is located at 2.01 and 2.07 Å respectively from the two carbon atoms of the base and at 1.89 Å from the apical carbon atom. The plane of the NiP₂ moiety is almost perpendicular to the base of the triangle (84.09°). This can be named *upright* conformation and is just opposite to that of the platinum complex.
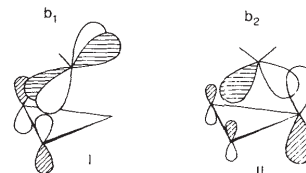
The bonding in both the metal complexes can be fairly well elucidated by considering the interactions of the b_1 and the b_2 orbitals of the MP₂ fragment (mainly metal d_{xz} and d_{yz} orbitals in nature) with the two π-set orbitals of the cyclopropenylium ion being the major bonding interactions in this complex[3].
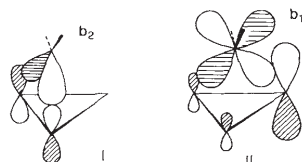
In the case of the platinum complex the b_2 orbital is favorably oriented for bonding interaction with the antibonding π* orbital I of the cyclopropenylium ion, while overlap of b_1 with II falls to a very low value.

A reversed situation is observed in the nickel complex. The 90° rotation of the NiP₂ fragment with respect to the $C_3Ph_3^{\oplus}$ ring as well as the very short Ni—C(apical) distance favors a large overlap of b_2 with II and a lower overlap of b_1 with I. Also the very short distance (1.35 Å) between the two basal carbon atoms in the $C_3Ph_3^{\oplus}$ ring, which is only a bit larger than the C—C double bond in the free ethylene molecule (1.337(2) Å)[4], suggests that their engagement in bonding with nickel is strongly reduced. (For a discussion see also ref.[5].)
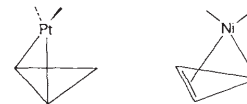
Experimental

All operations were performed under nitrogen and with oxygen-free solvents. Triphenylcyclopropenylium perchlorate (366 mg, 1 mmol) in methanol (20 ml) was added to a solution of (C₂H₄)Ni(PPh₃)₂ (611 mg, 1 mmol) in benzene (20 ml). On addition of (n-Bu)₄NPF₆ (386 mg, 1 mmol) in butanol (20 ml) and slow evaporation of the solvent, red crystals were formed: yield 75%.

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[2] Philips PW 1100 automated diffractometer. *a* = 15.815(4), *b* = 13.781(4), *c* = 12.764(4) Å, α = 114.06(9), β = 95.92(9), γ = 97.74(9) space group P̄1, *Z* = 2; *R* = 0.079 for 2919 reflections with |*I* < 3σ(*I*)|.
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Transition-Metal Complexes with Pyrazolyl Bridging Ligands between Very Different Metal Centers

By *Stephen R. Stobart, Keith R. Dixon, Donald T. Eadie, Jerry L. Atwood,* and *Michael D. Zaworotko*[*]

The structural characterization of transition-metal complexes with bridging pyrazolyl ligands[1] has thus far only

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