Regioselective or enantiogenic electrochemical and microbial reductions of 1,2-diketones

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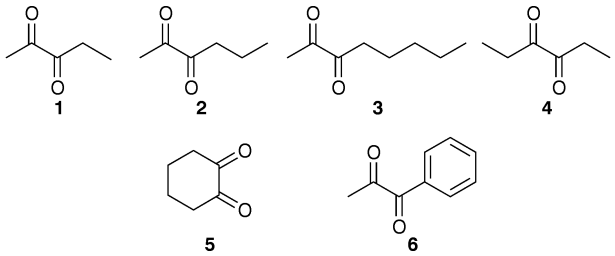
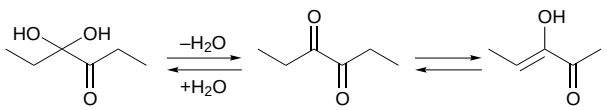
The electrochemical and microbial reduction of 1,2-diketones have been studied and the results compared among themselves and with those of previous works. The electrochemical reduction is highly selective and allows α-ketols to be obtained. The latter, being unreducible at the fixed potential used, never form diols. The anaerobic microbial reduction by *Proteus mirabilis* proves to be more chemo- and regioselective than that previously performed with other microorganisms. After two hours of incubation, the enantiomerically pure (2*S*)-α-ketols are isolated in high yield except in the case of 1,2-cyclohexanedione, for which the (1*S*,2*S*) diol is formed for all reaction times. The microbial reduction of the electrochemically generated racemic 2-hydroxycyclohexanone yields the sole (1*S*,2*S*) diol.

Réduction électrochimique ou microbiologique régioselective ou énantiogénique de 1,2-dicétones. Les résultats de la réduction électrochimique et microbiologique par *Proteus mirabilis* de six 1,2-dicétones ont été comparés entre eux et avec ceux obtenus dans des travaux antérieurs pour d'autres microorganismes. La méthode électrochimique, qui offre la possibilité d'imposer un pouvoir réducteur, conduit aux α-cétols en absence de toute trace de diols. L'action du microorganisme *Proteus mirabilis* s'est avérée beaucoup plus régiosélective que celle observée dans des études précédentes faisant intervenir d'autres microorganismes. Après deux heures d'incubation, les α-cétols de configuration (2*S*) sont obtenus énantiomériquement purs avec de bons rendements sauf pour la 1,2 cyclohexanedione qui donne directement le diol (1*S*,2*S*). La réduction microbiologique de la 2-hydroxycyclohexanone racémique générée électrochimiquement fournit le diol (1*S*,2*S*) par réduction énantiosélective du cétol (2*S*).

Regioselective or enantiogenic reactions have been frequently used in syntheses of biologically active compounds or natural product precursors.[1–4] In the field of regioselective and asymmetric synthesis, considerable effort has been made to obtain ketols and diols from prochiral dicarbonyl derivatives or olefines.[5–9] The present paper deals with the electrochemical and microbial reduction of the diketones:



In aqueous medium, the α-diketones **1**–**6** may exist under three forms in equilibrium:



The hydrated species is largely prevalent for alkyl diketones[10] whereas the enolic form is predominant in the case of cyclic α-diones.[11]

Electrochemistry can be successfully used for specific reductions (or oxidations) of organic molecules possessing more than one electroactive group.[12] On the other hand, microbial reactions are often the best way to prepare optically active products with very high enantiomeric excesses.[13] In this work we will assess the capability of the electrochemical method to reduce selectively one of the carbonyl groups and the possibility of microorganisms either to produce enantiomerically pure compounds from a prochiral center or to perform an enantiomeric recognition in the case of electrogenerated racemic mixtures.

Results and Discussion

Electrochemical reduction of the α-diketones 1–6

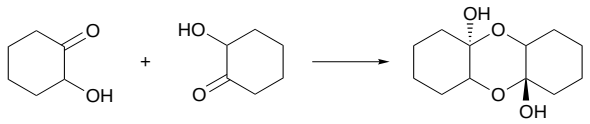
Numerous analytical studies have led to the establishment of detailed mechanisms concerning the electrochemical reduction of aliphatic or aromatic α-diketones according to the pH of aqueous solutions.[14–21] We have carried out all our electrolyses in buffered solutions at pH 7, thus allowing a comparison with microbial reductions. Under these conditions the cyclic voltammograms of dicarbonyl compounds **1**–**5** show identical two-electron reduction waves and on the reverse scan, a smaller anodic wave attributed to the oxidation of a dienolic structure R—C(OH)=C(OH)—R′ formed in the reduction process.[15] The aromatic diketone **6** is reduced in two steps: the first one ($E_{p_1} = -0.72$ V *vs.* SCE) corresponds to the reduction of the diketone[15] and the second, of weak intensity ($E_{p_2} = -1.15$ V *vs.* SCE), to that of an α-ketol[15] or a hydrated form of the initial dicarbonyl derivative.[16,17] As a comparison, the electrochemical reduction of α-diketones in an aprotic solvent takes place in two steps.[22]

Table 1 illustrates the results obtained from the electrolyses of compounds **1**–**6** in aqueous medium. In all the cases, the α-ketols are the main reaction products. We have never observed the formation of α-diols. The asymmetrical diketones

Table 1 Electrochemical reduction of α-diketones **1**–**6** at a fixed potential

α-Diketone	E_p/*vs.* SCE	α-Ketols/% $CH_3CHOHCOR$		$CH_3COCHOHR$	Side products/%
1	−0.86	28		52	20
2	−0.93	32		58	10
3	−1.05	38		57	5
6	−0.72	0.8		92	—
4	−0.88		86		14
5	−1.50		85	15	

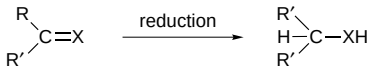
yielded a mixture of the two isomeric ketols, in which the 3-hydroxyketones are always the major product. Except for the aromatic diketone, we have observed the formation of side products. These, derived from diketones **1**–**4**, are very unstable and did not allow for purification on a silica gel column or by preparative gas chromatography. Their retention times in analytical gas chromatography and the fact that the crude reaction mixtures show, for the side products, the presence of three isomers in the case of the asymmetrical diketones **1**, **2**, **3** and only one for the symmetrical **4** lets us presume the formation of diastereomeric keto-pinacols by dimerization of the intermediate free radical. In the case of 1,2-cyclohexanedione, the impurity has been identified as cyclohexanone. The electroreductive cleavage of the C—OH bond in α-ketols has previously been observed.[14–18] We can also note that the α-ketol of 1,2-cyclohexanedione (adipoine) can slowly dimerize in aqueous solution:[23]



This reaction is favored by silica gel and therefore prevents any purification by silica gel chromatography. The dimer is, however, completely insoluble in diethyl ether and cannot be extracted from the aqueous solutions.

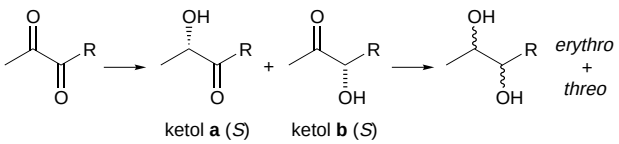
Microbial reduction of the α-diketones 1–6 by *Proteus mirabilis*

The synthesis of optically active natural products and biologically active compounds often requires chiral synthons as starting materials, most of them being obtained by enantiogenic reduction of prochiral moieties.[24–27]



The carbonyl function (X = O) is certainly one of the most studied and the use of enzymatic biocatalytic systems constituted of purified enzymes or whole cell microorganisms generally offers the advantage of producing enantiomerically pure compounds. The microbial reduction of dicarbonyl compounds by Baker's yeast, microorganisms or bacteria has been previously approached in our group[7] but in all cases, the asymmetrical α-diketones **1**, **3** and **6** have been reduced to a mixture of α-ketols and α-diols, even for very short reaction times (1 h, Table 2). The diols and α-ketols obtained were enantiomerically pure. Unfortunately, the reaction was never regioselective. In the particular case of 1,2-cyclohexanedione **5**, the formation of the α-ketol was never observed, regardless of the microorganism or reaction time used.[7] The diastereomeric diols were the sole products isolated. In continuation of our research, we present some results obtained under anaerobic conditions with *Proteus mirabilis*, a more selective microorganism allowing the formation of enantiomerically pure α-ketols using short reaction times (Table 3). In a first step the α-diketones **1**–**4** and **6** are reduced to the corresponding α-ketols, which can be further reduced to diols with longer reaction times. In contrast to the former microorganisms, it has been observed that *Proteus mirabilis* can induce a regiospecific reaction with the less hindered carbonyl group. Only the 2-hydroxyketones are obtained in high yields. In the case of 1,2-cyclohexanedione, it is unfortunately impossible to restrict the reaction to the reduction of only one carbonyl function. Even for short reaction times, the (1*S*,2*S*)-cyclohexanediol is isolated as the main reaction product. We can hypothesize that the (2*S*)-ketol is rapidly reduced to the (1*S*,2*S*)-diol. Electrochem-

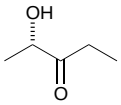
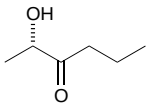
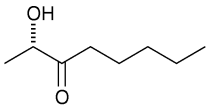
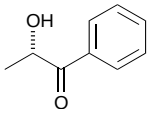
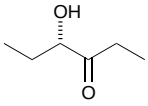
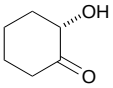
Table 2 Microbial reduction of α-diketones **1**, **3** and **6**[a]



α-Diketones	**1** R = C_2H_5			**3** R = C_5H_{11}			**6** R = C_6H_5		
Reaction products/%	Ketol **a**	Ketol **b**	Diols	Ketol **a**	Ketol **b**	Diols	Ketol **a**	Ketol **b**	Diols
Baker's yeast	17	14	69	35	7	58	70	—	— (30% ketone)
Aspergillus niger	4	12	84	2	4	94	—	50	50
Geotrichum candidum	25	15	60	29	7	64	60	—	17 (23% ketone)
Rodhotorula rubra	42	10	48	38	12	50	62	—	13 (25% ketone)

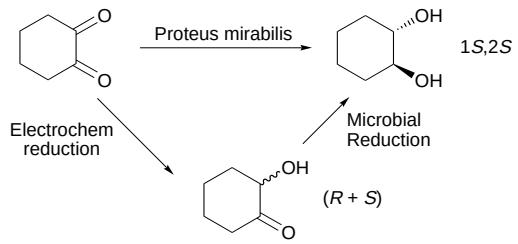
[a] Incubation time: 1h. Results for **6** from ref. 7.

Table 3 Microbial reduction of α-diketones **1**–**6** by *Proteus mirabilis*

Compound	Reaction time/h	α-Diketone/%	α-Ketol/%		Diols/%	
1	2	8		86	(2*S*,3*S*) (2*S*,3*R*)	4 2
	24	—		9	(2*S*,3*S*) (2*S*,3*R*)	84 7
2	2	1		95	(2*S*,3*S*) (2*S*,3*R*)	3 1
	24	—		52	(2*S*,3*S*) (2*S*,3*R*)	45 3
3	2	1		99	—	
	24	—		99	—	
6	2	18		82	—	
	24	7		98	—	
4	2	11		87	(3*S*,4*S*)	2
	24	—		2	(3*S*,4*S*)	98
5	2	70		3[a]	(1*S*,2*S*)	27
	24	11		2	(1*S*,2*S*)	87

[a] The ketol has not been isolated but only characterized by gas chromatography and ^{1}H and ^{13}C NMR spectrometry.

istry is able to produce the racemic (*R* + *S*)-2-hydroxycyclohexanone. We have submitted the racemic form of this α-ketol to an enantiospecific reduction by *Proteus mirabilis*. The reaction is controlled by GC analyses on chiral and non-chiral columns. We have observed the formation of the sole (1*S*,2*S*)-α-diol at all reaction times with an enantiomeric excess (ee) higher than 96%. For a reaction time of 24 h, 45% of the α-ketol was consumed. If the reaction is carried out for a longer time, the ketol progressively disappears without increasing the quantity of pure diastereomeric (1*S*,2*S*)-α-diol. We can tentatively explain this fact by an enantioselective recognition of the (2*S*)-ketol by the enzyme reductase with formation of the enantiomerically pure (1*S*,2*S*)-diol and the progressive dimerization of the (2*R*)-ketol to a nonbiologically reducible form.



All the isolated compounds have been characterized by comparison of their optical activity with that of authentic samples.[7,27] The enantiomeric excesses are defined by gas chromatography on a chiral column (Chirasil L-Valine or Lipodex E).

In conclusion, electrochemistry is a good chemospecific method for reducing α-diketones in aqueous medium owing to the possibility to regulate the reduction efficiency by applying the appropriate redox potentials. Only α-ketols are isolated, even in the case of cyclohexanedione. In the case of asymmetrical diketones, the technique appeared slightly regioselective for compounds **1**–**5** and highly regioselective for diketone **6**. The microbial reduction of the same diketones by *Proteus mirabilis* is particularly interesting compared to the results obtained with other microorganisms because of its high regio- and enantioselectivity. For short incubation times (1 h), contrary to electrochemistry, we observed only the reduction of the first carbonyl group (less hindered) and the isolated ketols are enantiomerically pure. These results complement those previously published because, in our first studies, we have never obtained pure ketols of 2,3-diketones with short alkyl chains (C_2 and C_3), even for an incubation time of one hour. The reaction products were always a mixture of isomeric ketols and diols. So, we now possess a choice of microorganisms giving simple access to α-ketols or α-diols.

Experimental

General methods

Cyclic voltammetry measurements were performed with a stationary mercury drop electrode and a Tacussel PRT 20-2X potentiostat. The reference electrode was a saturated calomel electrode (SCE). A Tacussel PRT 100-1X potentiostat coupled with a Tacussel IG5N integrator was used for controlled potential electrolyses, which were performed in a three-compartment glass cell joined by two glass frits. All the

macroscale reductions were carried out at a stirred mercury pool electrode (total area approximately 45 cm^2) with 400 μl (or 400 mg for solids) of substrate in 100 ml of a pH 7 Mac Ilvain buffered solution.

The microorganisms were all laboratory grown except Baker's yeast, which was purchased (Hirondelle, SI Lesaffre, Paris). *Proteus mirabilis* is obtained from Institut Pasteur (Paris, CIP 75.15). After culturing at 37 °C in a sterilized (20 min at 120°) medium [composed of yeast extract (Difco, 5 g), Tryptone (Difco, 20 g), glucose (5 g), K_2HPO_4 (5 g) and distilled water to make one litre of solution] for 9 h under anaerobic conditions, 50 μl of dione (or 50 mg for solids) were syringed through a septum. After incubation at 37 °C on a rotating table for the time appropriate to the formation of the desired product (2 h for α-ketones or longer times for diols), the mixture was filtered on sintered glass or centrifuged for ten minutes at 8000 rpm. The solution was then continually extracted with diethyl ether for 24 h. The overall yields were quite similar for electrochemical or microbial reductions. The culture of the other microorganisms mentioned have been previously described.[27]

Gas chromatography was performed using a Shimadzu GC 14 instrument equipped with a flame ionisation detector and DB1, Carbowax 20 M or Chirazil L-Valine and Lipodex E capillary columns for the measurement of enantiomeric excesses.

Substrates and solutions

The diketones **1**, **2**, **4**, **5** and **6** were purchased from Aldrich; 2,3-octanedione **3** was synthesized from 2-octanone according to a previously published method.[28] The pH 7 Mac Ilvaine buffered solution is obtained by dissolving 58.9 g of $Na_2HPO_4 \cdot 12\ H_2O$, 3.7 g of citric acid monohydrate and 5.44 g of KCl in distilled water to make one litre of solution. The α-ketols and diols were characterized by their optical rotation, ^1H and ^{13}C NMR spectra and comparison with authentic samples previously obtained.[7,27,29]

Reaction products

Microbial reduction by *Proteus mirabilis*. (*a*) Reduction of 2,3-pentanedione, **1**. After 2 h of incubation, the reaction products were chromatographed on a silica gel column. The eluent was pentane–ether, 80 : 20. The 2*S*-(+)-2-hydroxypentane-3-one is obtained in 63% yield. $[\alpha]_{578}^{25} = +44°$ ($c = 0.03$ $CHCl_3$), ee ⩾ 98%. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.10 (t, 3H), 1.38 (d, 3H), 2.47 (m, 2H), 3.5 (s, 1H exchangeable with D_2O), 4.22 (q, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 9 (C^5), 20.2 (C^1), 31 (C^4), 77.9 (C^2), 210 (C^3).

By incubating for 24 h, the (2*S*,3*S*) and (2*S*,3*R*) diols are formed with an overall yield of 85%. They are purified by chromatography on a silica gel column: eluent ethyl acetate. The diastereoisomer (2*S*,3*S*) is predominent (de 88%). $[\alpha]_{578}^{25} = -9°$ ($c = 0.03$ $CHCl_3$), ee ⩾ 98%. (2*S*,3*S*): ^1H NMR (400 MHz, $CDCl_3$) δ: 0.92 (t, 3H), 1.08 (d, 3H), 1.2–1.6 (m, 2H), 3.1–3.6 (m, 1H), 3.8 (s, 2H exchangeable with D_2O). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 7.6 (C^5), 16.6 (C^1), 23.5 (C^4), 67.7 (C^2), 74.7 (C^3).

(*b*) Reduction of 2,3-hexanedione, **2**. By following the same procedure, (2*S*)-(+)-2-hydroxyhexane-3-one is isolated in 66% yield after 2 h of incubation. The α-ketol is isolated by chromatography on a silica gel column (eluent ether–pentane, 40 : 60). $[\alpha]_{578}^{25} = +50°$ ($c = 0.03$ $CHCl_3$), ee ⩾ 98%. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.9 (t, 3H), 1.3 (d, 3H), 1.6 (m, 2H), 2.4 (m, 2H), 3.5 (s, 1H exchangeable with D_2O), 4.18 (q, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.8 (C^6), 17 (C^5), 19.7 (C^1), 39.3 (C^4), 76.7 (C^2), 210 (C^3).

The (2*S*,3*S*) diol is obtained in 41% yield after 24 h of incubation and purification on a silica gel column with ethyl acetate as eluent. The diastereomeric and enantiomeric excesses were 88% and 98%. $[\alpha]_{578}^{25} = -11°$ ($c = 0.03$ $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, 3H), 1.07 (d, 3H), 1.2–1.6 (m, 2H), 3.2–3.6 (m, 2H), 3.8 (s, 2H exchangeable with D_2O). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.5 (C^6), 17.2 (C^5), 18.6 (C^1), 34.9 (C^4), 70.0 (C^2), 74.9 (C^3).

(*c*) Reduction of 2,3-octanedione, **3**. After 2 h of incubation, (2*S*)-(+)-2-hydroxyoctane-3-one is isolated in 75% yield after purification on a silica gel column (eluent ether–pentane, 20 : 80). $[\alpha]_{578}^{25} = +63°$ ($c = 0.03$ $CHCl_3$). The diols are never formed, whatever the reaction time used. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.85 (t, 3H), 1.2–1.7 (m, 6H), 1.35 (d, 3H), 2.6 (m, 2H), 3.5 (s, 1H exchangeable with D_2O), 4.18 (q, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14 (C^8), 22.6, 23.5, 20 (C^1), 31.8 (C^7, C^6, C^5), 37.7 (C^4), 76.6 (C^2), 210.2 (C^3).

(*d*) Reduction of 1-phenylpropane-1,2-dione, **6**. The microbial reduction allows (2*S*)-(−)-2-hydroxy-1-phenylpropane-1-one to be obtained in 78% yield. $[\alpha]_{578}^{25} = -78°$ ($c = 0.03$ $CHCl_3$), ee ⩾ 98%. As observed for the 2,3-octanedione, the diols are never formed, even after 24 h of incubation.

(*e*) Reduction of 3,4-hexanedione, **4**. Incubation of the diketone for 2 h gave (4*S*)-(+)-4-hydroxyhexane-3-one in 67% yield. The α-ketol is isolated by chromatography on a silica gel column (eluent ether–pentane, 40 : 60). $[\alpha]_{578}^{25} = +70°$ ($c = 0.03$ $CHCl_3$), ee ⩾ 98%. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.85 (t, 3H), 1.05 (t, 3H), 1.56–1.82 (m, 2H), 2.44 (m, 2H), 3.35 (s, 1H exchangeable with D_2O), 4.41 (dd, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 7.6 (C^6), 8.9 (C^1), 27 (C^5), 31.2 (C^2), 77.2 (C^4), 213 (C^3).

(3*S*,4*S*)-(−)-Hexane-3,4-diol is obtained in 85% yield after 24 h of incubation. $[\alpha]_{578}^{25} = -16.5$ ($c = 0.03$ $CHCl_3$), ee ⩾ 98%. The reaction product was chromatographed on a silica gel column (eluent ethyl acetate). ^1H NMR (400 MHz, $CDCl_3$) δ: 0.9 (t, 6H), 1.42–1.54 (m, 4H), 3.30 (m, 2H), 4.10 (s, 2H exchangeable with D_2O). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.2 (C^1, C^6), 26.4 (C^2, C^5), 75.2 (C^3, C^4).

(*f*) Reduction 1,2-cyclohexanedione, **5**. The microbial reduction gave, after 24 h of incubation, (1*S*,2*S*)-(+)-cyclohexane-1,2-diol as the sole reaction product in 85% yield. Only 3% of the α-ketol has been formed and characterized by GC chromatography for a short reaction time (2 h). The diol is purified by chromatography on a silica gel column with ethyl acetate as eluent. $[\alpha]_{578}^{25} = +32°$ ($c = 0.03$ $CHCl_3$), ee ⩾ 98%. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.2 (m, 4H), 1.6–1.82 (m, 4H), 3.2 (m, 2H), 3.85 (2H exchangeable with D_2O). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.5 (C^4, C^5), 33.1 (C^3, C^6), 75.3 (C^1, C^2).

Electrochemical reductions. As examples, we will mention the electrochemical reduction of 1-phenylpropane-1,2-dione and cyclohexane-1,2-dione. At the fixed potential of −0.72 V *vs.* SCE, 1-phenylpropane-1,2-dione gives a mixture of 2-hydroxy-1-phenylpropane-1-one and 1-hydroxy-1-phenylpropane-2-one in a ratio 8 : 92 and in an overall yield of 85%. The reaction products were chromatographed on a silica gel column (eluent ethyl acetate–cyclohexane, 15 : 85). 2-Hydroxy-1-phenylpropane-1-one: ^1H NMR (400 MHz, $CDCl_3$) δ: 1.5 (d, 3H), 3.9 (s, 1H exchangeable with D_2O), 5.2 (q, 1H), 7.3–8.1 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.3 (C^3), 69.4 (C^2), 129.1, 129.5, 129.9, 133 (C arom), 202.5 (C^1). 1-Hydroxy-1-phenylpropane-2-one: ^1H NMR (400 MHz, $CDCl_3$) δ: 2.1 (s, 3H), 4.3 (s, 1H exchangeable with D_2O), 5.1 (s, 1H), 7.3–7.8 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 23.5 (C^3), 80.2 (C^1), 127.4, 128.8, 129.1, 136.2 (C arom), 207.3 (C^2).

(*R* + *S*)-2-Hydroxycyclohexane-1-one (adipoine) has been obtained by electrolysis at the fixed potential of −1.50 V *vs.* SCE. The monomeric α-ketol could not be chromatographed because of the dimerization reaction, which is catalysed by silica gel. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.63, 2.13 (H^5, $H^{5'}$), 1.50, 2.47 (H^3, $H^{3'}$), 1.74, 1.91 (H^4, $H^{4'}$), 2.37, 2.58 (H^6, $H^{6'}$),

3.85 (1H exchangeable with D_2O), 4.14 (H^2). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 23.3 (C^4), 27.4 (C^5), 36.6 (C^3), 39.4 (C^6), 75.3 (C^2), 211.3 (C^1). Dimer: mp = 130–131 °C. HRMS: calcd 228.2, exptal 228.1379. ^1H NMR [400 MHz, $(CD_3)_2SO$] δ: 1.1–1.75 (m, 8H), 3.35 (s, 2H exchangeable with D_2O), 3.87 (dd 2H). ^{13}C NMR [100 MHz, $(CD_3)_2SO$] δ: 22.2, 24.1, 27.6, 35.4 (C^4, $C^{4'}$, C^5, $C^{5'}$, C^6, $C^{6'}$), 72.2 (C^2, $C^{2'}$), 94.3 (C^1, $C^{1'}$).

References

1 M. P. Doyle and C. T. West, *Stereoselective Reductions*, Halsted Press, New York, 1976.
2 A. Hajos, *Complex Hydrides*, Elsevier, Amsterdam, 1979.
3 P. A. McNeil, N. K. Roberts and B. Bosnich, *J. Am. Chem. Soc.*, 1981, **103**, 2273 and references therein.
4 M. M. Midland, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, San Diego, 1983, vol. 2, p. 45.
5 M. Imuya and H. Ziffer, *J. Org. Chem.*, 1978, **43**, 3319.
6 A. Fauve and H. Veschambre, *Tetrahedron Lett.*, 1987, **28**, 5037.
7 R. Bel-Rhlid, Thesis, University of Clermont-Ferrand, 1990.
8 A. M. Martre, G. Mousset, S. Fabre and M. Prudhomme, *New J. Chem.*, 1983, **17**, 207.
9 S. Torii, P. Liu, N. Bhuvaneswari, C. Amatore and A. Jutand, *J. Org. Chem.*, 1996, **61**, 3055 and references therein.
10 N. Sleszynski and P. Zuman, *J. Org. Chem.*, 1987, **52**, 2622.
11 (*a*) J. P. Segretario, N. Sleszynski and P. Zuman, *J. Electroanal Chem.*, 1986, **214**, 259. (*b*) F. A. Long and R. Bekule, *J. Am. Chem. Soc.*, 1963, **85**, 2313.
12 (*a*) M. M. Baizer and H. Lund, *Organic Electrochemistry*, Marcel Dekker, 3rd edn., 1983. (*b*) M. M. Baizer, *Pure Appl. Chem.*, 1986, **58**, 889 and references therein.
13 (*a*) S. Servi, *Synthesis*, 1990, 1. (*b*) H. L. Holland, *Organic Synthesis with Oxidative Enzymes*, VCH, New York, 1992.
14 S. Letellier, *Electrochim. Acta.*, 1980, **25**,1051.
15 J. P. Segretario and P. Zuman, *J. Electroanal. Chem.*, 1986, 214.
16 J. M. Rodriguez-Mellado, J. L. Avila and J. J. Ruiz, *Can. J. Chem.*, 1985, **63**, 891.
17 M. A. Zon and J. M. Rodriguez-Mellado, *J. Electroanal. Chem.*, 1991, **318**, 283.
18 M. Fedoronko, J. Konigstein and K. Linek, *Collect Czech. Chem. Commun.*, 1967, **32**, 3998.
19 M. R. Montoya, M. A. Zon and J. M. Rodriguez-Mellado, *J. Electroanal. Chem.*, 1993, **353**, 217.
20 J. M. Rodriguez-Mellado and M. R. Montoya, *J. Electroanal. Chem.*, 1994, **365**, 71; *ibid.*, 1994, **371**, 215.
21 M. A. Zon and J. M. Rodriguez-Mellado, *J. Electroanal. Chem.*, 1992, **338**, 229.
22 (*a*) M. D. Ryan and D. H. Evans, *J. Electroanal. Chem.*, 1976, **67**, 333. (*b*) K. Boujlel and J. Simonet, *Tetrahedron Lett.*, 1979, **12**, 1063.
23 Beilstein, 1st edn., Edwards Brothers Inc., Michigan, 1944, vol. 8, part 2, p. 504.
24 J. Retey and J. A. Robinson, *Stereospecificity in Organic Chemistry and Enzymology*, VCH, Weinheim, 1982.
25 C. J. Sih and J. P. Rosazza, in *Applications of Biochemical Systems in Organic Chemistry*, ed. J. B. Jones, C. J. Sik and D. Perlman, Wiley, New York, 1976, vol. 10, pp. 69–106.
26 H. Izuka and A. Naito, *Microbial Conversion of Steroids and Alkaloids*, Springer, New York, 1981.
27 R. Bel-Rhlid, A. Fauve, M. F. Renard and H.Veschambre, *Biocatalysis*, 1992, **6**, 319.
28 R. Bel-Rhlid, A. Fauve and H. Veschambre, *J. Org. Chem.*, 1989, **54**, 3221.
29 R. Bel-Rhlid, M. F. Renard and H. Veschambre, *Bull. Soc. Chim. Fr.*, 1996, **133**, 1011.

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