Pergamon

Tetrahedron: *Asymmetry* 12 (2001) 847–852

TETRAHEDRON: *ASYMMETRY*

Baker's yeast reduction of α-methyleneketones

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Received 29 January 2001; accepted 6 March 2001

Abstract—The bioreduction of α-methyleneketones, $R^1C(=O)C(=CH_2)R^2$ (R^1 = Me, Et, Pr, *iso*-Bu, Ph, CH_2CH_2Ph; R^2 = Cl, Me, Et, *n*-Pr, *iso*-Pr, *n*-Bu, *n*-C_6H_{13}, Ph, CH_2Ph), was mediated by baker's yeast (*Saccharomyces cerevisiae*) to obtain the corresponding α-methylketones. The R^1 and R^2 groups had a significant influence on the rate and enantioselectivity of the reductions. The rate of C=C bond reduction was higher than that of C=O bond reduction. Only α-methyleneketones having R^1 = Me yielded α-methylketones in high enantioselectivity with e.e.s of 88–99%.

1. Introduction

In the last decade, whole cells and enzymes have been used extensively in organic synthesis to obtain homochiral products in a variety of organic reactions.[1] Baker's yeast has been widely used, mainly in the reduction of the carbonyl groups of prochiral ketones,[2] producing alcohols with high enantiomeric purity. Similarly, the carbon–carbon double bonds of prochiral alkenes may be reduced to obtain the corresponding saturated compounds with high enantiomeric excesses.

The α-methylketone structural moiety is present in a variety of compounds including drugs and pheromones.[3] In most cases, the absolute configuration of the α-carbon affects the bioactivity profile.[4] Ketones bearing a chiral α-carbon can be obtained by the enantioselective reduction of prochiral α-methyleneketones. In spite of a large number of studies involving the enantioselective bioreduction of the C=C bond α- to a ketone function,[5] there are few involving the bioreduction of α-methyleneketones.[6] Herein, we present a systematic study of the effect of R^1 and R^2 groups on the enantioselectivity and rate of the baker's yeast reduction of α-methyleneketones **2**.

2. Results and discussion

The α-methyleneketones **2a**–**2n** were prepared via the Mannich reaction by refluxing a solution of aqueous formaldehyde, the corresponding ketone **1a**–**1n** and a catalytic amount of morpholine in anhydrous acetic acid (Scheme 1).[7]

The reduction of **2** by baker's yeast was performed by stirring the reaction mixture at 30°C. We observed that ketone **3** and in some cases alcohol **4**, were obtained as reaction products from the C=C and C=O bond reductions, respectively (see Scheme 2).

As our interest lay in studying the effect of altering the R^1 and R^2 alkyl groups in these reduction reactions, samples were withdrawn from the reaction mixture after appropriate intervals of time, and analyzed by GCMS technique in order to determine the relative rate of reduction (Fig. 1).

In general, there was a large difference between the reduction rates of C=C and C=O bonds with baker's yeast. While C=C was reduced first and ketones **3a**–**3f** were obtained after 2 h, the appearance of alcohols **4a**–**4f** (17–100% of reaction progress) only occurs after reaction for 96–169 h (see Table 1). This chemoselectivity may be implemented as part of a synthetic strategy. In contrast, the reduction rate of the C=C bond of ketones **2h**–**2m** was slower than that of **2a**–**2f** and formation of alcohols **4h**–**4m** was not observed.

It is interesting that when R^1=Me (compounds **2a**–**2d**), the ketone reduction rates were the fastest, irrespective of the size of the R^2 group. When R^1 = Ph, the reduction rates of the ketones were dependent on the R^2 group size. When R^1 = Ph, the rates of reduction of the ketones with R^2 = Cl, Me and Et, **2e**–**2g**, were faster

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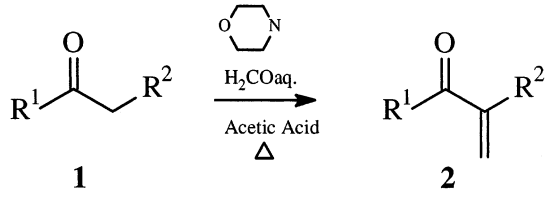
0957-4166/01/$ - see front matter
PII: S0957-4166(01)00134-3



	R^1	R^2		R^1	R^2
a	Me	*n*-Pr	**h**	Ph	*n*-Pr
b	Me	*n*-Hexyl	**i**	Ph	*n*-Bu
c	Me	Bn	**j**	Ph	Bn
d	Me	Ph	**k**	Et	Ph
e	Ph	Cl	**l**	*n*-Pr	Et
f	Ph	Me	**m**	CH_2CH_2Ph	Bn
g	Ph	Et	**n**	*iso*-Bu	*iso*-Pr

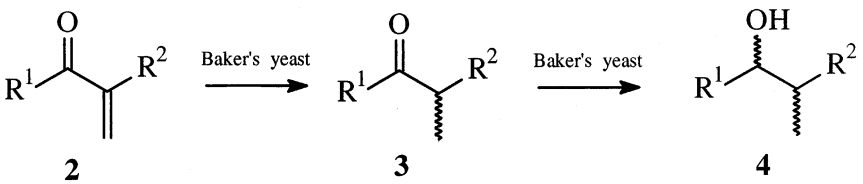
Scheme 1.

than the reduction rates of ketones **2h–2j** with R^2 = *n*-Pr, *n*-Bu and Bn.

In general, the rate of reductions was very sensitive to the size of the R^1 alkyl group. There was a marked difference in the reduction rate of ketone **2d** (R^1 = Me; R^2 = Ph), in comparison to ketone **2k** (R^1 = Et; R^2 = Ph). In the case of ketone **2n** (R^1 = *iso*-Bu; R^2 = *iso*-Pr) reduction did not occur.

The baker's yeast reduction of **2a–2d** (R^1 = Me) gave **3a–3d**, respectively with good to excellent e.e. (88 to >99%), irrespective of the size of the R^2 group. The configuration of ketones **3b–3d** may be assigned as (*R*)- by comparing $[\alpha]_D^{20}$ signals to literature data. Since the CD spectra of ketones **3a–3d** exhibit a distinct negative Cotton effect centered near 290 nm (Fig. 2) due to the carbonyl group, we can assign the (*R*)-configuration to ketone **3a**.[8]

When R^1 was Ph **2e–2j**, Et **2k**, Pr **2l** or $PhCH_2CH_2$ **2m**, the reduction products **3e–3n** were obtained with very poor e.e. Only α-methyleneketones having R^1 = Me yielded α-methylketones with high enantioselectivity. As the products **3a–3d** had (*R*)-configuration, it is reasonable to conclude that hydride transfers pre-



Scheme 2.

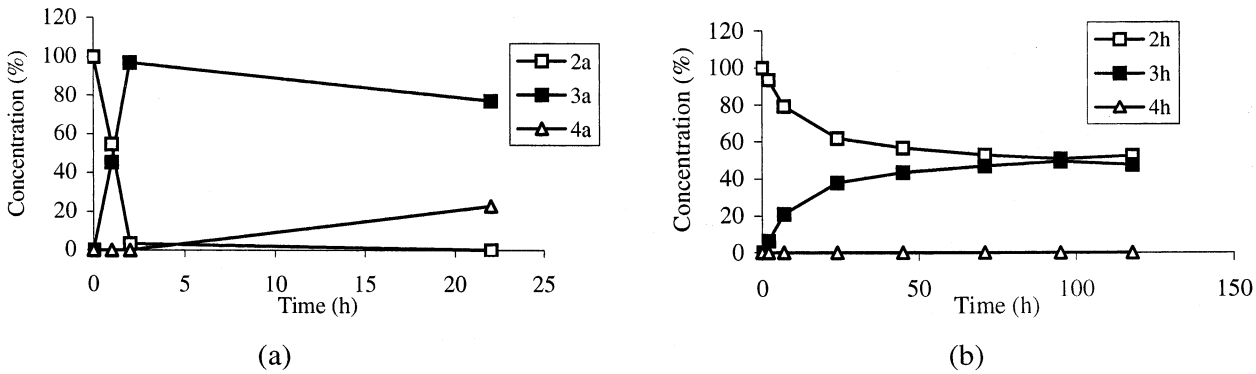


Figure 1. Profile of baker's yeast reduction of: (a) 3-propyl-3-buten-2-one **2a**; (b) 1-phenyl-2-propyl-2-propen-1-one **2h**.

Table 1. Baker's yeast reduction of α-methyleneketones **2** yielding α-methylketones **3** and alcohol **4** at 30°C

2	**3**					**4**	
	Reaction progress (%) after 2 h	e.e. (%)	$[\alpha]_D^{20}$ (*c*, solv)	$[\theta]$ (λ, nm) in MeOH	Conf.	Reaction time (reaction progress)	d.e. (%)
(a) R^1=Me; R^2=*n*-Pr	97	92	−8.8 (9.0, $CHCl_3$)	−31 (280)	*R*(−)[a]	168 h (20%)	53
(b) R^1=Me; R^2=*n*-Hexyl	70	>99	−17.1 (3.2, $CHCl_3$)	−420 (283)	*R*(−)[6b]	120 h (27%)	40
(c) R^1=Me; R^2=Bn	66	88	−28.0 (11.0, $CHCl_3$)	−1718 (285)	*R*(−)[6b]	114 h (17%)	91
(d) R^1=Me; R^2=Ph	100	88	−214.8 (6.2, $CHCl_3$)	−15507 (288)	*R*(−)[9]	169 h (35%)	88
(e) R^1=Ph; R^2=Cl	80	9	–	–		96 h (100%)	26
(f) R^1=Ph; R^2=Me	100	–	–	–		144 h (20%)	–
(g) R^1=Ph; R^2=Et	100	32	−1.1 (oil)		*R*(−)[10]	n.r.	–
(h) R^1=Ph; R^2=*n*-Pr	6	3	–	–		n.r.	–
(i) R^1=Ph; R^2=*n*-Bu	5	4	–	–		n.r.	–
(j) R^1=Ph; R^2=Bn	16	14	–	–		n.r.	–
(k) R^1=Et; R^2=Ph	34	12	–	–	–	n.r.	–
(l) R^1=*n*-Pr; R^2=Et	40	16	–	–	–	n.r.	–
(m) $R^1=CH_2CH_2Ph$; R^2=Bn	6	14	–	–		n.r.	–
(n) R^1=*iso*-Bu; R^2=*iso*-Pr	n.r.	–				n.r.	–

[a] Inferred from CD spectrum.

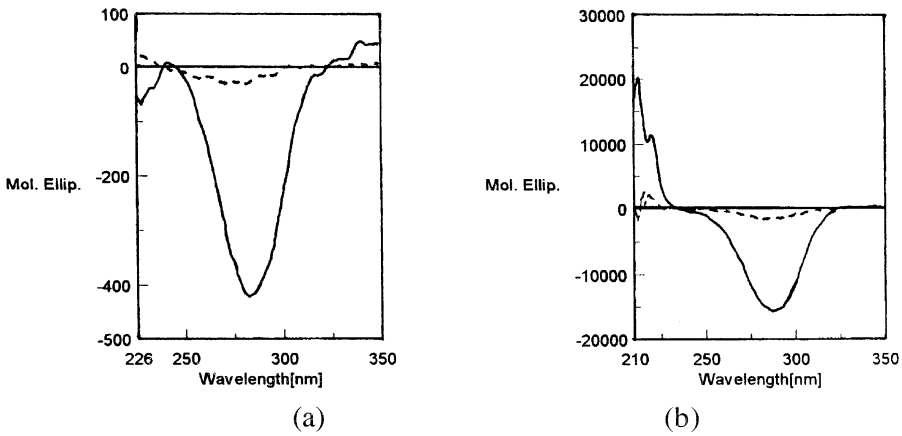


Figure 2. CD spectra at 25°C of: (a) **3a** *R*(−) (---) and **3b** *R*(−) (—); (b) **3c** *R*(−) (---) and **3d** *R*(−)(—), respectively.

ferentially to the *Si*-face of the C=C bond of **2a**–**2d** (Fig. 3).

The results indicate that the active site of the principal enzyme responsible for hydride transference to α-methyleneketones is highly restricted with respect to the R^1 group: Chain homologation by one or two carbons in R^1 appears responsible for the poor e.e. values of products **3k** and **3l** (12 and 16% e.e., respectively), in comparison to **3d** (88% e.e.). In addition, the fact that the reduction rates of **2h**–**2n** are lower than those of **2a**–**2d**, indicates that assembly of the appropriate transition state on the active site of the enzyme with ketones **2h**–**2n** is not favored and as a result the reduction mediated by the yeast either loses stereospecificity, or other pro-(*S*)- and pro-(*R*)- enzymes present in the yeast may compete in the reaction.

The baker's yeast reduction of intermediate ketones **3c** and **3d**, which have aromatic groups at R^2, gave the alcohols **4c** and **4d** in good diastereoisomeric excess (d.e.), whereas the baker's yeast reduction of the ketones **3a** and **3b** gave alcohols **4a** and **4b** with poor d.e.

3. Conclusions

The baker's yeast reduction of the alkene function of α-methyleneketones **2** were faster than those of the carbon–oxygen double bonds, showing that this chemoselectivity may be used as an important strategy in synthetic organic chemistry. The stereoselectivity and reduction rate of the carbon–carbon double bond is affected markedly by the R^1 and R^2 groups. Only α-methyleneketones having R^1=Me produced the corresponding α-methylketone in high enantioselectivity.

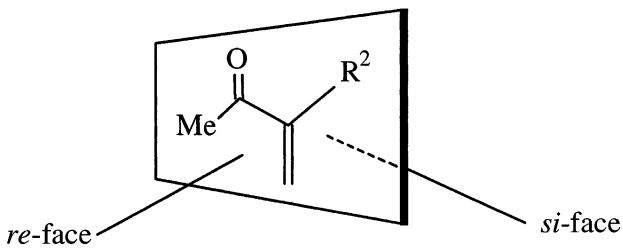


Figure 3. *Re*- and *Si*-faces of the alkenic bond of α-methyleneketones **2a**–**d**.

4. Experimental

The IR spectra were recorded on a BOMEM MB SERIES Hartmann & Braun spectrometer. The ^{1}H NMR and ^{13}C NMR were recorded on a VARIAN-INOVA spectrometer. Mass spectra were recorded on a Shimadzu GC–MS-QP 5000 gas chromatograph/mass spectrometer and with helium as carrier gas. A 30 m×0.25 mm I.D. capillary column of fused silica SUPELCO SIMPLICITY 1™ was used and the chiral column employed in the determination of enantiomeric excess (e.e.) was a 25 m×0.25 mm I.D. CHIRASIL-DEX from CHROMPACK. An injector temperature of 230°C and a detector temperature of 280°C, with the column at 50°C for 3 min; then using a rate of 20°C/min up to 280°C, with a pressure of 100 kPa and gas flow of 80 mL/min, was used. HRMS were obtained on a Fison VG Autoespec. Optical rotations were measured using a Carl Weiss POLAMAT A polarimeter. CD spectra were recorded on a Jasco-J720 spectropolarimeter at 25°C. Preparative column chromatography was carried out using silica gel 60 (Merck).

4.1. General procedure for the preparation of α-methyleneketones

Aqueous formaldehyde (24 mL, 37% solution, 0.3 mol) and a catalytic quantity of morpholine (3 drops), were added to a solution of ketone **1** (0.1 mol) in glacial acetic acid (90 mL). The resulting solution was refluxed overnight. Subsequently, the reaction mixture was cooled and neutralized with aqueous NaOH (0.1 M). The products were extracted three times with ethyl acetate. The organic layer was washed with aqueous $NaHCO_3$ (10%) and brine and dried over magnesium sulfate. The solvent was evaporated. The crude oil was purified by silica gel column chromatography to obtain the α-methyleneketone **2**.

4.2. General procedure for the biotransformations of 2

The α-methyleneketone **2** (0.1 mol) was added to a mixture of dry baker's yeast (Emulzint® 5 g) in water (100 mL) at 30°C. The resulting mixture was maintained at 30°C with constant stirring. Samples were withdrawn from the reaction mixture at appropriate intervals and analyzed by the GC/MS technique.

Subsequently, at the end of the reactions, Celite®, ethyl acetate (50 mL) and brine (50 mL) were added to the reaction mixture, and stirring was continued for 30 min. The cells–Celite mixture was filtered off and the filtrate extracted three times with ethyl acetate. The organic layer was washed with aqueous $NaHCO_3$ (10%) and brine, dried over magnesium sulfate and the solvent was evaporated. The crude oil was purified by silica gel column chromatography to obtain the α-methylketone **3** and in some cases, the alcohol **4**.

4.3. 3-Propyl-3-buten-2-one 2a

IR (film) 2961, 2933, 1681, 1364, 1145, 938 cm^{-1}; ^{1}H NMR δ 0.92 (t, 3H, $J=7.4$ Hz), 1.43 (sx, 2H, $J=7.4$ Hz), 2.23 (t, 2H, $J=7.4$ Hz), 2.33 (s, 3H), 5.75 (s, 1H), 6.01 (s, 1H); MS m/z 112 (M^+, 3%), 97 (30%), 79 (1%), 69 (30%), 55 (10%), 43 (100%), 41 (80%).

4.4. 3-Methyl-2-hexanone 3a

IR (film) 2926, 2851, 1745, 1463, 1369, 1239 cm^{-1}; ^{1}H NMR δ MS m/z 114 (M^+, 3%), 99 (3%), 72 (14%), 55 (5%), 43 (100%); ^{1}H NMR δ 0.91 (t, 3H, $J=6.96$ Hz), 1.07 (d, 3H, $J=6.96$ Hz), 1.20–1.70 (m, 4H), 2.13 (s, 3H), 2.50 (m, 1H).

4.5. 3-Hexyl-3-buten-2-one 2b

IR (film) 2957, 2926, 2858, 1684, 1465, 1365, 1148, 936 cm^{-1}, ^{1}H NMR δ 0.88 (m, 3H), 1.30 (m, 8H), 2.20 (m, 2H), 2.33 (s, 3H), 5.74 (s, 1H), 5.99 (s, 1H); MS m/z 154 (M^+, 2%), 139 (10%), 125 (2%), 111 (36%), 85 (21%), 69 (78%), 55 (57%), 41 (100%).

4.6. 3-Methyl-2-nonanone 3b

IR (film) 2959, 2929, 2857, 1713, 1361, 1171 cm^{-1}; ^{1}H NMR δ 0.88 (t, 3H, $J=6.96$ Hz), 1.08 (d, 3H, $J=7.00$ Hz), 1.30 (m, 10H), 1.60 (m, 1H), 2.13 (s, 3H); MS m/z 156 (M^+, 1%), 141 (1%), 113 (1%), 99 (1%), 72 (56%), 57 (21%), 43 (100%).

4.7. 3-Benzyl-3-buten-2-one 2c

IR (film) 3085, 3063, 3028, 2925, 1676, 1495, 1363, 733, 698, 505 cm^{-1}; ^{1}H NMR δ 2.33 (s, 3H), 3.59 (s, 2H), 5.63 (s, 1H); 6.07 (s, 1H), 7.2 (m, 5H); MS m/z 160 (M^+, 25%), 159 (25%), 145 (20%), 115 (40%), 91 (30%), 77 (5%), 43 (100%). HRMS found m/z: 160.0889; calcd for $C_{11}H_{12}O$ $[M]^+$: 160.0888

4.8. 3-Methyl-4-phenyl-2-butanone 3c

IR (film) 3028, 2971, 2933, 1713, 1449, 1351, 1165, 737, 700 cm^{-1}; ^{1}H NMR δ 1.08 (d, 3H, $J=7.10$ Hz), 2.08 (s, 3H), 2.56 (dd, 1H, $J=13.67$ Hz, $J=7.81$ Hz), 2.82 (m, 1H, $J=6.80$ Hz, $J=7.10$ Hz, $J=7.80$ Hz), 2.98 (dd, 1H, $J=13.67$ Hz, $J=6.80$ Hz), 7.13–7.35 (m, 5H); MS m/z 162 (M^+, 20%), 147 (17%), 129 (2%), 119 (12%), 103 (2%), 91 (100%), 77 (2%), 65 (12%), 43 (100%).

4.9. 3-Phenyl-3-buten-2-one 2d

IR (film) 3105, 3057, 2926, 2856, 1685, 1497, 1365, 1173, 950, 779, 704 cm^{-1}; ^{1}H NMR δ 2.44 (s, 3H), 5.96 (s, 1H), 6.17 (s, 1H), 7.34 (m, 5H); MS m/z 146 (M^+, 39%), 131 (19%), 103 (100%), 77 (39%), 63 (6%), 51 (40%), 43 (88%). HRMS found m/z: 146.0730; calcd for $C_{10}H_{10}O$ $[M]^+$: 146.0731.

4.10. 3-Phenyl-2-butanone 3d

IR (film) 3029, 2978, 2932, 1718, 1495, 1453, 1356, 768, 702, 545 cm^{-1}; ^{1}H NMR δ 1.39 (d, 3H, $J=7.02$ Hz), 2.04 (s, 3H), 3.74 (q, 1H, $J=7.02$ Hz), 7.22–7.33 (m, 5H); MS m/z 148 (M^+, 6%), 133 (2%), 115 (1%), 105 (100%), 91 (2%), 77 (20%), 63 (2%), 51 (15%), 43 (63%).

4.11. 2-Chloro-1-phenyl-2-propen-1-one 2e

IR (film) 3114, 3063, 3028, 1675, 1449, 964, 697 cm^{-1}; ^1H NMR δ 6.06 (s, 1H), 6.27 (s, 1H), 6.60 (m, 5H); MS m/z 166 (M^+, 20%), 138 (2%), 131 (5%), 105 (100%), 77 (40%), 61 (10%), 51 (65%); HRMS found m/z: 166.0184; calcd for C_9H_7ClO $[M]^+$: 166.0185

4.12. 2-Chloro-1-phenyl-1-propanone 3e

IR (film) 3063, 2985, 2932, 1691, 1595, 1447, 956, 720, 683 cm^{-1}, ^1H NMR δ 1.74 (d, 3H, $J=6.60$ Hz), 5.25 (q, 1H, $J=6.60$ Hz), 7.40–8.10 (m, 5H); MS m/z 168 (M^+, 2%), 132 (2%), 105 (100%), 77 (47%), 63 (2%), 51 (36%).

4.13. 2-Methyl-1-phenyl-2-propen-1-one 2f

IR (film) 3062, 2927, 1656, 1449, 1330, 1200, 754, 714 cm^{-1}; ^1H NMR δ 2.05 (s, 3H), 5.60 (s, 1H), 5.88 (s, 1H), 7.40–7.70 (m, 5H); MS m/z 146 (M^+, 20%), 131 (2%), 118 (20%), 105 (100%), 91 (2%), 77 (80%), 51 (50%), 41 (20%). HRMS found m/z: 146.0749; calcd for $C_{10}H_{10}O$ $[M]^+$: 146.0731.

4.14. 2-Methyl-1-phenyl-1-propanone 3f

IR (film) 3065, 2972, 1681, 1449, 1387, 1222, 979, 790, 702 cm^{-1}; ^1H NMR δ 1.22 (d, 6H, $J=6.96$ Hz), 3.56 (hep, 1H, $J=6.96$ Hz), 7.40–7.96 (m, 5H); MS m/z 148 (M^+, 6%), 134 (1%), 105 (100%), 91 (1%), 77 (42%), 51 (25%).

4.15. 2-Ethyl-1-phenyl-2-propen-1-one 2g

IR (film) 3062, 2966, 1658, 1448, 979, 752, 703 cm^{-1}; ^1H NMR δ 1.12 (t, 3H, $J=7.53$ Hz), 2.49 (q, 2H, $J=7.53$ Hz), 5.56 (s, 1H), 5.80 (s, 1H), 7.40–7.70 (m, 5H); MS m/z 160 (M^+, 20), 159 (22%), 145 (25%), 131 (15%), 117 (10%), 105 (100%), 91 (3%), 77 (80%), 51 (40%), 39 (12%). HRMS found m/z: 160.0887; calcd for $C_{11}H_{12}O$ $[M]^+$: 160.0888.

4.16. 2-Methyl-1-phenyl-1-butanone 3g

IR (film) 3062, 2935, 2875, 1682, 1598, 1448, 1219, 970, 701 cm^{-1}; ^1H NMR δ 0.91 (t, 3H, $J=7.32$ Hz), 1.18 (d, 3H, $J=6.60$ Hz), 1.48 (m, 1H), 1.90 (m, 1H), 3.40 (m, 1H), 7.40–7.97 (m, 5H); MS m/z 162 (M^+, 7%), 144 (1%), 134 (7%), 105 (100%), 91 (2%), 77 (43%), 63 (1%), 51 (21%).

4.17. 1-Phenyl-2-propyl-2-propen-1-one 2h

IR (film) 3084, 3062, 2960, 2932, 2872, 1657, 1445, 982, 753, 706, 694 cm^{-1}; ^1H NMR δ 0.96 (t, 3H, $J=7.32$ Hz), 1.53 (sx, 2H, $J=7.32$ Hz), 2.45 (t, 2H, $J=7.32$ Hz), 5.58 (s, 1H), 5.82 (s, 1H), 7.40–7.80 (m, 5H); MS m/z 174 (M^+, 10%), 173 (12%), 159 (20%), 145 (15%), 132 (12%), 131 (12%), 105 (100%), 77 (80%), 51 (40%), 41 (25%). HRMS found m/z: 174.1048; calcd for $C_{12}H_{14}O$ $[M]^+$: 174.1045.

4.18. 2-Methyl-1-phenyl-1-pentanone 3h

IR (film) 3065, 2959, 2935, 2873, 1679, 1596, 971, 703 cm^{-1}; ^1H NMR δ 0.90 (t, 3H, $J=7.32$ Hz), 1.19 (d, 3H, $J=6.84$ Hz), 1.34 (m, 2H), 1.42 (m, 1H), 1.78 (m, 1H), 3.50 (sx, 1H, $J=6.84$), 7.40–7.90 (m, 5H); MS m/z 176 (M^+, 2%), 147 (2%), 134 (20%), 105 (100%), 91 (2%), 77 (36%), 51 (17%).

4.19. 1-Phenyl-2-buthyl-2-propen-1-one 2i

IR (film) 3085, 2958, 2930, 2873, 1658, 981, 752, 695 cm^{-1}; ^1H NMR δ 0.92 (t, 3H, $J=7.32$ Hz), 1.32–1.44 (m, 4H), 2.46 (t, 2H, $J=7.50$ Hz), 5.56 (s, 1H), 5.80 (s, 1H), 7.40–7.80 (m, 5H). MS m/z 188 (M^+, 10%), 187 (10%), 173 (2%), 159 (18%), 145 (18%), 131 (15%), 117 (5%), 105 (100%), 91 (5%), 77 (70%), 51 (30%), 41 (20%). HRMS found m/z: 188.1207; calcd for $C_{13}H_{16}O$ $[M]^+$: 188.1201.

4.20. 2-Methyl-1-phenyl-1-hexanone 3i

IR (film) 3062, 2959, 2933, 2872, 1682, 1594, 970, 702 cm^{-1}; ^1H NMR δ 0.86 (m, 3H), 1.23 (d, 3H, $J=6.60$ Hz), 1.30–1.50 (m, 5H), 1.80 (m, 1H), 3.45 (sx, 1H, $J=6.60$ Hz), 7.40–7.97 (m, 5H); MS m/z 190 (M^+, 2%), 171 (1%), 161 (1%), 147 (2%), 134 (41%), 115 (1%), 105 (100%), 91 (2%), 77 (50%), 69 (2%), 51 (20%).

4.21. 2-Benzyl-1-phenyl-2-propen-1-one 2j

IR (film) 3085, 3062, 3029, 2925, 1648, 1495, 985, 756, 698; ^1H NMR δ 3.80 (s, 2H), 5.67 (s, 1H), 5.74 (s, 1H), 7.20–7.70 (m, 10H); MS m/z 222 (M^+, 3%), 221 (3%), 210 (22%), 191 (1%), 178 (1%), 165 (1%), 152 (1%), 131 (3%), 116 (3%), 105 (100%), 91 (10%), 77 (41%), 65 (5%), 51 (17%). HRMS found m/z: 222.1044; calcd for $C_{16}H_{14}O$ $[M]^+$: 222.1045.

4.22. 2-Methyl-1,3-diphenyl-1-propanone 3j

IR (film) 3085, 3062, 3028, 2970, 2931, 2872, 1680, 1595, 1450, 1229, 972, 740, 697 cm^{-1}; ^1H NMR δ 1.20 (d, 3H, $J=6.84$ Hz), 2.68 (dd, 1H, $J=13.67$ Hz, $J=7.81$ Hz), 3.16 (dd, 1H, $J=13.67$ Hz, $J=6.35$ Hz), 3.76 (m, 1H); MS m/z 224 (M^+, 13%), 209 (2%), 191 (1%), 181 (2%), 165 (1%), 145 (1%), 131 (2%), 117 (2%), 105 (100%), 91 (19%), 77 (31%), 65 (5%), 51 (13%).

4.23. 2-Phenyl-1-penten-3-one 2k

IR (film) 3060, 2979, 2934, 1685, 1494, 1121, 939, 774, 703 cm^{-1}; ^1H NMR δ 1.11 (t, 3H, $J=7.31$ Hz), 2.73 (q, 2H, $J=7.31$ Hz), 5.84 (s, 1H), 6.07 (s, 1H), 7.26–7.34 (m, 5H); MS m/z 160 (M^+, 30%), 145 (1%), 131 (17%), 115 (1%), 103 (100%), 91 (1%), 77 (37%), 63 (3%), 57 (42%). HRMS found m/z: 160.0887; calcd for $C_{11}H_{12}O$ $[M]^+$: 160.0888.

4.24. 2-Phenyl-3-pentanone 3k

IR (film) 3056, 3024, 2976, 2937, 1714, 1602, 1496, 1454, 759, 701 cm^{-1}; ^1H NMR δ 0.96 (t, 3H, $J=7.32$

Hz), 1.40 (d, 3H, $J=6.97$), 2.36 (m, 2H), 3.76 (q, 1H, $J=6.97$ Hz); MS m/z 162 (M^+, 4%), 133 (4%), 115 (1%), 105 (82%), 91 (3%), 77 (19%), 57 (100%), 51 (13%).

4.25. 2-Ethyl-1-hexen-3-one 2l

IR (film) 2965, 2875, 1680, 1458, 934 cm^{-1}, ^1H NMR δ 0.94 (t, 3H, $J=7.32$ Hz), 1.03 (t, 3H, $J=7.45$ Hz), 1.64 (sx, 2H, $J=7.32$ Hz), 2.29 (q, 2H, $J=7.45$ Hz), 2.66 (t, 2H $J=7.32$ Hz), 5.71 (s, 1H), 5.98 (s, 1H); MS m/z 126 (M^+, 3%), 111 (7%), 97 (14%), 83 (86%), 71 (9%), 55 (100%), 43 (63), 41 (30%), 39 (40%).

4.26. 3-Methyl-4-heptanone 3l

IR (film) 2964, 2883, 1715, 1463 cm^{-1}; ^1H NMR δ 0.87 (t, 3H, $J=7.32$ Hz), 0.91 (t, 3H, $J=7.32$ Hz), 1.06 (d, 3H, $J=6.84$ Hz), 1.38 (m, 1H), 1.59–1.69 (m, 3H), 2.40–2.46 (m, 3H); MS m/z 128 (M^+, 6%), 113 (1%), 100 (4%), 85 (8%), 71 (60%), 57 (71%), 43 (100%).

4.27. 2-Benzyl-5-phenyl-1-penten-3-one 2m

IR (film) 3084, 3061, 3028, 2922, 1678, 1449, 1073, 943, 741, 699; ^1H NMR δ 2.91 (t, 2H, $J=8.0$ Hz), 3.01 (t, 2H, $J=8.0$ Hz), 3.60 (s, 2H), 5.60 (s, 1H), 6.05 (s, 1H), 7.15–7.30 (m, 10H); MS m/z 250 (M^+, 22%), 235 (2%), 217 (2%), 202 (2%), 191 (2%), 172 (5%), 159 (25%), 145 (25%), 129 (20%), 117 (70%), 91 (100%), 77 (20%), 65 (30%), 51 (20%), 39 (40%). HRMS found m/z: 250.1356; calcd for $C_{18}H_{18}O$ $[M]^+$: 250.1358.

4.28. 2-Methyl-1,5-diphenyl-3-pentanone 3m

IR (film) 3086, 3062, 3027, 2927, 1712, 1496, 1454, 743, 700 cm^{-1}; ^1H NMR δ 1.05 (d, 3H, $J=6.84$ Hz), 2.56 (m, 2H), 2.70–2.80 (m, 4H), 2.94 (m, 1H), 7.10–7.30 (m, 10H). MS m/z 252 (M^+, 5%), 234 (1%), 219 (1%), 202 (1%), 191 (1%), 181 (1%), 161 (2%), 147 (12%), 133 (24%), 119 (12%), 105 (50%), 91 (100%), 77 (12%), 65 (13%), 51 (9%), 41 (17%).

4.29. 2-Isopropyl-5-methyl-1-hexen-3-one 2n

IR (fim) 2958, 2871, 1676, 1464, 1366, 924 cm^{-1}; ^1H NMR δ 0.928 (d, 6H, $J=6.6$ Hz), 1.02 (d, 6H, $J=6.6$ Hz), 2.10 (m, 3H), 2.93 (hept, 1H, $J=6.6$ Hz), 5.66 (s, 1H), 5.93 (s, 1H). MS m/z 154 (M^+, 5%), 139 (60%), 125 (8%), 111 (10%), 97 (100%), 85 (20%), 69 (90%), 57 (80%), 41 (100%).

Acknowledgements

We thank FAPESP for financial support, CNPq for a scholarship for E.P.S.F.

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