A New Protocol for a Regioselective Aldol Condensation as an Alternative Convenient Synthesis of *β*-Ketols and α,*β*-Unsaturated Ketones

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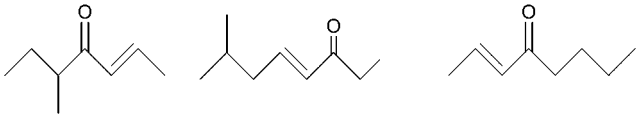
Abstract: A general and convenient synthesis of *β*-ketols and α,*β*-alkenones has been achieved by a Knoevenagel condensation of a *β*-ketoacid with an aldehyde in aqueous medium. Saponification of a *β*-ketoester by an aqueous KOH 10% solution gives the potassium salt of the *β*-ketoacid, which is condensed in situ with an aldehyde at pH 7.8−8.0, at 60 °C for 5−6 h. The intermediate *β*-ketocarboxylate is smoothly decarboxylated in the reaction medium, giving the *β*-ketol in high yield (75−90%). Acidification of the reaction mixture at pH 1 and heating at 70 °C under vigorous stirring for 6 h, leads directly to the corresponding α,*β*-unsaturated ketone in good yield (65−75%).

Introduction

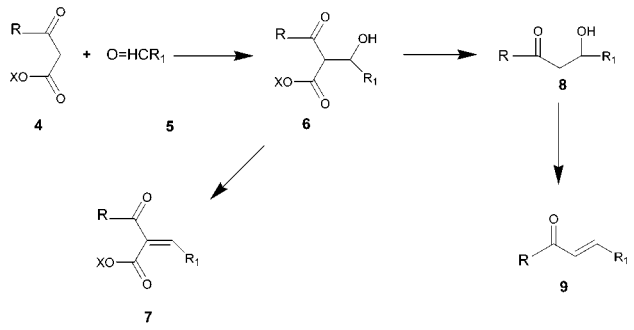
There is a general interest in the synthesis of alkenones, because this structural unit is the main function of various natural fragrant compounds and pheromones, and also it is a versatile intermediate in the synthesis of various natural products. For example (*E*)-5-methylhept-2-en-4-one **1** (filbertone) has been isolated from hazelnuts,[1] (*E*)-7-methyloct-4-en-3-one **2** from the marine sponge *Plakortis zygompha*,[2] and (*E*)-2-octen-4-one **3** has been found as a volatile constituent of raw and roasted carob.[3]



1 **2** **3**

The most common access to this structural unit is by the aldol condensation, a reaction that is amply documented and described.[4] Significant improvement on the regioselectivity of the reaction can be obtained by a preformed specific enol equivalent such as a kinetic enolate,[5] an O-silylated enolate,[6] or by the use of adequate catalysts.[7] The one-step synthesis of alkenones by the Horner−Emmons−Wadsworth reaction[8] is also well-known.

Scheme 1



a X = CH_3, CH_2CH_3

b X = H

c X = Na, K

β-Ketoesters **4a** have been utilized as active methylene compounds in Knoevenagel condensations with aldehydes,[9] giving α-alkenyl-*β*-ketoesters **7a** (Scheme 1). An approach to the α,*β*-alkenone unit could be the saponification and decarboxylation of the α-alkenyl-*β*-ketoester **7a**. However, usual alkaline hydrolysis of the *β*-ketoesters for the production of a ketone is often complicated by a competing fission reaction that affords esters or acids, particularly when the α position is substituted.[10] For this reason this approach has not been used for the regiospecific synthesis of α,*β*-unsaturated ketones.

It has been reported that *β*-ketoacids **4b** (Scheme 1) give condensation reactions with aldehydes to yield *β*-ketols or α,*β*-unsaturated ketones.[11,12] However, the overall yields are low and the experimental conditions do not allow for an extensive application of the method. The main inconvenience is that the *β*-ketoacid **4b** has to be carefully isolated from its aqueous solution before the condensation with the aldehyde.[12] The isolation of the thermally unstable *β*-ketoacids is not a simple procedure, especially for multigram preparations. The extraction of a *β*-ketoacid from an aqueous solution and the condensation of the solvent have to be done rapidly at a temperature below 30 °C, and the crude acid must be kept at −20 °C, not longer than one week.[12] Moreover, the condensation with the aldehyde was accomplished either in pyridine[12] or DMF,[13] solvents that are difficult to handle in large scale preparations. The reported conden-

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(1) (a) Jauch, J.; Schmalzing, D.; Schuring, V.; Emberger, R.; Hopp, R.; Kospel, M.; Silberzahn, W.; Werkhoff, P. *Angewante Chem., Int., Ed. Engl.* **1989**, *28*, 1022−1023. (b) Jauch, J.; Czesla, H.; Schuring, V. *Tetrahedron* **1999**, *55*, 9787−9792.

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(3) Cantalejo, M. J. *J. Agric. Food Chem.* **1997**, *45*, 1345−1350.

(4) Nielsen, A. T.; Houlihan, W. J. In *Organic Reactions*; John Wiley & Sons: New York, 1968; vol. 16, pp 1−438.

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(8) Wadsworth, W. S. In *Organic Reactions*; John Wiley & Sons: New York, 1977; vol. 25, pp 73−250.

(9) Jones, G. In *Organic Reactions*: John Wiley & Sons: New York, 1967; vol. 15, pp 204−599.

(10) House, H. O. In *Modern Synthetic Methods*, 2nd ed.; Benjamin, W. A., Ed.; New York, 1972; pp 492−546.

(11) (a) Schopf, C.; K.Thierfelder, K. *Liebigs Ann. Chem.* **1935**, *518*, 127−155. (b) Stiles, M.; Wolf, D.; G. V. Hudson, G. V. *J. Am. Chem. Soc.* **1959**, *81*, 628−632.

(12) Grayson, D. H.; Tuite, M. R. J. *J. Chem. Soc., Perkin Trans. 1* **1986**, 2137−2142.

(13) Naf, F.; Decorzant, R.; W.Thommen, W. *Helv. Chim. Acta* **1982**, *65*, 2212−2223.

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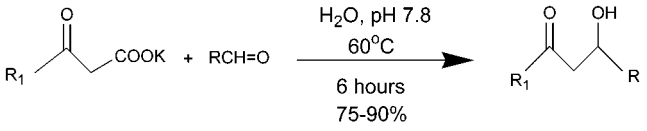
Scheme 2



sation of benzaldehyde with acetoacetic acid **4b** (Scheme 1) in neutral phosphate buffer was accomplished in 14 days, and the β-ketol **8** was isolated in low yield.[11] Even though the experimental conditions in the above reports were not attractive and the reported yields were moderate, we anticipated that the condensation of a β-ketoacid with an aldehyde could be a general synthetic approach to α,β-alkenones.

In this paper a new very simple protocol for the condensation of a β-ketoacid with an aldehyde to the corresponding β-ketol and/or $\alpha\beta$-unsaturated ketone is described, providing a highly regioselective aldol condensation alternative. The utility of the method has been illustrated by the synthesis of the (*E*)-5-methylhept-2-en-4-one (filbertone) **1**, the (*E*)-7-methyloct-4-en-3-one **2**, the (*E*)-2-octen-4-one **3** and a series of other simple α,β-unsaturated ketones and β-ketols.

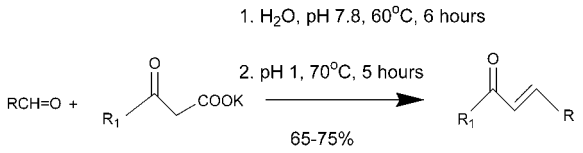
Results and Discussion

During the present study for a regiospecific synthesis of α,β-unsaturated ketones, our effort was focused on the conditions for a direct condensation of a β-ketoacid with an aldehyde. To avoid the tedious isolation of pure β-ketoacids, their sodium or potassium salts in an aqueous solution are used. For this purpose, a β-ketoester is smoothly saponified by an aqueous alkali metal hydroxide solution, at room-temperature overnight, giving a clear homogeneous solution of its alkali metal salt. The pH of the obtained aqueous solution is adjusted to 7.8−8.0, by addition of a buffer of pH 8, and then the addition of the aldehyde is followed. If the pH is higher than 8.5, the self-condensation of the aldehyde is the main reaction. If the pH is lower than 7.5, the reaction is very slow and the procedure becomes nonpractical. In the case of a condensation with a water insoluble aldehyde, a phase transfer catalyst has to be added in the reaction mixture. Finally, depending on the nature and the availability of the reagents, an excess of one of the reactants can be used to improve the yield.

The reaction is better accomplished at 60 °C. In most of the cases the aldehyde has reacted in less than 6 h, without any self-condensation taking place (Scheme 2). When the aldehyde is volatile (e.g., acetaldehyde, propionaldehyde), the reaction mixture is first stirred at room temperature for 2 h and then heated at 40 °C, until the reaction is complete. Then, the reaction mixture is cooled at room temperature, and the β-ketol, which is the unique reaction product, can be easily isolated, by extraction with a common solvent. The main impurity is the corresponding α,β-unsaturated ketone, which has never been found at a concentration of more than 2%. Distillation of the crude product gave the β-ketol in excellent purity and very good yield (75−90%).

The results of some representative condensations of β-ketoesters and aldehydes for the synthesis of β-ketols are summarized in Table 1. The α-branched β-ketoesters such as ethyl 2-methylacetoacetate and ethyl 2-ethylacetoacetate (entry10, Table 1) failed to condense with an aldehyde even after 3 days. Also the condensation with a ketone (entry 11, Table 1) was unsuccessful.

Scheme 3



The dehydration of an isolated pure β-ketol was studied under various conditions. Reflux in benzene or toluene in the presence of *p*-toluenesunfonic acid, HCl (gas), or anhydrous $CuSO_4$ gave the α,β-unsaturated ketone in good yield. However, the final product was contaminated with the corresponding β,γ-unsaturated ketone at a proportion ranging from 5 to 15%. We found that excellent regioselectivity and very good yield (75−92%) on the dehydration of pure β-ketol can be obtained by heating its aqueous emulsion at pH 1 at 70 °C for 5 h (Table 1).

It is worth mentioning that the formation of the α,β-unsaturated ketone can be achieved as a one-step procedure, i.e., without the isolation of the intermediate β-ketol. Therefore, when the condensation of the β-ketoacid with an aldehyde is finished, the reaction medium is acidified by concentrated hydrochloric acid to pH 1 and heated at 60−70 °C with stirring until the dehydration is accomplished. In most of the cases the dehydration is complete after 5 h and the product can be easily recovered by a simple extraction of the reaction medium (Scheme 3). Thus, if the α,β-unsaturated ketone is the desired product, the intermediate β-ketol does not need to be isolated.

The above one-pot procedure is successfully applied for the synthesis of the natural compounds (*E*)-5-methylhept-2-en-4-one **1** (filbertone), (*E*)-7-methyloct-4-en-3-one **2**, (*E*)-2-octen-4-one **3** and for a series of other simples α,β-unsaturated ketones, which are illustrated in Table 1.

In conclusion, a new simple protocol for the condensation of a β-ketoacid with an aldehyde, to β-ketol and/or α,β-alkenone, has been described. The presented method provides a general regioselective alternative to the aldol condensation, particularly convenient in practical terms. The advantages lie in the mildness of experimental conditions, the short reaction time, the availability of reagents, and the high yield of pure products.

Experimental Section

IR spectra were obtained in 5% CCl_4 solutions. ^{1}H NMR spectra were recorded on a 200 MHz spectrometer in $CDCl_3$ (with TMS as internal standard). Mass spectra were taken on a GC-MS system at 70 eV. GC analyses were performed on carbowax 20M 50m or SE30 50m fused silica capillary columns. All aldehydes were washed with an aqueous 10% $NaHCO_3$ solution, dried over anhydrous Na_2SO_4, and then purified by distillation. Acetaldehyde and propionaldehyde, however, were used without further purification, provided that their acidity was less than 1%. Ethyl acetoacetate, ethyl 3-oxopentanoate, and ethyl 3-oxoheptanoate are commercially available (Aldrich), and they were used without further purification. Ethyl 3-oxo-4-methylhexanoate was prepared according to the reported procedure,[14] from 2-methylbutyryl chloride.

Preparation of β-Ketol. Into a cold (+10 °C) aqueous 2 M solution of KOH (520 mL, 1.05 mol) was added the β-ketoester (1 mol), and the solution was stirred overnight at room temper-

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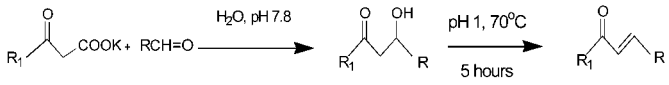
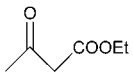
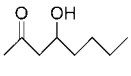
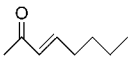
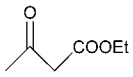
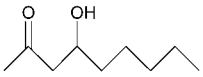
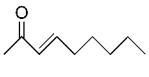
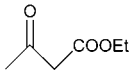
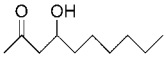
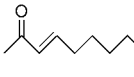
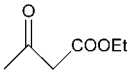
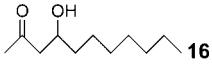
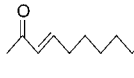
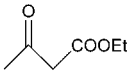
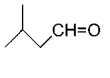
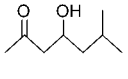
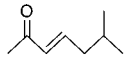
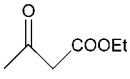
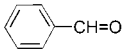
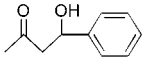
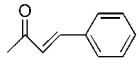
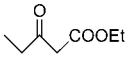
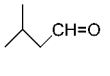
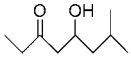
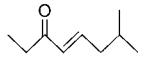
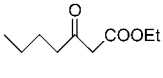
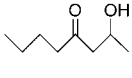
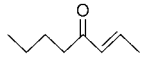
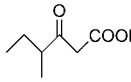
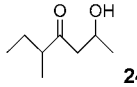
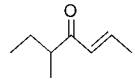
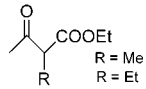
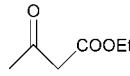
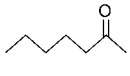
Table 1. Synthesis of *β*-ketols and α,*β*-Unsaturated Ketones



	β-Ketoester	Aldehyde	Time/Temp. Hours/ °C	β-ketol	Yield (%)	αβ-unsaturated ketone	Yield[a] (%)	One pot Procedure Yield (%)
1			5.0/60	 **10**	80	 **11**	85	74
2			5.0/ 60	 **12**	75	 **13**	88	70
3			5.0/60	 **14**	72	 **15**	82	66
4			7.0/60	 **16**	70	 **17**	78	65
5			5.0/60	 **18**	85	 **19**	92	75
6			5.0/60	 **20**	54[b]	 **21**	85	72
7			5.0/60	 **22**	90	 **2**	76	65
8		$CH_3CH=O$	5.0/40	 **23**	78	 **3**	92	67
9		$CH_3CH=O$	4.0/40	 **24**	75	 **1**	86	64
10	 R = Me R = Et		72/60	No reaction	---			
11			72/60	No reaction	---			

[a] Yields refer to the dehydration of pure *β*-ketol. [b] The isolated product contains also 27% of the 1-phenyl-1-buten-3-one **21**.

ature. A solution of tetrabutylammonium hydrogenosulfate ($TBAHSO_4$ 1.7 g, 5 mmol) in water (10 mL) was added, followed by a phosphate buffer pH 8 (Na_2HPO_4−NaOH) (100 mL). The pH of the final solution was adjusted at 7.8 using 0.1 N NaOH or 0.1 N HCl. Then the aldehyde (0.5 mol) was added, and the reaction mixture was stirred for 5−7 h at 60 °C. In the case of volatile aldehydes as acetaldehyde or propionaldehyde, the reaction mixture was first stirred at room temperature for 2 h and then at 40 °C. When GC analysis indicated complete consumption of the starting aldehyde, the reaction mixture was taken to room temperature and extracted with diethyl ether or CH_2Cl_2 (3 × 150 mL). The organic phase was washed with water (100 mL) and dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude product, which is contaminated with less than 2% of the corresponding α,*β*-unsaturated ketone, is purified by distillation under vacuum giving the *β*-ketol in excellent purity.

Dehydration of Isolated *β*-Ketol. The pure *β*-ketol was added to an equal volume of water, and the well-stirred emulsion was acidified by concentrated HCl to pH 1 and then heated under vigorous stirring at 70 °C, until the end of the reaction, generally 5 h. After being cooled to room temperature, the reaction medium was extracted with diethyl ether or CH_2Cl_2 (3 × 150 mL). The organic phase was washed with water (100 mL) and saturated aqueous $NaHCO_3$ (100 mL) and dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The product was purified by distillation under vacuum, to give pure α,*β*-unsaturated ketone.

One-Pot Preparation of α,*β*-Unsaturated Ketones. The general procedure for the preparation of *β*-ketols was followed until the reaction of the aldehyde and the *β*-ketoester was complete. Then, concentrated HCl (150 mL) was added, until pH 1, and the reaction mixture was heated under vigorous stirring at 70 °C for 5 h. Following the previously described workup, pure α,*β*-unsaturated ketone was obtained.

4-Hydroxyoctan-2-one (10). Obtained from ethyl acetoacetate (130 g, 1 mol) and *n*-valeraldehyde (43.0 g, 0.5 mol) as a colorless liquid (57.6 g, yield 80%): bp 88−92 °C/1.5 mmHg (lit.,[15] 45−47 °C/0.1 mmHg); IR (cm^{-1}) 3550, 1700; ^1H NMR *δ* 0.80 (t, *J* = 7.2 Hz, 3H), 1.02−1.26 (m, 6H), 2.21 (s, 3H) 2.48−2.58 (m, 2H), 4,00 (m, 1H); MS *m*/*z* (relative intensity) 126 (5, M − 18), 111 (5), 97 (2), 87 (51), 55 (19), 43 (100).

4-Hydroxynonan-2-one (12). Obtained from ethyl acetoacetate (130 g, 1 mol) and *n*-hexanal (50 g, 0.5 mol) as a colorless

(15) Curran, D. P. *J. Am. Chem. Soc.* **1983**, *105*, 5826−5833.

liquid (59.1 g, yield 75%): bp 95−100 °C/2 mmHg (lit.,[16] 60 °C/0,1 mmHg); IR (cm^{-1}) 3520, 1700; ^1H NMR δ 0.80 (t, J = 7.2 Hz, 3H), 1.00−1.22 (m, 8H), 2.10 (s, 3H), 2.50−2.62 (m, 2H), 3.80−4.00 (m, 1H); MS *m/z* (relative intensity) 143 (1, M − 15), 140 (3), 111 (3), 97 (2), 87 (42), 58 (11), 55 (12), 43 (100).

4-Hydroxydecan-2-one (14). Obtained from ethyl acetoacetate (130 g, 1 mol) and *n*-heptanal (57 g, 0.5 mol) as a colorless liquid (62.0 g, yield 72%): bp 120−125 °C/3 mmHg (lit.,[17] 67 °C/0.5 mmHg); IR (cm^{-1}) 3540, 1705; ^1H NMR δ 0.80 (t, J = 7.2 Hz, 3H), 1.10−1.25 (m, 10H), 2.14 (s, 3H), 2.45−2.52 (m, 2H) 4.00−4.20 (m, 1H); MS *m/z* 154 (3, M − 18), 139 (2), 111 (3), 97 (5), 87 (56), 69 (7), 58 (14), 43 (100).

4-Hydroxyundecan-2-one (16). Obtained from ethyl acetoacetate (130 g, 1 mol) and *n*-octanal (64 g, 0.5 mol) as a colorless liquid (65.3 g, yield 70%): bp 98−100 °C/0.5 mmHg; IR(cm^{-1}) 3550, 1705; ^1H NMR δ 0.82 (t, J = 7.2 Hz, 3H), 1.10−1.30 (m, 12H), 2.15 (s, 3H), 2.50−2.64 (m, 2H), 3.90−4.20 (m, 1H); MS *m/z* 171 (1, M − 15), 125 (2), 110 (3), 87 (35), 69 (10), 58 (8), 55 (9), 43 (100).

4-Hydroxy-6-methylheptan-2-one (18). Obtained from ethyl acetoacetate (130 g, 1 mol) and isovaleraldehyde (43 g, 0.5 mol) as a colorless liquid (61.0 g, yield 85%): bp 60−62 °C/0.7 mmHg; IR (cm^{-1}) 3540, 1700; ^1H NMR δ 0.80 (d, J = 6.7 Hz, 6H), 1.01−1.06 (m, 1H), 1.28−1.32 (m, 1H), 1.65−1.69 (m, 1H), 2.05 (s, 3H), 2.41−2.44 (m, 2H), 3.98−4.00 (m, 1H); MS *m/z* (relative intensity) 129 (3, M − 15), 111 (6), 108 (9), 87 (35), 69 (16), 58 (24), 55 (16), 43 (100).

1-Phenyl-1-hydroxybutan-3-one (20). Obtained from ethyl acetoacetate (130 g, 1 mol) and benzaldehyde (53 g, 0.5 mol), as a yellowish liquid (54.0 g), containing also the corresponding unsaturated ketone 1-phenyl-1-buten-3-one (**21**). GC-MS analysis of the obtained product showed the presence of 1-phenyl-1-hydroxybutan-3-one[18] and of 1-phenyl-1-buten-3-one[7] at a ratio of 2:1. The above compounds were identified by their mass spectra, which were consistent with the literature.[7,18]

5-Hydroxy-7-methyloctan-3-one (22). Obtained from ethyl 3-oxopentanoate (26.0 g, 0.2 mol) and isovaleraldehyde (17.2 g, 0.2 mol) as a colorless liquid (28.1 g, yield 90%): bp 65−67 °C/1 mmHg); IR (cm^{-1}) 3550, 1705; ^1H NMR δ 0.81 (d, J = 7.0 Hz, 6H), 0.95 (t, J = 7.2 Hz, 3H), 1.02 (m, 1H), 1.31−1.38 (m, 1H), 1.66−1.71 (m, 1H), 2.30−2.45 (m, 4H), 3.99−4.03 (m, 1H); MS *m/z* (relative intensity) 143 (5, M − 15), 129 (9), 111 (31), 101 (35), 69 (42), 57 (100), 55 (38), 43 (88).

2-Hydroxyoctan-4-one (23). Obtained from ethyl 3-oxoheptanoate (86 g, 0.5 mol) and acetaldehyde (31.5 g, 0.75 mol) as a colorless liquid (56.1 g, yield 78%): bp 60−62 °C/0,8 mmHg (lit.,[19] 61−62 °C/1,0 mmHg); IR (cm^{-1}) 3500, 1706; ^1H NMR δ 0.93 (t, J = 7.2 Hz 3H), 1.18 (d, J = 6.8 Hz, 3H), 1.35 (m, 2H), 1.56 (m, 2H), 2.42 (t, J = 6.4 Hz, 2H), 2.52−2.60 (m, 2H), 4.12 (m, 1H); MS *m/z* (relative intensity) 144 (1, M^+), 129 (2), 103 (10), 87 (16), 85 (19), 69 (27), 58 (45), 43 (100).

2-Hydroxy-5-methylheptan-4-one (24). Obtained from ethyl 3-oxo-4-methylhexanoate (43 g, 0.25 mol) and acetaldehyde (13.2 g, 0.3 mol) as a colorless liquid (24.8 g, yield 75%): bp 62−65 °C/1,0 mmHg (lit.,[20] 40 °C/0,025 mmHg); IR (cm^{-1}) 3500, 1705; ^1H NMR δ 0.72 (t, J = 7.4 Hz, 3H), 0.91 (d, J = 7.1 Hz, 3H), 1.03 (d, J = 6.3 Hz, 3H), 1.20−1.28 (m, 2H), 2.26−2.33 (m, 1H), 2.44−2.48 (m, 2H), 4.05−4.07 (m, 1H); MS *m/z* (relative intensity) 144 (1, M^+), 116 (3), 103 (7), 87 (42), 85 (9), 69 (12), 57 (52), 43 (100).

3-Octen-2-one (11). Obtained from ethyl acetoacetate (130 g, 1 mol) and *n*-valeraldehyde (43 g, 0.5 mol) as a colorless liquid (46.5 g, yield 74%): bp 60−62 °C/2 mmHg; IR (cm^{-1}) 1696, 1675, 1627, 980; ^1H NMR δ 0.88 (t, J = 7.2 Hz, 3H), 1.20−1.80 (m, 4H), 2.20 (m, 2H), 2.30 (s, 3H), 6.00 (d, J = 16.5 Hz, 1H), 6.68 (dt, J = 16.5 and 7.0 Hz, 1H); MS *m/z* (relative intensity) 126 (6, M^+), 111 (14), 97 (29), 71 (15), 69 (21), 57 (63), 55 (100), 43 (64).

3-Nonen-2-one (13). Obtained from ethyl acetoacetate (130 g, 1 mol) and *n*-hexanal (50 g, 0.5 mol) as a yellowish liquid (49 g, yield 70%): bp 70−75 °C/4 mmHg (lit.,[21] 106−107 °C/32 mmHg); IR (cm^{-1}) 1696, 1676,1627, 981; ^1H NMR δ 0.85 (t, J = 7.2 Hz, 3H), 1.15−1.68 (m, 6H), 2.15−2.26 (m, 2H), 2.28 (s, 3H), 6.02 (d, J = 16.0 Hz, 1H), 6.70 (dt, J = 6.8 and 16.0 Hz, 1H); MS *m/z* (relative intensity) 140 (12, M^+), 125 (35), 111 (10), 97 (20), 82 (11), 71 (19), 55 (100), 43 (71).

3-Decen-2-one (15). Obtained from ethyl acetoacetate (130 g, 1 mol) and *n*-heptanal (57 g, 0.5 mol) as a clear yellowish liquid (45.3 g, yield 66%): bp 80−83 °C/3 mmHg (lit.,[22] 104−109 °C/20 mmHg); IR (cm^{-1}) 1697, 1676, 1627, 976; ^1H NMR δ 0.80 (t, J = 7.0 Hz, 3H), 1.18 (bs, 6H), 1.33−1.35 (m, 2H), 2.12 (s, 3H), 2.09−2.14 (m, 2H), 5.95 (d, J = 16.0 Hz, 1H), 6.65 (dt, J = 6.6 and 16.0 Hz, 1H); MS *m/z* (relative intensity) 154 (4, M^+), 139 (18), 125 (6), 111 (9), 97 (21), 69 (42), 55 (82), 43 (100).

3-Undecen-2-one (17). Obtained from ethyl acetoacetate (130 g, 1 mol) and *n*-octanal (64 g, 0.5 mol) as a clear yellowish liquid (54.6 g, yield65%): bp 80−83 °C/3 mmHg (lit.,[23] 68 °C/0,5 mmHg); IR (cm^{-1}) 1695, 1675, 1626, 980; ^1H NMR δ 0.85 (t, J = 7.2 Hz, 3H), 1.22 (bs, 8H), 1.33−1.36 (m, 2H), 2.20 (s, 3H), 2.12−2.26 (m, 2H), 6.00 (d, J = 16.2 Hz, 1H), 6.70 (dt, J = 7.0 and 16.2 Hz, 1H); MS *m/z* (relative intensity) 168 (1, M^+), 153 (10), 125 (4), 97 (14), 83 (9), 69 (31), 55 (62), 43 (100).

6-Methyl-3-hepten-2-one (19). Obtained from ethyl acetoacetate (130 g, 1 mol) and isovaleraldehyde (43 g, 0.5 mol) as a yellowish liquid (47.0 g, yield 75%): bp 83−85 °C/20 mmHg (lit.,[24] 43 °C/3 mmHg); IR (cm^{-1}) 1699, 1674, 1628, 983; ^1H NMR δ 0.85 (d, J = 6.6 Hz, 6H), 1.70 (m, 1H), 2.04 (t, J = 7.0 Hz, 2H), 2.17 (3H, s), 6.00 (d, J = 16.0 Hz, 1H), 6.70 (dt, J = 7.0 and 16.0 Hz, 1H); Ms *m/z* (relative intensity) 126 (6, M^+), 111 (25), 108 (12), 84 (32), 71 (15), 69 (85), 55 (62), 43 (100).

1-Phenyl-1-buten-3-one (21). Obtained from ethyl acetoacetate (130 g, 1 mol) and benzaldehyde (53 g, 0.5 mol) as a clear colorless liquid (52.5 g, yield 72%): bp 96−98 °C/1 mmHg (lit.,[7] 160 °C/27 mmHg); IR (cm^{-1}) 1692, 1668, 1626, 1610, 976; ^1H NMR δ 2.32 (s, 3H), 6.62 (d, J = 16.0 Hz, 1H), 7.20−7.60 (m, 6H); MS *m/z* (relative intensity) 145 (30, M − 1), 131 (80), 103 (100).

7-Methyl-4-octen-3-one (2). Obtained from ethyl 3-pentanoate (26 g, 0.2 mol) and isovaleraldehyde (17 g, 0.2 mol) as a yellowish liquid (18.0 g, yield 65%): bp 53−55 °C/1 mmHg (lit.,[2] 92−94 °C/30 mmHg); IR (cm^{-1}) 1702, 1677, 1632, 983; ^1H NMR δ 0.84 (d, J = 6.8 Hz, 6H), 1.01 (t, J = 7.3 Hz, 3H), 1.66−1.70 (m, 1H), 2.01 (t, J = 7.0 Hz, 2H), 2.48 (q, J = 7.3 Hz, 2H), 5.97 (d, J = 16.5 Hz, 1H), 6.72 (dt, J = 6.9 and 16.5 Hz, 1H); MS *m/z* (relative intensity) 140 (5, M^+), 111 (28), 97 (1), 83 (4), 69 (21), 55 (100), 57 (10), 43 (27).

2-Octen-4-one (3). Obtained from ethyl 3-oxo-heptanoate (86 g, 0.5 mol) and acetaldehyde (31.5 g, 0.75 mol) as a clear yellowish liquid (45.5 g, yield 67%): bp 50−52 °C/4 mmHg (lit.,[25] 68−70 °C/17 mmHg); IR (cm^{-1}) 1697, 1677, 1633, 971; ^1H NMR δ 0.88 (t, J = 6.0 Hz, 3H), 1.25−1.98 (m, 2H), 1.54−1.65 (m, 2H), 1.94 (d, J = 7.2 Hz, 3H), 2.55 (t, J = 7.0 Hz, 2H), 6.15 (d, J = 16.0 Hz, 1H), 6.82 (dq, J = 7.0 and 16.0 Hz, 1H); MS *m/z* 126 (1, M^+), 111 (11), 97 (2), 84 (38), 69 (100), 57 (5), 55 (5), 41 (80).

5-Methyl-2-hepten-4-one (1). Obtained from ethyl 4-methyl-3-oxo-hexanoate (40 g, 0.23 mol) and acetaldehyde (10.2 g, 0,23 mol) as a clear yellowish liquid (18.8 g, yield 64%): bp 65−70 °C/16 mmHg (lit.,[1] 70 °C/20 mmHg); IR (cm^{-1}) 1692, 1671, 1631, 969; ^1H NMR δ 0.86 (t, J = 7.5 Hz, 3H), 1.06 (d, J = 7.0 Hz, 3H), 1.32−1.45 (m, 1H), 1.61−1.75 (m, 1H), 1.88 (d, J = 6.8 Hz 3H), 2.58−2.70 (m, 1H), 6.18 (d, J = 15.7 Hz, 1H), 6.88 (dq, J = 15.7 and 6.8 Hz, 1H); MS *m/z* 126 (8, M^+), 111 (15), 98 (17), 69 (100), 57 (5), 41 (75).

JO0200872

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