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Iron(III) Tosylate in the Preparation of Dimethyl and Diethyl Acetals from Ketones and β -Keto Enol Ethers from Cyclic β -Diketones

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Iron(III) Tosylate in the Preparation of Dimethyl and Diethyl Acetals from Ketones and β-Keto Enol Ethers from Cyclic β-Diketones

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Abstract: An efficient method for conversion of ketones to their corresponding dimethyl and diethyl acetals and of cyclic β-diketones into β-keto enol ethers using $Fe(OTs)_3$ as a catalyst is described.

Keywords: Diethyl acetals, dimethyl acetals, iron(III) tosylate, β-keto enol ethers, ketones

INTRODUCTION

Dialkyl acetals are one of the most frequently used protective groups for aldehydes and ketones.[1] The acetalization reaction is widely used in organic synthesis and is typically achieved by treatment of the carbonyl compound with the alcohol and/or the corresponding orthoformate in the presence of protic acids, Lewis acids, or acidic catalysts. Some methods for the preparation of dimethyl and diethyl acetals include homogeneous catalysts such as PTSA,[2] $PhSO_2NHOH$,[3] triflic acid,[4] HCl,[5] DCC-$SnCl_4$,[6] TMSOTf,[7] $LaCl_3$,[8] $Sc(OTf)_3$,[9] $Bi(OTf)_3$,[10] $Bi(NO_3)_3$,[11] $RuCl_3$,[12] $TiCl_4$,[13] $In(OTf)_3$,[14] $B_{10}H_{14}$,[15] [Hmin]BF_4,[16] $LiBF_4$,[17] $Cu(BF_4)_2$,[18] iodine,[19] $FeCl_3$,[20] DDQ,[21] $ZrCl_4$,[22] NBS,[23] and tetrabutylammonium tribromide (TBATB).[24] On the other hand, some solid

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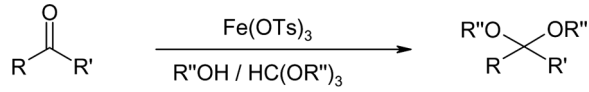
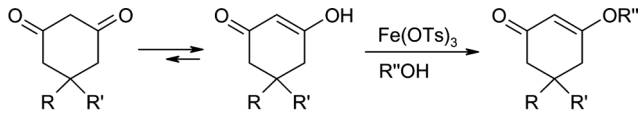


1a : R= alkyl, aryl
1b : R'= H, alkyl, aryl

2: R"= Me, Et

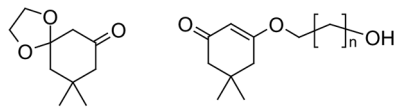
Scheme 1.

catalysts[25] such as sulphonic resins,[26] acidic montmorillonite clay,[27] montmorillonite clay K 10–PTSA,[28] and zeolites,[29] in the presence of trimethyl orthoformate and montmorillonite clay K 10,[30] Ce-exchanged clay,[31] siliceous mesoporous silica,[32] and amorphous SO_3H-SiO_2[33] with methanol have also been employed for the preparation of dimethyl acetals. Acetalization is more easily achieved from aldehydes than from ketones, and a literature survey shows that a few methods are available for the preparation of diethyl acetals in comparison with those employed to obtain dimethyl acetals. Ketone reactivity generally follows the order acyclic ≈ cyclohexanones >



3a : R= H, R'= H
3b : R= H, R'= Me
3c: R= Me, R'= Me

4



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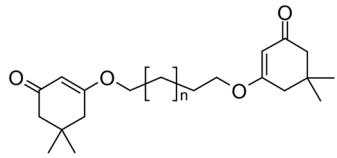
6 : n=1
7 : n=2
8 : n=3



9 : n= 1
10 : n= 3

Scheme 2.

cyclopentanones > α,β-unsaturated ketones ≈ α,α-disubstituted ketones >> aromatic ketones. The preparation of dialkyl acetals from diaryl ketones is more difficult, and standard methods for acetalization generally fail. Acetalization rate in diaryl ketones is strongly influenced by both the presence of two favorable aryl groups by way of the stabilization of the intermediate cation and by the unfavourable steric crowding during the initial formation of a hemiacetal.

Here we report on an alternative and efficient method for the preparation of dimethyl and diethyl acetals from aldehydes and especially from ketones, including diaryl ketones, with the use of $Fe(OTs)_3$[34] as a catalyst (Scheme 1). Likewise, iron(III) tosylate acts as a good catalyst in the formation of β-keto enol ethers from cyclic β-diketones (Scheme 2).

RESULTS AND DISCUSSION

Initially we explored the preparation of dimethyl and diethyl acetals from aldehydes by treatment with the alcohol and the corresponding orthoformate in the presence of variable amounts of iron(III) tosylate. This reagent is relatively inexpensive to prepare in high yield, easy to handle in relation with other iron(III) salts, and can be stored indefinitely at room temperature under an inert atmosphere.

After several assays, we found that aldehydes could be readily converted to their corresponding dialkyl acetals in excellent yields by using 3 mol% $Fe(OTs)_3$ as a catalyst at room temperature (Table 1).

Table 1. Protection of aldehydes as dimethyl and diethyl acetals with ROH/$HC(OR)_3$ catalyzed by $Fe(OTs)_3$[a]

Entry	Substrate	ROH	Temp	Time	Yield (%)
1	4-Bromobutanal	MeOH	rt	30 min	>99
2	Heptaldehyde	MeOH	rt	30 min	97
3	Benzaldehyde	MeOH	rt	30 min	>99
4	Benzaldehyde	EtOH	rt	30 min	>99
5	Anisaldehyde	MeOH	rt	60 min	96
6	Anisaldehyde	EtOH	rt	90 min	98
7	3-Bromobenzaldehyde	EtOH	rt	30 min	>99
8	4-Chlorobenzaldehyde	EtOH	rt	60 min	95
9	*trans*-Cinnamaldehyde	EtOH	rt	120 min	86
10	Furfural	EtOH	rt	30 min	92

[a]The structures of the products were established from their spectral (^{1}H NMR, ^{13}C NMR, and MS) data.

Likewise, we examined the possibility of extending this methodology to the preparation of the corresponding acetals from ketones under identical conditions. Most of the ketones tested were efficiently converted into their dimethyl and diethyl acetals at room temperature or under reflux conditions with the alcohol as solvent (Table 2). Only in the case of dicyclohexyl ketone (entries 25 and 26) was the formation of the acetal not observed, and only minimal amounts of the corresponding vinyl ethers were detected, probably due to the large steric impediment induced by the two cyclohexyl groups contiguous to the carbonyl group. A β-keto ester such as ethyl acetoacetate under these conditions afforded mixtures 3 : 1 (acetal–enol ether) with high overall yield. With diaryl ketones, the best results were obtained with the use of 5 mol% $Fe(OTs)_3$ at reflux. Dimethyl acetals were formed in excellent yields including 9-fluorenone dimethyl acetal (entry 35), which is difficult to prepare using other known acetalization methods.[4,10] The yields of diethyl acetals from diaryl ketones decrease in relation to those of the corresponding dimethyl acetals and in the case of 4,4′-dichlorobenzophenone (entry 32) and 4-nitrobenzophenone (entry 34) the conversions are significantly low, even after long reaction times, with the greater part of the starting ketones being recovered unreacted.

Finally, we explored the use of $Fe(OTs)_3$ in the preparation of β-keto enol ethers from cyclic β-diketones (Scheme 2). β-Keto enol ethers are very valuable synthetic intermediates,[35] and they have been widely used in the construction of various biologically active compounds.[36] Several methods have been reported to prepare β-keto enol ethers from cyclic β-diketones such as methylation with diazomethane,[35a] reaction with alcohols and PTSA,[37] and reaction with alcohols catalyzed by $TiCl_4$,[13] iodine,[38] $B(C_6F_5)_3$,[39] $Yb(OTf)_3$,[40] CAN,[41] or $HClO_4$–SiO_2.[42] β-Keto enol ethers also have been prepared from 3-chloro-cycloalk-2-enones by treatment with methoxide.[43]

Reaction of cyclic β-diketones with various alcohols in the presence of $Fe(OTs)_3$(5 mol%) as a catalyst afforded the corresponding β-keto enol ethers in good to high yields (Table 3). Generally reactions were carried out at reflux with the alcohols acting as solvents or with the use of toluene or 1,2-dichloroethane. In the reactions with methanol (entries 1, 11, and 14), β-keto enol ethers were cleanly obtained in high yields at room temperature. When a β-diketone such as dimedone (**3c**) reacts with primary diols(entries 23–26), under the described conditions, the distribution of the obtained compounds clearly depends on their chain length. Thus, in the reaction with 1,2-ethanediol (entry 23), together with the corresponding β-keto enol ether **6**, significant amounts (25% overall yield) were isolated of the

Table 2. Protection of ketones as dimethyl and diethyl acetals with ROH/$HC(OR)_3$ catalyzed by $Fe(OTs)_3$[a]

Entry	Substrate	ROH	Temp	Time	Yield (%)
1	Acetophenone	MeOH	rt	4 h	99
2	Acetophenone	EtOH	rt	4 h	98
3	Benzylideneacetophenone	MeOH	reflux	2 h	95
4	Benzylideneacetophenone	EtOH	reflux	2 h	84
5	1,5-Diphenylpentan-3-one	MeOH	rt	4 h	99
6	1,5-Diphenylpentan-3-one	EtOH	rt	5 h	94
7	1,3-Diphenylacetone	MeOH	rt	2 h	97
8	1,3-Diphenylacetone	EtOH	rt	4 h	95
9	Cyclohexanone	MeOH	rt	30 min	98
10	Cyclohexanone	EtOH	rt	1 h	96
11	2-Methylcycloxanone	MeOH	rt	2 h	96
12	2-Methylcyclohexanone	EtOH	rt	3 h	94
13	1,4-Cyclohexanedione	MeOH	rt	30 min	98[b]
14	1,4-Cyclohexanedione	EtOH	rt	30 min	96[b]
15	Cycloheptanone	MeOH	rt	1 h	92
16	Cycloheptanone	EtOH	rt	5 h	69
17	Cyclooctanone	MeOH	rt	4 h	92
18	Cyclooctanone	EtOH	rt	4 h	87
19	Cyclododecanone	MeOH	rt	1 h	99
20	Cyclododecanone	EtOH	rt	3 h	98
21	Chloroacetone	EtOH	rt	2 h	91
22	3-Octanone	MeOH	rt	2 h	84
23	d,l-Camphor	MeOH	rt	24 h	77
24	d,l-Camphor	EtOH	rt	24 h	51
25	Dicyclohexyl ketone	MeOH	NR[c]	—	—
26	Dicyclohexyl ketone	EtOH	NR[c]	—	—
27	Benzophenone[d]	MeOH	reflux	6 h	99
28	Benzophenone[d]	EtOH	reflux	10 h	96
29	4,4′-Dimethoxybenzophenone[d]	MeOH	reflux	8 h	98
30	4,4′-Dimethoxybenzophenone[d]	EtOH	reflux	48 h	78
31	4,4′-Dichlorobenzophenone[d]	MeOH	reflux	24 h	97
32	4,4′-Dichlorobenzophenone[d]	EtOH	reflux	24 h	60 (98)[e]
33	4-Nitrobenzophenone[d]	MeOH	reflux	36 h	96
34	4-Nitrobenzophenone[d]	EtOH	reflux	48 h	28 (99)[e]
35	9-Fluorenone[d]	MeOH	reflux	24 h	99
36	9-Fluorenone[d]	EtOH	reflux	24 h	80
37	Ethyl acetoacetate	MeOH	rt	3 h	70/28[f]
38	Ethyl acetoacetate	EtOH	rt	3 h	67/27[f]

[a]The structures of the products were established from their spectral (^1H NMR, ^{13}C NMR, and MS) data.

[b]Yield of bis-acetal at C_1 and C_4.

[c]Only miniscule amounts of the corresponding enol ether were detected.

[d]5 mol% of $Fe(OTs)_3$ was used.

[e]Yield based on conversion in parentheses.

[f]Acetal/Ethyl(2E)-3-ethoxy-2-butenoate.

Table 3. $Fe(OTs)_3$-catalyzed etherification of cyclic β-diketones[a]

Entry	Substrate	R″OH[b]	Temp	Time	Yield (%)
1	**3a**	Methanol	rt	4 h	99
2	**3a**	Ethanol	reflux	3 h	95
3	**3a**	Propanol	reflux	4 h	94
4	**3a**	Isopropanol	reflux	6 h	81
5	**3a**	Butanol	reflux	4 h	92
6	**3a**	Isobutanol	reflux	6 h	82
7	**3a**	Propargyl alcohol	reflux	6 h	87
8	**3a**	Allyl alcohol	reflux	6 h	77
9	**3a**	Benzyl alcohol[c]	reflux	6 h	83
10	**3a**	Cyclohexanol[c]	reflux	6 h	69
11	**3b**	Methanol	rt	2 h	98
12	**3b**	Ethanol	reflux	3 h	87
13	**3b**	Isopropanol	reflux	6 h	85
14	**3c**	Methanol	rt	2 h	98
15	**3c**	Ethanol	reflux	3 h	96
16	**3c**	Propanol	reflux	4 h	93
17	**3c**	Isopropanol	reflux	6 h	81
18	**3c**	Butanol	reflux	4 h	91
19	**3c**	Isobutanol	reflux	6 h	85
20	**3c**	Cyclohexanol[c]	reflux	6 h	82
21	**3c**	Propargyl alcohol	reflux	6 h	82
22	**3c**	Benzyl alcohol[c]	reflux	6 h	79
23	**3c**	1,2-Ethanediol[d]	reflux	4 h	25/66[e]
24	**3c**	1,3-Propanediol[d]	reflux	6 h	87[f]
25	**3c**	1,4-Butanediol[d]	reflux	12 h	37/35[g]
26	**3c**	1,6-Hexanediol[d]	reflux	12 h	70[h]
27	**3c**	4-Hydroxybutyl acetate[d]	reflux	12 h	64

[a]The structures of the products were established from their spectral (^{1}H NMR, ^{13}C NMR, and MS) data.

[b]Unless otherwise stated, alcohol acts as solvent.

[c]In toluene.

[d]In 1,2-dichloroethane.

[e]β-Ketodioxolane **5**/β-keto enol ether **6**.

[f]β-Keto enol ether **7**.

[g]β-Keto enol ether **8**/bis-β-keto enol ether **9**.

[h]Bis-β-keto enol ether **10**. Only minimal amounts of the corresponding β-keto enol ether was isolated (0.9%).

β-keto acetal **5**, whereas the use of 1,3-propanediol (entry 24) gave exclusively the formation of the β-keto enol ether **7**. The reaction with 1,4-butanediol (entry 25) led to a mixture of the β-keto enol ether **8** and the corresponding bis-β-enol ether **9**, the latter resulting from the reaction of both hydroxyl groups of the diol with the

β-diketone. Acetylation of **6** led to a compound identical with that obtained by reaction of dimedone with 4-hydroxybutyl acetate (entry 27). Lastly, the reaction of dimedone with 1,6-hexanediol (entry 26) under the described conditions led exclusively to the formation of bis-β-enol ether **10**.

In conclusion, a simple and efficient method has been developed for the protection of carbonyl groups that is especially applicable to protect a wide variety of ketones, as dimethyl and diethyl acetals, in high yields, using easy-to-handle $Fe(OTs)_3$ as a Lewis acid catalyst in the presence of the corresponding alkyl orthoformate as water scavenger. In the same way, $Fe(OTs)_3$ also acts as a good catalyst in the preparation of β-keto enol ethers from cyclic β-diketones and alcohols.

EXPERIMENTAL

Iron(III) tosylate was prepared as described in Ref. 34. Methanol and ethanol were dried by passage through Linde-type 4 A molecular sieves. Other alcohols and solvents were dried by conventional methods, and orthoesters were used as received. Cyclic β-diketones were recrystallized prior to use. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 300 spectrometer at 300 and 75 MHz respectively in C_6D_6 as a solvent, and δ values are expressed in parts per million. The mass spectra were recorded on a VG Autoscope (Fisons Instruments) spectrometer.

General Procedure for Preparation of Dialkyl Acetals

To a stirred solution of $Fe(OTs)_3$ (17 mg, 0.03 mmol) and trialkyl orthoformate (0.32 ml, 3 mmol) in the corresponding dry alcohol (5 ml) the carbonyl compound (1 mmol) neat or dissolved in the minimal amount of dry alcohol was added. The mixture was stirred at room temperature or under reflux under an inert atmosphere for the specified time, and the reaction was monitored by TLC or GC. The reaction was quenched by addition of a saturated aqueous $NaHCO_3$ (10 ml) solution and stirring for 10 min at room temperature. The resulting mixture was extracted with dichloromethane or ether, the organic phase was dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The pure acetals were obtained from the crude by crystallization or chromatography over silica gel or neutral alumina with mixtures of hexane–EtOAc as eluents.

General Procedure for Preparation of Cyclic β-Keto Enol Ethers

Method A

To a stirred solution of the β-diketone (1 mmol) in the appropriate alcohol, which acts as solvent, 5 ml of $Fe(OTs)_3$ (38 mg, 0.05 mmol) were added. The resulting mixture was heated at reflux under an inert atmosphere, and the reaction was monitored by TLC. The mixture was cooled to room temperature, poured into a saturated aqueous $NaHCO_3$ solution (10 ml), and stirred at room temperature for 10 min. After extraction with dichloromethane or ethyl acetate, the combined organic phases were dried over anhydrous $MgSO_4$ and concentrated at reduced pressure. The β-keto enol ethers obtained were purified by chromatography on silica gel or neutral alumina with mixtures of hexane–EtOAc as eluents.

Method B

To a stirred solution of the β-diketone (1 mmol) in toluene or 1,2-dichloroethane (10 ml), the alcohol (3 mmol) and $Fe(OTs)_3$ (38 mg, 0.05 mmol) were added, and the resulting mixture was heated at reflux under an inert atmosphere. The reaction was monitored by TLC. Workup was done as in method A.

All the products were characterized by ^{1}H NMR, ^{13}C NMR, and mass spectral analysis.

Selected Spectral Data

Benzylideneacetophenone diethyl acetal: A colorless oil; ^{1}H NMR δ: 7.79 (d, J = 7.9 Hz, 2 H), 7.28–6.96 (m, 9 H), 6.22 (d, J = 16.0 Hz, 1 H), 3.58–3.35 (m, 4 H), 1.16 (dd, J = 6.9, 7.0 Hz, 6 H); ^{13}C NMR δ: 142.0, 136.5, 131.7, 130.4, 128.3, 127.8, 127.5, 127.4, 127.0, 126.6, 100.9, 56.9, 14.9; MS m/z (%): 282 (M^+, 29), 237 (M^+-OEt, 55), 77 (100).

1,5-Diphenylpentan-3-one dimethyl acetal: A colorless oil; ^{1}H NMR δ: 7.28–7.16 (m, 10H), 3.14 (s, 6 H), 2.75–2. 70 (m, 4 H), 2.14–2.08 (m, 4 H); ^{13}C NMRδ: 141.9, 128.3, 128.2, 125.7, 102.4, 47.1, 34.2, 30.5; MS m/z (%): 253 (M^+-OMe, 9), 179 (100), 91 (96).

1,5-Diphenylpentan-3-one diethyl acetal: A light yellow oil; ^{1}H NMR δ: 7.29–7.15 (m, 10 H), 3.49 (ddd, J = 7.0, 7.0, 7.0 Hz, 4 H), 2.79–2.73 (m, 4 H), 2.18–2.12 (m, 4 H), 1.22 (dd, J = 7.0, 7.0 Hz, 6 H); ^{13}C NMR, δ: 142.1, 128.2, 128.1, 125.7, 102.2, 54.9, 35.4, 30.3, 15.2; MS m/z (%): 267 (M^+- OEt, 8), 207 (85), 91 (100).

1,3-Diphenylacetone diethyl acetal: A colorless oil; ^{1}H NMR δ: 7.37–7.16 (m, 10 H), 3.59–3.51 (m, 4 H), 3.02 (s, 4 H), 1.23 (dd, $J = 6.9$, 7.0 Hz, 3 H), 1.22 (dd, $J = 7.0$ Hz, 3 H); ^{13}C NMR δ: 137.2, 130.4, 127.7, 126.0, 103.0, 55.3, 40.1, 15.0; MS m/z (%): 239 (M^+-OEt, 12), 193 (80), 91 (100).

2-Methylcyclohexanone diethyl acetal: A colorless oil; ^{1}H NMR δ: 3.45–3.25 (m, 4 H), 2.17–2.03 (m, 1 H), 1.94–1.82 (m, 1 H), 1.77–1.68 (m, 1 H), 1.55–1.31 (m, 6 H), 1.11–1.03 (m, 6 H), 0.96 (d, $J = 7.2$ Hz, 3 H); ^{13}C NMR δ: 101.5, 54.3, 53.8, 34.3, 29.2, 28.2, 22.8, 20.0, 15.2, 15.1, 13.9; MS m/z (%): 186 (M^+, 39), 141 (M^+-OEt, 80), 129 (100).

Cycloheptanone diethyl acetal: A colorless oil; ^{1}H NMR δ: 3.49 (ddd, $J = 7.0$, 7.0, 7.0 Hz, 4 H), 1.89–1.80 (m, 4 H), 1.59–1.43 (m, 8 H), 1.13 (dd, $J = 7.0$, 7.0 Hz, 6 H); ^{13}C NMR δ: 103.8, 54.8, 37.0, 29.0, 21.8, 15.3; MS m/z (%): 186 (M^+, 8), 141 (M^+-OEt, 97), 129 (100).

Cyclooctanone diethyl acetal: A colorless oil; ^{1}H NMR δ: 3.39 (ddd, $J = 7.0$, 7.0, 7.0 Hz, 2 H), 3.38 (ddd, $J = 7.0$, 7.0, 7.0 Hz, 2 H), 1.88–1.80 (m, 4 H), 1.62–1.42 (m, 10 H), 1.13 (dd, $J = 7.0$, 7.0 Hz, 3 H), 1.12 (dd, $J = 7.0$, 7.0 Hz, 3 H); ^{13}C NMR δ: 103.3, 54.73, 31.3, 28.1, 24.4, 21.4, 15.3; MS m/z (%): 200 (M^+, 20), 155 (M^+-OEt, 83), 129 (100).

Cyclododecanone diethyl acetal: A colorless oil; ^{1}H NMR δ: 3.41 (ddd, $J = 7.0$, 7.0, 7.0 Hz, 4 H), 1.77–1.68 (m, 4 H), 1.40–1.30 (m, 18 H), 1.15 (dd, $J = 7.0$, 7.0 Hz, 6 H); ^{13}C NMR δ: 103.4, 54.8, 30.3, 26.2, 26.0, 22.3, 21.9, 19.4, 15.2; MS m/z (%): 256 (M^+, 7), 211, M^+- OEt, 76), 129 (100).

Chloroacetone diethyl acetal: A colorless oil; ^{1}H NMR δ: 3.34 (s, 2H), 3.35–3.22 (m, 4 H), 1.33 (s, 3 H), 1.02 (dd, $J = 7.0$, 7.0 Hz, 6 H); ^{13}C NMR δ: 99.7, 55.8, 46.4, 20.7, 14.9; MS m/z (%): 316 (M^+, 5), 271 (M^+- OMe, 100).

d,l-Camphor diethyl acetal: A colorless oil; ^{1}H NMR δ: 3.63–3.50 (m, 1 H), 3.44–3.25 (m, 3 H), 2.23–2.11 (m, 1 H), 1.94–1.82 (m, 1 H), 1.82–1.74 (m, 1 H), 1.59 (dd, $J = 4.7$, 4.7 Hz, 1 H), 1.40–1.32 (m, 3 H), 1.08 (dd, $J = 7.0$, 7.1 Hz, 3 H), 1,07 (dd, $J = 7.0$, 7.0 Hz, 3 H), 1.07 (s, 3 H), 1.04 (s, 3 H), 0.82 (s, 3 H); ^{13}C NMR δ: 108.7, 57.4, 55.1, 53.3, 50.1, 44.8, 42.0, 29.7, 27.7, 21.1, 20.8, 15.7, 15.5, 12.6; MS m/z (%): 226 (M^+, 22), 211 (8), 181(M^+-OEt, 25), 95 (100).

Ethyl acetoacetate diethyl acetal: A colorless oil; ^{1}H NMR δ: 3.94 (ddd, $J = 7.1$, 7.1, 7.1 Hz, 2 H), 3.52–3.30 (m, 4 H), 2.70 (s, 2 H), 1.60 (s, 3 H), 1.08 (dd, $J = 7.0$, 7.1 Hz, 6 H), 0.94 (dd, $J = 7.1$, 7.1 Hz, 3 H); ^{13}C NMR δv: 169.2, 99.8, 60.0, 56.0, 43.4, 23.1, 15.4, 14.1; MS m/z (%): 159 (M^+-OEt, 100).

Ethyl (2E)-3-ethoxy-2-butenoate: A light yellow oil; ^{1}H NMRδ: 5.05 (s,1 H), 4.13 (ddd, $J = 7.1$, 7.1, 7.1 Hz, 2 H), 3.21 (ddd, $J = 7.0$, 7.0, 7.0 Hz, 2 H), 2.43 (s, 3 H), 1.08 (dd, $J = 7.1$, 7.1 Hz, 3 H),

0.86 (dd, $J = 7.0$, 7.0 Hz, 3 H); ^{13}C NMR δ: 172.0, 167.6, 91.7, 63.4, 59.2, 19.1, 14.6, 14.0; MS m/z (%): 158 (M^+, 18), 113 (M^+-OEt, 84), 85 (100).

3-Cyclohexyloxy-5,5-dimethyl-2-cyclohexen-1-one (Table 3, entry 20): A light yellow oil; ^{1}H NMR δ: 5.46 (s, 1 H), 3.83–3.78 (m, 1 H), 2.10 (s, 2 H), 1.94 (s, 2 H), 1.64–1.59 (m, 2 H), 1.47–1.41 (m, 2 H), 1.33–1.24 (m, 3 H), 1.07–0.93 (m, 3 H), 0.77 (s, 6 H); ^{13}C NMR δ: 196.6, 172.7, 102.0, 75.0, 50.5, 42.9, 31.6, 30.7, 27.6, 25.1, 23.1; MS m/z (%): 222 (M^+, 11), 141 (100).

9,9-Dimethyl-1,4-dioxaspiro[4.5]decan-7-one (5): A colorless oil; ^{1}H NMR δ: 3.36 (s, 4 H), 2.44 (s, 2 H), 1.91 (s, 2 H), 1.62 (s, 2 H), 0.87 (s, 6 H); ^{13}C NMR δ: 204.9, 109.8, 63.8, 53.5, 50.3, 46.6, 31.9, 29.1; MS m/z (%): 184 (M^+, 5), 127 (100).

3-(2-Hydroxyethoxy)-5,5-dimethyl-2-cyclohexen-1-one (6): A colorless oil; ^{1}H NMR δ: 5.33 (s, 1 H), 3.37–3.34 (m, 2 H), 3.29–3.26 (m, 2 H), 2.05 (s, 2 H), 1.87 (s, 2 H), 0.73 (s, 6 H); ^{13}C NMR δ: 198.2, 175.4, 101.5, 69.7, 59.9, 50.3, 42.2, 31.6, 27.5; MS m/z (%): 184 (M^+, 25), 169 (8), 141 (65), 85 (100). Acetate: ^{1}H NMR δ: 5.25 (s, 1 H), 3.92–3.85 (m, 2 H), 3.26–3.23 (m, 2 H), 2.01 (s, 2 H), 1.86 (s, 2 H), 1.60 (s, 3 H), 0.70 (s, 6 H).

3-(3-Hydroxypropoxy)-5,5-dimethyl-2-cyclohexen-1-one (7): A colorless oil; ^{1}H NMR δ: 5.46 (s, 1H), 3.61–3.58 (m, 2 H), 3.51–3.46 (m, 2 H), 2.06 (s, 2 H), 1.87 (s, 2 H), 1.66–1.60 (m, 2 H), 0.73 (s, 6 H); ^{13}C NMR δ: 198.3, 175.5, 101.5, 65.5, 58.3, 50.3, 42.3, 31.6, 31.5, 27.5; MS m/z (%): 198 (M^+, 9), 183 (11), 141 (95), 85 (100). Acetate: ^{1}H NMR δ: 5.33 (s, 1 H), 3.95–3.91 (m, 2 H), 3.27–3.23 (m, 2 H), 2.06 (s, 2 H), 1.84 (s, 2 H), 1.66 (s, 3 H), 1.62–1.53 (m, 2 H), 0.73 (s, 6 H).

3-(4-Hydroxybutoxy)-5,5-dimethyl-2-cyclohexen-1-one (8): White crystals (CH_2Cl_2–hexane); mp 62–64 °C; ^{1}H NMR δ: 5.43 (s, 1 H), 3.50–3.38 (m, 4 H), 2.08 (s, 2 H), 1.90 (s, 2 H), 1.62–1.53 (m, 2 H), 1.49–1.40 (m, 2 H), 0.75 (s, 6 H); ^{13}C NMR δ: 197.6, 174.8, 101.5, 67.9, 61.4, 50.4, 42.3, 31.6, 28.8, 27.6, 25.0; MS m/z (%): 212 (M^+, 18), 141 (42), 85 (51), 84 (100). Acetate: ^{1}H NMR δ: 5.35 (s, 1 H), 3.88–3.84 (m, 2 H), 3.22–3.18 (m, 2 H), 2.08 (s, 2 H), 1.89 (s, 2 H), 1.67 (s, 3 H), 1.38–1.28 (m, 4 H), 0.76 (s, 6 H); ^{13}C NMR δ: 196.5, 173.8, 169.5, 101.5, 67.1, 63.2, 50.4, 42.2, 31.5, 27.5, 24.9, 24.7, 19.9; MS m/z (%): 254 (M^+, 24), 239 (18), 179 (43), 55 (100). This compound is identical to the product obtained in the reaction of dimedone with 4-hydroxybutyl acetate (Table 3, entry 27).

Compound 9: White crystals (CH_2Cl_2–hexane); mp 140–142 °C; ^{1}H NMR δ: 5.37 (s, 2 H), 3.24–3.18 (m, 4 H), 2.10 (s, 4 H), 1.93 (s, 4 H), 1.34–1.28 (m, 4 H), 0.76 (s, 12 H); ^{13}C NMR δ: 196.6, 173.8, 101.8, 67.1, 50.5, 43.4, 31.6, 27.6, 24.8; MS m/z (%): 334 (M^+, 15), 179 (100).

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