Controlled Release of Perfumery Aldehydes and Ketones by *Norrish* Type-II Photofragmentation of α-Keto Esters in Undegassed Solution

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Alkyl or aryl α-keto esters of primary or secondary alcohols decompose upon irradiation at 350–370 nm from the intermediate triplet state into aldehydes or ketones in polar, as well as apolar solvents. The use of these keto esters as delivery systems for the controlled release of perfumery aldehydes and ketones was investigated by photoirradiation in the presence of oxygen with a Xe or UV lamp, as well as outdoor sunlight. Systematic GC/MS analysis of the irradiated solutions showed that, under these conditions, the desired *Norrish* type-II fragmentation of the ester side chain is the predominant reaction pathway in most of the cases. γ-H Abstraction from the alkyl side chain of alkyl keto esters, as well as an intramolecular *Paternò-Büchi* reaction or epoxidation of the alkene function in different citronellyl α-keto esters were identified as the most important side reactions. Some of the experimental findings have been rationalized on the basis of *ab initio* and density-functional calculations. (Cyclohexyl)oxoacetates and oxo(phenyl)acetates were found to be the most suitable precursors for the desired perfumery applications.

1. Introduction. – Aldehydes and ketones are important classes of fragrances that are present in all kinds of perfumes. However, many of them are very volatile and can, after application, only be perceived over a relatively short period of time. Furthermore, as constituents of perfumes for a variety of different bodycare or household applications, such as shampoos, soaps, all purpose cleaners, fabric softeners, or detergent powders, they are often too hydrophilic and thus easily carried away by water during various rinsing processes instead of staying on substrates like hair, skin, or fabrics.

To prolong the desired odor perception of this class of compounds, we have prepared a series of photolabile, hydrophobic, non-volatile fragrance precursors as potential delivery systems for the controlled release of perfumery aldehydes and ketones in typical bodycare and household applications. In this publication, we describe the fragrance release from α-keto esters upon irradiation with artificial light sources, as well as natural sunlight in the presence of O_2 [1]. Some interesting fragrances for release in functional perfumery are depicted in *Fig. 1* [2].

The photolysis of alkyl or aryl α-keto esters of primary or secondary alcohols has been intensively studied since the early sixties [3–7]. It was found that these esters decompose from their intermediate triplet state into aldehydes or ketones upon irradiation at 350–370 nm in polar, as well as apolar solvents [7–11]. Most of the photoirradiations described in the literature were carried out in degassed solutions in the absence of O_2. The relatively good yields of the fragmentation process have allowed the use of α-keto esters as intermediates for the transformation of primary or secondary alcohols to aldehydes and ketones, respectively [12].

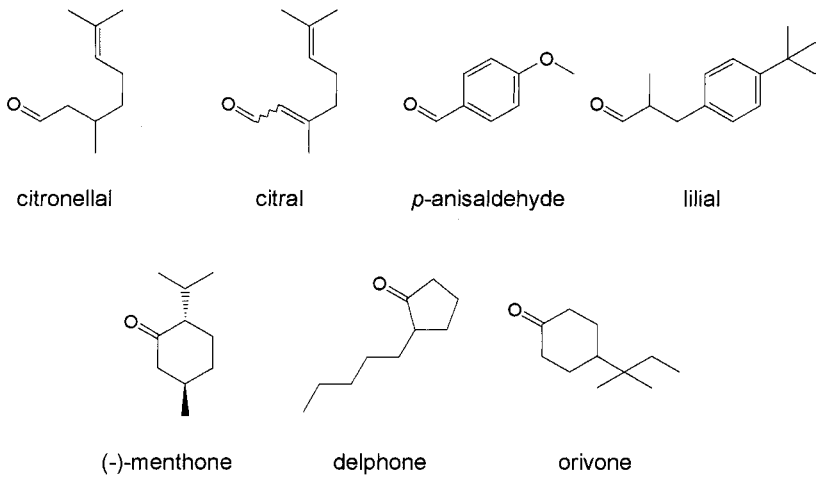


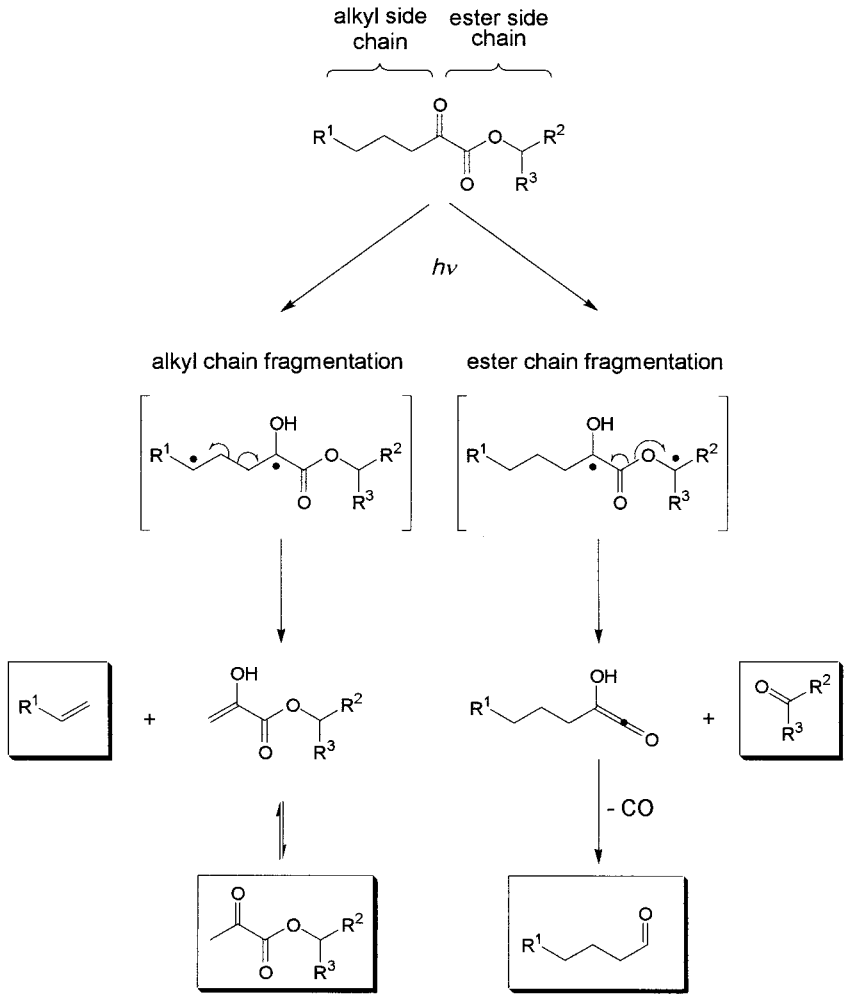
Fig. 1. *Structures and trivial names of typical perfumery aldehydes and ketones* [2] (*Lilial* and *Orivone* are registered trademarks of *Givaudan-Roure* and *Int. Flavors and Fragrances*, respectively)

The accepted general mechanism is based on a *Norrish* type-II fragmentation of the triplet state of the irradiated keto ester [7–9]. As a first step, this process involves the formation of a 1,4-diradical by *intramolecular* γ-H abstraction from the ester side chain by the carbonyl O-atom in its excited triplet state, followed by C(α)–O(β) bond cleavage. This results in the formation of the carbonyl compound together with a hydroxy ketene derivative, which then loses CO to form an aldehyde (*Scheme 1*) [7–9]. In the case of long-chain alkyl α-keto acids or esters, an intramolecular H shift from the alkyl moiety to the carbonyl O-atom has been observed, yielding an alkene and, after tautomerization, an α-keto acid or ester (*Scheme 1*) [13]. *Intermolecular* H abstraction, which has even been observed in apolar, non-H-donating solvents, results in the formation of different dimeric structures [4][9].

All these processes are based on an electronic $n \rightarrow \pi^*$ transition from the ground state to the excited singlet state $^1(n \rightarrow \pi^*)$ of the C=O group, followed by a rapid intersystem crossing to the triplet state $^3(n \rightarrow \pi^*)$. The $n \rightarrow \pi^*$ transitions from the ground state to the excited singlet state have, in general, small molar absorption coefficients (ε) due to an unfavorable overlap of the orbitals. The most reactive C=O groups are those in which these excited states are the lowest energy states of the C=O function [14].

Since O_2 quenches the triplet state of C=O compounds [15], the investigation of its role in the *Norrish* type-II photooxidation is an important prerequisite for the use of α-keto esters as efficient delivery systems in functional perfumery. So far, only a few authors have reported the influence of O_2 on the mechanism of the photoirradiation of α-keto esters [5][10][11][16][17]. *Pirrung* and *Tepper*, for example, proposed a mechanism invoking the formation of a 1,3,4-trioxane intermediate resulting from the reaction of molecular O_2 with the previously formed 1,4-diradical [10]. Alternatively the formation of a hydroperoxide as a possible intermediate was described by *Hu* and *Neckers* [16]. Further reaction of both species should yield CO_2 and a carboxylic acid besides the desired carbonyl compound. On the other hand, the formation of CO_2 in the

Scheme 1. *Mechanism for the Intramolecular H-Abstraction from the Alkyl or Ester Side Chain of α-Keto Esters in Degassed Solution*



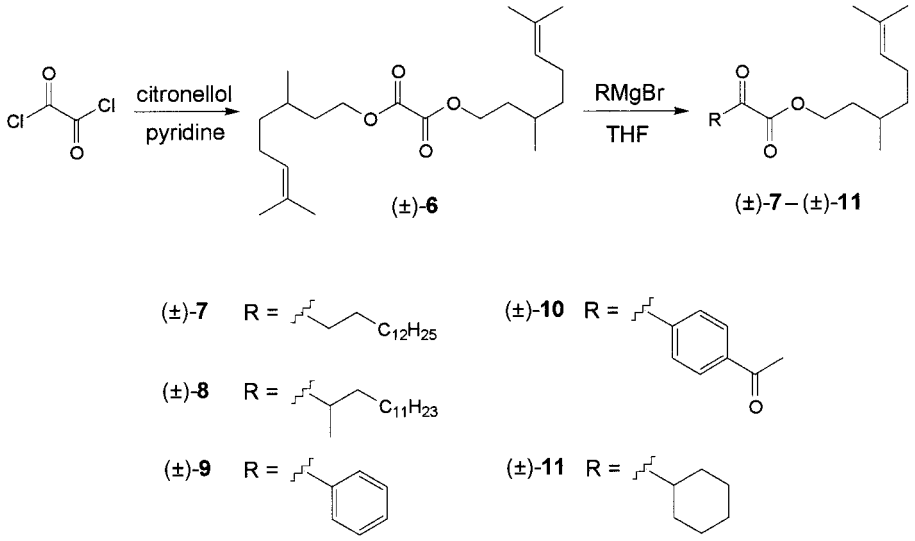
presence of O_2 could also be explained by the direct reaction of singlet oxygen with the α-keto ester. *Davidson et al.*, however, found that singlet oxygen does not seem to play a major role in the reaction and they proposed a mechanism involving an electron transfer from the excited keto ester to the oxygen ground state [11]. This would lead to the formation of peracid intermediates, presumably in competition with the *Norrish* type-II fragmentation. That higher yields of the desired fragmentation products were observed in oxygenated rather than in degassed solutions suggests that the intermediate 1,4-diradical is either not completely or inefficiently intercepted by oxygen [11][16], a finding that is particularly important for the desired applications.

This publication describes the synthesis of various new α-keto esters and their capacity to serve as delivery systems for perfumery aldehydes and ketones upon exposure to sunlight in the presence of O_2. The structure of the precursor substrates has been optimized by a detailed study of the fragmentation reactions in order to maximize the desired fragrance release. In addition, the experimental findings have been rationalized on the basis of semi-empirical or *ab initio* and density-functional calculations.

2. Results and Discussion. – 2.1. *Synthesis of α-Keto Esters.* A large number of protocols for the preparation of α-keto esters have been reported (see, *e.g.*, [18]). Commercially available α-keto acids can directly be esterified with different alcohols in the presence of TsOH under azeotropic removal of water [19], under *N,N′*-dicyclohexylcarbodiimide (DCC) coupling conditions in the presence of 4-(dimethylamino)pyridine (DMAP) [9][20] or with pyridine [12] from their corresponding acid chlorides [21]. Thus α-keto esters **1**–**5** (*cf. Table 1*) were prepared by esterification of commercially available 2-oxopropanoic (pyruvic), 2-oxobutanic, 2-oxopentanoic, and 3-methyl-2-oxopentanoic acid with citronellol (= 3,7-dimethyloct-6-en-1-ol) or geraniol (= (*E*)-3,7-dimethylocta-2,6-dien-1-ol).

For the preparation of other α-keto esters, the reaction of alkyl or aryl *Grignard* reagents with alkyl oxalates [22] was chosen as the most versatile method. Starting from alkyl oxalates, which can be prepared directly from oxalyl chloride, the corresponding keto esters are obtained upon addition of *ca.* 1 equiv. of alkyl or aryl *Grignard* reagent in yields ranging from 40 to 80%. To have a series of compounds releasing the same perfumery chemical from different keto ester substrates, a large quantity of dicitronellyl oxalate (**6**) was prepared and then reacted with a variety of alkyl or aryl *Grignard* reagents, to yield keto esters **7**–**11** as illustrated in *Scheme 2* [22]. In some

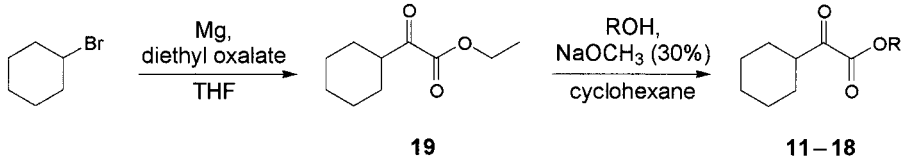
Scheme 2. *Reaction Sequence for the Tailor-Made Synthesis of Citronellyl α-Keto Esters* **7**–**11**

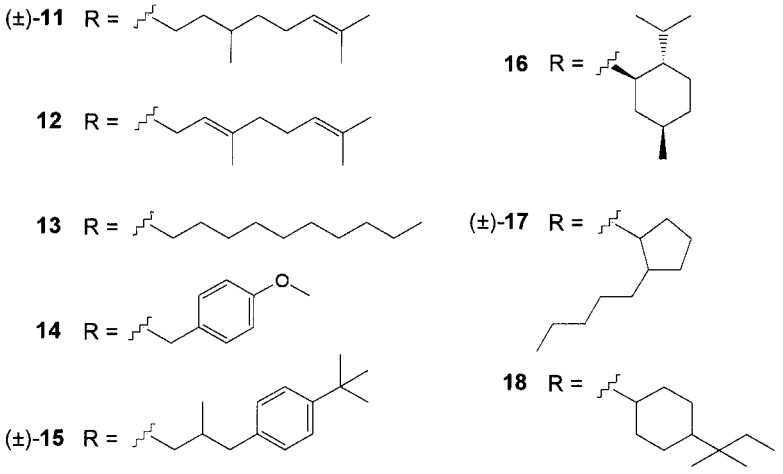


cases, the separation of the α-keto ester from the unreacted dicitronellyl oxalate was found to be difficult, and an additional purification step (MPLC) was required to obtain the pure compounds.

Finally, to compare the release of different aldehydes or ketones from the same α-keto-ester substrate (cyclohexyl)oxoacetates **11**–**18** were prepared from ethyl ester **19** by transesterification in cyclohexane in the presence of small amounts of MeONa (30% in MeOH) as depicted in *Scheme 3*. Citronellyl (cyclopentyl)oxoacetate (**20**) and geranyl oxo(phenyl)acetate (**21**) were prepared in the same way from their corresponding ethyl esters **22** and **23**, of which the latter is commercially available.

Scheme 3. *Synthesis of (Cyclohexyl)oxoacetates* **11**–**18**





2.2. *Photoirradiations of α-Keto Esters in Undegassed Solutions and in the Neat State.* Most of the photoirradiations described in the literature have been carried out with high- or medium-pressure Hg lamps in degassed solutions. In view of the desired application as a delivery system, we investigated the photoirradiation of α-keto esters **1**–**5**, **7**–**18**, **20**, and **21** in undegassed solutions under realistic daylight conditions. Photoirradiations carried out with outdoor sunlight may lack reproducibility, since light intensity varies during the day, reaching a maximum value around noon. The spectral irradiance of Xe arc lamps, which are generally used to simulate sunlight in different technical applications, was found to match the standard solar spectrum [23] with good reproducibility. The photolysis experiments were, therefore, carried out with a Xe lamp

(*Heraeus Suntest CPS* at 460 W m^{-2})[1]) and compared to a UV lamp (*UVP Model UVL-28*, 8 W at 360 nm)[2]), as well as outdoor sunlight irradiations (*Geneva*, autumn 1998 and 1999).

Ca. 0.08M solutions of the different α-keto esters in the indicated solvent were prepared by adding 1 ml of a 0.01M solution of decanol (used as an internal standard for the GC analysis) to 5 ml of a 0.01M solution of the α-keto ester. These solutions were then irradiated during 3 h in 10-ml volumetric *Pyrex* glass flasks. For the irradiations in the neat state, 5 ml of 0.03M solutions of α-keto ester in pentane were transferred to 10-ml volumetric flasks. Pentane was then removed *in vacuo*, and the samples were irradiated under the aforementioned conditions during 3.5 h. After the irradiation, 5 ml of pure MeCN and 1 ml of a 0.03M solution of decanol in MeCN (used as internal standard) were added. In each case, a control experiment was performed in the dark (one of the samples was wrapped in Al foil).

The amount of the perfumery aldehyde or ketone released, as well as the quantity of unreacted starting material, were determined by analytical GC (*Table 1*), and the formation and identification of side products were systematically investigated by GC/MS.

GC/MS Analysis of the irradiated solutions unambiguously proved that all the aforementioned α-keto esters had yielded the desired aldehyde or ketone in moderate to good yields after 3 h of irradiation (*Table 1*). Excellent yields are obtained for the alkyl keto esters, and (cyclohexyl)oxoacetates **11**–**18**, in particular, released the targeted fragrances in up to quantitative amounts.

As a general trend, it was observed that the keto esters derived from secondary alcohols undergo photofragmentation to form ketones in a much higher yield than the corresponding formation of aldehydes from the keto esters of primary alcohols. This is probably due to the higher stability of the intermediate 1,4-diradical (see *Scheme 1*) in the case of secondary alcohols as compared to the primary alcohol derivatives. This difference is particularly apparent in the experiments carried out in the neat state (*Table 1*).

The direct comparison of the different light sources used (Xe lamp, UV lamp, and outdoor sunlight) showed that the results obtained from the irradiations with the Xe lamp are much closer to the real sunlight conditions than those carried out with the UV lamp. This is nicely illustrated by the amount of unreacted starting material and the composition of the product mixture after the irradiations (*Table 1*).

Solvents that are potential hydrogen-radical sources can interfere with the desired *Norrish* type-II fragmentation by H-transfer to the intermediate diradical, resulting in the formation of dimers or photoreduction products [4][6][7]. Comparison of the irradiation results of citronellyl keto esters **3**, **4**, and **7**–**11** in different solvents (*Table 1*) shows the formation of citronellal to be roughly independent of the solvent. Only in the

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[1]) This value corresponds to the total energy between 300 and 800 nm as indicated by the producer. Note that the irradiation energy may vary with the lifetime of the lamp. Indeed, our measurements for the lamp used in our experiments indicated an average irradiation intensity of *ca.* 80000–100000 lux, which corresponds to 115–150 W m^{-2} (1 lux = 0.00147 W m^{-2} at 555 nm). In our case, these values were found to be comparable to outdoor sunlight irradiation (60000–100000 lux).

[2]) The lamp irradiates at 360 nm, which is the wavelength needed for the desired photooxidations. An average light intensity of 2700 lux = 4 W m^{-2} was measured.

Table 1. *Results of the Photoirradiations of Different α-Keto Esters in Solution and in Their Neat State* (all numbers are average values of 2 or 3 samples)

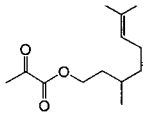
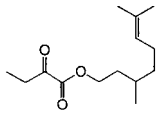
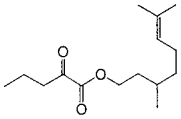
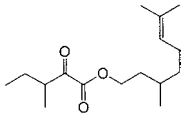
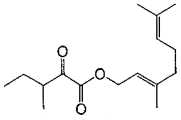
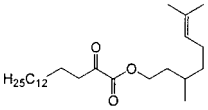
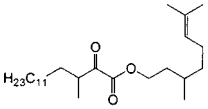
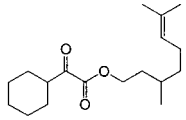
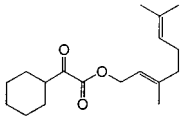
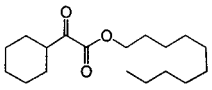
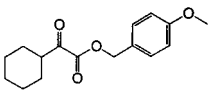
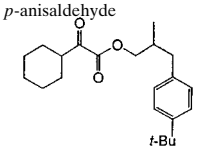
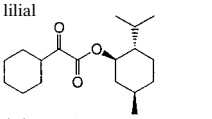
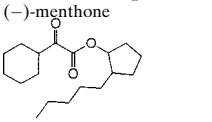
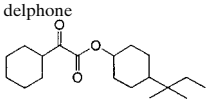
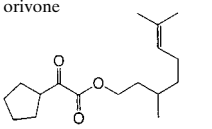
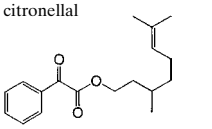
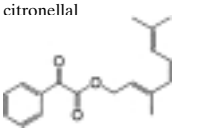
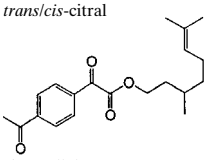
Structure of irradiated substrate and name(s) of released compound(s)	No.	Light source	Yield of released compound (remaining starting material)[a]) [mol-%]							
			Toluene 3 h	Cumene 3 h	EtOH 3 h	i-PrOH 3 h	Acetone 3 h	AcOEt 3 h	MeCN 3 h	Neat 3.5 h
 Citronellal	**1**	Xe	30 (5)			5 (65)			29 (15)	
		UV sunlight	44 (< 5)			4 (45)[c])			30 (45)	
 Citronellal	**2**	Xe	33 (5)			11 (40)			27 (5)	
		UV sunlight	50 (5)			10 (35)[c])			29 (15)	
 Citronellal	**3**	Xe	38 (5)[b])		17 (−)[c])	9 (25)[c])			31 (10)[b])	1 (45)
		UV	13 (75)	10 (55)	2 (−)[c])	9 (45)	7 (60)	11 (85)	7 (95)	
		sunlight	21 (5)			13 (20)			21 (5)	0 (55)
 Citronellal	**4**	Xe	55 (< 5)[b])		45 (−)[c])	30 (15)[c])			36 (< 5)[b])	5 (40)
		UV	19 (60)	18 (50)	7 (90)	5 (85)	16 (65)	17 (55)	14 (65)	
		sunlight	23 (< 5)			30 (20)			15 (5)	< 1 (55)
 *trans*/*cis*-Citral	**5**	Xe	15/26 (< 5)			6/26 (20)			7/12 (20)	0 (35)
		UV sunlight	17/21 (20)			6/35 (20)			7/11 (35)	
 citronellal/tridecene	**7**	Xe	5/38 (35)[b])		2/n.d. (−)[c])	2/24 (45)[c])			3/32 (40)	1/10 (35)
		UV	0/5 (85)	0/4 (100)	0/3 (−)[c])	0/5 (70)		0/5 (90)	0/5 (95)	
		sunlight	7/42 (35)			3/21 (55)			0/37 (25)	0/6 (75)
 citronellal/dodecene	**8**	Xe	11/n.d. (30)[b])		6/n.d. (−)[c])					2/11 (30)
		UV sunlight	2/6 (85)	2/5 (70)	0/2 (−)[c])	0/3 (−)[c])	0/5 (80)	2/5 (85)	1/6 (80)	
 citronellal	**11**	Xe	≈45 (< 5)[b])		43 (−)[c])	22 (20)			16 (< 5)	3 (35)
		UV	25 (65)	24 (70)	7 (−)[c])	9 (90)	21 (65)	12 (60)	13 (70)	
		sunlight	38 (< 5)			35 (15)			18 (< 5)	< 1 (45)[b])
 *trans*/*cis*-citral	**12**	Xe	26/43 (< 5)			10/33 (30)			11/19 (20)	< 1/0 (50)
		UV sunlight	19/25 (5)			10/48 (30)			11/17 (30)	

Table 1 (cont.)

Structure of irradiated substrate and name(s) of released compound(s)	No.	Light source	Yield of released compound (remaining starting material)[a]) [mol-%]							
			Toluene 3 h	Cumene 3 h	EtOH 3 h	i-PrOH 3 h	Acetone 3 h	AcOEt 3 h	MeCN 3 h	Neat 3.5 h
 decanal		Xe	52 (0)			28 (5)			27 (< 5)	5 (45)
		UV								
	13	sunlight	52 (5)			26 (5)			25 (5)	4 (55)
 *p*-anisaldehyde		Xe	81 (5)			20 (25)[c])			66 (30)	
		UV								
	14	sunlight	86 (5)							
 lilial		Xe	69 (< 5)			49 (15)			52 (< 5)	
		UV								
	15	sunlight	63 (5)			47 (15)			53 (5)	
 (−)-menthone		Xe	quant. (< 5)			53 (10)			91 (< 5)	75 (40)
		UV								
	16	sunlight	quant. (10)			44 (10)			86 (5)	21 (50)
 delphone		Xe	76 (< 5)			53 (15)			75 (< 5)	
		UV								
	17	sunlight				51 (10)			73 (10)	
 orivone		Xe	93 (< 5)			65 (20)			88 (10)	
		UV								
	18	sunlight	93 (5)			57 (15)			83 (5)	
 citronellal		Xe	24 (< 5)			17 (15)			20 (5)	
		UV								
	20	sunlight	37 (5)						22 (15)	
 citronellal		Xe	11 (< 5)		17 (−)[c])				16 (15)[b])	< 1 (< 5)
		UV	13 (65)	12 (65)	5 (85)	4 (50)	13 (50)	11 (55)	7 (80)	
	9	sunlight	27 (< 5)			6 (30)			15 (20)	0 (< 5)
 *trans*/*cis*-citral		Xe	10/10 (5)			3/3 (25)			6/7 (5)	
		UV								
	21	sunlight	10/9 (< 5)			2/2 (25)			8/9 (5)	
 citronellal		Xe	9 (20)[b])		3 (−)[c])					< 1 (< 5)
		UV	4 (55)			0 (35)		4 (40)	2 (45)	
	10	sunlight								

[a]) Amount of remaining starting material rounded to ±5%. [b]) Amount of starting material estimated from blank sample. [c]) Yield not or only approximatively determined due to transesterification.

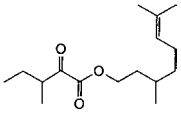
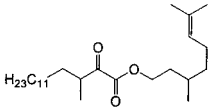
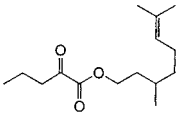
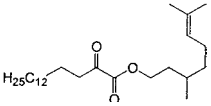
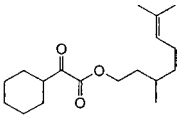
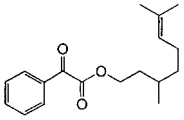
photolyses carried out in EtOH or i-PrOH was less of the desired aldehyde obtained [6]. It is interesting to note that the irradiations carried out in cumene or i-PrOH, which can form more stable (tertiary) radicals than their corresponding homologs, toluene or EtOH, and thus may serve more easily as external hydrogen-radical sources to compete with the intramolecular H-abstraction process, do not significantly reduce the formation of citronellal (*Table 1*). In the photolysis of **11**, the formation of photoreduction products, such as citronellyl (cyclohexyl)hydroxyacetate, which is probably due to H abstraction from the solvent [4], was observed only when using EtOH or i-PrOH rather than cumene or toluene.

2.3. *Investigation of Side Products Formed upon Photoirradiation*. Systematic GC/MS analysis of the product mixtures obtained after irradiation of the α-keto-esters with either one of the three light sources in different solvents revealed the formation of the same side products under certain conditions. Comparison of the mass spectra of the products from irradiation of (cyclohexyl)oxoacetates **11**–**18** in either toluene or MeCN showed that small amounts of cyclohexyl carboxylic acid were formed in most cases. In the series of citronellyl α-keto esters **1**–**5**, **7**–**11** and **20**, which was investigated in more detail, the formation of the same side products was observed under certain conditions. For example, in some of the photolyses performed in EtOH or i-PrOH, the formation of small quantities of citronellol indicates that partial transesterification takes place in these solvents. This was confirmed by the detection of ethyl ester **19** as one of the side products resulting from the irradiation of **11** in EtOH (Xe lamp) or by the formation of ethyl 2-oxohexadecanoate (**24**) from **7** under the same conditions.

Table 2 lists a series of compounds that have been identified as side products by irradiation of different citronellyl α-keto esters under various conditions. Compounds **1** and **2**, for example, were each formed from only two of the substrates (**1** from **3**, and **7** and **2** from **4** and **8**), and their formation was solvent independent. Due to the similarity of the alkyl chains of the respective substrates and the fact that tridecene and dodecene were formed upon photolysis of **7** and **8**, respectively, the formation of **1** and **2** can be rationalized by alkyl-chain fragmentation and tautomerization of the intermediate enolates (*Scheme 4*) [13]. This was confirmed by comparison of the mass spectra and GC retention times. It is interesting to note that alkyl-chain fragmentation as a side reaction should not theoretically reduce the yield of citronellal formed, since the remaining compounds (esters **1** and **2**) can still release the desired aldehyde by ester-side-chain fragmentation in a second reaction step (see *Table 1*).

Comparison of the yield of citronellal released from different α-keto ester substrates shows that the highest amount of aldehyde was obtained from those compounds in which γ-H abstraction from the alkyl chain is either impossible (**1**, **2**, or **9**) or sterically unfavorable (**11** and **20**) (*Table 1*). In cases where γ-H abstractions from both the alkyl and the ester side chain are possible (**3**, **4**, **7**, and **8**), the yield of citronellal liberated upon ester-chain fragmentation decreases dramatically with increasing chain length. The higher stability of a secondary radical formed by γ-H abstraction from the long alkyl side chains of **7** and **8**, as compared to a primary radical formed from **3** and **4**, together with the lower C–H bond energy of a CH_2 as opposed to a CH_3 group facilitates γ-H abstraction from the longer alkyl chains. If secondary radicals can be formed from both the ester and the alkyl side-chain fragmentation (as this is the case for **7** and **8**), the difference in relative energies of the intermediate 1,4-

Table 2. *Side Products Formed upon Photolysis of Different Citronellyl α-Keto Esters under Different Irradiation Conditions* (GC/MS Analysis)

Irradiated compound	No.	Solvent	Side product formed		
			Xe	UV	Sunlight
	**4**	toluene	**2**, **25**, **26**	**26**	**25**, **26**
		cumene		**26**	
		MeCN		**25**, **26**	**25**, **26**
		i-PrOH	**2**		**2**
		acetone		**2**, **25**, **26**	
		AcOEt		**2**, **25**, **26**	
		neat	**26**		
	**8**	toluene	**2**	**2**	
		i-PrOH		**2**	
		EtOH	**2**		
	**3**	toluene			**25**
		MeCN	**1**, **25**		**1**, **25**
		i-PrOH	**1**		
	**7**	toluene	**1**		**1**
		MeCN	**1**		**1**
		i-PrOH	**1**		**1**
		EtOH	**1**		
		neat	**1**		
	**11**	toluene	**25**, **27**	**25**, **27**	**25**
		MeCN	**25**, **27**	**27**	**25**, **27**
		acetone		**27**	
		neat	**27**		
	**9**	toluene	**25**, **29**	**29**	**25**, **29**
		cumene		**29**	
		MeCN	**25**, **29**	**29**	**25**, **29**
		i-PrOH		**29**	**29**
		EtOH	**29**		
		acetone		**29**	
		AcOEt		**29**	

diradicals may indicate the preference for one or the other pathway. Comparison of the relative energies obtained by density-functional calculations [24] of the diradicals (in their triplet state) [25], resulting from γ-H-abstraction from ethyl 2-oxohexanoate showed that the diradical resulting from alkyl-chain fragmentation is only 0.9 kcal/mol lower in energy than the one formed by ester-chain fragmentation (*Fig. 2*).

Besides the stability of the intermediately formed diradical, other parameters, such as the energy of the optimal conformation for the H abstraction, need to be considered, since they may contribute considerably to the formation of the transition state of the photoreaction. To further rationalize the preference for alkyl-chain fragmentation, *ab initio Hartree-Fock* and density-functional calculations [24] were carried out for different conformations of the ester and alkyl side chains of α-keto esters before H abstraction. *Ihmels* and *Scheffer* recently investigated the geometric requirements for γ-H abstraction in *Norrish* type-II fragmentations by analyzing data derived from X-

Scheme 4. *Alkyl-Chain Fragmentation of Citronellyl α-Keto Esters* **3**, **4**, **7**, *and* **8**

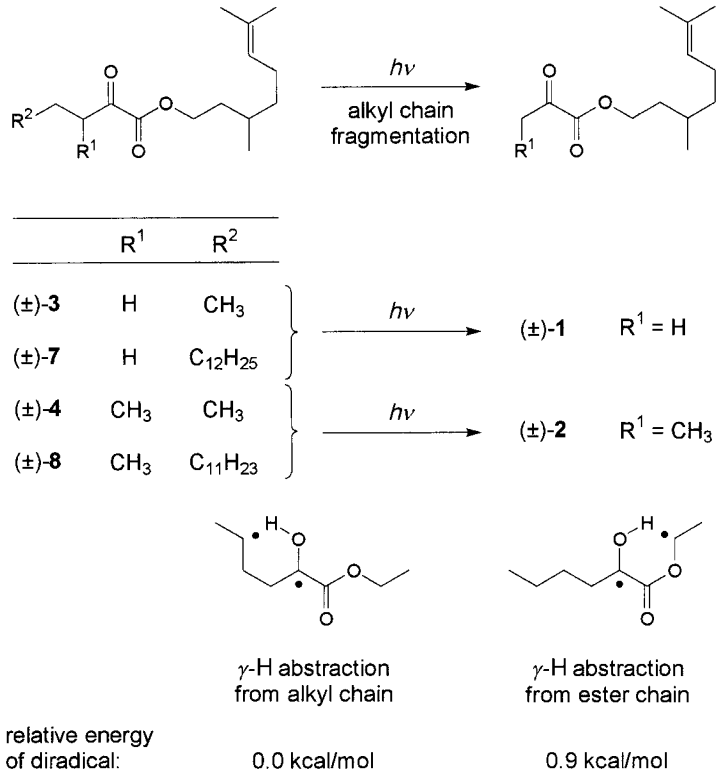


Fig. 2. *Schematic representation and calculated relative energies* (pBP/DN**) *of the triplet 1,4-diradicals resulting from γ-H abstraction of the alkyl or ester chain of ethyl 2-oxohexanoate*

ray crystallography [26]. They found that abstraction occurs preferentially when the C=O ··· H distance is close to the sum of the *van der Waals* radii (2.72 Å), and when the H-atom can deviate 50–60° from the plane that contains the n orbital of the O-atom involved in the abstraction process.

Our calculations, which are summarized in *Fig. 3* and *Table 3*, are in good agreement with the values reported by *Ihmels* and *Scheffer* for an optimal γ-H abstraction and reflect the preference for H abstraction from the alkyl rather than the ester side chain. The lowest-energy conformation required for fragmentation of the ester chain (conformer B in *Fig. 3*) was found to be 7–8 kcal/mol less stable than conformer A, which leads to the undesired fragmentation (*Table 3*). A lower energy difference of 4.37 kcal/mol was also previously determined by *Hu* and *Neckers* with semi-empirical AM1 calculations [27].

The energy difference calculated for the four most stable conformations of the alkyl side chain (conformers C–F and C′–F′ in *Fig. 3*, bottom) is less pronounced, slightly favoring an orientation where γ-H abstraction from the alkyl side chain is facile (conformers D and D′, *Fig. 3*). Introducing a Me group into an α-position of the

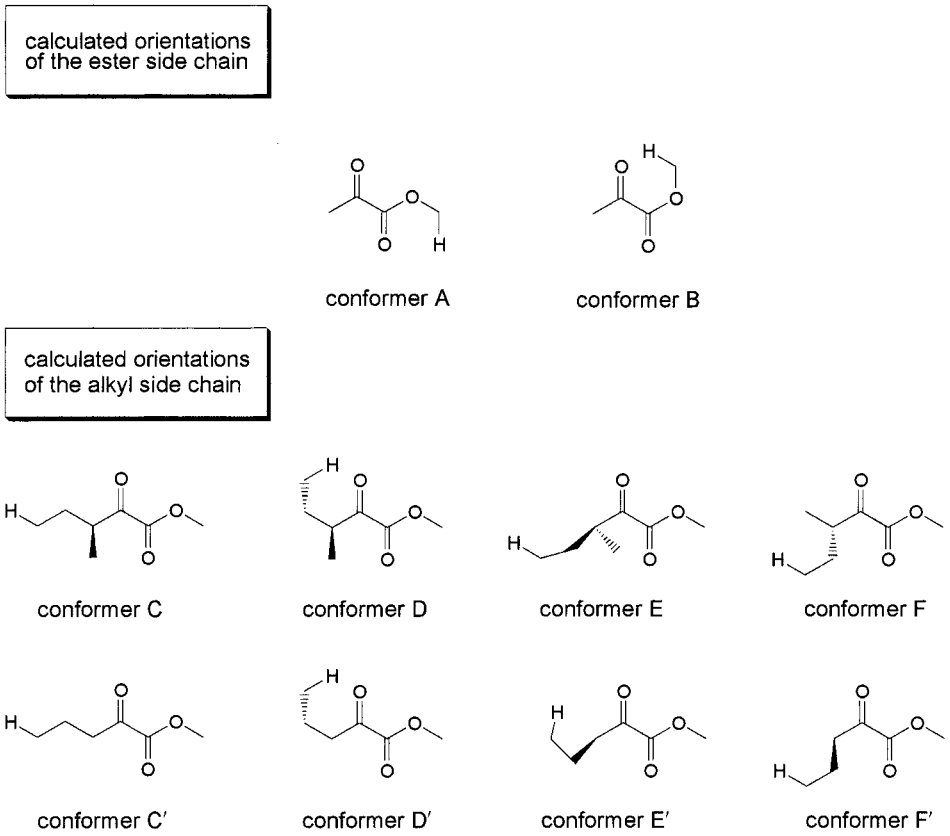


Fig. 3. *Schematic representation of the calculated most stable conformations of the ester* (top) *and alkyl* (bottom) *side chains in α-keto esters*

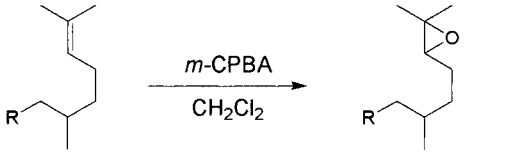
Table 3. Ab initio *Calculated Relative* Hartree-Fock *and Density-Functional Energies for the Conformers Shown in* Fig. 3. ω represents the deviation of the abstractable γ-H from the plane containing the oxygen n orbital. The main conformers C, D, E, F, and C′, D′, E′, and F′ were obtained by the *Monte Carlo* procedure with the MM2 molecular force field as implemented in *MacroModel* [39]

	Relative energies		O···H Distance	ω
	HF/6-31G* [kcal/mol]	pBP/DN** [kcal/mol]	pBP/DN** [Å]	pBP/DN** [°]
Conformer A	0.0	0.0	4.48	
Conformer B	7.9	7.4	2.53	
Conformer C	0.6	1.0	4.77	
Conformer D	0.0	0.0	2.75	54.3
Conformer E		1.5	3.21	
Conformer F		0.1	4.99	
Conformer C′		0.0	4.84	
Conformer D′		0.5	2.71	40.0
Conformer E′		0.8	3.13	
Conformer F′		1.1	4.83	

photoactive C=O function does not significantly influence the difference in energy of the preferentially adopted conformations, although the experimental findings listed in *Table 1* suggest an increase of steric hindrance of the alkyl side chain.

Among the series of compounds that have been obtained under different conditions (*Table 2*), only **25**, which was assigned as (±)-6,7-epoxy-3,7-dimethyloctanal, was formed independently of the starting material *and* the solvent used. It is thus derived from either the citronellyl ester side chain or the citronellal resulting from the photolysis, and not dependent on the keto-acid part of the precursor molecule. An independent synthesis of **25** by epoxidation of citronellal with *m*-chloroperbenzoic acid (*m*-CPBA) in CH_2Cl_2 (*Scheme 5*) [28] confirmed this structural assignment. Studies of the epoxidation of alkenes in the presence of α-diketones [29] or α-keto esters and acids [17] have previously been reported.

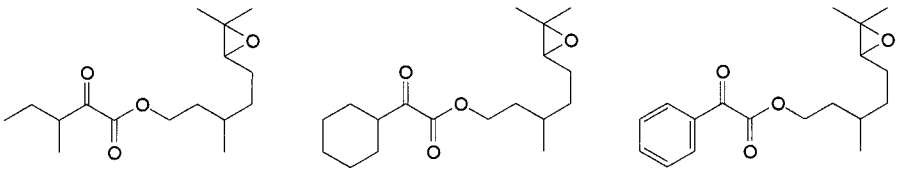
Scheme 5. *Epoxidation of Citronellol* (R = CH_2OH) *and Citronellal* (R = CHO) *with* m-*CPBA*



(±)-**35** R = CH_2OH

(±)-**25** R = CHO

Compound **26** (*Table 2*), was only obtained from substrate **4**, independent of the solvent. Because its structure could not be unambiguously assigned from its mass spectrum, **26** was isolated by preparative GC on a *OV-101* stationary phase in order to have sufficient quantities to record its ^{1}H- and ^{13}C-NMR spectra. The structural assignment (*Fig. 4*) was then confirmed by epoxidation of citronellol with *m*-CPBA (*Scheme 5*) [30], followed by transesterification with ethyl 3-methyl-2-oxopentanoate. By analogy, **27** and **28** (*Fig. 4*) were synthesized by transesterification of their ethyl esters and fully characterized. Whereas **27** was generated in the photoirradiations of **11** (*Table 2*), only traces of **28** were found upon photolysis of **9** in ethyl acetate (UV lamp), although the presence of **25** in many other cases may suggest the formation of **28** as intermediate generated in the photoreaction.



(±)-**26** (±)-**27** (±)-**28**

Fig. 4. *Structures of α-keto ester derivatives* **26**–**28** *identified as possible side products formed upon photoirradiation of citronellyl α-keto esters in the presence of* O_2

To elucidate its structure, small quantities of compound **29** were isolated as a diastereoisomeric mixture by preparative GC from a solution of **9** in MeCN, which was irradiated for 3 h with a Xe lamp. The ^{1}H- and ^{13}C-NMR spectra of the major isomer were found to be identical to those described by *Hu* and *Neckers* for an oxetane resulting from the intramolecular *Paternò-Büchi* reaction of **9** [27]. Two possible structures, namely **29a**–**d** and **30a**–**d** (*Fig. 5*) can theoretically be expected, depending on the orientation of the alkene C=C bond towards the C=O function. The ^{13}C-NMR spectrum is in agreement only with structure **29**, since the observation of two *singlets* at *ca*. 83 ppm suggests that these two C-atoms should be directly connected to an O-atom, whereas the *doublet* recorded at 53 ppm indicates a C-atom that is further removed from the same O-atom. Our structural assignment is in agreement with the compound reported by *Hu* and *Neckers* [31].

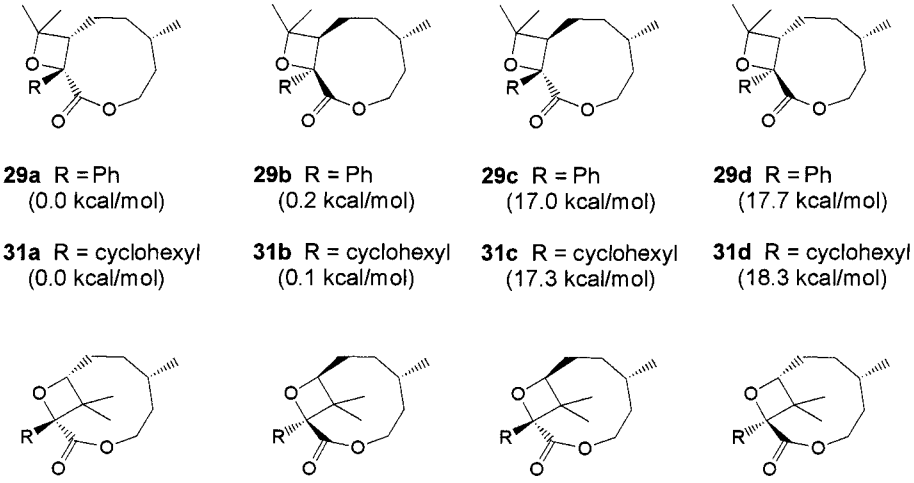


Fig. 5. *Structures and relative energies* (MM2, in kcal/mol) *of oxetane derivatives* **29**–**32**, *resulting from different orientations of the alkene C=C bond towards the C=O function in the intramolecular* Paternò-Büchi *reaction of* **9** *or* **11**

To rationalize the formation of the *Paternò-Büchi* adduct **29** rather than its regioisomer **30**, all four possible configurations of the two isomers were minimized based on MM2 calculations [32] (see *Exper. Part*). The most stable structures ((*S*,*S*)-**29a**, (*R*,*R*)-**29b**, (*S*,*R*)-**30a**, and (*R*,*S*)-**30b**) are *cis*-configured with respect to the oxetane ring (*Fig. 5*). Calculations for **29a** and **30a** were then further optimized by semi-empirical PM3 [33] and density-functional methods. Oxetane **29a** was found to be by 5.0 (MM2), 7.2 (PM3), or 7.6 kcal/mol (pBP/DN**) more stable than **30a**. Similar results were obtained for the cyclohexyl analogs **31** and **32** (*Fig. 5*), where **31a** is by 4.5 (MM2), 7.2 (PM3), or 9.8 kcal/mol (pBP/DN**) lower in energy than its regioisomer

32a. This difference in energy is probably due to the relatively large ring strain in **30a** and **32a**.

The oxetane formation proceeds *via* attack of the electrophilic O-atom of the excited C=O group in its $^3(n \rightarrow \pi^*)$ triplet state to the alkene to form a triplet 1,4-diradical that undergoes intersystem crossing to the singlet 1,4-diradical before closure to the oxetane [34]. Based on the orientation of the alkene towards the C=O group in the intramolecular *Paternò-Büchi* reaction of **9**, two different regioisomeric 1,4-diradicals can be formed to give rise to isomers **29** and **30**, respectively (*Fig. 6*). Since, at first sight, intermediate A, yielding the less stable isomer **30**, should be more stable than B, giving rise to **29**, ring strain may play an important role in the formation of the observed product by compensating for the relative stability of the radicals. We, therefore, decided to investigate the relative energies of the diradicals by density-functional calculations, which were carried out on the previously optimized structures of **29a** and **30a** by cutting the corresponding C–C bond and calculating the energies of the resulting diradicals in their singlet and triplet states at C–C distances varying between 2.2 and 3.0 Å. The singlet as well as the triplet states of intermediate B (*Fig. 6*) were found to be lower in energy than intermediate A at all calculated distances, in agreement with the experimental results.

A summary of the different photochemical reactions of citronellyl alkyl or aryl α-keto esters such as **4**, **9**, and **11** in undegassed solutions is presented in *Scheme 6*. The

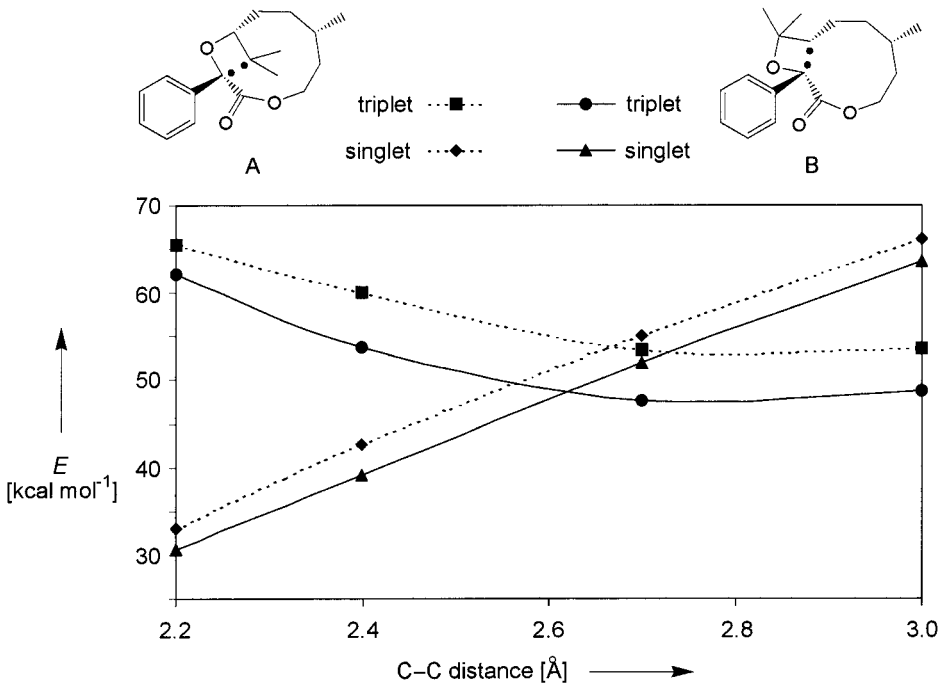
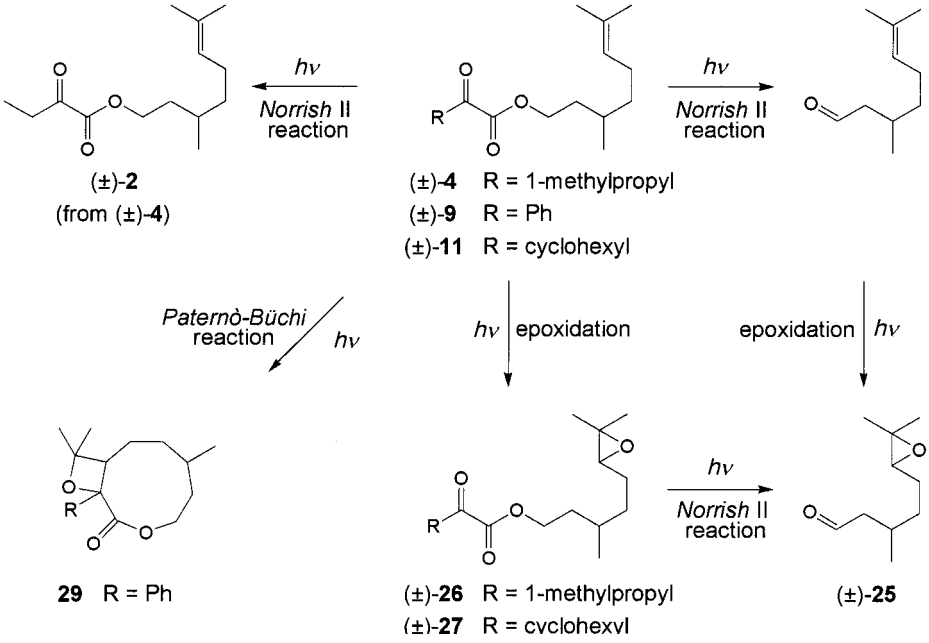


Fig. 6. *Relative singlet- and triplet-state energies obtained by density-functional calculations of diradicals A and B yielding oxetanes* **30a** *and* **29a**, *respectively.* The relative energies were calculated with respect to the most stable structure **29a**

Scheme 6. *Photochemical Reaction Pathways of Alkyl and Aryl α-Keto Esters of Citronellol in Undegassed Solutions*



main reaction is the desired *Norrish* type-II fragmentation from the ester side chain. Only when γ-H-abstractions from the alkyl side chain is preferred, as in the case of **7** or **8**, is the formation of terminal alkenes the predominant reaction.

It is interesting to note that, in the case of aryl keto ester **9**, the intramolecular *Paternò-Büchi* reaction is preferred to epoxidation of the alkene function, whereas, in the case of alkyl keto esters **4** and **11**, the formation of epoxides rather than oxetanes is observed, although the formation of traces of the latter can not be completely ruled out. Since the structures of oxetanes **29a** and **31a** are of similar energy, the preference for *Paternò-Büchi* cyclization of Ph derivative **9** is most probably due to electronic rather than steric factors. Note that all reaction pathways displayed in *Scheme 6* involve the $^3(n \rightarrow \pi^*)$ triplet state of the α-keto group as intermediate, the energy of which thus determines the observed product distribution.

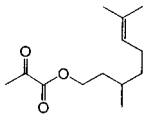
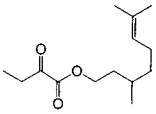
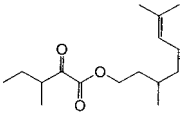
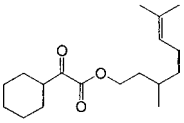
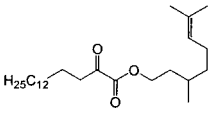
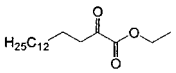
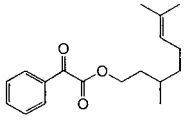
To compare the relative importance of the different reaction pathways, the amounts of the reaction products obtained by photolysis of keto esters **1**, **2**, **4**, **7**, **9**, and **11**, as well as **24** as control substrate were investigated at different concentrations in toluene.

2.4. *Quantitative Analysis of Reaction Product Distribution at Different Concentrations.* To quantify the product distribution of the reactions depicted in *Scheme 6*, concentration-dependent photoirradiations were carried out for some model compounds. Undegassed 0.005, 0.01, 0.025, 0.05, and 0.1M solutions of **1**, **2**, **4**, **7**, **9**, **11**, and **24** were individually irradiated in toluene for 3 h with a Xe lamp at an average light intensity of 108500 lux. Decanol, which was added before the irradiations at a concentration of 20 mol-%, was used as an internal standard for the GC analyses. The

formation of the calibrated compounds was verified by GC/MS analysis of the irradiated 0.1M solutions.

As discussed above, besides the *Norrish* type-II fragmentation of the ester or alkyl side chain, the formation of citronellal epoxide **25** is the major side reaction. The amounts of the different products identified range between 3 and 25% for the epoxide, 35 and 38% for the tridecene obtained from alkyl chain fragmentation, and 10 and 70% for citronellal formed by ester-chain fragmentation (*Scheme 6* and *Table 4*). It was found that the formation of citronellal, which is the desired reaction for the targeted applications, decreases with increasing concentration, whereas the formation of epoxide **25** and the amount of remaining starting material increase. Since, ideally, very low concentrations of the precursor molecules would be used in

Table 4. *Concentration-Dependent Quantitative Analysis of Reaction Products Formed upon Photolysis of Different α-Keto Esters in Undegassed Toluene*

Compound irradiated		Compounds formed	Yield from 0.005M solution [mol-%]	Yield from 0.01M solution [mol-%]
	**1**	citronellal	56	46
		25	3	6
		remaining **1**	20	16
	**2**	citronellal	70	53
		25	8	15
		remaining **2**	16	9
	**4**	citronellal	67	54
		25	11	18
		26	1	2
		2	< 1	1
		remaining **4**	3	3
	**11**	citronellal	56	46
		25	16	19
		27	1	1
		remaining **11**	2	3
	**7**	citronellal	19	16
		25	0	1
		tridecene	36	35
		1	26	27
		remaining **7**	22	26
	**24**	tridecene	38	33
		remaining **24**	29	37
	**9**	citronellal	31[a])	10[a])
		25	26[a])	21[a])
		28	0[a])	0[a])
		remaining **9**	2[a])	5[a])

[a]) Results based on external standard calibrations.

the targeted applications, the use of α-keto esters in controlled-release systems is advantageous.

The amount of decanol, which was used as an internal standard for the GC analysis, was found to decrease during irradiation at high keto ester concentrations when compared to non-irradiated standard solutions. Although the comparison of internal and external standard calibrations showed no significant difference in the case of the 0.005 and 0.01M solutions, a significant decrease of decanol, was observed in the photolyses carried out at concentrations between 0.025 and 0.1M. This suggests that the alcohol may participate in the reaction pathway during the photoreaction (for example as an external H$^{\bullet}$-radical donor). Interestingly, irradiations carried out in EtOH or i-PrOH as solvents did not quench the desired photoreaction (*Table 1*).

As it was mentioned before, epoxide **28** was not formed upon photoirradiation of phenyl keto ester **9**. The formation of aldehyde **25** may then be explained by partial epoxidation of preliminarily released citronellal. In the photolysis of the alkyl keto esters **4** and **11**, where no *Paternò-Büchi* reaction has been observed, very small amounts of epoxides **26** and **27**, respectively, were detected.

3. Conclusions. – α-Keto esters have been found to be very efficient delivery systems for the controlled release of perfumery aldehydes and ketones. Photooxidation with outdoor sunlight or Xe lamps in the presence of O_2 released the desired aldehydes and ketones in moderate-to-good yields after only 3 h of irradiation. High yields for the desired fragmentation reaction were observed, especially at the low concentrations necessary for the targeted use in bodycare or household applications, such as shampoos, all purpose cleaners, fabric softeners, or powdered detergents.

Norrish type-II fragmentation is the major reaction pathway in all of the cases studied in this work. If γ-H abstraction from the alkyl side chain is possible, the formation of a terminal alkene and, after tautomerization, a new α-keto ester with a shorter alkyl chain are preferred to the ester-chain fragmentation, which liberates the desired aldehyde or ketone. The relative energy of the intermediate 1,4-diradical, resulting from alkyl-chain fragmentation, was calculated to be by 0.9 kcal/mol more stable than that resulting from ester-chain fragmentation. Furthermore, *ab initio Hartree-Fock* and density-functional calculations have shown that the favorable conformation for ester-chain H abstraction is by 7–8 kcal/mol less stable than the unfavorable ground-state conformation. The energetically favored alkyl-chain fragmentation, however, can be easily avoided by the choice of keto-ester substrates such as (cyclohexyl)oxoacetates **11**–**18** or oxo(phenyl)acetates **9** and **21**. Due to the higher stability of the intermediate diradicals, α-keto esters derived from a secondary alcohol generally undergo photofragmentation with much higher yields than the keto esters of primary alcohols.

For several citronellyl α-keto esters, epoxidation of the alkene function and the intramolecular *Paternò-Büchi* reaction were identified as the most important side reactions. Whereas, in the photolysis of aryl keto ester **9**, the intramolecular oxetane formation is preferred to epoxidation of the citronellyl moiety, the inverse was found in the case of alkyl keto esters **4** and **11**. Based on NMR analysis together with computer simulations, the structure of *Paternò-Büchi* adduct was established as **29**.

In conclusion, the results obtained in this study have been the basis of bodycare and household applications in functional perfumery, where α-keto esters have been found to successfully release perfumery aldehydes and ketones upon exposure to daylight [1][35].

Experimental Part

General. Commercially available reagents and solvents were used without further purification if not stated otherwise. Reactions were carried out in standard glassware under N_2, and yields are not optimized. Column chromatography: silica gel *60* Å (35–70 μ from *SDS*). Anal. GC: *Carlo Erba MFC 500* chromatograph equipped with a *Fisons AS 800* autosampler and a *J & W Scientific DB1* capillary column (15 m, 0.32 mm i.d.) at 70 or 80° for 10 min, then to 260° (10°C/min), He pressure 50 kPa, injection volume 0.5 μl, injection temp. 250°, detector temp. 280°. Prep. GC: *Varian Star 3600 CX* instrument combined wtih a *Hewlett Packard HP 3395 Integrator* or on a *HP 6890 GC System* coupled with a *Joint Analytical Systems (JAS)* fraction collector and a *HP 6890 Series Injector*. MPLC: *Ismatec Instruments* medium-pressure pump and a *LKB Bromma 2111 Multirac* fraction collector. Light intensities were measured with a *Lutron LX-107* light meter. UV/VIS Spectra: *Perkin Elmer Lambda 14* spectrometer, λ in nm (ε). IR Spectra: *Perkin Elmer 1600 FTIR* spectrometer, $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Bruker AMX-360* spectrometer, δ in ppm downfield from Me_4Si as standard, J in Hz. GC/MS: *HP 5890* or *6890 GC System* equipped with a *Supelco SPB-1* cap. column (30 m, 0.25 mm i.d.) at 70° for 10 min, then to 260° (10°C/min), He flow *ca*. 1 ml/min, coupled with a *HP MSD 5972* or *5973* quadrupole mass spectrometer, electron energy *ca*. 70 eV, fragment ions *m/z* (rel. int. in % of the base peak).

Computational Methods. The geometries of the different structures were identified by the *Monte Carlo* procedure with the MM2 molecular force field [32] as implemented in *MacroModel* V6.0 [36]. Only the lowest-energy conformers/isomers were considered for further calculations and discussions. The geometries of these conformers/isomers were then fully optimized by standard *ab initio* and density-functional methods (pBP/DN**, comparable to the highest conventional *ab initio* models (MP2)) in the *SPARTAN V5.0* program (*Wavefunction, Inc.*, Irvine, CA, 1997). All calculations were carried out on a *Silicon Graphics SGI R10000* computer.

(±)-3,7-Dimethyloct-6-enyl 2-Oxopropanoate ((±)-**1**). *Method A* [19]. A stirred soln. of 5.56 g (63 mmol) of 2-oxopropionic acid and 19.68 g (126 mmol) of citronellol (= 3,7-dimethyloct-6-en-1-ol) in 150 ml of toluene was heated for 35 h under reflux with azeotropic removal of H_2O. After cooling to r.t., the mixture was extracted with Et_2O (2×), 10% $NaHCO_3$, sat. NaCl, dried (Na_2SO_4) and concentrated *in vacuo*. CC (SiO_2; pentane/Et_2O 9:1): 2.81 g (20%) of (±)-**1**. Colorless oil. UV/VIS (hexane): 388 (sh, 3), 378 (sh, 5), 369 (sh, 8), 360 (sh, 10), 345 (14), 334 (14), 319 (sh, 12), 284 (sh, 9). IR (neat): 2961*m*, 2915*m*, 2873*m*, 2856*m*, 1728*s*, 1454*m*, 1378*m*, 1357*m*, 1297*m*, 1266*m*, 1203*w*, 1134*s*, 1051*m*, 1024*w*, 982*m*, 937*m*, 830*m*, 771*w*, 720*m*, 663*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.15–5.03 (*m*, 1 H); 4.37–4.18 (*m*, 2 H); 2.47 (*s*, 3 H); 2.10–1.88 (*m*, 2 H); 1.87–1.71 (*m*, 1 H); 1.71–1.47 (*m*, 2 H); 1.68 (*s*, 3 H); 1.60 (*s*, 3 H); 1.46–1.28 (*m*, 1 H); 1.28–1.12 (*m*, 1 H); 0.94 (*d*, J = 6.3, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 191.96 (*s*); 160.92 (*s*); 131.52 (*s*); 124.37 (*d*); 65.06 (*t*); 36.89 (*t*); 35.14 (*t*); 29.39 (*d*); 26.73 (*q*); 25.71 (*q*); 25.33 (*t*); 19.36 (*q*); 17.66 (*q*). EI-MS: 226 (3, M^+), 208 (5), 183 (9), 155 (14), 138 (15), 137 (20), 124 (3), 123 (29), 121 (3), 110 (5), 109 (20), 96 (8), 95 (45), 83 (15), 82 (28), 81 (51), 70 (10), 69 (100), 68 (14), 67 (23), 57 (5), 56 (8), 55 (34), 53 (7), 43 (41), 42 (5), 41 (40), 39 (6), 29 (4), 27 (3).

(±)-3,7-Dimethyloct-6-enyl 2-Oxobutanoate ((±)-**2**). As described above (*Method A*) with 6.43 g (63 mmol) of 2-oxobutyric acid, 19.68 g (126 mmol) of citronellol, and 150 ml of toluene for 24 h. CC (SiO_2; pentane/Et_2O 9:1): 7.80 g (52%) of (±)-**2**. Colorless oil. UV/VIS (hexane): 397 (sh, 1), 383 (sh, 3), 373 (sh, 6), 356 (sh, 12), 341 (16), 330 (16), 318 (sh, 14), 268 (sh, 12). IR (neat): 2961*m*, 2914*m*, 2879*m*, 2857*m*, 1725*s*, 1456*m*, 1404*w*, 1379*m*, 1351*w*, 1273*m*, 1242*m*, 1173*w*, 1144*m*, 1097*s*, 1041*m*, 982*m*, 946*w*, 881*w*, 830*m*, 760*w*, 737*w*, 700*m*, 678*m*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.14–5.02 (*m*, 1 H); 4.40–4.20 (*m*, 2 H); 2.86 (*q*, J = 7.3, 2 H); 2.09–1.88 (*m*, 2 H); 1.87–1.68 (*m*, 1 H); 1.68 (*s*, 3 H); 1.68–1.45 (*m*, 2 H); 1.60 (*s*, 3 H); 1.45–1.29 (*m*, 1 H); 1.29–1.15 (*m*, 1 H); 1.13 (*t*, J = 7.1, 3 H); 0.94 (*d*, J = 6.3, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 195.09 (*s*); 161.32 (*s*); 131.51 (*s*); 124.40 (*d*); 64.87 (*t*); 36.90 (*t*); 35.17 (*t*); 32.89 (*t*); 29.40 (*d*); 25.71 (*q*); 25.34 (*t*); 19.37 (*q*); 17.66 (*q*); 6.97 (*q*). EI-MS: 240 (1, M^+), 222 (3), 183 (8), 155 (12), 139 (3), 138 (20), 137 (15), 124 (3), 123 (31), 121 (3), 110 (4), 109 (16), 97 (3), 96 (9), 95 (43), 94 (3), 83 (17), 82 (31), 81 (51), 80 (3), 79 (2), 70 (8), 69 (100), 68 (13), 67 (19), 57 (63), 56 (7), 55 (30), 53 (6), 43 (6), 42 (4), 41 (38), 39 (5), 29 (17), 27 (5).

(±)-3,7-Dimethyloct-6-enyl 2-Oxopentanoate ((±)-**3**). As described above (*Method A*) with 4.33 g (37 mmol) of 2-oxopentanoic acid and 11.65 g (75 mmol) of citronellol for 65 h. CC (SiO_2; toluene/AcOEt

9:1, and SiO_2; heptane/Et_2O 95:5) afforded 3.79 g of crude product, which was distilled (*Kugelrohr*) to give 2.52 g (27%) of (±)-**3**. Colorless oil. UV/VIS (hexane): 398 (sh, 1), 376 (sh, 10), 357 (sh, 10), 342 (sh, 20), 331 (20), 281 (sh, 20), 268 (sh, 30), 241 (sh, 280). IR (neat): 2965*s*, 2931*s*, 2877*m*, 1750*m*, 1728*s*, 1457*m*, 1380*m*, 1287*w*, 1261*m*, 1178*w*, 1146*w*, 1118*m*, 1055*m*, 1037*w*, 943*w*, 832*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.13–5.03 (*m*, 1 H); 4.36–4.21 (*m*, 2 H); 2.80 (*t*, *J* = 7.1, 2 H); 2.10–1.89 (*m*, 2 H); 1.83–1.70 (*m*, 1 H); 1.68 (*s*, 3 H); 1.67 (*q*, *J* = 7.3, 2 H); 1.63–1.47 (*m*, 2 H); 1.60 (*s*, 3 H); 1.45–1.29 (*m*, 1 H); 1.28–1.12 (*m*, 1 H); 0.96 (*t*, *J* = 6.9, 3 H); 0.94 (*d*, *J* = 6.3, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 194.63 (*s*); 161.44 (*s*); 131.52 (*s*); 124.40 (*d*); 64.88 (*t*); 41.21 (*t*); 36.91 (*t*); 35.19 (*t*); 29.43 (*d*); 25.71 (*q*); 25.35 (*t*); 19.37 (*q*); 17.67 (*q*); 16.54 (*t*); 13.52 (*q*). EI-MS: 254 (1, M^+), 183 (6), 155 (7), 138 (15), 137 (10), 123 (26), 118 (3), 109 (17), 95 (41), 83 (15), 82 (32), 81 (54), 71 (87), 69 (100), 67 (23), 55 (34), 43 (66), 41 (72), 27 (14).

(±)-3,7-Dimethyloct-6-enyl 3-Methyl-2-oxopentanoate ((±)-**4**). As described above (*Method A*) with 4.85 g (38 mmol) of 3-methyl-2-oxopentanoic acid and 11.66 g (74 mmol) of citronellol in 130 ml of toluene for 72 h. CC (SiO_2; toluene/AcOEt 9:1) afforded 10 g of crude product, which was fractionally distilled to give 3.65 g (36%) of (±)-**4**. Colorless oil. B.p. 94°/0.2 mbar. UV/VIS (hexane): 394 (sh, 4), 382 (sh, 10), 374 (sh, 10), 365 (sh, 10), 350 (sh, 20), 336 (20), 268 (sh, 30), 241 (sh, 180). IR (neat): 2966*s*, 2929*s*, 2877*m*, 1749*m*, 1728*s*, 1460*m*, 1380*m*, 1267*m*, 1254*m*, 1165*m*, 1115*w*, 1087*w*, 1051*m*, 1001*w*, 961*w*, 829*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.12–5.04 (*m*, 1 H); 4.36–4.24 (*m*, 2 H); 3.18–3.06 (*m*, 1 H); 2.08–1.88 (*m*, 2 H); 1.86–1.67 (*m*, 2 H); 1.68 (*s*, 3 H); 1.65–1.10 (*m*, 5 H); 1.60 (*s*, 3 H); 1.28 (*d*, *J* = 6.8, 3 H); 0.94 (*d*, *J* = 6.4, 3 H); 0.92 (*t*, *J* = 7.6, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 198.22 (*s*); 162.21 (*s*); 131.51 (*s*); 124.40 (*d*); 64.74 (*t*); 43.64 (*d*); 36.92 (*t*); 35.23 (*t*); 29.43 (*d*); 25.71 (*q*); 25.36 (*t*); 24.93 (*t*); 19.35 (*q*); 17.66 (*q*); 14.55 (*q*); 11.35 (*q*). EI-MS: 268 (1, M^+), 138 (10), 123 (14), 109 (7), 95 (18), 85 (32), 81 (26), 69 (51), 57 (100), 41 (53), 29 (18).

*(±)-(*E*)-3,7-Dimethylocta-2,6-dienyl 3-Methyl-2-oxopentanoate* ((±)-**5**). As described above (*Method A*) with 4.85 g (38 mmol) of 3-methyl-2-oxopentanoic acid and 11.5 g (75 mmol) of geraniol (=(*E*)-3,7-dimethylocta-2,6-dien-1-ol) in 130 ml of toluene for 24 h. CC (SiO_2; heptane/AcOEt 95:5) afforded 7.68 g of crude product, which was fractionally distilled to give 4.04 g (40%) of (±)-**5**. Colorless oil. B.p. 82°/0.2 mbar. UV/VIS (hexane): 393 (sh, 5), 382 (sh, 9), 374 (sh, 13), 364 (sh, 17), 357 (sh, 19), 350 (sh, 21), 335 (23). IR (neat): 2966*m*, 2929*m*, 2878*m*, 1746*m*, 1723*s*, 1670*w*, 1454*m*, 1377*m*, 1338*w*, 1274*m*, 1244*m*, 1163*m*, 1107*w*, 1085*w*, 1039*s*, 999*m*, 959*m*, 913*m*, 827*w*, 796*w*, 772*w*, 742*w*, 705*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.46–5.35 (*m*, 1 H); 5.14–5.04 (*m*, 2 H); 4.77 (*d*, *J* = 7.1, 2 H); 3.20–3.07 (*m*, 1 H); 2.20–2.00 (*m*, 4 H); 1.83–1.66 (*m*, 1 H); 1.74 (*s*, 3 H); 1.68 (*s*, 3 H); 1.60 (*s*, 3 H); 1.52–1.36 (*m*, 1 H); 1.13 (*d*, *J* = 7.1, 3 H); 0.92 (*t*, *J* = 7.5, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 198.29 (*s*); 162.10 (*s*); 144.01 (*s*); 131.97 (*s*); 123.58 (*d*); 117.13 (*d*); 62.94 (*t*); 43.66 (*d*); 39.53 (*t*); 26.22 (*t*); 25.66 (*q*); 24.92 (*t*); 17.69 (*q*); 16.57 (*q*); 14.46 (*q*); 11.35 (*q*). EI-MS: 266 (1, M^+), 138 (3), 137 (28), 136 (6), 135 (5), 95 (10), 93 (6), 91 (3), 85 (9), 82 (4), 81 (52), 79 (3), 77 (3), 70 (6), 69 (100), 68 (12), 67 (12), 57 (30), 55 (5), 53 (6), 41 (26), 39 (5), 29 (5).

Bis(3,7-dimethyloct-6-enyl) Ethane-1,2-dioate ((±)-**6**). Oxalyl chloride (10 ml, 116 mmol) was added dropwise to a stirred soln. of 36.37 g (233 mmol) of citronellol in 300 ml of pyridine at 0° over a period of 30 min. The formation of a white precipitate was observed. The soln. was allowed to warm to r.t. overnight and was quenched with H_2O, extracted with Et_2O (2×), H_2SO_4 (10%) (2×), $NaHCO_3$ (10%), and NaCl soln. (sat.). The org. layer was dried (Na_2SO_4), concentrated at reduced pressure, and filtered over a short plug (SiO_2; heptane/Et_2O 1:1). CC (SiO_2, heptane/Et_2O 9:1) gave 18.55 g (43%) of (±-**6**). Colorless oil. R_f(heptane/Et_2O 9:1) 0.38. IR (neat): 2965*s*, 2925*s*, 2873*m*, 2856*m*, 1770*s*, 1745*s*, 1457*m*, 1380*m*, 1347*w*, 1312*m*, 1250*w*, 1170*s*, 1122*w*, 1044*w*, 941*m*, 886*w*, 831*w*, 792*w*, 756*w*, 742*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.13–5.04 (*m*, 1 H); 4.40–4.23 (*m*, 2 H); 2.08–1.87 (*m*, 2 H); 1.85–1.71 (*m*, 1 H); 1.70–1.50 (*m*, 2 H); 1.68 (*s*, 3 H); 1.60 (*s*, 3 H); 1.43–1.29 (*m*, 1 H); 1.29–1.13 (*m*, 1 H); 0.94 (*d*, *J* = 6.3, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 158.04 (*s*); 131.45 (*s*); 124.42 (*d*); 65.59 (*t*); 36.91 (*t*); 35.08 (*t*); 29.42 (*d*); 25.70 (*q*); 25.36 (*t*); 19.36 (*q*); 17.65 (*q*). EI-MS: 336 (0.1, M^+), 138 (18), 123 (30), 109 (16), 95 (38), 81 (51), 69 (100), 55 (30), 41 (46), 29 (5).

(±)-3,7-Dimethyloct-6-enyl 2-Oxohexadecanoate ((±)-**7**). *Method B.* A *Grignard* reagent prepared from 5.54 g of 1-bromotetradecane (20 mmol) and 0.54 g of Mg (22.5 mmol) in 20–25 ml of THF [37] was added dropwise to a stirred soln. of 8.0 g (22 mmol) of (±)-**6** in 50 ml of THF at −78° over a period of 30 min [22]. The mixture was slowly warmed to −10°, and the reaction was quenched with 25 ml of a sat. soln. of NH_4Cl. The mixture was extracted with Et_2O and H_2O (2×), and the org. phase was dried (Na_2SO_4). CC (2×) (SiO_2; heptane/Et_2O 95:5): 3.21 g (39%) of (±)-**7**. Colorless oil. R_f(heptane/Et_2O 95:5) 0.63. UV/VIS (hexane): 376 (sh, 10), 359 (sh, 20), 343 (sh, 20), 279 (260), 272 (sh, 250), 242 (530). IR (neat): 2958*m*, 2924*s*, 2854*s*, 1728*s*, 1465*m*, 1458*m*, 1400*w*, 1378*m*, 1271*m*, 1128*w*, 1088*w*, 1062*m*, 945*w*, 831*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.12–5.03 (*m*, 1 H); 4.35–4.21 (*m*, 2 H); 2.81 (*t*, *J* = 7.3, 2 H); 2.09–1.88 (*m*, 2 H); 1.87–1.69 (*m*, 1 H); 1.68 (*s*, 3 H); 1.69–1.47 (*m*, 2 H); 1.60 (*s*, 3 H); 1.45–1.14 (*m*, 26 H); 0.94 (*d*, *J* = 6.3, 3 H); 0.88 (*t*, *J* = 6.9, 3 H). ^{13}C-NMR

(90.6 MHz, $CDCl_3$): 194.77 (*s*); 161.48 (*s*); 131.49 (*s*); 124.41 (*d*); 64.86 (*t*); 39.38 (*t*); 36.93 (*t*); 35.20 (*t*); 31.96 (*t*); 29.68 (3×) (*t*); 29.61 (*t*); 29.45 (2×) (*t*); 29.39 (*t*); 29.33 (*t*); 29.01 (*t*); 25.71 (*q*); 25.37 (*t*); 23.05 (*t*); 22.71 (*t*); 19.38 (*q*); 17.66 (*q*); 14.12 (*q*). EI-MS: 225 (11), 183 (14), 155 (8), 139 (7), 138 (55), 137 (28), 124 (6), 123 (52), 121 (5), 111 (4), 110 (7), 109 (27), 97 (9), 96 (16), 95 (70), 94 (8), 85 (16), 83 (28), 82 (50), 81 (97), 80 (10), 71 (26), 70 (11), 69 (100), 68 (11), 67 (21), 57 (54), 56 (12), 55 (47), 43 (48), 42 (10), 41 (55), 39 (7), 29 (12).

(±)-3,7-Dimethyloct-6-enyl 3-Methyl-2-oxopentadecanoate ((±)-**8**). As described above (*Method B*) with 5.0 g (18 mmol) of 2-bromotetradecane, 0.58 g (24 mmol) of Mg and 7.32 g (20 mmol) of (±)-**6** in 50 ml of THF. CC (3×) (SiO_2; heptane/Et_2O 95:5): 2.52 g (34%) of (±)-**8**. Colorless oil. R_f(heptane/Et_2O 95:5) 0.46. UV/VIS (hexane): 394 (sh, 4), 383 (sh, 10), 373 (sh, 10), 365 (sh, 20), 349 (sh, 20), 336 (20), 284 (sh, 10), 269 (sh, 20), 241 (sh, 140). IR (neat): 3440*w*, 2958*s*, 2924*s*, 2854*s*, 2730*w*, 1749*s*, 1725*s*, 1460*m*, 1378*m*, 1350*w*, 1266*m*, 1173*w*, 1146*w*, 1112*w*, 1053*m*, 1032*m*, 943*w*, 887*w*, 830*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.13–5.04 (*m*, 1 H); 4.36–4.23 (*m*, 2 H); 3.23–3.10 (*m*, 1 H); 2.10–1.87 (*m*, 2 H); 1.87–1.64 (*m*, 1 H); 1.68 (*s*, 3 H); 1.64–1.47 (*m*, 2 H); 1.60 (*s*, 3 H); 1.46–1.16 (*m*, 24 H); 1.13 (*d*, J = 6.7, 3 H); 0.94 (*d*, J = 6.3, 3 H); 0.88 (*t*, J = 6.9, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 198.33 (*s*); 162.20 (*s*); 131.50 (*s*); 124.40 (*d*); 64.75 (*t*); 42.21 (*d*); 36.93 (*t*); 35.23 (*t*); 31.92 (*t*); 29.68 (*t*); 29.66 (2×) (*t*); 29.59 (2×) (*t*); 29.45 (2×) (*t*); 29.37 (*t*); 27.01 (*t*); 25.71 (*q*); 25.37 (*t*); 22.70 (*t*); 19.35 (*q*); 17.66 (*q*); 15.01 (*q*); 14.12 (*q*). EI-MS: 408 (1, M^+), 255 (4), 197 (3), 183 (12), 155 (8), 141 (4), 139 (9), 138 (76), 137 (21), 127 (7), 123 (46), 113 (9), 109 (19), 99 (15), 96 (15), 95 (57), 94 (8), 85 (47), 83 (25), 82 (52), 81 (89), 80 (14), 71 (65), 70 (10), 69 (100), 68 (10), 67 (18), 57 (94), 56 (17), 55 (51), 43 (61), 41 (69), 39 (7), 29 (15), 27 (6).

(±)-3,7-Dimethyloct-6-enyl 2-Oxo-2-phenylacetate ((±)-**9**; for an alternative synthesis, see [27]). As described above (*Method B*) with 3.14 g of 1-bromobenzene (20 mmol), 0.55 g of Mg (22 mmol) in 20 ml of Et_2O, and 8.0 g (22 mmol) of (±)-**6** in 50 ml of Et_2O. CC (SiO_2; heptane/Et_2O 95:5) allowed a partial separation of the product from remaining **6**. MPLC on a *Lobar* column (SiO_2 (*Merck*); heptane/Et_2O 97:3) finally afforded 3.5 g (61%) of pure (±)-**9**. Bright yellow oil. R_f(heptane/Et_2O 97:3) 0.16. UV/VIS (hexane): 370 (sh, 30), 352 (40), 340 (sh, 40), 294 (sh, 1020), 252 (10350), 248 (10360). IR (neat): 3065*w*, 2962*s*, 2926*s*, 2872*m*, 2855*m*, 1738*s*, 1693*s*, 1597*m*, 1581*m*, 1451*m*, 1379*m*, 1322*m*, 1313*m*, 1300*m*, 1246*w*, 1198*s*, 1175*s*, 1122*w*, 1042*w*, 1030*w*, 1003*m*, 998*m*, 941*w*, 831*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 8.04–7.97 (*m*, 2 H); 7.69–7.62 (*m*, 1 H); 7.55–7.45 (*m*, 2 H); 5.12–5.03 (*m*, 1 H); 4.50–4.36 (*m*, 2 H); 2.15–1.90 (*m*, 2 H); 1.90–1.75 (*m*, 1 H); 1.75–1.50 (*m*, 2 H); 1.66 (*s*, 3 H); 1.59 (*s*, 3 H); 1.45–1.32 (*m*, 1 H); 1.32–1.15 (*m*, 1 H); 0.96 (*d*, J = 6.3, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 186.50 (*s*); 164.02 (*s*); 134.87 (*d*); 132.56 (*s*); 131.51 (*s*); 130.02 (*d*); 128.90 (*d*); 124.40 (*d*); 64.85 (*t*); 36.93 (*t*); 35.30 (*t*); 29.44 (*d*); 25.69 (*q*); 25.38 (*t*); 19.38 (*q*); 17.66 (*q*). EI-MS: 288 (1, M^+), 270 (4), 155 (4), 152 (3), 138 (9), 137 (10), 123 (11), 109 (8), 106 (10), 105 (100), 96 (3), 95 (20), 83 (3), 82 (12), 81 (24), 78 (3), 77 (36), 70 (3), 69 (26), 68 (5), 67 (10), 57 (3), 56 (3), 55 (11), 53 (3), 51 (10), 43 (4), 42 (3), 41 (28), 39 (5), 29 (4), 27 (4).

2-(4-Bromomethyl)-2-methyl-1,3-dioxolane (**33**) [38]. 4-Bromoacetophenone (10.0 g, 50 mmol), 7.0 g (112 mmol) of ethylene glycol, and a few crystals of TsOH were dissolved in 100 ml of toluene, and the mixture was heated overnight under reflux with azeotropic removal of H_2O. After cooling to r.t., the mixture was concentrated *in vacuo*. CC (SiO_2; heptane/Et_2O 9:1) afforded 11.4 g (93%) of a colorless oil, which easily crystallized. R_f(heptane/Et_2O 9:1) 0.39. UV/VIS (hexane): 287 (sh, 400), 274 (sh, 1300), 270 (sh, 1800), 259 (sh, 6700), 252 (7800), 227 (sh, 61800), 220 (75600), 217 (sh, 75000). IR (neat): 3084*w*, 3060*w*, 2990*m*, 2957*s*, 2928*s*, 2890*s*, 2856*m*, 2670*w*, 1911*w*, 1691*m*, 1657*w*, 1591*m*, 1575*w*, 1482*m*, 1470*w*, 1443*m*, 1393*m*, 1373*m*, 1249*m*, 1222*w*, 1196*s*, 1144*m*, 1118*m*, 1092*m*, 1079*m*, 1040*s*, 1010*s*, 947*m*, 873*s*, 826*s*. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.49–7.42 (*m*, 2 H); 7.39–7.32 (*m*, 2 H); 4.08–3.96 (*m*, 2 H); 3.80–3.69 (*m*, 2 H); 1.62 (*s*, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 142.49 (*s*); 131.30 (*d*); 127.17 (*d*); 121.86 (*s*); 108.43 (*s*); 64.47 (*t*); 27.52 (*q*). EI-MS: 244, 242 (1, 1, M^+), 230 (14), 229 (97), 227 (100), 213 (5), 211 (5), 186 (4), 185, 183 (51, 53), 157, 155 (14, 14), 148 (4), 133 (5), 104 (8), 103 (9), 102 (8), 89 (3), 87 (26), 77 (12), 76 (16), 75 (14), 74 (7), 63 (4), 51 (7), 50 (13), 43 (41), 39 (3), 29 (7).

(±)-3,7-Dimethyloct-6-enyl [4-(2-Methyl-1,3-dioxolan-2-yl)phenyl]-2-oxoacetate ((±)-**34**). As described above (*Method B*) with 4.66 g (20 mmol) of **33**, 0.54 g (22 mmol) of Mg, and 8.0 g (22 mmol) of **6** in 50 ml of THF. CC (SiO_2; heptane/Et_2O 8:2): 4.35 g (58%) of (±)-**34**. Slightly yellow oil. R_f(heptane/Et_2O 8:2) 0.25. UV/VIS (hexane): 370 (sh, 40), 353 (60), 340 (sh, 60), 296 (sh, 1300), 258 (13890). IR (neat): 2963*s*, 2926*s*, 1736*s*, 1690*s*, 1607*s*, 1573*m*, 1505*w*, 1455*m*, 1407*m*, 1374*m*, 1347*w*, 1314*m*, 1294*w*, 1250*m*, 1199*s*, 1175*s*, 1146*w*, 1122*w*, 1100*w*, 1078*m*, 1039*m*, 1018*w*, 989*m*, 948*w*, 890*w*, 876*m*, 861*m*, 833*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.98 (*d*, J = 8.3, 2 H); 7.62 (*d*, J = 8.7, 2 H); 5.12–5.04 (*m*, 1 H); 4.50–4.36 (*m*, 2 H); 4.13–4.00 (*m*, 2 H); 3.82–3.70 (*m*, 2 H); 2.10–1.90 (*m*, 2 H); 1.90–1.75 (*m*, 1 H); 1.72–1.54 (*m*, 2 H); 1.67 (*s*, 3 H); 1.65 (*s*, 3 H); 1.60 (*s*, 3 H); 1.45–1.32 (*m*, 1 H); 1.30–1.16 (*m*, 1 H); 0.96 (*d*, J = 6.3, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 186.04 (*s*); 163.97 (*s*); 150.64 (*s*); 132.12 (*s*); 131.53 (*s*); 130.15 (*d*); 125.97 (*d*); 124.39 (*d*); 108.39 (*s*); 64.89 (*t*); 64.65 (2×) (*t*); 36.93 (*t*); 35.30 (*t*); 29.44 (*d*); 27.38 (*q*); 25.70 (*q*); 25.37 (*t*); 19.38 (*q*); 17.66 (*q*). EI-MS: 374 (7, M^+), 359 (8), 356 (3),

192 (32), 191 (100), 148 (24), 138 (16), 133 (6), 123 (14), 119 (76), 109 (9), 104 (15), 95 (22), 91 (8), 87 (18), 81 (30), 69 (26), 55 (10), 43 (12), 41 (21), 29 (3).

(±)-3,7-Dimethyloct-6-enyl (4-Acetylphenyl)-2-oxoacetate ((±)-**10**). To a soln. of 4.2 g (13 mmol) of **34** in 30 ml of THF, 5 ml of H_2SO_4 (50%) were added. The mixture was heated at 40° for 5 h, then extracted with Et_2O (2×), and sat. solns. of $NaHCO_3$ (2×) and NaCl (2×). The org. layer was dried (Na_2SO_4) and concentrated. CC (SiO_2; heptane/Et_2O 1:1): 2.0 g (47%) of (±)-**10**. Yellow oil. R_f(heptane/Et_2O 1:1) 0.50. UV/VIS (hexane): 384 (sh, 60), 367 (sh, 100), 343 (sh, 150), 310 (sh, 1230), 301 (sh, 1660), 266 (17910), 260 (18440). IR (neat): 3051*w*, 2964*s*, 2926*s*, 2872*m*, 2856*m*, 1736*s*, 1693*s*, 1607*w*, 1570*m*, 1500*m*, 1457*m*, 1434*m*, 1407*m*, 1379*m*, 1359*m*, 1318*m*, 1307*m*, 1260*s*, 1199*s*, 1176*s*, 1117*w*, 1075*m*, 992*s*, 959*m*, 861*m*, 832*m*. ^{1}H-NMR (360 MHz, $CDCl_3$): 8.17–8.02 (*m*, 4 H); 5.12–5.04 (*m*, 1 H); 4.53–4.37 (*m*, 2 H); 2.66 (*s*, 3 H); 2.14–1.90 (*m*, 2 H); 1.90–1.75 (*m*, 1 H); 1.73–1.53 (*m*, 2 H); 1.67 (*s*, 3 H); 1.60 (*s*, 3 H); 1.46–1.32 (*m*, 1 H); 1.32–1.12 (*m*, 1 H); 0.96 (*d*, *J* = 6.3, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 197.19 (*s*); 185.55 (*s*); 163.25 (*s*); 141.33 (*s*); 135.67 (*s*); 131.57 (*s*); 130.28 (*d*); 128.56 (*d*); 124.34 (*d*); 65.19 (*t*); 36.91 (*t*); 35.26 (*t*); 29.43 (*d*); 26.94 (*q*); 25.70 (*q*); 25.35 (*t*); 19.37 (*q*); 17.67 (*q*). EI-MS: 330 (4, M^+), 194 (4), 149 (5), 148 (43), 147 (100), 138 (4), 137 (11), 123 (10), 120 (4), 119 (11), 109 (10), 104 (12), 96 (4), 95 (21), 91 (15), 83 (5), 82 (13), 81 (29), 77 (6), 76 (8), 69 (38), 68 (5), 67 (11), 65 (3), 57 (3), 56 (3), 55 (12), 53 (3), 50 (3), 43 (15), 41 (30), 39 (5), 29 (4), 27 (3).

(±)-3,7-Dimethyloct-6-enyl 2-Cyclohexyl-2-oxoacetate ((±)-**11**). As described above (*Method B*) with 3.24 g (20 mmol) of freshly distilled 1-bromocyclohexane, 0.55 g (22 mmol) of Mg, and 8.0 g (22 mmol) of (±)-**6** in 50 ml of THF. CC (SiO_2, toluene/AcOEt 95:5) allowed a partial separation of the product from remaining **6**. MPLC on a *Lobar* column (SiO_2 (*Merck*), heptane/Et_2O 97:3): 1.69 g (29%) of pure (±)-**11**. Colorless oil. UV/VIS (hexane): 394 (sh, 4), 375 (sh, 11), 366 (sh, 14), 350 (sh, 18), 338 (19). IR (neat): 2932*s*, 2856*m*, 1747*m*, 1727*s*, 1451*m*, 1379*m*, 1311*w*, 1276*m*, 1230*m*, 1183*w*, 1173*w*, 1140*m*, 1118*w*, 1082*m*, 1067*m*, 1050*w*, 1029*w*, 997*m*, 942*w*, 895*w*, 837*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.12–5.04 (*m*, 1 H); 4.36–4.22 (*m*, 2 H); 3.07–2.95 (*m*, 1 H); 2.09–1.85 (*m*, 4 H); 1.85–1.64 (*m*, 3 H); 1.68 (*s*, 3 H); 1.64–1.47 (*m*, 2 H); 1.60 (*s*, 3 H); 1.43–1.13 (*m*, 8 H); 0.93 (*d*, *J* = 6.3, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 197.65 (*s*); 162.17 (*s*); 131.51 (*s*); 124.39 (*d*); 64.71 (*t*); 46.34 (*d*); 36.91 (*t*); 35.21 (*t*); 29.44 (*d*); 27.46 (*t*); 25.72 (*t*); 25.36 (*t*); 25.30 (*t*); 19.35 (*q*); 17.66 (*q*). EI-MS: 294 (1, M^+), 183 (4), 138 (13), 137 (4), 123 (14), 111 (16), 110 (3), 109 (6), 96 (4), 95 (16), 84 (7), 83 (100), 82 (15), 81 (22), 80 (3), 69 (29), 68 (4), 67 (11), 56 (4), 55 (42), 54 (3), 53 (5), 43 (4), 42 (4), 41 (38), 39 (8), 29 (6), 27 (4). Compound (±)-**11** was alternatively prepared from **19** by *Method C* as described below[3]).

Ethyl 2-Cyclohexyl-2-oxoacetate (**19**) [22a,d]. A *Grignard* reagent prepared from 24.45 g of 1-bromocyclohexane (150 mmol) and 4.32 g of Mg (180 mmol) in 70 ml THF [37] was added dropwise (during 40 min) to a stirred soln. of 14.6 g (0.10 mol) of diethyl oxalate in 150 ml of THF at −70°. The formation of a precipitate was observed, and another 100 ml of THF were added. The mixture was slowly warmed to −10° and poured onto ice, saturated with NaCl, extracted with Et_2O (2×) and washed with a sat. soln. of NH_4Cl (2×) and H_2O (pH *ca.* 7). The org. phase was dried (Na_2SO_4) and concentrated. Fractional distillation gave 9.86 g (54%) of **19**. Colorless oil. B.p. 54°/0.1–1.5 mbar. UV/VIS (hexane): 394 (sh, 5), 375 (sh, 10), 366 (sh, 15), 350 (sh, 20), 337 (20), 285 (sh, 7). IR (neat) 2982*w*, 2930*m*, 2854*m*, 1722*s*, 1449*m*, 1366*w*, 1272*m*, 1229*m*, 1184*w*, 1140*m*, 1112*w*, 1081*m*, 1066*s*, 1014*m*, 991*m*, 923*w*, 894*w*, 855*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.32 (*q*, *J* = 7.1, 2 H); 3.1–2.97 (*m*, 1 H); 1.97–1.85 (*m*, 2 H); 1.85–1.74 (*m*, 2 H); 1.74–1.64 (*m*, 1 H); 1.45–1.13 (*m*, 5 H); 1.37 (*t*, *J* = 7.1, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 197.65 (*s*); 162.03 (*s*); 62.19 (*t*); 46.29 (*d*); 27.51 (*t*); 25.73 (*t*); 25.32 (*t*); 14.06 (*q*). EI-MS: 184 (2, M^+), 112 (3), 111 (33), 110 (3), 84 (6), 83 (100), 81 (3), 67 (5), 56 (3), 55 (54), 54 (5), 53 (5), 42 (3), 41 (23), 39 (12), 29 (20), 28 (3), 27 (13).

*(*E*)-3,7-Dimethylocta-2,6-dienyl 2-Cyclohexyl-2-oxoacetate* ((±)-**12**). *Method C*. A soln. of 25.20 g (137 mmol) of **19**, 25.56 g (166 mmol) of geraniol, and 1 ml of $NaOCH_3$ (30% in MeOH) in 150 ml of cyclohexane was heated with a water separator under reflux overnight. After cooling to r.t., the mixture was taken up in Et_2O, washed with a sat. soln. of NaCl (pH *ca.* 7), dried (Na_2SO_4), filtered, and concentrated. CC (SiO_2; heptane/Et_2O 9:1) and fractional distillation: 23.36 g (58%) of (±)-**12**. Colorless oil. B.p. 130°/0.1 mbar. UV/VIS (hexane): 394 (sh, 5), 384 (sh, 8), 375 (sh, 14), 366 (sh, 17), 358 (sh, 20), 350 (sh, 22), 336 (24). IR (neat): 2926*m*, 2853*m*, 1743*m*, 1721*s*, 1670*w*, 1449*m*, 1376*m*, 1341*w*, 1331*w*, 1309*w*, 1273*m*, 1267*m*, 1227*m*, 1183*w*, 1139*m*, 1111*w*, 1080*m*, 1063*s*, 1027*w*, 993*s*, 915*m*, 895*w*, 830*w*, 805*w*, 787*w*, 739*w*, 729*w*, 718*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.45–5.35 (*m*, 1 H); 5.12–5.03 (*m*, 1 H); 4.76 (*d*, *J* = 7.1, 2 H); 3.09–2.95 (*m*, 1 H); 2.17–1.98 (*m*, 4 H); 1.98–1.85 (*m*, 2 H); 1.84–1.75 (*m*, 2 H); 1.74 (*s*, 3 H); 1.73–1.62 (*m*, 1 H); 1.68 (*s*, 3 H); 1.60 (*s*, 3 H); 1.43–1.14 (*m*, 5 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 197.70 (*s*); 162.08 (*s*); 143.97 (*s*); 131.97 (*s*); 123.59 (*d*);

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[3]) We thank *Hervé Pamingle* (*Firmenich SA*) for preparing 50 g of (±)-**11** by this method.

117.16 (*d*); 62.90 (*t*); 46.38 (*d*); 39.55 (*t*); 27.49 (*t*); 26.23 (*t*); 25.73 (*t*); 25.67 (*q*); 25.31 (*t*); 17.69 (*q*); 16.58 (*q*). EI-MS: 292 (1, M^+), 138 (3), 137 (24), 136 (4), 135 (3), 111 (9), 95 (9), 93 (9), 91 (3), 84 (4), 83 (54), 82 (4), 81 (55), 79 (4), 77 (3), 70 (6), 69 (100), 68 (12), 67 (12), 55 (24), 53 (6), 43 (2), 41 (25), 39 (5).

Decyl 2-Cyclohexyl-2-oxoacetate (**13**). As described above (*Method C*) with 6.21 g (33.4 mmol) of **19**, 5.75 g (36.4 mmol) of decanol, 0.5 ml of $NaOCH_3$ (30% in MeOH), and 50 ml of cyclohexane. Fractional distillation: 3.85 g (39%) of **13**. Colorless oil. B.p. 118–126°/0.2 mbar. UV/VIS (hexane): 394 (sh, 4), 382 (sh, 8), 376 (sh, 11), 367 (sh, 14), 358 (sh, 17), 350 (sh, 19), 336 (19), 314 (sh, 17), 302 (sh, 15). IR (neat): 2924*s*, 2852*m*, 1745*m*, 1723*s*, 1466*m*, 1450*m*, 1377*w*, 1330*w*, 1310*w*, 1290*w*, 1274*m*, 1229*m*, 1183*w*, 1139*m*, 1117*w*, 1082*m*, 1065*m*, 1028*w*, 995*m*, 929*w*, 895*w*, 867*w*, 802*w*, 785*w*, 720*m*, 662*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.24 (*t*, *J* = 6.7, 2 H); 3.07–2.96 (*m*, 1 H); 1.98–1.85 (*m*, 2 H); 1.85–1.60 (*m*, 5 H); 1.44–1.14 (*m*, 19 H); 0.88 (*t*, *J* = 6.9, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 197.70 (*s*); 162.22 (*s*); 66.27 (*t*); 46.37 (*d*); 31.90 (*t*); 29.51 (*t*); 29.49 (*t*); 29.30 (*t*); 29.17 (*t*); 28.42 (*t*); 27.48 (*t*); 25.80 (*t*); 25.74 (*t*); 25.32 (*t*); 22.69 (*t*); 14.11 (*q*). EI-MS: 296 (2, M^+), 112 (7), 111 (88), 110 (3), 84 (7), 83 (100), 67 (3), 57 (5), 56 (3), 55 (23), 43 (7), 41 (10).

4-Methoxybenzyl 2-Cyclohexyl-2-oxoacetate (**14**). As described above (*Method C*) with 6.62 g (35.9 mmol) of **19**, 6.06 g (43.9 mmol) of 4-methoxybenzyl alcohol, 0.5 ml of $NaOCH_3$ (30% in MeOH), and 50 ml of cyclohexane. CC (SiO_2, heptane/Et_2O 7:3) afforded one fraction of the pure product **14** together with another fraction of lower purity. The latter was rechromatographed (SiO_2; heptane/Et_2O 8:2) to yield a total of 1.15 g (12%) of pure **14**. Slightly yellow oil. UV/VIS (hexane): 395 (sh, 5), 375 (sh, 15), 367 (sh, 18), 360 (sh, 21), 352 (sh, 24), 337 (26), 324 (sh, 25), 312 (sh, 24), 288 (sh, 230), 280 (1520), 274 (1790), 268 (sh, 1590), 265 (sh, 1520), 259 (sh, 1170). IR (neat): 3001*w*, 2929*m*, 2853*m*, 1806*w*, 1721*s*, 1612*m*, 1586*m*, 1514*s*, 1461*m*, 1449*m*, 1424*w*, 1369*w*, 1303*m*, 1271*m*, 1246*s*, 1225*s*, 1174*s*, 1138*s*, 1112*m*, 1080*m*, 1063*s*, 1031*s*, 996*s*, 984*s*, 946*w*, 916*w*, 895*m*, 849*w*, 821*s*, 755*w*, 719*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.38–7.30 (*m*, 2 H); 6.94–6.85 (*m*, 2 H); 5.21 (*s*, 2 H); 3.81 (*s*, 3 H); 3.08–2.94 (*m*, 1 H); 1.98–1.83 (*m*, 2 H); 1.83–1.71 (*m*, 2 H); 1.71–1.56 (*m*, 1 H); 1.41–1.10 (*m*, 5 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 197.39 (*s*); 161.94 (*s*); 160.04 (*s*); 130.51 (*d*); 126.81 (*s*); 114.08 (*d*); 67.58 (*t*); 55.31 (*q*); 46.41 (*d*); 27.46 (*t*); 25.70 (*t*); 25.27 (*t*). EI-MS: 276 (1, M^+), 122 (10), 121 (100), 91 (3), 83 (7), 78 (5), 77 (4), 55 (9), 41 (3).

*(±)-3-[4-(*tert*-Butyl)phenyl]-2-methylpropyl 2-Cyclohexyl-2-oxoacetate* ((±)-**15**). As described above (*Method C*) with 4.8 g (26.1 mmol) of **19**, 4.0 g (21.5 mmol) of 3-[4-(*tert*-butyl)phenyl]-2-methylpropanol (obtained by reduction of (±)-3-[4-(*tert*-butyl)phenyl]-2-methylpropanal (*Lilial*) with $LiAlH_4$ in Et_2O, 0.5 ml of $NaOCH_3$ (30% in MeOH), and 40 ml of cyclohexane. CC (SiO_2; heptane/Et_2O 8:2): 3.43 g (46%) of (±)-**15**. Colorless oil. UV/VIS (hexane): 393 (sh, 4), 384 (sh, 7), 375 (sh, 12), 366 (sh, 15), 357 (sh, 18), 351 (sh, 20), 336 (22), 322 (sh, 20), 271 (270), 263 (330), 257 (280), 251 (240), 244 (sh, 240). IR (neat). 3089*w*, 3055*w*, 3021*w*, 2953*m*, 2928*m*, 2855*m*, 1723*s*, 1512*m*, 1450*m*, 1410*w*, 1387*w*, 1364*w*, 1310*w*, 1270*m*, 1226*m*, 1183*w*, 1139*m*, 1112*w*, 1079*m*, 1064*m*, 998*m*, 963*w*, 954*w*, 919*w*, 892*w*, 843*w*, 800*w*, 718*w*, 674*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.35–7.27 (*m*, 2 H); 7.12–7.05 (*m*, 2 H); 4.14 (*A* of *ABX*, *J* = 10.7, 5.6, 1 H); 4.07 (*B* of *ABX*, *J* = 10.7, 6.7, 1 H); 3.06–2.95 (*m*, 1 H); 2.70 (*A* of *ABX*, *J* = 13.7, 6.5, 1 H); 2.48 (*B* of *ABX*, *J* = 13.7, 7.7, 1 H); 2.28–2.12 (*m*, 1 H); 1.97–1.86 (*m*, 2 H); 1.86–1.74 (*m*, 2 H); 1.74–1.63 (*m*, 1 H); 1.45–1.15 (*m*, 5 H); 1.31 (*s*, 9 H); 0.98 (*d*, *J* = 6.7, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 197.52 (*s*); 162.24 (*s*); 149.01 (*s*); 136.34 (*s*); 128.75 (*d*); 125.27 (*d*); 70.11 (*t*); 46.44 (*d*); 39.08 (*t*); 34.43 (*d*); 34.38 (*s*); 31.39 (*q*); 27.44 (*t*); 25.71 (*t*); 25.30 (*t*); 16.77 (*q*). EI-MS: 345 (1, $[M+H]^+$), 344 (6, M^+), 329 (6), 234 (9), 233 (52), 231 (4), 189 (10), 188 (27), 177 (13), 174 (7), 173 (31), 159 (5), 148 (6), 147 (45), 145 (8), 133 (3), 132 (23), 131 (29), 119 (4),118 (3), 117 (19), 116 (3), 115 (5), 112 (3), 111 (40), 105 (5), 91 (9), 84 (7), 83 (100), 57 (14), 55 (20), 41 (9).

*(1*R*,2*S*,5*R*)-5-Methyl-2-(1-methylethyl)cyclohexyl 2-Cyclohexyl-2-oxoacetate* (**16**) [20]. As described above (*Method C*) with 25.03 g (136 mmol) of **19**, 25.70 g (165 mmol) of (−)-menthol, and 1 ml of $NaOCH_3$ (30% in MeOH) in 150 ml of cyclohexane. Fractional distillation: 23.14 g (58%) of **16**. Colorless oil. B.p. 122°/0.33 mbar. UV/VIS (hexane): 394 (sh, 5), 383 (sh, 8), 375 (sh, 12), 366 (sh, 16), 360 (sh, 18), 351 (sh, 20), 337 (22). IR (neat): 2949*m*, 2928*m*, 2854*m*, 1717*s*, 1450*m*, 1387*w*, 1370*m*, 1332*w*, 1311*w*, 1274*m*, 1230*m*, 1181*w*, 1139*m*, 1111*w*, 1081*m*, 1064*m*, 1037*w*, 1027*w*, 1006*w*, 995*s*, 980*m*, 951*m*, 912*m*, 894*m*, 869*w*, 844*m*, 802*w*, 787*w*, 717*m*. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.83 (*td*, *J* = 10.9, 4.36, 1 H); 3.05–2.94 (*m*, 1 H); 2.08–1.99 (*m*, 1 H); 1.96–1.62 (*m*, 8 H); 1.59–1.45 (*m*,2 H); 1.44–0.99 (*m*, 7 H); 0.93 (*d*, *J* = 6.7, 3 H); 0.90 (*d*, *J* = 7.1, 3 H); 0.77 (*d*, *J* = 7.1, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 198.09 (*s*); 162.16 (*s*); 76.71 (*d*); 46.79 (*d*); 46.32 (*d*); 40.49 (*t*); 34.10 (*t*); 31.50 (*d*); 27.37 (*t*); 26.25 (*d*); 25.76 (*t*); 25.32 (*t*); 25.26 (*t*); 23.38 (*t*); 21.95 (*q*); 20.67 (*q*); 16.17 (*q*). EI-MS: 294 (1, M^+), 154 (4), 140 (4), 139 (33), 138 (8), 111 (9), 97 (16), 95 (5), 84 (7), 83 (100), 81 (12), 71 (3), 69 (19), 67 (5), 57 (13), 55 (33), 43 (5), 41 (11).

(±)-2-Pentylcyclopentyl 2-Cyclohexyl-2-oxoacetate ((±)-**17**). As described above (*Method C*) with 6.62 g (36 mmol) of **19**, 6.80 g (44 mmol) of (±)-2-pentylcyclopentanol, and 1 ml of $NaOCH_3$ (30% in MeOH) in

50 ml of cyclohexane for 24 h. CC (SiO_2; heptane/Et_2O 8:2) afforded 5.91 g (55%) of a yellow oil (mixture of diastereoisomers). The UV/VIS spectrum indicated the presence of a colored impurity. UV/VIS (hexane): 395 (sh, 4), 383 (sh, 7), 374 (sh, 11), 366 (sh, 14), 358 (sh, 16), 349 (sh, 19), 320 (sh, 23), 303 (sh, 34), 289 (sh, 43). IR (neat): 2924*m*, 2853*m*, 1806*w*, 1719*s*, 1461*w*, 1449*m*, 1376*w*, 1311*w*, 1275*m*, 1254*w*, 1229*m*, 1183*w*, 1139*m*, 1116*w*, 1081*m*, 1064*m*, 1028*w*, 996*m*, 968*w*, 925*w*, 894*w*, 844*w*, 724*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.35–5.28 (*m*, 1 H); 4.96–4.89 (*m*, 1 H); 3.05–2.88 (*m*, 2 H); 2.10–1.55 (*m*, 10 H); 1.53–1.10 (*m*, 13 H); 0.93–0.80 (*m*, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 197.99 (*s*); 162.29 (*s*); 162.26 (*s*); 83.72 (*d*); 80.36 (*d*); 46.58 (*d*); 46.42 (*d*); 45.39 (*d*); 44.81 (*d*); 33.49 (*t*); 32.53 (*t*); 32.07 (*t*); 31.94 (*t*); 31.80 (*t*); 30.20 (*t*); 29.61 (*t*); 29.12 (*t*); 28.18 (*t*); 27.60 (*t*); 27.46 (*t*); 27.38 (*t*); 25.32 (*t*); 22.76 (*t*); 22.59 (*t*); 22.03 (*t*); 14.05 (*q*). EI-MS: 139 (8), 138 (7), 111 (11), 97 (25), 95 (3), 84 (7), 83 (100), 82 (5), 81 (4), 71 (4), 69 (22), 67 (9), 57 (11), 55 (29), 54 (3), 43 (4), 41 (12), 39 (3), 29 (3).

4-(1,1-Dimethylpropyl)cyclohexyl 2-Cyclohexyl-2-oxoacetate (**18**). As described above (*Method C*) with 6.62 g (36 mmol) of **19**, 7.40 g (43.5 mmol) of 4-(1,1-dimethylpropyl)cyclohexan-1-ol, and 1 ml of $NaOCH_3$ (30% in MeOH) in 50 ml of cyclohexane. CC (SiO_2; heptane/Et_2O 8:2): afforded 4.78 g (43%) of a mixture *cis*-**18**/*trans*-**18** (*ca.* 38:62). Slightly yellow oil. UV/VIS (hexane): 394 (sh, 4), 385 (sh, 7), 375 (sh, 12), 367 (sh, 15), 339 (sh, 35), 326 (40), 312 (sh, 38), 297 (sh, 34), 283 (33), 272 (sh, 36). IR (neat): 2929*s*, 2855*m*, 1800*w*, 1719*s*, 1462*w*, 1448*m*, 1387*w*, 1377*w*, 1364*w*, 1323*w*, 1309*w*, 1274*m*, 1254*w*, 1228*m*, 1182*w*, 1160*w*, 1140*m*, 1108*w*, 1081*m*, 1064*m*, 1047*w*, 1005*w*, 995*s*, 948*w*, 928*w*, 906*w*, 894*w*, 875*w*, 830*w*, 805*w*, 780*w*, 745*w*, 719*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.21–5.14 (*m*, 1 H (*cis*)); 4.85–4.72 (*tt*, J = 11.3, 4.6, 1 H (*trans*)); 3.07–2.91 (*m*, 1 H); 2.17–1.04 (*m*, 21 H); 0.83–0.77 (*m*, 9 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): *trans*-isomer: 198.07 (*s*); 161.85 (*s*); 76.16 (*d*); 46.35 (*d*); 44.21 (*d*); 34.60 (*s*); 32.75 (*t*); 31.90 (*t*); 27.49 (*t*); 25.75 (*t*); 25.38 (*t*); 24.97 (*t*); 24.27 (*q*); 8.10 (*q*); *cis*-isomer: 198.07 (*s*); 161.62 (*s*); 72.28 (*d*); 46.81 (*d*); 44.58 (*d*); 34.82 (*s*); 32.49 (*t*); 30.49 (*t*); 27.46 (*t*); 25.75 (*t*); 25.30 (*t*); 24.17 (*q*); 21.22 (*t*); 8.10 (*q*). EI-MS: 153 (4), 152 (3), 137 (4), 123 (10), 111 (14), 98 (4), 97 (55), 95 (5), 84 (4), 83 (60), 81 (12), 72 (6), 71 (100), 69 (13), 67 (11), 57 (15), 56 (3), 55 (51), 54 (4), 53 (3), 43 (32), 41 (22), 39 (4), 29 (7), 27 (4).

Ethyl 2-Cyclopentyl-2-oxoacetate (**22**) [22d]. A *Grignard* reagent, prepared from 64.0 g of freshly distilled bromocyclopentane (0.43 mol) and 11.0 g of Mg (0.45 mol) in 360 ml of dry Et_2O [37] and filtered under N_2, was added dropwise (during 4 h) to a stirred soln. of 48.2 g (0.33 mol) of diethyl oxalate in 300 ml of dry Et_2O at $-40°$ [22]. The mixture was slowly warmed to 0° and poured into a sat. soln. of NH_4Cl, extracted with Et_2O, and washed with H_2O (pH *ca.* 7). The org. phase was dried (Na_2SO_4) and concentrated. Fractional distillation gave 27.1 g (48%) of a colorless oil in sufficient purity for further derivatization. CC (SiO_2; heptane/Et_2O 8:2) of 2.50 g afforded 2.04 g of **22** at high purity. B.p. 42°/0.1 mbar. UV/VIS (hexane): 389 (sh, 3), 371 (sh, 9), 359 (sh, 13), 345 (sh, 15), 336 (15). IR (neat): 3483*w*, 2956*m*, 2869*m*, 1723*s*, 1684*m*, 1469*w*, 1449*m*, 1399*w*, 1372*w*, 1318*w*, 1296*m*, 1254*s*, 1194*m*, 1159*m*, 1140*m*, 1091*s*, 1043*s*, 1029*s*, 952*m*, 906*m*, 858*m*, 780*m*, 708*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.32 (*q*, J = 7.1, 2 H); 3.56–3.44 (*m*, 1 H); 1.98–1.75 (*m*, 4 H); 1.75–1.57 (*m*, 4 H); 1.37 (*t*, J = 7.1, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 196.73 (*s*); 161.98 (*s*); 62.24 (*t*); 47.42 (*d*); 28.32 (*t*); 26.05 (*t*); 14.05 (*q*). EI-MS: 170 (5, M^+), 98 (4), 97 (48), 96 (4), 70 (6), 69 (100), 68 (3), 67 (6), 55 (4), 41 (22), 39 (7), 29 (5), 27 (4).

(±)-3,7-Dimethyloct-6-enyl 2-Cyclopentyl-2-oxoacetate ((±)-**20**). As described above (*Method C*) with 6.07 g (35.6 mmol) of **22**, 6.80 g (43.6 mmol) of citronellol, and 0.5 ml of $NaOCH_3$ (30% in MeOH) in 50 ml of cyclohexane. CC (SiO_2; heptane/Et_2O 7:3): 5.28 g (53%) of (±)-**20**. Yellow oil. UV/VIS (hexane): 389 (sh, 4), 366 (sh, 12), 345 (sh, 17), 336 (17). IR (neat): 3493*w*, 2957*m*, 2916*m*, 2869*m*, 1798*w*, 1724*s*, 1687*m*, 1451*m*, 1377*m*, 1354*w*, 1259*m*, 1190*m*, 1164*m*, 1144*m*, 1091*m*, 1047*m*, 1027*m*, 984*w*, 945*m*, 829*m*, 782*w*, 739*w*, 717*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.13–5.03 (*m*, 1 H); 4.40–4.20 (*m*, 2 H); 3.54–3.42 (*m*, 1 H); 2.10–1.71 (*m*, 7 H); 1.71–1.45 (*m*, 6 H); 1.68 (*s*, 3 H); 1.60 (*s*, 3 H); 1.43–1.30 (*m*, 1 H); 1.29–1.13 (*m*, 1 H); 0.94 (*d*, J = 6.3, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 196.66 (*s*); 162.11 (*s*); 131.51 (*s*); 124.40 (*d*); 64.75 (*t*); 47.48 (*d*); 36.90 (*t*); 35.22 (*t*); 29.40 (*d*); 28.27 (*t*); 26.05 (*t*); 25.71 (*q*); 25.35 (*t*); 19.35 (*q*); 17.66 (*q*). EI-MS: 280 (1, M^+), 183 (6), 155 (3), 138 (20), 137 (6), 123 (22), 109 (9), 98 (3), 97 (39), 96 (7), 95 (21), 83 (6), 82 (15), 81 (23), 70 (7), 69 (100), 68 (5), 67 (9), 55 (10), 53 (3), 41 (25), 39 (4).

*(*E*)-3,7-Dimethylocta-2,6-dienyl 2-Oxo-2-phenylacetate* (**21**). As described above (*Method C*) with 17.6 g (99 mmol) of ethyl 2-oxo-2-(phenyl)acetate, 18.5 g (120 mmol) of geraniol, and 1.5 ml of $NaOCH_3$ (30% in MeOH) in 170 ml of cyclohexane. CC (SiO_2; heptane/Et_2O 8:2): 14.5 g (52%) of **21**. Slightly yellow oil. UV/VIS (hexane): 412 (sh, 3), 396 (sh, 9), 370 (sh, 29), 352 (42), 343 (41), 331 (sh, 36), 294 (sh, 900), 284 (sh, 1400), 252 (10700). 247 (10900). IR (neat): 2966*w*, 2913*m*, 2853*w*, 1731*s*, 1687*s*, 1596*m*, 1580*w*, 1450*m*, 1376*m*, 1341*w*, 1317*w*, 1291*m*, 1192*s*, 1171*s*, 1108*w*, 1071*w*, 1028*w*, 1002*m*, 967*s*, 935*w*, 915*w*, 900*w*, 860*w*, 823*w*, 806*w*, 744*m*, 865*s*, 676*s*. ^{1}H-NMR (360 MHz, $CDCl_3$): 8.04–7.97 (*m*, 2 H); 7.69–7.62 (*m*, 1 H); 7.55–7.46 (*m*, 2 H); 5.52–5.54 (*m*, 1 H); 5.13–5.04 (*m*, 1 H); 4.91 (*d*, J = 7.2, 2 H); 2.20–2.03 (*m*, 4 H); 1.78 (*s*, 3 H); 1.67 (*s*, 3 H); 1.60

(*s*, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 186.46 (*s*); 163.90 (*s*); 144.40 (*s*); 134.85 (*d*); 132.58 (*s*); 132.03 (*s*); 130.04 (*d*); 128.87 (*d*); 123.55 (*d*); 117.07 (*d*); 63.00 (*t*); 39.56 (*t*); 26.24 (*t*); 25.68 (*q*); 17.70 (*q*); 16.63 (*q*). EI-MS: 286 (1, M^+), 137 (10), 136 (18), 135 (16), 121 (10), 107 (7), 106 (8), 105 (68), 95 (7), 94 (9), 93 (45), 92 (13), 91 (15), 82 (3), 81 (30), 80 (11), 79 (12), 78 (4), 77 (45), 70 (6), 69 (100), 68 (4), 67 (15), 65 (4), 55 (5), 53 (9), 51 (13), 50 (4), 43 (4), 42 (3), 41 (43), 39 (9), 29 (4), 27 (3).

Ethyl 2-Oxohexadecanoate (**24**). As described above (*Method B*) with 5.54 g (20 mmol) of 1-bromotetradecane, 0.54 g (22.5 mmol) of Mg, and 3.21 g (22 mmol) of diethyl oxalate in 50 ml of THF at $-40°$. CC (SiO_2; heptane/Et_2O 8:2): 3.61 g (61%) of **24**. White crystals. UV/VIS (hexane). 397 (sh, 2), 375 (sh, 8), 357 (sh, 14), 342 (18), 332 (18), 319 (sh, 16), 294 (sh, 8). IR (neat): 2953*m*, 2916*s*, 2870*m*, 2847*s*, 1722*s*, 1472*m*, 1462*m*, 1397*m*, 1367*m*, 1354*w*, 1339*w*, 1320*m*, 1301*m*, 1283*m*, 1262*m*, 1241*m*, 1218*m*, 1192*m*, 1157*w*, 1129*m*, 1103*m*, 1071*s*, 1061*m*, 1042*m*, 1018*m*, 997*m*, 974*w*, 927*w*, 918*w*, 888*w*, 859*m*, 815*w*, 795*w*, 770*w*, 730*m*, 719*m*, 698*w*, 678*m*. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.40–4.24 (*m*, 2 H); 2.82 (*t*, $J = 7.5$, 2 H); 1.69–1.57 (*m*, 2 H); 1.37 (*t*, $J = 7.1$, 3 H); 1.35–1.20 (*m*, 22 H); 0.88 (*t*, $J = 6.7$, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 194.83 (*s*); 161.34 (*s*); 62.34 (*t*); 39.31 (*t*); 31.95 (*t*); 29.68 (*t*, 4 ×); 29.60 (*t*); 29.44 (*t*); 29.38 (*t*); 29.32 (*t*); 28.98 (*t*); 23.02 (*t*); 22.71 (*t*); 14.14 (*q*); 14.02 (*q*). EI-MS: 298 (4), 226 (17), 225 (100), 123 (3), 109 (3), 95 (5), 85 (7), 83 (4), 81 (3), 71 (13), 69 (4), 57 (12), 55 (7), 43 (9), 41 (6), 29 (5).

(±)-6,7-Epoxy-3,7-dimethyloctan-1-ol ((±)-**35**) [30b]. Citronellol (3.0 g, 19.2 mmol) and 6.0 g of fine powdered $NaHCO_3$ were dissolved under Ar in 60 ml of CH_2Cl_2. After cooling to 0° (ice bath), 4.75 g (21.2 mmol) of *m*-chloroperbenzoic acid (70%), dissolved in 60 ml of CH_2Cl_2, were added dropwise over a period of 10 min. The ice bath was removed, and the mixture left stirring for 24 h. *Ca.* 10 ml of an aq. soln. of sodium sulfite (10%) were added to destroy the residual peracid. After addition of 30–50 ml of a sat. soln. of $NaHCO_3$, the biphasic soln. was extracted with CH_2Cl_2 (3 ×) and washed with H_2O. The org. layer was dried (Na_2SO_4) and concentrated to give 3.25 g (98%) of a colorless oil as a mixture of diastereoisomers. The spectral analyses were in agreement with those described in [39].

(±)-6,7-Epoxy-3,7-dimethyloctanal ((±)-**25**). The compound was prepared as described above for **35** with 3.0 g (19.5 mmol) of citronellal. *Kugelrohr* distillation gave 1.75 g (53%) of an unstable, colorless oil (mixture of diastereoisomers). B.p. *ca.* 110°/0.05 mbar. IR (neat): 3468*w*, 2956*m*, 2925*m*, 2872*m*, 2819*w*, 2716*w*, 1721*s*, 1458*m*, 1431*w*, 1409*w*, 1378*m*, 1329*w*, 1249*m*, 1182*w*, 1119*m*, 1097*w*, 1072*w*, 1048*w*, 1022*m*, 979*w*, 943*w*, 899*m*, 890*m*, 869*m*, 795*m*, 740*w*, 677*m*. ^{1}H-NMR (360 MHz, (D_6)acetone): 9.77–9.69 (*m*, 1 H); 2.63 (*t*, $J = 5.9$, 1 H); 2.51–2.39 (*m*, 1 H); 2.33–2.21 (*m*, 1 H); 2.18–2.03 (*m*, 1 H); 1.64–1.27 (*m*, 4 H); 1.23 (*s*, 3 H); 1.22 (*s*, 3 H); 0.96 (*d*, $J = 6.7$, 3 H). ^{13}C-NMR (90.6 MHz, (D_6)acetone): 202.72 (*d*); 64.19 (*d*); 57.97 (*s*); 57.87 (*s*); 51.43 (*t*); 51.26 (*t*); 34.26 (*d*); 28.45 (*d*); 27.09 (*t*); 25.03 (*q*); 20.16 (*q*); 20.02 (*q*); 18.92 (*q*); 18.89 (*q*). EI-MS: 155 (6), 127 (7), 113 (6), 112 (9), 111 (3), 98 (4), 97 (54), 95 (15), 93 (4), 86 (4), 85 (42), 84 (33), 83 (13), 81 (9), 79 (6), 72 (4), 71 (20), 70 (10), 69 (38), 68 (12), 67 (15), 60 (3), 59 (100), 58 (9), 57 (22), 56 (26), 55 (31), 53 (5), 44 (4), 43 (43), 42 (18), 41 (48), 40 (4), 39 (20), 31 (4), 29 (12), 27 (10).

(±)-6,7-Epoxy-3,7-dimethyloctyl 3-Methyl-2-oxopentanoate ((±-(**26**). *Ca.* 100 mg of (±)-**4** were irradiated with a Xe lamp for 3 h. The compound was taken up with solvent, and small quantities of pure **26** were isolated by repetitive prep. GC on a 500 × 4 mm glass column filled with a *OV-101* stationary phase (10% on 80/100 *Supelcoport*) from 150° with 5°/min to 200° and a He flow of 75 ml/min. Larger quantities of **26** were prepared as described above (*Method C*) with 0.78 g (4.2 mmol) of (±)-ethyl 3-methyl-2-oxopentanoate, 1.00 g (5.8 mmol) of **35**, and 10 drops of $NaOCH_3$ (30% in MeOH) in 10 ml of cyclohexane for 3 days. Distillation (*Kugelrohr*) afforded 0.75 g (45%) of a colorless oil as a mixture of stereoisomers. B.p. *ca.* 160°/0.05 mbar. UV/VIS (hexane): 393 (sh, 3), 383 (sh, 6), 374 (sh, 9), 365 (sh, 12), 356 (sh, 15), 349 (16), 335 (17), 289 (31), 281 (34). IR (neat): 3440*w*, 2962*m*, 2925*m*, 2875*m*, 1724*s*, 1459*m*, 1433*w*, 1378*m*, 1326*w*, 1265*m*, 1249*m*, 1164*m*, 1119*m*, 1094*w*, 1047*s*, 1013*m*, 1001*m*, 960*m*, 893*w*, 868*m*, 858*m*, 792*m*, 705*w*, 678*m*. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.38–4.24 (*m*, 2 H); 3.20–3.07 (*m*, 1 H); 2.74-2.66 (*m*, 1 H); 1.90–1.70 (*m*, 2 H); 1.70–1.20 (*m*, 6 H); 1.31 (*s*, 3 H); 1.27 (*s*, 3 H); 1.14 (*dd*, $J = 7.4$, 1.5, 3 H); 0.96 (*d*, $J = 6.4$, 3 H); 0.92 (*dt*, $J = 7.4$, 1.0, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 198.14 (*s*); 162.02 (*s*); 64.65 (*d*); 64.54 (*t*); 64.41 (*d*); 58.25 (*s*); 43.59 (*d*); 35.24 (*t*); 35.06 (*t*); 33.47 (*t*); 29.72 (*d*); 26.35 (*t*); 26.27 (*t*); 29.42 (*t*, *q*); 19.33 (*q*); 19.23 (*q*); 18.72 (*q*); 18.67 (*q*); 14.59 (*q*); 14.54 (*q*); 11.35 (*q*). EI-MS: 169 (3), 156 (6), 155 (4), 141 (3), 123 (3), 113 (12), 109 (6), 99 (5), 98 (6), 97 (51), 96 (3), 95 (13), 86 (7), 85 (87), 84 (4), 83 (10), 82 (6), 81 (9), 71 (13), 70 (3), 69 (28), 68 (7), 67 (6), 59 (25), 58 (7), 57 (100), 56 (6), 55 (41), 43 (22), 42 (5), 41 (31), 39 (6), 29 (11), 27 (3).

(±)-6,7-Epoxy-3,7-dimethyloctyl 2-Cyclohexyl-2-oxoacetate ((±)-**27**). As described above (*Method C*) with 0.90 g (4.9 mmol) of **19**, 1.15 g (6.7 mmol) of **35**, and 2–3 drops of $NaOCH_3$ (30% in MeOH) in 15 ml of cyclohexane. CC (SiO_2; heptane/Et_2O 8:2) afforded 1.05 g (69%) of a colorless oil as a mixture of stereoisomers. B.p. *ca.* 200°/0.05 mbar. UV/VIS (hexane): 395 (sh, 4), 384 (sh, 7), 375 (sh, 11), 366 (sh, 15), 357

(sh, 17), 350 (sh, 19), 337 (20), 321 (sh, 19), 290 (sh, 16), 281 (sh, 22), 273 (sh, 26). IR (neat): 2956*m*, 2926*m*, 2854*m*, 1722*s*, 1450*m*, 1377*m*, 1327*w*, 1310*w*, 1289*w*, 1274*m*, 1252*m*, 1228*m*, 1183*w*, 1139*m*, 1119*m*, 1082*m*, 1066*m*, 1027*w*, 996*m*, 942*w*, 894*w*, 869*m*, 788*w*, 740*w*, 717*w*, 679*w*. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.37–4.23 (*m*, 2 H); 3.09–2.93 (*m*, 1 H); 2.69 (*t*, *J* = 6.1, 1 H); 1.96–1.73 (*m*, 5 H); 1.73–1.15 (*m*, 12 H); 1.31 (*s*, 3 H); 1.27 (*s*, 3 H); 0.96 (*d*, *J* = 6.3, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 197.53 (*s*); 162.14 (*s*); 64.47 (*t*); 64.38 (*d*); 58.28 (*s*); 58.18 (*s*); 46.33 (*d*); 35.25 (*t*); 35.08 (*t*); 33.51 (*t*); 33.48 (*t*); 29.72 (*d*); 27.47 (*t*); 26.36 (*t*); 26.28 (*t*); 25.71 (*t*); 25.28 (*t*); 24.88 (*q*); 19.34 (*q*); 19.24 (*q*); 18.73 (*q*); 18.68 (*q*). EI-MS: 113 (6), 112 (3), 111 (38), 110 (3), 109 (5), 97 (28), 95 (7), 85 (9), 84 (7), 83 (100), 82 (5), 81 (6), 71 (6), 69 (15), 68 (4), 67 (5), 59 (12), 57 (5), 56 (3), 55 (38), 43 (11), 42 (3), 41 (15), 39 (4).

(±)-6,7-Epoxy-3,7-dimethyloctyl 2-Oxo-2-phenylacetate ((±)-**28**). As described above (*Method C*) with 0.75 g (5.2 mmol) of ethyl 2-oxo-2-(phenyl)acetate, 1.00 g (5.8 mmol) of **35**, and 3 drops of $NaOCH_3$ (30% in MeOH) in 10 ml of cyclohexane. CC (SiO_2; heptane/Et_2O 8:2) afforded 0.77 g (49%) of a slightly yellow oil as a mixture of diastereoisomers. UV/VIS (hexane): 413 (sh, 4), 393 (sh, 12), 369 (sh, 35), 352 (47), 340 (46), 330 (sh, 38), 293 (sh, 1100), 284 (sh, 1600), 252 (11400), 249 (11400). IR (neat): 3064*w*, 2958*m*, 2923*m*, 2870*w*, 1733*s*, 1687*s*, 1596*m*, 1451*m*, 1379*m*, 1318*m*, 1297*m*, 1249*w*, 1196*s*, 1173*s*, 1120*m*, 1028*w*, 983*s*, 943*w*, 894*w*, 869*w*, 832*w*, 796*w*, 745*m*, 677*s*. ^{1}H-NMR (360 MHz, $CDCl_3$): 8.05–7.96 (*m*, 2 H); 7.71–7.62 (*m*, 1 H); 7.57–7.47 (*m*, 2 H); 4.52–4.37 (*m*, 2 H); 2.73–2.65 (*m*, 1 H); 1.93–1.77 (*m*, 1 H); 1.75–1.20 (*m*, 6 H); 1.30 (*s*, 3 H); 1.26 (*s*, 3 H); 0.98 (*d*, *J* = 6.3, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): 186.38 (*s*); 163.94 (*s*); 134.92 (*d*); 132.47 (*s*); 130.02 (*d*); 128.92 (*d*); 64.62 (*t*); 64.39 (*d*); 58.32 (*s*); 35.31 (*t*); 35.15 (*t*); 33.51 (*t*); 33.46 (*t*); 29.68 (*d*); 26.35 (*t*); 26.29 (*t*); 24.87 (*q*); 19.34 (*q*); 19.26 (*q*); 18.73 (*q*); 18.68 (*q*). EI-MS: 304 (1, M^+), 171 (3), 153 (3), 152 (4), 125 (3), 113 (5), 106 (9), 105 (100), 97 (9), 95 (5), 85 (5), 83 (6), 82 (3), 81 (3), 77 (26), 71 (6), 69 (15), 68 (3), 67 (3), 59 (8), 57 (5), 56 (4), 55 (19), 51 (7), 43 (16), 42 (3), 41 (15), 39 (4), 29 (5), 27 (3).

(±)-6,10,10-Trimethyl-1-phenyl-3,11-dioxabicyclo[7.2.0]undecan-2-one ((±)-**29**) [27][31]. A soln. of 95.4 mg of (±)-**9** in 2 ml of MeCN was irradiated for 3 h with a Xe lamp. Repetitive prep. GC using a 1500 × 5.5 mm glass column filled with an apolar *OV-101* stationary phase at 70° for 10 min then to 230° with 8°/min yielded a colorless oil as a mixture of diastereoisomers. ^{1}H-NMR (360 MHz, $CDCl_3$): major isomer: 7.56–7.50 (*m*, 2 H); 7.42–7.33 (*m*, 2 H); 7.33–7.24 (*m*, 1 H); 4.82–4.74 (*m*, 1 H); 3.86–3.74 (*m*, 1 H); 2.97–2.86 (*m*, 1 H); 2.20–1.20 (*m*, 7 H); 1.41 (*s*, 3 H); 1.24 (*s*, 3 H); 0.93 (*d*, *J* = 6.7, 3 H). ^{13}C-NMR (90.6 MHz, $CDCl_3$): major isomer. 171.57 (*s*); 141.98 (*s*); 127.98 (*d*); 127.42 (*d*); 126.03 (*d*); 84.25 (*s*); 82.63 (*s*); 66.24 (*t*); 52.71 (*d*); 31.49 (*d*); 30.82 (*q*); 30.57 (*t*); 30.31 (*t*); 23.96 (*q*); 21.15 (*q*); 17.89 (*t*). EI-MS: 288 (2, M^+), 244 (15), 229 (5), 173 (5), 160 (5), 159 (29), 157 (4), 145 (3), 129 (3), 128 (3), 122 (3), 115 (7), 106 (9), 105 (100), 95 (3), 81 (4), 77 (18), 69 (4), 55 (3), 41 (4).

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REFERENCES

[1] Parts of this publication are the subject of a patent application: J. Pika, A. Herrmann, C. Vial, to *Firmenich SA*, PCT Int. Patent Appl. WO 99/60990, 1999; *Chem. Abstr.* **2000**, *132*, 15499.
[2] S. Arctander, 'Perfume and Flavor Chemicals', published by the author, Montclair, 1969.
[3] G. S. Hammond, P. A. Leermakers, N. J. Turro, *J. Am. Chem. Soc.* **1961**, *83*, 2395.
[4] N. C. Yang, A. Morduchowitz, *J. Org. Chem.* **1964**, *29*, 1654.
[5] P. A. Leermakers, M. E. Ross, G. F. Vesley, P. C. Warren, *J. Org. Chem.* **1965**, *30*, 914.
[6] D. S. Kendall, P. A. Leermakers, *J. Am. Chem. Soc.* **1966**, *88*, 2766.
[7] E. S. Huyser, D. C. Neckers, *J. Org. Chem.* **1964**, *29*, 276.
[8] a) R. S. Davidson, D. Goodwin, *J. Chem. Soc., Perkin Trans. 2* **1982**, 993; b) M. V. Encinas, E. A. Lissi, A. Zanocco, L. C. Stewart, J. C. Scaiano, *Can. J. Chem.* **1984**, *62*, 386; c) J. C. Scaiano, M. V. Encinas, E. A. Lissi, A. Zanocco, P. K. Das, *J. Photochem.* **1986**, *33*, 229; d) Y. Chiang, A. J. Kresge, P. Pruszynski, N. P. Schepp, J. Wirz, *Angew. Chem.* **1990**, *102*, 810; *Angew. Chem., Int. Ed.* **1990**, *29*, 792.
[9] S. Hu, D. C. Neckers, *J. Org. Chem.* **1996**, *61*, 6407.
[10] M. C. Pirrung, R. J. Tepper, *J. Org. Chem.* **1995**, *60*, 2461.
[11] a) R. S. Davidson, D. Goodwin, J. E. Pratt, *Tetrahedron* **1983**, *39*, 1069; b) R. S. Davidson, D. Goodwin, J. E. Pratt, *Tetrahedron* **1983**, *39*, 2373.

[12] R. W. Binkley, *J. Org. Chem.* **1976**, *41*, 3030.
[13] a) T. R. Evans, P. A. Leermakers, *J. Am. Chem. Soc*. **1968**, *90*, 1840; b) R. S. Davidson, D. Goodwin, P. Fornier de Violet, *Tetrahedron Lett*. **1981**, *22*, 2485; c) A. L. Zanocco, E. A. Soto, E. A. Lissi, J. C. Scaiano, *J. Photochem. Photobiol. A, Chem*. **1990**, *53*, 77.
[14] A. M. Braun, M.-T. Maurette, E. Oliveros, 'Photochemical Technology', J. Wiley & Sons, Chichester, 1991 and refs. cit. therein.
[15] R. D. Small Jr., J. C. Scaiano, *J. Am. Chem. Soc*. **1978**, *100*, 4512.
[16] S. Hu, D. C. Neckers, *J. Photochem. Photobiol. A, Chem*. **1998**, *118*, 75.
[17] Y. Sawaki, Y. Ogata, *J. Am. Chem. Soc*. **1981**, *103*, 6455.
[18] J. M. Brown, in 'Comprehensive Organic Chemistry', Eds. D. Barton, W. D. Ollis, I. O. Sutherland, Pergamon Press, Oxford, 1979, Vol. 2, pp. 779–813 and refs. cit. therein.
[19] a) Organikum; 17th Ed., VEB Verlag der Wissenschaften, Berlin 1988, p. 403; b) D. Basavaiah, T. K. Bharathi, P. Rama Krishna, *Synth. Commun.* **1992**, *22*, 941.
[20] R. Pelzer, H.-D. Scharf, H. Buschmann, J. Runsink, *Chem. Ber*. **1989**, *122*, 1187.
[21] H. C. J. Ottenheijm, J. H. M. de Man, *Synthesis* **1975**, 163.
[22] a) R. W. Stoughton, to *Mallinckrodt Chem. Works*, US Patent 2,338,064, 1943; *Chem. Abstr.* **1944**, *38*, 3422(1); b) W. J. Middleton, E. M. Bingham, *J. Org. Chem.* **1980**, *45*, 2883; c) L. M. Weinstock, R. B. Currie, A. V. Lovell, *Synth. Commun.* **1981**, *11*, 943; d) Y. Akiyama, S. Takebayashi, T. Kawasaki, M. Sakamoto, *Chem. Pharm. Bull*. **1984**, *32*, 1800; e) X. Creary, *J. Org. Chem*. **1987**, *52*, 5026; f) M. Ramboud, M. Bakasse, G. Duguay, J. Villieras, *Synthesis* **1988**, 564.
[23] R. M. Sayre, C. Cole. W. Billhimer, J. Stanfield, R. D. Ley, *Photodermatol. Photoimmunol. Photomed*. **1990**, *7*, 159.
[24] a) R. G. Parr, W. Yang, 'Density Functional Methods in Atoms and Molecules', Oxford University Press, New York, 1989; b) J. W. Labanowski, J. Andzelm, 'Density Functional Methods in Chemistry', Springer Verlag, New York, 1991.
[25] T. Bally, W. T. Borden, in 'Reviews in Computational Chemistry', Eds. K. B. Lipkowitz, D. B. Boyd, VCH Publishers, New York, 1990, Vol. 13, pp. 1–88.
[26] H. Ihmels, J. R. Scheffer, *Tetrahedron* **1999**, *55*, 885.
[27] S. Hu, D. C. Neckers, *J. Org. Chem*. **1997**, *62*, 564.
[28] T. Shono, Y. Matsumura, J. Hayashi, K. Inoue, F. Iwasaki, T. Itoh, *J. Org. Chem*. **1985**, *50*, 4967.
[29] N. Shimizu, P. D. Bartlett, *J. Am. Chem. Soc*. **1976**, *98*, 4193.
[30] a) G. Ohloff, B. Lienhard, *Helv. Chim. Acta* **1965**, *48*, 182; b) T. Petrzilka, M. Demuth, *Helv. Chim. Acta* **1974**, *57*, 121.
[31] S. Hu, D. C. Neckers, *J. Org. Chem*. **1997**, *62*, 6820.
[32] a) N. L. Allinger, *J. Am. Chem. Soc*. **1997**, *99*, 8127; b) U. Burkert, N. L. Allinger, 'Molecular Mechanics', American Chemical Society, Washington D.C., 1982.
[33] J. J. P. Stewart, *J. Comput. Chem*. **1989**, *10*, 209.
[34] S. C. Freilich, K. S. Peters, *J. Am. Chem. Soc*. **1985**, *107*, 3819, and refs. cit. therein.
[35] A. Herrmann, C. Debonneville, V. Laubscher, L. Aymard, *Flavour Fragr. J.*, in press.
[36] F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Henrickson, W. C. Still, *J. Comput. Chem.* **1990**, *11*, 440.
[37] H. Gilman, N. B. St. John, F. Schulze, *Org. Synth.*, *Coll. Vol. II* **1943**, 425.
[38] R. G. Neville, *J. Org. Chem*. **1959**, *24*, 111.
[39] K. J. Barr, S. C. Berk, S. L. Buchwald, *J. Org. Chem*. **1994**, *59*, 4323.

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