170. Synthesis of (+)-(2*S*,6*S*)-*trans*-α-Irone and of (−)-(2*S*,6*S*)-*trans*-γ-Irone[1])

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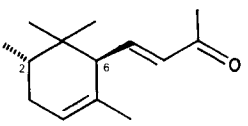
(26. VII. 89)

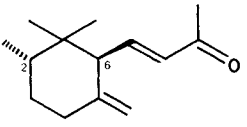
A 3:1 mixture of (+)-(2*S*,6*S*)-*trans*-α-irone ((+)-**1**) and (−)-(2*S*,6*S*)-*trans*-γ-irone ((−)-**2**) has been synthesized with *ca.* 70% e.e. by the ene reaction of (−)-(*S*)-**3** and but-3-yn-2-one.

Introduction. – One of the main constituents of *Iris* oil is (+)-(2*S*,6*S*)-*trans*-α-Irone[2]) ((+)-(2*S*,6*S*)-**1**) [1–3]. In spite of more than forty years of synthetic activity around the irones[3]), there were only a few attempts to prepare them enantioselectively. *Yoshikoshi* and coworkers [5] described the synthesis of (−)-(2*R*,6*R*)-**1** from (+)-(*R*)-citronellal, and more recently, *Rautenstrauch et al.* [2] reported a route to (+)-**1** from (−)-α-pinene by a variant of *Eschinazi*'s synthesis [6].

The natural occurrence of *trans*-γ-irone (**2**) of as yet unkown absolute configuration has only been proved very recently [2]. Nevertheless, three syntheses of the racemate (±)-**2** [7–9] and one of (+)-(*2R,6R*)-**2** [5] have already been reported.



(+)-(2*S*,6*S*)-**1**[2])



(−)-(2*S*,6*S*)-**2**[2])

In pursuit of our interest in the synthesis of irones[4]), we describe now the preparation of the title compounds (+)-(2*S*,6*S*)-**1** and (−)-(2*S*,6*S*)-**2**. Our approach is based on the potentially straightforward ene reaction of (−)-(*S*)-1,3,3,4-tetramethylcyclohex-1-ene ((−)-**3**) with but-3-yn-2-one *(vide infra)*. *Prins* reactions of (±)-**3** have been described [11–13], and ene reactions of butynone [14] have also been mentioned[5]).

Results and Discussion. – First, the *Lewis*-acid-catalysed ene reaction of but-3-yn-2-one with (±)-**3** was investigated. The required olefin was prepared by *Wolff-Kishner*

[1]) Presented by *D. Helmlinger* at the Meeting of the Swiss Chemical Society, Bern, October 18th, 1985.

[2]) This numbering is according to the IUPAC rules for the nomenclature of carotenoids (see [2]), and we will use it when referring to irones in order to avoid confusion. In the *Exper. Part* and for the discussion of the NMR spectra, the IUPAC rules for general organic chemistry are followed.

[3]) See ref. 4–9 in [4] for the literature up to 1979.

[4]) For the stereoselective synthesis of (±)-*cis*-α-irone, see [10a], for that of (±)-*cis*-γ-irone, see [10b].

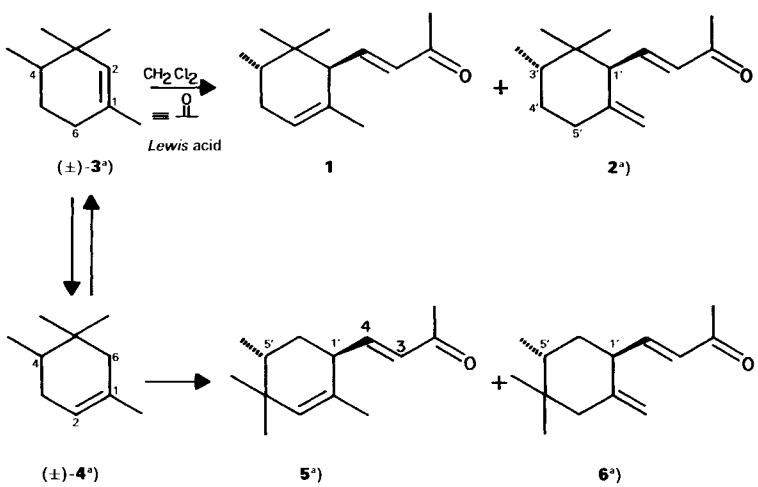
[5]) Ene reactions of the closely related ethyl propynoate are reported in more detail [15].

Table. Lewis-*Acid-Catalysed Ene Reaction of* (±)-**3**. In CH_2Cl_2, at r.t.

Lewis acid	Overall yield [%]	Composition [%][7])			
		1	**2**	**5**	**6**
$ZnCl_2$	51	42	20	15	15
$ZnBr_2$	51	51	24	6.5	10
ZnI_2	60.5	75	20	0.6	4

reduction of 2,2,4-trimethylcyclohex-3-ene-1-carbaldehyde [16][6]) in 80% yield. Reaction of (±)-**3** with but-3-yn-2-one in the presence of $ZnCl_2$ in CH_2Cl_2 furnished a mixture of four main products in 51% yield, *i.e.* **1**, **2**, **5**, and **6** (see *Scheme 1* and the *Table*). Small amounts of cyclobutene derivatives were also detected as a mixture of four components (*ca.* 2.5%, GC/MS) which we did not elucidate further. The *trans* configuration of the 1,3-disubstituted cyclohexene ring could be established for all four compounds by NMR spectroscopy and by comparison with authentic samples[8]).

Scheme 1



a) Systematic numbering.

^{1}H-NMR Experiments with **5**. Irradiation of CH_3–C(5′) showed H–C(5′) as a *dd* at 1.5 ppm with $J \approx 12$ and 3 Hz; this is in agreement with the pseudoaxial position of H–C(5′) and a pseudoequatorial one of CH_3–C(5′). On the other hand, irradiation of H–C(4) resulted in the appearance of H–C(1′) as a *dd* at 2.72 ppm with $J \approx 6$ and *ca.* 2.3 Hz, which is in accord with a pseudoequatorial H–C(1′) and a pseudoaxial side chain.

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[6]) From this common intermediate, *i.e.* from the corresponding alcohol, *cis*-α- and *cis*-γ-irone have been prepared [10].

[7]) All compounds are stable under the reaction conditions ($ZnCl_2$ or ZnI_2, but-3-yn-2-one in CH_2Cl_2, 3 days).

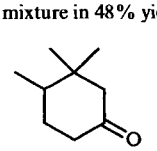
[8]) Racemic *trans*-α-irone (**1**) is the main constituent (51%) of *Irone alpha*® *(Givaudan)*; *cis*-α-irone and *cis*-γ-irone have been synthesized by ourselves [10]; a 3:1 mixture of *trans*-γ-irone and *cis*-γ-irone was at our disposal, kindly furnished by the late Prof. *Leyendecker* [17].

^{1}H-NMR Experiments with **6**. Double-resonance experiments with an [Eu(fod)$_3$]-complexed solution revealed H–C(5') again as a *dd* with $J \approx 11$ and 3.3 Hz, indicating H–C(5') to be pseudoaxial. At the same time, $J(1',6') \approx 4$ and 5 Hz could be deduced, establishing H–C(1') to be pseudoequatorial and the side chain pseudoaxial. Thus, both **5** and **6** have a *trans*-relationship between the substituents on C(1') and C(5'), and both prefer a conformation with pseudoaxial side chain.

The preference of **1** to adopt a conformation with pseudoaxial side chain has already been discussed [1] [2] [8]. Also **2** prefers a conformation with pseudoaxial side chain, as established by a [Eu(fod)$_3$]-shifted ^{1}H-NMR spectrum, in which H_{ax}–C(4') is visible at 1.45 ppm as a *dddd*: $J_{gem} \approx J(4'_{ax},3'_{ax}) \approx J(4'_{ax},5'_{ax}) \approx 12$ Hz, $J(4'_{ax},5'_{eq}) \approx 5$ Hz. From this follows that CH_3–C(3') is pseudoequatorial, *i.e.* the compound being *trans*, the side chain must be pseudoaxial.

Having also the *cis* isomers at our disposal[8]), the *trans*/*cis* ratio of the ene-reaction products **1** and **2** was easily determined to be *ca.* 20 by GLC analysis. This high selectivity is better than anticipated on grounds of the examples in [15b]. In want of the *cis* analogues of **5** and **6**, we can only state that the *trans*/*cis* ratio in these products, based on GLC analysis, is probably even more in favour of the *trans* products than in the case of **1** and **2**.

For a more efficient preparation of **5** and **6**, we used also a 3:1 mixture (±)-**4**/(±)-**3** which was obtained by methylcuprate addition on 3,4-dimethylcyclohex-2-en-1-one [19] followed by a *Grignard* reaction on the resulting 3,3,4-trimethylcyclohexanone [20] (**7**); Dehydration of the resulting 1,3,3,4-tetramethylcyclohexan-1-ol (**8**) with oxalic acid furnished (±)-**4**/(±)-**3** in a 3:1 ratio (*cf.* [21]). Ene reaction of this mixture with butynone ($ZnCl_2$, CH_2Cl_2, r.t.) led to the following mixture in 48% yield: 6.5% of **1**, 3% of **2**, 42% of **5**, and 42% of **6**.



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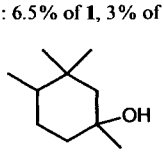

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The formation of the isomeric compounds **5** and **6** from (±)-**3** shows that prior to the ene reaction partial isomerisation (±)-**3** → (±)-**4** must have taken place[9]). To avoid the formation of these unwanted isomers **5** and **6**, we changed the *Lewis* acid *(Table)*. Reaction with $ZnBr_2$ showed a considerable improvement with only 6.5% of **5** and 10% of **6** being formed, and ZnI_2 not only raised the overall yield to 60.5%, but suppressed the formation of **5** and **6** nearly completely[10]).

The favoured *trans* configuration of the four products **1**, **2**, **5**, and **6** can be rationalised in the following manner. CH_3–C(4) in (±)-**3** and -**4** are pseudoequatorial. In the transition state the butynone/*Lewis* acid complex will approach (±)-**3** and -**4** from the *trans* side with respect to this pseudoequatorial CH_3 group. This is notably the side with the pseudoequatorial CH_3 of the geminal dimethyl group, and also with the pseudoaxial H–C(6) in (±)-**3** and -**4**, the transfer of which leads to **1** and **5**, respectively [15c]. In an analogous transition state, the transfer of an H-atom from CH_3–C(1) in (±)-**3** and -**4** leads to the γ-derivatives **2** and **6**, respectively.

Next, we prepared (–)-(*S*)-**3** in order to be able to carry out the ene reaction in the non-racemic series. Thus, aldehyde (–)-(*S*)-**9** [22] [23] ($[\alpha]_D^{20} = -49.2$ ($c = 1.14$, $CHCl_3$))

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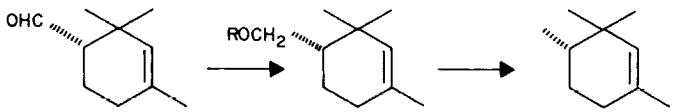
[9]) Cyclohexene (±)-**3** is completely stable when treated with $ZnCl_2$ in CH_2Cl_2, but obviously, it is not stable when butynone is also present. Probably, the proton necessary for isomerisation (see also [11]) originates from the complex between butynone and $ZnCl_2$.

[10]) Other *Lewis* acids like $TiCl_4$, $SnCl_4$, $AlEt_2Cl$, $CdCl_2$, $HgCl_2$ gave lower yields of different, partly unknown mixtures.

was reduced to alcohol (−)-(*S*)-**10** [23] ($[\alpha]_D^{20} = -30.6$ ($c = 1.0$, $CHCl_3$)). These two [α] values correspond to 82 and 73.5% e.e., respectively, when compared with the values of *Pfander et al.* [21], indicating a slight racemisation during $LiAlH_4$ reduction of (−)-(*S*)-**9**. For a double check, we recorded the NMR spectrum of the acetate (−)-(*S*)-**11** in the presence of an optishift reagent. The splitting of each of the geminal dimethyl groups in the ratio of *ca.* 85:15 indicated an e.e. of 70%. Finally, hydride reduction of the mesylate (−)-(*S*)-**12** furnished (−)-(*S*)-**3** ($[\alpha]_D^{20} = -68$ ($c = 1$, $CHCl_3$))[11]).

Scheme 2



(−)-(*S*)-**9** (−)-(*S*)-**10** R = H; (−)-(*S*)-**11** R = Ac; (−)-(*S*)-**12** R = Ms (−)-(*S*)-**3**

The ene reaction of (−)-(*S*)-**3** with butynone in the presence of ZnI_2 yielded (+)-(2*S*,6*S*)-*trans*-α-irone ((+)-(2*S*,6*S*)-**1**) and (−)-(2*S*,6*S*)-*trans*-γ-irone ((−)-(2*S*,6*S*)-**2**) in the ratio of 3:1.

The optical purity of (+)-(2*S*,6*S*)-**1** was *ca.* 70% as expected from the starting material (−)-(*S*)-**3** (see (−)-(*S*)-**11**); the $[\alpha]_D^{20} = +297$ ($c = 1$, $CHCl_3$) is in good agreement with the literature values [1] [2] [5] and also with NMR experiments in the presence of optishift reagents where the signal of one of the geminal dimethyl groups split up in the ratio of *ca.* 85:15. The optical purity of (−)-(2*S*,6*S*)-**2** should be the same as that of the α-isomer. In fact, optishift experiments confirmed this showing again one of the geminal dimethyl groups in a *ca.* 85:15 ratio. However, the optical rotation ($[\alpha]_D^{20} = -43.3$ ($c = 0.8$, CH_2Cl_2; GLC 100%)) is not in agreement with the only other literature value [5], which is $[\alpha]_D^{20} = +57$ ($c = 0.33$, CH_2Cl_2) for a sample with a reported 76% e.e.

Whe thank Mr. *M. Graf* and Miss *C. Ebner* for experimental work, Mr. *J. Märki* for the NMR spectra, and Dr. *J. Schmid* for the mass spectra.

Experimental Part

General. Column chromatography: silica gel *60 Merck* (0.04–0.063) neat or impregnated with 10% $AgNO_3$. TLC: silica gel plates *60 F_{254} (Merck)*; detection by UV light or/and reagent prepared from *p*-anisaldehyde (1 ml), conc. H_2SO_4 (2 ml), and AcOH (100 ml). GLC: *C. Erba Fractovap 2101 AC*, capillary column *UCON 50 HB 5100* (30 m, 0.3 mm). $[\alpha]_D$: *Perkin Elmer 141* polarimeter. IR: *Perkin Elmer 257*. NMR: ^1H spectra on *Bruker AM-400*, ^{13}C spectra on *Varian XL-100* at 25 MHz, in $CDCl_3$ with TMS as internal standard, chemical shifts in ppm, coupling constants *J* in Hz. The enantiomeric excess (e.e.) has been determined by ^1H-NMR in presence of [Eu(hfc)$_3$] (= tris{3-[(heptafluoropropyl)hydroxymethylidene]camphorato}europium(III); *Aldrich*). MS: *Varian MAT CH-5* instrument; 70 eV, relative peak intensities in % of the base peak (= 100%).

[11]) The direct *Wolff-Kishner* reduction of (−)-(*S*)-**9** caused complete racemisation (see [13]).

1,3,3,4-Tetramethylcyclohex-1-ene ((±)-**3**). For 1.5 h, 2,2,4-trimethylcyclohex-3-ene-1-carbaldehyde ((±)-**9**) [16] (15 g, 0.1 mol) was heated to reflux in the mixture of K_2CO_3 (25 g, 0.18 mol), hydrazine hydrate *(Fluka, purum)* (25.7 g, 0.5 mol) triethylene glycol (250 ml). Then, (±)-**3** was distilled from the mixture through a small column at 80–100°/*ca.* 30 Torr. The H_2O which separated was re-added into the reaction flask. The product was dried and redistilled at 55–58°/20 Torr: 11 g (79.5%). ^{1}H-NMR: 5.07 (br. *s*, H–C(2)); 1.98–1.73 (*m*, 2 H); 1.62 (*s*, CH_3–C(1)); 1.54–1.48 (*m*, 1 H); 1.42–1.35 (*m*, 2 H); 0.94, 0.77 (2 *s*, 2 CH_3–C(3)); 0.86 (*d*, CH_3–C(4)). MS: 138 (17, M^+), 123 (100), 105 (5), 96 (41), 93 (6), 91 (14), 81 (80), 79 (13), 77 (10), 69 (12), 67 (21), 57 (22), 55 (25), 43 (20), 41 (33), 39 (18).

3,3,4-Trimethylcyclohexanone (**7**). To the soln. of CH_3MgI (0.45 mol) in Et_2O (140 ml), prepared from Mg (10.4 g) and CH_3I (64.4 g), CuCl (0.7 g) was added at r.t. To this soln., 3,4-dimethylcyclohex-2-en-1-one [19] (40 g, 0.32 mol) in Et_2O (70 ml) was added at 0–5° during 3 h. The mixture was stirred over night at 20° and worked up as usual. The crude product (41 g) was purified on silica gel (hexane + 2% Et_2O) to yield, after distillation at 60–62°/1.5 Torr, 23.6 g (52%) of **7**. IR (film): 1715, 1370, 1295, 1245, 1195, 1080. ^{1}H-NMR: 2.35–2.3 (*m*, 2 H); 2.22, 2.11 (*AB*, *q*, $J \approx 13$, 2 H–C(2)); 1.93–1.85 (*m*, 1 H); 1.78–1.68 (*m*, 1 H); 1.62–1.54 (*m*, 1 H); 1.0, 0.78 (2*s*, 2 CH_3–C(3)); 0.95 (*d*, CH_3–C(4)). MS: 140 (12, M^+), 125 (6), 112 (1), 107 (2), 98 (5), 83 (71), 69 (13), 56 (100), 55 (58), 43 (28), 41 (46), 39 (24).

1,3,3,4-Tetramethylcyclohexan-1-ol (**8**). To the soln. of CH_3MgI (45 mmol) in Et_2O (20 ml), prepared from Mg (1.1 g) and CH_3I (6.3 g), **7** (5 g, 35 mmol) in Et_2O (15 ml) was added. After 3.5 h reflux and workup as usual, bulb-to-bulb distillation at 80°/1 Torr gave 4.9 g (90%) of **8**. M.p. (pentane) 60–62°. IR ($CHCl_3$): 3600, 1450, 1350, 1190, 1040, 895. ^{1}H-NMR: 1.67–1.23 (*m*, 6 H); 1.22–1.12 (*m*, 1 H); 1.17 (*s*, 3 H); 1.02–0.97 (br. *s*, OH); 0.95 (*s*, 3 H); 0.86 (*s*, 3 H); 0.845 (*d*, 3 H). MS: 156 (1, M^+), 141 (90), 123 (80), 99 (80), 83 (50), 71 (100).

1,4,5,5-Tetramethylcyclohex-1-ene ((±)-**4**) *and 1,3,3,4-Tetramethylcyclohex-1-ene* ((+)-**3**). For 1.5 h, **8** (5 g) and anh. oxalic acid (1.9 g) were heated at 120°. Usual workup yielded 3.5 g (80%) of a 3:1 mixture (±)-**4**/(±)-**3**. ^{1}H-NMR of (±)-**4**: 5.28 (*m*, H–C(2)); 1.61 (br. *s*, CH_3–C(1)); 0.9, 0.75 (2 *s*, 2 CH_3–C(5)); 0.83 (*d*, CH_3–C(4)).

*(3E)-4-(*trans*-2′,4′,4′,5′-Tetramethylcyclohex-2′-en-1′-yl)but-3-en-2-one* (**5**) *and (3E)-4-(*trans*-4′,4′,5′-Trimethyl-2′-methylidenecyclohex-1′-yl)but-3-en-2-one* (**6**). To a soln. of (±)-**4**/(±)-**3** (3:1, 3.4 g, 25 mmol) in CH_2Cl_2 (30 ml) and but-3-yn-2-one [24] (1.8 g, 26 mmol), $ZnCl_2$ (5.2 g, 38 mmol) was added and stirred for 48 h at r.t. After usual workup, the crude product (4.3 g) was chromatographed on silica gel (hexane/Et_2O 95:5) to give 2.6 g (51%) of a mixture of 6.5% of **1**, 3% of **2**, 42% of **5**, and 42% of **6**. Chromatography on $AgNO_3$-impregnated silica gel (hexane/Et_2O 93:7 → 90:10) gave pure **5** and **6**.

5: IR (film): 1700, 1680, 1620, 1360, 1250, 990. ^{1}H-NMR: 6.74 (*dd*, $J(4,3) \approx 16$, $J(4,1') \approx 8$, H–C(4)); 6.01 (*dd*, $J(3,4) = 16$, $J(3,1') \approx 0.5$, H–C(3)); 5.28 (br. *s*, H–C(3′)); 2.72 (*ddd*, $J(1',4) \approx 8$, $J(1',6'ax) \approx 6$, $J(1',6'eq) \approx 2.3$, H–C(1′)); 2.27 (*s*, CH_3(1)); 1.68 (*ddd*, $J(6'ax,5'ax) \approx 12$, $J(6'ax,6'eq)) \approx 13$, $J(6'ax,1') \approx 6$, H_{ax}–C(6′)); 1.5 (*m*, $J(5'ax,6'ax) \approx 12$, $J(5'ax,6'eq) \approx 3$, $J(5'ax, CH_3$–C(5)) ≈ 7, H_{ax}–C(5′)); 1.43 (*ddd*, $J(6'eq,6'ax) \approx 13$, $J(6'eq, 1') \approx 2.3$, $J(6'eq,5'ax) \approx 3$, H_{eq}–C(6′)); 0.79, 0.96 (2*s*, 2 CH_3–C(4′)); 0.86 (*d*, $J \approx 7$, CH_3–C(5′)). MS: 206 (13, M^+), 191 (51), 173 (7), 163 (16), 149 (22), 133 (38), 121 (53), 107 (30), 95 (41), 91 (27), 79 (13), 71 (24), 67 (13), 55 (33), 43 (100).

6: IR (film): 1700, 1680, 1620, 1360, 1250. ^{1}H-NMR: 6.88 (*dd*, $J(4,3) = 16$, $J(4,1') = 6$, H–C(4)); 6.09 (*dd*, $J(3,4) \approx 16$, $J(3,1') \approx 2$, H–C(3)); 4.76 (*m*, CH_2=C(2′)); 3.13 (*m*, H–C(1′)); 2.26 (*s*, CH_3(1)); 1.87, 2.01 (*AB*, *q*, $J(3',3') = 13$, CH_2(3′)); 0.85 (*d*, $J \approx 7$, CH_3–C(5′)); 0.73, 0.915 (*2s*, 2 CH_3–C(4′)), after addition of [Eu(fod)$_3$]: 4.24 (*m*, $J(1',6'eq) \approx 5$, $J(1',6'ax) \approx 4$, $J(1',4) \approx 6$, H–C(1′)); 2.27, 2.78 (*AB*, *q*, $J(3',3') \approx 10$, CH_2(3′)); 2.29 (*ddd*, $J(6'eq,6'ax) \approx 13$, $J(6'eq,1') \approx 5$, $J(6'eq,5'ax) \approx 3.3$, H_{eq}–C(6′)); 2.17 (*m*, $J(5'ax,6'ax) \approx 11$, $J(5'ax,6'eq) \approx 3.3$, $J(5'ax, CH_3$–C(5′)) ≈ 7, H_{ax}–C(5′)); 2.08 (*ddd*, $J(6'ax,6'eq) \approx 13$, $J(6'ax,5'ax) \approx 11$, $J(6'ax,1') = 4$, H_{ax}–C(6′)). MS: 206 (1, M^+), 191 (17), 163 (63), 149 (8), 135 (11), 121 (41), 107 (47), 93 (33), 83 (33), 79 (27), 70 (22), 55 (55), 43 (100).

*(–)-(*S*)-2,2,4-Trimethylcyclohex-3-ene-1-carbaldehyde* ((–)-**9**). Preparation according to [22]. $[\alpha]_D^{20} = -49.2$ ($c = 1.14$, $CHCl_3$; *cf.* [23]).

*(–)-(*S*)-2,2,4-Trimethylcyclohex-3-ene-1-methanol* ((–)-**10**). Preparation according to [23]. $[\alpha]_D^{20} = -30.6$ ($c = 1.0$, $CHCl_3$).

*(–)-(*S*)-2,2,4-Trimethylcyclohex-3-ene-1-methyl Acetate* ((–)-**11**). From (–)-**10** with Ac_2O and pyridine. B.p. 55–60°/0.01 Torr (bulb-to-bulb). $[\alpha]_D^{20} = -21.9$ ($c = 1.09$, $CHCl_3$). IR (film): 1740, 1370, 1390, 1240, 1040, 970, 905, 845. ^{1}H-NMR: 5.03 (*m*, H–C(3)); 4.22 ('*dd*', $J = 10, 4$, *A* of *ABX*, 1 H, AcOCH_2); 3.87 ('*dd*', $J = 10, 9$, *B* of *ABX*, 1 H, AcOCH_2); 2.06 (*s*, Ac); 1.62 (*s*, CH_3–C(4)); 1.03, 0.85 (2 *s*, 2 CH_3–C(2)); after addition of [Eu(hfc)$_3$], each of the 2 $(CH_3)_2$C signals was split into 2 *s* in the ratio of *ca.* 85:15 at 1.28 and 1.12 ppm. MS: 136 (26, M^+ – AcOH), 121 (95), 107 (12), 96 (20), 93 (56), 81 (32), 67 (8), 53 (11), 43 (100).

(−)-(S)-2,2,4-Trimethylcyclohex-3-ene-1-methyl Methanesulfonate ((*S*)-**12**). A soln. of (−)-**10** (30.8 g, 0.2 mol) in pyridine (100 ml) was treated dropwise with CH_3SO_2Cl (25.7 g, 0.22 mol) at 5°. After further stirring at r.t. for 4 h, the mixture was poured on ice and extracted with CH_2Cl_2. The org. phase was washed with 2N HCl and H_2O and dried ($MgSO_4$): 42.7 g (92%) of **12**. IR (film): 1380, 1180, 990, 960, 860. ^{1}H-NMR: 5.02 (*m*, H–C(3)); 4.37 (*dd*, $J \approx 9, 5$, 1 H CH_2O); 4.01 (*dd*, $J \approx 9, 9$; 1 H, CH_2O); 3.02 (*s*, CH_3SO_3); 1.63 (*s*, CH_3–C(4)); 1.06, 0.85 (2 *s*, 2 CH_3–C(2)). MS: 232 (M^+, 0.5), 136 (20), 121 (100), 105 (14), 96 (15), 93 (46), 81 (22), 79 (21), 67 (6), 55 (8), 53 (5), 41 (7).

(−)-(S)-1,3,3,4-Tetramethylcyclohex-1-ene ((−)-(*S*)-**3**). To a suspension of $LiAlH_4$ (10.5 g, 0.27 mol) in THF (300 ml), the soln. of (*S*)-**12** (42.7 g, 0.18 mol) in THF (50 ml) was added dropwise within 15 min. Thereupon, the mixture was heated under reflux for 4 h. After stirring overnight at r.t., $Na_2SO_4 \cdot 10\,H_2O$ was slowly added until the excess of $LiAlH_4$ was destroyed. Usual workup with H_2O and pentane and distillation at 35–60°/*ca.* 25 Torr furnished 21 g (85%) of a crude product which was purified on silica gel (pentane) and distilled on a 10-cm column at 45–46°/11 Torr: 12.5 g (50.4%) of pure (−)-(*S*)-**3**. $[\alpha]_D^{20} = -66.7$ ($c = 1.0$, cyclohexane), $[\alpha]_D^{20} = -68.9$ ($c = 1.0$, $CHCl_3$; *cf.* [13]).

(+)-(1'S,5'S,3E)-4-(2',5',6',6'-Tetramethylcyclohex-2'-en-1'-yl)but-3-en-2-one (= (+)-(2*S*,6*S*)-*trans*-α-Irone; (+)-**1**) *and (−)-(1'S,3'S,3E)-4-(2',2',3'-Trimethyl-6'-methylidenecyclohex-1'-yl)but-3-en-2-one* (= (−)-(2*S*,6*S*)-*trans*-γ-Irone; (−)-**2**). The mixture of (−)-(*S*)-**3** (6.9 g, 50 mmol), but-3-yn-2-one (4.0 g, 58 mmol) and ZnI_2 (18.5 g, 58 mmol) in CH_2Cl_2 (60 ml) was stirred at r.t. for 4½ days. Then, more but-3-yn-2-one (4 g, 58 mmol) was added and the mixture stirred for further 3 days. Solvent evaporation gave 31 g of residue which, upon chromatography on silica gel (hexane→hexane/Et_2O 9:1), yielded 6.6 g (64%) of a crude mixture of 72% of (+)-**1**, 20% of (−)-**2**, and small amounts of **5**, **6**, and β-irone. This mixture was finally separated on silica gel impregnated with 10% $AgNO_3$ (hexane/Et_2O 9:1).

(+)-**1**[12]): $[\alpha]_D^{20} = +297$ ($c = 1.1$, $CHCl_3$). GLC: 100% pure. ^{1}H-NMR: 6.69 (*dd*, $J \approx 16$, 10, H–C(4)); 6.03 (*d*, $J \approx 16$, H–C(3)); 5.49–5.44 (*m*, H–C(3')); 2.28 (*d*, $J \approx 10$, H–C(1')); 2.25 (*s*, CH_3(1)); 2.1–2.02 (*m*, H–C(4')); 1.75–1.62 (*m*, H–C(4'), H–C(5')); 1.58–1.55 (*m*, CH_3–C(2')); 0.85, 0.82 (2 *s*, 2 CH_3–C(6')); 0.84 (*d*, CH_3–C(5')). ^{13}C-NMR: 197 (*s*, C(2)); 147.6 (*d*, C(4)); 131.8 (*d*, C(3)); 131.4 (*s*, C(2')); 122.5 (*d*, C(3')); 55.8 (*d*, C(1')); 34.6 (*s*, C(6')); 31.7 (*t*, C(4')); 31.2 (*d*, C(5')); 26.2 (*q*, C(1)); 25.8 (*q*, CH_3–C(6')); 21.9 (*q*, CH_3–C(2')); 20.1 (*q*, CH_3–C(6')); 14.5 (*q*, CH_3–C(5')). MS: 206 (12, M^+), 191 (2), 163 (2), 136 (38), 121 (80), 109 (12), 93 (73), 77 (22), 65 (8), 55 (24), 43 (100).

(−)-**2**[12]): $[\alpha]_D^{20} = -43.3$ ($c = 0.8$, CH_2Cl_2; *cf.* [5]). ^{1}H-NMR: 7.07 (*dd*, $J \approx 16, 9$; H–C(4)); 6.09 (*dd*, $J \approx 16, 0.5$, H–C(3)); 4.77–4.75 (*m*, 1 H, CH_2=C(6')); 4.68–4.5 (*m*, 1 H, CH_2=C(6')); 2.64 (*d*, $J \approx 9$, H–C(1')); 2.24 (*s*, CH_3(1)); 2.25–2.2 (*m*, CH_2(5')); 1.69–1.58 (*m*, CH_2(4')); 1.38–1.28 (*m*, H–C(3')); 0.89, 0.81 (2 *s*, 2 CH_3–C(2')); 0.86 (*d*, CH_3–C(3')). ^{13}C-NMR: 198.4 (*s*, C(2)); 147.7 (*s*, C(6')); 147.5 (*d*, C(4)); 131.7 (*d*, C(3)); 110.3 (*t*, CH_2=C(6')); 59.4 (*d*, C(1')); 37.5 (*s*, C(2')); 36.1 (*d*, C(3')); 31.3 (2*t*, C(4'), C(5')); 27.1 (*q*, C(1)); 26.9 (*q*, CH_3–C(2')); 21.3 (*q*, CH_3–C(2')); 15.4 (*q*, CH_3–C(3')). MS: 206 (2, M^+), 191 (3), 178 (5), 173 (3), 163 (23), 149 (19), 135 (8), 121 (74), 109 (34), 93 (26), 81 (55), 67 (13), 55 (57), 43 (100).

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