Structure/Odor Relationships of (–)- and (+)-β-Vetivone, and Their Demethyl Derivatives

Short Communication

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Dedicated with best wishes to Prof. Dr. *W. Fleischhacker* on the occasion of his 67th birthday

(–)-β-Vetivone ((–)-**3a**), one of the main constituents of vetiver oil, was submitted to a structure/odor relationship study. The influence of the Me groups at the cyclohexenone ring and of the configuration on the odor was examined. Detailed ^{1}H- and ^{13}C-NMR-spectroscopic data were collected, and the absolute configurations were determined by CD methods.

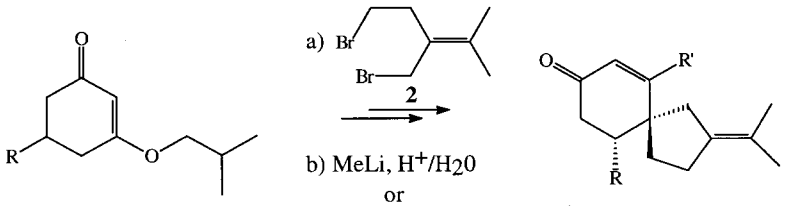
Introduction. – Vetiver oil is, besides the essential oils of sandalwood and patchouli, one of the most important fragrance compounds with woody odor for perfumery industries. The harmonious melting of the heavy-sweet, woody, and earthy notes of the vetiver aroma is unique. Until now, reconstitution of the pleasant vetiver aroma with synthetic compounds has not been achieved, unlike sandalwood, where, *e.g.*, a mixture of isocamphanyl-cyclohexanols (*ca.* 1000 t/year) [2] have been found to mimic its odor. In continuation of our structure/odor relationship studies of vetiver compounds with the aim to devise a synthetic reconstitution strategy allowing the determination of the structural elements necessary for exhibiting the desired odor [3–5], we focused our interest on (–)-β-vetivone ((–)-**3a**). The overwhelming majority of authors attribute to this spirocyclic compound an important and significant role for the typical vetiver aroma [6]. In preceding studies on structure/odor relationships, we examined the odorous character of chiral cyclohexenone derivatives which possess a partial structure of **3a** [7]. In the following, the influence of chirality on the odorous properties of (–)-β-vetivone ((–)-**3a**) is studied. Furthermore, the contributions of the Me groups at the cyclohexenone ring to the scent are examined by synthesizing and evaluating the chiral demethyl derivatives **3b**,**c** of **3a**.

Results and Discussion. – The straightforward route to the chiral target molecules was based on the racemic β-vetivone synthesis by *Stork* and coworkers [8] followed by resolution of the antipodes. Thus, the enol ethers **1a** and **1b** [8][10] underwent spirocyclization at C(4) with dibromide **2** [11] in THF/DMPU (= 1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1*H*)-one). The following reaction with MeLi and H^+/H_2O

[1]) Part of the Ph. D. Thesis [1].

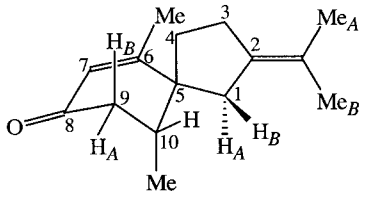
furnished compounds **3a** [12] and **3b**, respectively, as racemates. Treatment of the spirocyclic intermediate obtained by the reaction of **1a** and **2** with $LiAlH_4$ and H^+/H_2O led to **3c** (for the synthesis of 10-*epi*-**3c**, see [13]).

Scheme 1



1a R = Me
b R = H

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

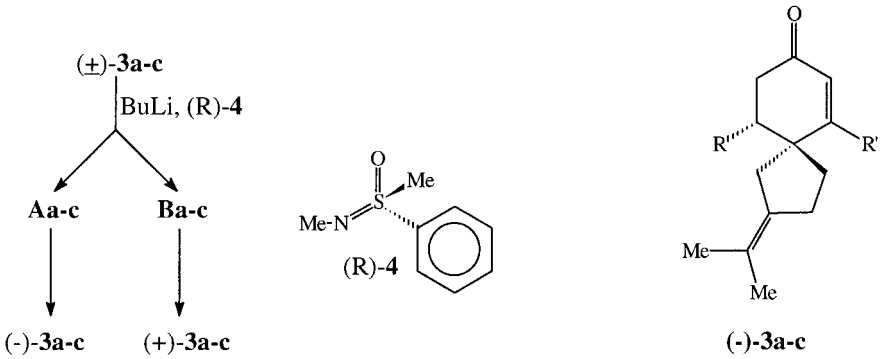


(–)-**3a**

NOEs: H_A-C(1)/Me_B-C=C(2), Me-C(6)
H_B-C(1)/Me_B-C=C(2), Me-C(10)
CH_2(3)/Me_A-C=C(2), CH_2(4)
CH_2(4)/H_B-C(9)
H_A-C(9)/Me-C(10)
H_B-C(9)/H-C(10)

Resolution of the racemates of **3a**–**c** was carried out by reaction with lithiated (–)-(*R*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine (**4**) [14–16] which proceeded with excellent facial selectivity affording MPLC- and TLC-separable mixtures of two diastereoisomeric sulfoximine adducts **Aa**–**c**, and **Ba**–**c**, respectively (*Scheme 2*). The separation was controlled by HPLC, thus realizing a diastereoisomer excess (de) of > 99%. The sulfoximine adducts **Aa**–**Bc** were each submitted to thermolysis in refluxing toluene yielding the enantiomerically pure compounds **3a**–**c**. The elucidation of the absolute configurations of the chiral nor-β-vetivone derivatives **3b**,**c** was realized by comparison of their CD data with those of (+)- and (–)-β-vetivone ((+)- and (–)-**3a**) [17][18] and consideration of the 'helicity rule' for enones. Signs of both π-π^* and the rather weak n-π^* band of conjugated cyclohexenones are usually correctly predicted, if one assumes half-chair conformation and applies the 'helicity rule' for transoid enones [19][20]. According to this rule, oppositely signed CEs for these bands can be expected. Furthermore, disubstitution at C(4) seems to have no consequences to this rule unless half-chair conformation of the cyclohexenone ring is prevented [19][21][22]. The CD spectrum of (–)-β-vetivone ((–)-**3a**) shows a negative π-π^* (band I) *Cotton*-effect at 249 (see *Fig. 1*). It is remarkable that the expected positive n-π^* band is followed by a negative band. But, that bisignate n-π^* band may reflect the presence of two n-π^* transitions and can be found also in the CD spectra of 5-methylcyclohexenone [19] and other cyclohexenones [23]. The observed curve profiles of (–)- and (+)-**3c** follow the helicity rule in an ideal way with an intense band I and a 'normal' n-π^* band, which are

Scheme 2. *Resolution of β-Vetivone* (**3a**) *and Derivatives* **3b,c**, *and Absolute Configuration of (−)-***3a – c**



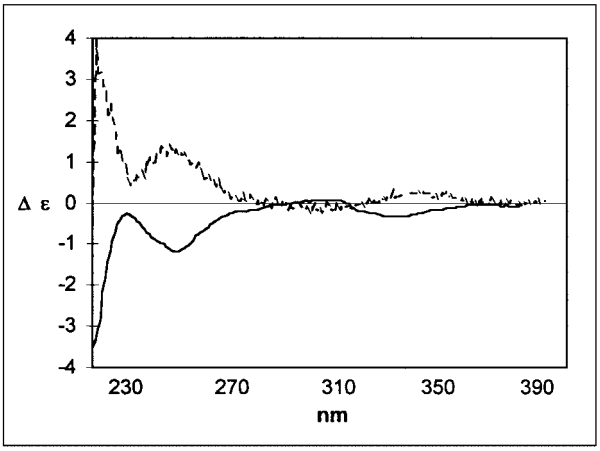


Fig. 1. *CD Spectra of (−)-β-Vetivone* ((−)-**3a**; —) *and (+)-β-Vetivone* ((+)-**3a**; - - -)

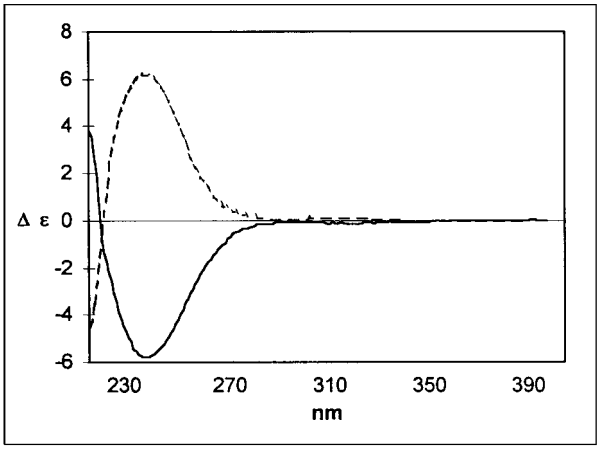


Fig. 2. *CD Spectra of (−)-***3b**; (—) *and (+)-***3b** (- - -)

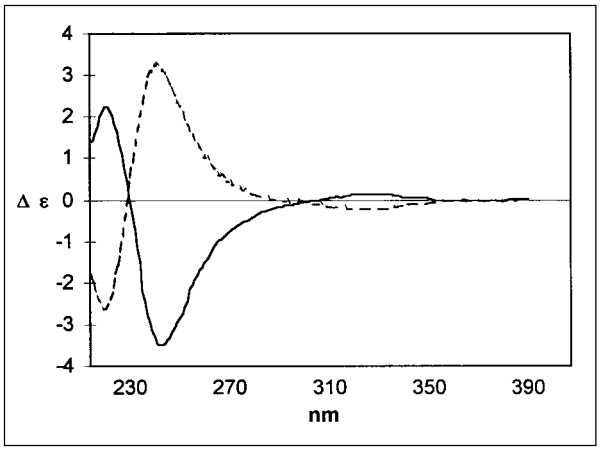


Fig. 3. *CD Spectra of (−)-***3c**; (—) *and (+)-***3c** (---)

oppositely signed (see *Fig. 3*). The CD spectra of (−)- and (+)-**3b**, which lack the Me group at C(10), show intense negative and positive, *Cotton* effects (band I), respectively, at 235 as expected, but the n-π^* band is nearly undetectable (see *Fig. 2*).

Confirmation of the structures of target compounds **3a**–**c** as well as full and unambiguous assignments of all ^{1}H- and ^{13}C-NMR signals (see *Exper. Part*) were achieved by a combination of different NMR techniques, such as NOE-difference spectroscopy [24], APT [25], HMQC [26], COSY-45 [27], long-range INEPT [28] experiments with selective excitation, 1D-HETCOR [29], and 1D-TOCSY spectra [30]. For compounds **3a** and **3c**, the axial position of Me–C(10) follows from the splitting patterns of the signals of CH_2(9) showing relatively small (4.3–6.6 Hz) vicinal coupling constants H–C(10), which consecutively must arise from (axial, equatorial) and (equatorial, equatorial) couplings. The most important through-space connectivities found in a series of NOE-difference experiments with β-vetivone (**3a**) are shown in *Scheme 1*. It should be emphasized that our NMR experiments confirm the structure of **3a** proposed by *McCurry* and *Singh* [31] and support 'half-chair' conformation of the cyclohexenone system. The ^{1}H-NMR data of **3a** correspond well with those given in [18][31–33]; however, only a few selected resonances have been assigned there. To the best of our knowledge, no ^{13}C-NMR data have been published so far for β-vetivone (**3a**) and closely related structures.

The odorous impression of the demethyl derivatives (−)-**3b** and (+)-**3b** can be summarized as intense cresolic. Enantiomer (−)-**3c** exhibits a sweet coumarine-like odor with a woody note, and (+)-**3c** a woody smell with a quinoline-like by-note. Surprisingly, the odor of (−)-β-vetivone ((−)-**3a**) can be described as a quinoline-like, fruity (cassis, grapefruit) aroma with a woody by-note. There could not be detected any odor reminiscent to the pleasant vetiver aroma; (+)-**3a** exhibits an unpleasant cresolic, medicinal note. It is doubtful why the overwhelming majority of authors attribute a typical vetiver scent to β-vetivone and describe it as one of the main odorants of this essential oil. Maybe this wrong description results from examinations of β-vetivone

samples which were obtained from the essential oil and contained traces of highly intensive odorous contaminations. The only study that is in accordance with our results, to the best of our knowledge, was published by *Maurer* who stated that (−)-β-vetivone exhibits an odor lacking the typical odor characteristics associated with vetiver [34]. The results of this publication remain uncited and seem to be ignored, and β-vetivone is described wrongly as usual, *e.g.*, as one of three odor-donating components of vetiver oil [6], as contributing significantly [35][36] and with a characteristic woody and root-like odor [37]. In summary, it could be demonstrated that configuration has a great impact on the character of the odor of β-vetivone (**3a**) and its demethyl analogue **3c**. Furthermore, it is shown that the typical odor descriptors do not stem from this compound nor from these partial structures. A further search for compounds with partial structures of β-vetivone with the aim to mimic the vetiver odor, therefore, seems not promising (see also [7]).

We are indepted to Mr. *W. Höppner* and *V. Hausmann*, perfumers of *Dragoco Vienna*, for the organoleptic analyses of all new compounds.

Experimental Part

1. *General*. All reactions were carried out under Ar. THF and Et_2O were distilled over $LiAlH_4$. TLC: *Merck-F-254* (No. 5554) precoated sheets; visualization by anisaldehyde/H_2SO_4 or by UV. Column chromatography (CC): *Merck KG 60 F 254*, 70–230 mesh ASTM (No. 7734). HPLC: *Merck Hitachi LaChrom-7000* apparatus, pump *L 7100*, UV/VIS detector *L-7420* or *L-4200*; *LiChroprep®-100-RP-18* column (5 ml, 125 × 4 mm; *Merck* (No. 50943)); detection at 266 nm. M.p.: *Kofler* apparatus; uncorrected. Circular dichroism (CD): *Jobin-Yvonne-CD-6* dichrographe; at 20°; $l = 1$ cm; in EtOH, $c = 10^{-4}$–10^{-5} mol/l^{-1}; in λ ($\Delta\varepsilon$). IR Spectra: *Perkin-Elmer-298* spectrophotometer; $\tilde{\nu}_{max}$ in cm^{-1}. ^{1}H-NMR Spectra: *Bruker AC 80* (80 MHz) and *Varian Unityplus 300* (300 MHz); δ in ppm rel. to Me_4Si (= 0 ppm), J in Hz. ^{13}C-NMR: *Varian Unityplus 300* (75 MHz); δ rel. to Me_4Si (= 0 ppm). GC/MS: *Hewlett-Packard 5890/5970* spectrometer: *m/z* (rel. %).

2. *(±)-6,10-Dimethyl-2-(1-methylethylidene)spiro[4.5]dec-6-en-8-one* (β-Vetivone; (±)-**3a**) *and (±)-10-Methyl-2-(1-methylethylidene)spiro[4.5]dec-6-en-8-one* ((±)-**3c**). Enol ether **1a** was treated with dibromide **2** (instead of the analogous dichloride, and HMPA was substituted by DMPU) according to [8] furnishing the 4,4-spirocyclized enol ether (yield: 38%). Subsequent reaction either with MeLi and H^+/H_2O furnished (±)-**3a** (yield: 61%) or with $LiAlH_4$ and H^+/H_2O yielded (±)-**3c** (yield: 83%).

*Data of (±)-***3a**: Colorless crystals. M.p. 42–44° ([18]: 37–38°, [38]: 38–41°, [8]: 40–44°, [39]: 44–44.5°, [12]: 43.5–46°, [40]: 44–46°, [41]: 46–48°, [42]: 47–48°, [43]: 48–49°, [44]: 49–50°, [31]: 53–54.5°). IR (KBr): 2910, 1670, 1445, 1380. ^{1}H-NMR ($CDCl_3$): 0.96 (d, $J = 6.8$, Me_{ax}–C(10)); 1.62 (m, Me_B); 1.66 (m, Me_A); 1.88 (d, $J = 1.3$, Me–C(6)); 1.95 (m, CH_2(4)); 2.07 (m, H–C(10)); 2.19 (ddd, $J = 16.9$, 4.5, 0.9, H_{eq}–C(9)); 2.28 (m, 1 H–C(1)); 2.39 (m, CH_2(3)); 2.43 (m, 1 H–C(1)); 2.64 (dd, $J = 16.9$, 4.7, H_{ax}–C(9)); 5.78 (m, 1 H–C(7)). ^{13}C-NMR ($CDCl_3$): 16.6 (Me_{ax}–C(5)); 20.9 (Me_B); 21.1 (Me_A); 21.6 (Me–C(6)); 29.4 (C(3)); 37.7 (C(4)); 38.0 (C(1)); 39.0 (C(10)); 42.9 (C(9)); 51.0 (C(5)); 122.6 (Me_2C=); 126.0 (C(7)); 133.8 (C(2)); 167.0 (C(6)); 198.9 (C(8)). MS: 218 (68, M^+), 161 (57), 136 (100), 133 (58), 121 (73), 105 (51), 91 (96), 83 (50), 79 (67), 77 (70). Anal. calc. for $C_{15}H_{22}O$ (218.34): C 82.52, H 10.16; found: C 82.74, H 10.18.

*Data of (±)-***3c**: Colorless oil. IR (NaCl, liquid film): 2980, 2920, 1680, 1200. ^{1}H-NMR ($CDCl_3$): 1.00 (d, $J = 6.7$, Me_{ax}–C(10)); 1.64 (m, Me_A, Me_B); 1.87 (m, CH_2(4)); 2.13 (m, H–C(10)); 2.24 (m, H_{eq}–C(9), 1 H–C(1)); 2.28 (m, 1 H–C(1)); 2.39 (m, CH_2(3)); 2.61 (dd, $J = 16.4$, 4.3, H_{ax}–C(9)); 5.86 (d, $J = 10.1$, H–C(7)); 6.70 (dd, $J = 10.1$, 1.1, H–C(6)). ^{13}C-NMR ($CDCl_3$): 16.4 (Me_{ax}–C(5)); 20.9 (Me_B); 21.1 (Me_A); 28.7 (C(3)); 37.9 (C(10)); 38.0 (C(4)); 38.9 (C(1)); 43.7 (C(9)); 48.1 (C(5)); 123.8 (Me_2C=); 126.6 (C(7)); 132.5 (C(2)); 157.1 (C(6)); 199.5 (C(8)). MS: 205 (12, $[M+1]^+$), 204 (100, M^+), 162 (36), 147 (35), 119 (45), 107 (37), 93 (32), 91 (66), 83 (40). Anal. calc. for $C_{14}H_{20}O$ (204.29): C 82.30, H 9.87; found: C 82.03, H 10.03.

3. *(±)-6-Methyl-2-(1-methylethylidene)spiro[4.5]dec-6-en-8-one* ((±)-**3b**). As described for **3a**, with enol ether **1b**, **2**, MeLi, and H^+/H_2O: (±)-**3b** as colorless crystals (yield: 49%). M.p. 90–92° (Et_2O/petroleum ether; [42]: 89–90°). IR (KBr): 2980, 2940, 2920, 2860, 1720, 1615, 1480. ^{1}H-NMR ($CDCl_3$): 1.60 (m, Me_A, Me_B); 1.65 (m, 1 H–C(4)); 1.81 (m, 2 H–C(10)); 1.90 (d, $J = 1.3$, Me–C(6)); 1.90 (m, 1 H–C(4)); 2.26 (m, 1 H–C(1)); 2.34 (m, CH_2(3), 1 H–C(1)); 2.36 (m, 2 H–C(9)); 5.80 (m, H–C(7)). ^{13}C-NMR ($CDCl_3$): 20.3 (*Me*–C(6));

20.5 (Me_B); 21.1 (Me_A); 28.5 (C(3)); 33.1 (C(10)); 34.5 (C(9)); 34.8 (C(4)); 39.7 (C(1)); 46.6 (C(5)); 123.5 ($Me_2C=$); 127.4 (C(7)); 132.7 (C(2)); 167.2 (C(6)); 199.3 (C(8)). MS: 205 (16, $[M+1]^+$), 204 (100, M^+), 161(65), 148(71), 147(33), 133(57), 122(52), 121(50), 120(54), 70(60). Anal. calc. for $C_{14}H_{20}O$ (204.30): C 82.20, H 9.80; found: C 81.95, H 9.67.

4. *Separation of the Racemates of (±)-***3a–c**. 4.1. *Sulfoximine Adducts* **Aa–c** *and* **Ba–c**. To a suspension of 2 equiv. of (–)-(*R*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine (**4**) in abs. THF (2 ml/100 mg of **4**), 3 equiv. of 1.6M soln. of BuLi in hexane were added at 0° under Ar. After stirring for 15 min at r.t., the mixture was cooled to –78°, and 1 equiv. of (±)-**3a–c** in THF was added within *ca.* 5 min. Stirring was continued for further 4 h. During this time, the mixture was allowed to warm up to –20°. The mixture was treated with an aq. 3 : 10 NH_4Cl/NaCl soln. and extracted with Et_2O affording adducts **Aa**/**Ba** (from (±)-**3a**), **Ab**/**Bb** (from (±)-**3b**), and **Ac**/**Bc** (from (±)-**3c**), resp. The adducts were separated by MPLC (**Aa**/**Ba** and **Ac**/**Bc**; MeOH/H_2O 3 : 1) or TLC (**Ab**/**Bb**; petroleum ether/AcOEt 3 : 2).

Data of **Aa**: Yield: 50%. $[\alpha]_D^{20} = +117.44$ ($c = 5.1$, EtOH). IR (NaCl, liquid film): 3280, 3060, 2920, 1655, 1445, 1240. ^{1}H-NMR ($CDCl_3$): 0.97 (d, $J = 6.9$, 3 H); 1.59–2.58 (m, 18 H); 2.63 (s, 3 H); 3.22 (AB('q'), $J_{AB} = 13.8$, $\Delta\nu_{AB} = 52.9$, 2 H); 5.13 (s, 1 H); 6.84 (s, 1 H); 7.55–7.89 (m, 5 H). ^{13}C-NMR ($CDCl_3$): 145.1; 139.1; 135.8; 133.0; 129.5; 128.9; 126.5; 120.6; 71.2; 63.0; 49.7; 40.1; 37.2; 36.7; 35.6; 30.5; 28.9; 21.0; 20.9; 20.0; 16.6. MS: 387 (2, M^+), 218(14), 154(32), 140(54), 125(68), 107(59), 91(68), 77(100), 67(53), 51 (58).

Aa/**Ba**: Anal. calc. for $C_{23}H_{33}NO_2S$ (387.59): C 71.28, H 8.58, N 3.61; found: C 71.06, H 8.39, N 3.51.

Data of **Ba**: Yield: 22%. $[\alpha]_D^{20} = -75.44$ ($c = 2.3$, EtOH). IR (NaCl, liquid film): 3280, 3060, 2920, 1655, 1445, 1240. ^{1}H-NMR ($CDCl_3$): 0.82 (d, $J = 6.6$, 3 H); 1.52–1.34 (m, 18 H); 2.66 (s, 3 H); 3.30 (AB('q'), $J_{AB} = 13.8$, $\Delta\nu_{AB} = 48.7$, 2 H); 5.80 (s, 1 H); 7.27–7.88 (m, 5 H). ^{13}C-NMR ($CDCl_3$): 143.6; 139.2; 135.9; 133.0; 129.5; 128.9; 125.3; 120.6; 70.7; 65.4; 49.6; 42.7; 36.7; 36.5; 35.1; 30.6; 28.9; 21.0, 20.9; 20.1; 16.6. MS: 387 (4, M^+), 218(19), 154(37), 140(54), 125(67), 107(61), 91(80), 77(100), 67(43), 51(47).

Data of **Ab**: Yield: 34%. $[\alpha]_D^{20} = +23.6$ ($c = 0.96$, EtOH). IR (NaCl, liquid film): 3280, 3060, 2925, 1655, 1445, 1230. ^{1}H-NMR ($CDCl_3$): 1.25–2.30 (m, 19 H); 2.63 (s, 3 H); 3.21 (AB('q'), $J_{AB} = 13.7$, $\Delta\nu_{AB} = 101.5$, 2 H); 5.18 (s, 1 H); 7.58–7.90 (m, 5 H). ^{13}C-NMR ($CDCl_3$): 144.1; 139.0; 134.1; 133.1; 129.5; 128.9; 127.4; 122.4; 70.3; 64.3; 54.6; 39.8; 35.7; 32.2; 30.6; 28.9; 28.7; 21.1; 20.9; 19.1. MS: 373 (3, M^+), 204(13), 140(36), 125(61), 106(46), 79(43), 77(100), 65(31), 51(50).

Ac/**Bc**: Anal. calc. for $C_{22}H_{31}NO_2S$ (373.56): C 70.74, H 8.36, N 3.75; found: C 71.00, H 8.25, N 3.60.

Data of **Bb**: Yield: 45%. M.p. 120–122° (petroleum ether/AcOEt). $[\alpha]_D^{20} = +89.56$ ($c = 0.7$, EtOH). IR (KBr): 3260, 3060, 2920, 1650, 1445, 1245. ^{1}H-NMR ($CDCl_3$): 1.41–2.43 (m, 19 H); 2.63 (s, 3 H); 3.22 (AB('q'), $J_{AB} = 13.8$, $\Delta\nu_{AB} = 75.7$, 2 H); 5.20 (s, 1 H); 6.77 (br. s, 1 H); 7.54–7.89 (m, 5 H). ^{13}C-NMR ($CDCl_3$): 143.7; 139.0; 134.1; 133.1; 129.5; 128.9; 128.0; 122.4; 70.7; 63.5; 45.7; 40.9; 35.0; 32.1; 31.3; 28.9; 28.6; 21.1; 20.9; 19.0. MS: 373 (1, M^+), 204(6), 140(35), 125(53), 121(22), 106(40), 93(39), 91(63), 79(44), 77(00), 67(50), 55(59).

Data of **Ac**: Yield. 39%. $[\alpha]_D^{20} = +144.32$ ($c = 8.1$, EtOH). IR (NaCl, liquid film): 3280, 3060, 2925, 1650, 1480, 1240. ^{1}H-NMR ($CDCl_3$): 0.99 (d, $J = 6.0$, 3 H); 1.36–2.29 (m, 15 H); 2.63 (s, 3 H); 3.26 (AB('q'), $J_{AB} = 13.8$, $\Delta\nu_{AB} = 51.3$, 2 H); 5.34 (d, $J = 10.0$, 1 H); 5.62 (d, $J = 10.0$, 1 H); 6.93 (br. s, 1 H); 7.55–7.90 (m, 5 H). ^{13}C-NMR ($CDCl_3$): 139.0; 138.6; 133.9; 133.0, 129.5; 128.9; 128.4; 122.1; 71.5; 62.3; 46.9; 40.8; 37.2; 37.0; 34.8; 28.9; 28.4, 21.0; 20.8, 16.3. MS: 373 (1, M^+), 204(9), 154(22), 140(24), 124(47), 106(42), 91(56), 77(100), 55(53), 51(60).

Ab/**Bb**: Anal. calc. for $C_{22}H_{31}NO_2S$ (373.56): C 70.74, H 8.36, N 3.75; found: 70.85, H 8.19, N 3.56.

Data of **Bc**: Yield: 26%. $[\alpha]_D^{20} = -64.35$ ($c = 5.4$, EtOH). IR (NaCl, liquid film): 3270, 3060, 2920, 1650, 1445, 1240. ^{1}H-NMR ($CDCl_3$): 0.85 (d, $J = 6.6$, 3 H); 1.51–2.32 (m, 15 H); 2.66 (s, 3 H); 3.32 (AB('q'), $J_{AB} = 13.8$, $\Delta\nu_{AB} = 51.7$, 2 H); 5.71 (d, $J = 10.0$, 1 H); 6.05 (d, $J = 10.0$, 1 H); 6.94 (br. s, 1 H); 7.55–7.89 (m, 5 H). ^{13}C-NMR ($CDCl_3$): 139.0; 137.3; 134.0; 133.1; 129.5; 128.9; 127.3; 122.0; 70.9; 65.3; 46.8; 43.4; 36.8; 36.7; 34.2; 28.9; 18.5; 21.0; 20.8; 16.2. MS: 373 (1, M^+), 204(10), 124(23), 106(26), 91(26), 86(64), 84(100), 77(50), 55(30), 51(37).

4.2. *Thermolysis of the Sulfoximine Adducts* **Aa–c** *and* **Ba–c**. A soln. of adduct in toluene (2 ml/mmol) was heated under reflux for 16 h. The mixture was evaporated and the residue submitted to TLC (petroleum ether/AcOEt 65 : 35).

*(5*R*,10*R*)-6,10-Dimethyl-2-(1-methylethylidene)spiro[4.5]dec-6-en-8-one* (*β-Vetivone*; (–)-**3a**): Yield: 82%. $[\alpha]_D^{20} = -45.63$ ($c = 2.3$, EtOH; [45]: –19, [46]: –23.6, [39]: –24.1, [47]: –38.9, [18]: –43.45, [48]: –47.1). CD: 249 (–1.17), 318 (+0.075), 348 (–0.34).

*(5*S*,10*S*)-6,10-Dimethyl-2-(1-methylethylidene)spiro[4.5]dec-6-en-8-one* ((+)-**3a**): Yield: 58%. $[\alpha]_D^{20} = +44.48$ ($c = 0.7$, EtOH; [49]: +38 and +62.6). CD: 242 (+1.33), 310 (–0.17), 348 (+0.25).

(5S)-6-Methyl-2-(1-methylethylidene)spiro[4.5]dec-6-en-8-one ((−)-**3b**): Yield: 50%. $[\alpha]_D^{20} = -87.26$ ($c = 0.8$, EtOH). CD: 235 (−5.93)

(5R)-6-Methyl-2-(1-methylidene)spiro[4.5]dec-6-en-8-one ((+)-**3b**): Yield: 59%. $[\alpha]_D^{20} = +90.95$ ($c = 1.2$, EtOH). CD: 235 (+6.20).

(5R,10R)-10-Methyl-2-(1-methylethylidene)spiro[4.5]dec-6-en-8-one ((−)-**3c**): Yield: 51%. $[\alpha]_D^{20} = -47.15$ ($c = 2.3$, EtOH). CD: 240 (−3.47), 338 (+0.17).

(5S,10S)-10-Methyl-2-(1-methylethylidene)spiro[4.5]dec-6-en-8-one ((+)-**3c**): Yield: 61%. $[\alpha]_D^{20} = +44.91$ ($c = 1.8$, EtOH). CD: 240 (+3.27), 337 (−0.20).

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