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Synthesis and structure of nitrones derived from 2-trifluoromethyl bornane 3-imines

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ABSTRACT

Upon treatment with (trifluoromethyl)trimethylsilane (CF_3SiMe_3), 3-(*N*-alkyl or 3-*N*-aryl)imines of camphorquinone of type **1** smoothly undergo stereoselective conversion to yield 2-*endo*-trifluoromethylated 1:1 adducts **2**, which, after subsequent desilylation with sodium borohydride in boiling alcoholic solutions, were converted into imino alcohols **3**. Unexpectedly, oxidation of **3** with *m*-CPBA resulted in the formation of a new type of trifluoromethylated nitrones **5** (and not the expected oxaziridines) in a stereoselective manner. In the case of **5a**, the (*Z*)-configuration of the C=N double bond of the nitrone unit was unambiguously established by an X-ray crystal-structure determination. However, photolysis of **5a** led to the *exo*,*exo*/*exo*,*endo* mixture of the isomeric oxaziridine **7**; the two stereoisomers were separated chromatographically.

1. Introduction

In spite of the fact that camphor and its derivatives attract attention as readily available, enantiomerically pure building blocks and ligands for stereocontrolled synthesis [1,2], very little is known about fluorinated derivatives of camphor. Fluorination of camphor-3-carboxylic acid used as an *endo*/*exo* mixture with SF_4 at room temperature was reported to give, depending on the reaction conditions, the corresponding acid fluoride or 3-(trifluoromethyl)-camphor as a mixture of *endo* and *exo* isomers [3]. On the other hand, isoketopinic acid, treated with SF_4 at 100 °C, was converted into the corresponding 2,2-difluorocarboxylic acid fluoride. In this case, no trifluoromethylated derivative was reported.

Recently, we showed that camphorquinone monoimines **1** smoothly undergo a nucleophilic trifluoromethylation with the Ruppert-Prakash reagent (CF_3SiMe_3) to give the corresponding (2-trifluoromethyl)imine silylethers **2** in a diastereoselective manner. The latter products, upon treatment with sodium borohydride, were converted into imino alcohols **3** in excellent yields [4] (Scheme 1). As shown in the same paper, acidic hydrolysis of the primary adducts **2** gave the corresponding trifluoromethylated (α-hydroxy)ketone. On the other hand, the reduction of **3** with DIBAL-H afforded the α-trifluoromethylated β-amino alcohols **4**, and the major products were identified as the *cis*-isomers.

Oxidation reactions of *N*-substituted camphor imines have been extensively studied, and the formation of oxaziridines as the exclusive products was reported [5]. Typically, the oxidations were performed with peroxides and gave the *endo*-oxaziridines as the major or exclusive product. The so-called 'Davis oxaziridine' has gained special importance as an excellent chiral O-transfer reagent, used in enantioselective oxidation reactions [6].

Nitrones are isomers of oxaziridines and belong to the group of well-known and widely explored 1,3-dipoles. It is worth mentioning that under photochemical or thermal conditions, the isomeric nitrones and oxaziridines can be interconverted [7]. Interestingly, the *N*-methyl nitrones derived from camphorquinone were obtained via a non-oxidative method by the treatment of its monooxime with diazomethane [8].

The aim of the present study was the synthesis of oxaziridines and/or nitrones containing the trifluoromethylated camphor skeleton via oxidation of imino alcohols **3**. To the best of our knowledge, this type of optically active nitrones (or oxaziridines) has not been reported so far.

2. Results and discussion

The trifluoromethylated imino alcohols **3** were prepared according to the method described earlier [4]. The structures of the racemic *N*-methyl and *N*-ethyl derivatives **3a**,**b** had previously

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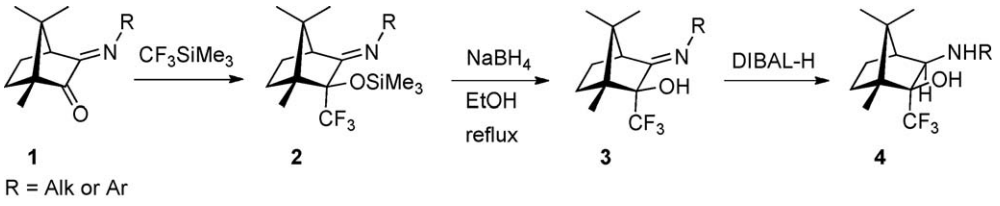
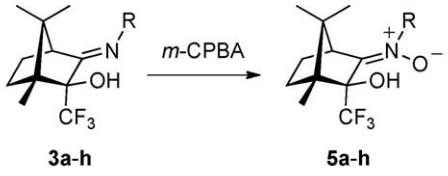
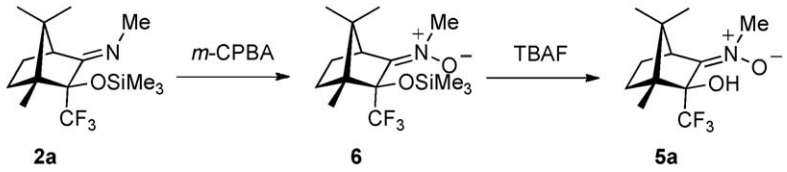


Scheme 1.



a: R = Me, **b**: R = Et, **c**: R = *i*Pr, **d**: R = *t*Bu, **e**: R = *c*Hex, **f**: R = CH(Ph)Me, **g**: R = Ph, **h**: R = 4-MeOC$_6$H$_4$



Scheme 2.

been established by X-ray crystallography [4]. Oxidation of **3a**–**h** with *m*-CPBA in dichloromethane at room temperature afforded, after *ca.* 2 h reaction time, only one product in each case in 82–94% yield. In the case of the reaction with **3a**, the ^{19}F NMR spectrum of the crude product displayed only one signal located at −67.1 ppm, indicating that the reaction occurred stereoselectively. In addition, the IR and the ^{13}C NMR spectra revealed the presence of a C=N group (1642 cm^{-1} and 153.1 ppm, respectively). After crystallisation, the elemental analysis corresponded with the formula $C_{12}H_{18}F_3NO_2$, *i.e.*, a monoxidated product. These data indicated that the obtained product was the nitrone **5a** and not the corresponding oxaziridine (Scheme 2). Oxidation experiments with **3a**, carried out at lower temperature (0 °C and −30 °C), led to the same result.

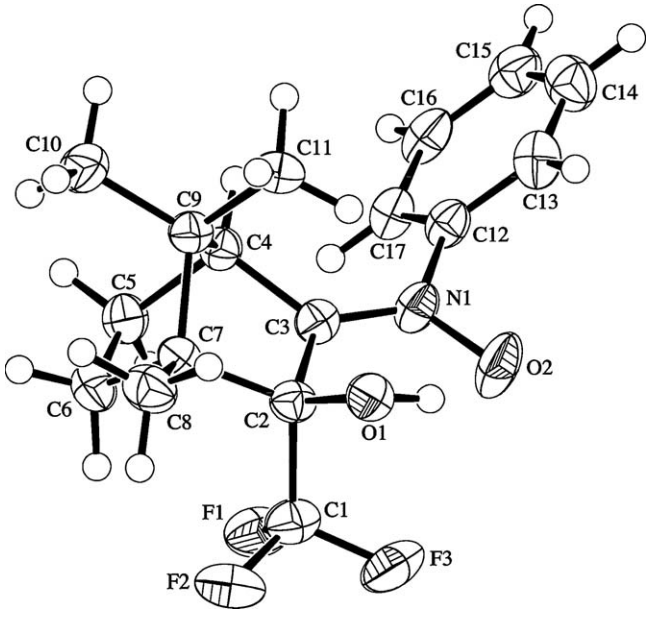


Fig. 1. ORTEP-plot [10] of the molecular structure of **5g** (50% probability ellipsoids, arbitrary numbering of the atoms).

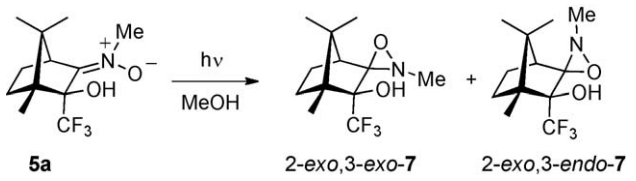
Analogously, treatment of **3b**–**h** afforded crystalline products, which displayed similar spectroscopic data. In all cases, the structure of the corresponding nitrone of type **5** was proposed for the isolated product. Finally, the structure of **5g** with (*Z*)-configuration was unambiguously established by X-ray crystallography (Fig. 1). The crystal-structure shows that the hydroxy group forms an intramolecular hydrogen bond with the nitrone O-atom. This interaction creates a six-membered loop that can be described by a graph set motif [9] of S(6).

In addition to the presented reactions with imines **3**, the oxidation of the trimethylsilyloxy derivative **2a** with *m*-CPBA in CH_2Cl_2 solution was performed at ca. 0–5 °C, and the product isolated after typical workup was identified as the silylated nitrone derivative **6** (Scheme 2). The ^{13}C NMR spectrum revealed the expected absorption of the C=N group at 150.2 ppm. The subsequent desilylation with TBAF yielded the known product **5a**.

The typical procedures applied for the synthesis of nitrones are the condensation of hydroxylamines with carbonyl compounds or the methylation of monooximes of 1,2-diketones with diazomethane [2b,11]. On the other hand, the oxidation of imines is a known protocol for the preparation of oxaziridines [7,12]. Therefore, the formation of nitrones **5** from the imino alcohols **3** is an unexpected result. Considering the reaction pathway, the initial formation of the corresponding oxaziridines and subsequent ring opening under the reaction conditions cannot be excluded.

It is worth mentioning that the oxidation of *N*-alkylaminoacetonitriles with excess *m*-CPBA leads to the *N*-oxide of the corresponding cyanomethylidene amines (nitrones) [13]. In this case, electron-deficient cyanomethylidene amines are likely intermediates. Based on this result, we propose that the strongly electron-withdrawing CF_3 group is responsible for the formation of nitrones **3** and not oxaziridines from the imino derivatives of type **3** and the O-silylated analogue **2a**.

In order to prepare an oxaziridine derivative, the nitrone **5a** was irradiated in methanolic solution with UV-light (mercury lamp), and the progress of the reaction was controlled by means of TLC.



5a 2-*exo*,3-*exo*-**7** 2-*exo*,3-*endo*-**7**

Scheme 3.

After 60 min, the irradiation was stopped, and the crude product was analyzed by ^{19}F NMR spectroscopy. Along with two main products disclosing two singlets located at −70.5 and −71.3 ppm, respectively, some smaller signals indicated the presence of non-identified minor products resulting from photodecompositions.

After chromatographic separation, two main fractions were isolated as colourless solids in 70% overall yield. The IR spectra of both compounds confirmed the absence of a C=N group. Correspondingly, in the ^{13}C NMR spectra, no absorption above 125 ppm was observed (absence of C=N), and the characteristic signals at 92.3 ppm (major product) and 93.4 ppm (minor product) were attributed to the C(3)-atom of the oxaziridines **7** (Scheme 3). These chemical shifts fit satisfactorily with values reported for a series of oxaziridines (79.2–85.2 ppm) [13].

In the ^{19}F NMR spectra of the separated isomers **7**, the presence of only one signal in each case confirmed the purity of the samples. In the case of the main isomer, the signal located at −70.5 ppm appeared as a broad one, whereas the minor isomer showed a sharp singlet at −71.3 ppm. The broadening of the signal in the first case may result from a through-space interaction of the CF_3 group with the *endo*-oriented MeN group. Based on this assumption, the structure of the major isomer is proposed as 2-*exo*,3-*exo*-**7** (Scheme 3).

The attempted photo-isomerisation of the Ph substituted nitrone **5g** resulted in the formation of a complex mixture and, after column chromatography only unidentified decomposition products were isolated.

Nitrones are widely explored as useful building blocks in organic synthesis, and their [2 + 3]-cycloaddition reactions with diverse dipolarophiles are well documented [11b,c]. In order to check if trifluoromethylated nitrones of type **5**, derived from camphor, are able to react with typical C=N or C=C dipolarophiles, in analogy to already described reactions with similar systems [2b,11d], THF solutions containing equimolar amounts of **5a** and phenyl isocyanate or **5g** and fumaronitrile, respectively, were heated under reflux for 10 h. After this time, in both cases, the starting materials were recovered unchanged in nearly quantitative yields. Apparently, steric hindrance in nitrones **5** prevents the formation of the corresponding [2 + 3]-cycloadduct.

3. Conclusions

The trifluoromethylated imino alcohols **3** undergo oxidation with *m*-CPBA yielding the corresponding nitrones **5** instead of the corresponding oxaziridines. This rather unexpected result is probably caused by the substitution pattern of the imine, and the influence of the CF_3 group may play a crucial role. The new type of trifluoromethylated nitrones, which can be prepared conveniently in enantiomerically pure form, can be further explored for stereocontrolled reactions. Moreover, they can be tested as a new type of ligands for organocatalysis.

4. Experimental

4.1. General experimental procedures

Melting points were determined on a Melt-Temp. II apparatus (Aldrich) in capillaries and are uncorrected. The ^1H, $^{13}C\{^1H\}$ and ^{19}F NMR spectra were recorded in $CDCl_3$ with TMS or CCl_3F as the internal standards using Bruker AC-200 or Bruker ARX-300 spectrometers. Assignments of signals in ^{13}C NMR spectra were made on the basis of DEPT 135 experiments. The IR spectra were measured using a NEXUS FT-IR spectrophotometer. The MS spectra (CI, EI, ESI) were obtained using LKB-2091, Finnigan MAT-95, or Bruker Esquire LC spectrometers. Optical rotations were measured on a PERKIN-ELMER 241 MC spectropolarimeter for λ = 589 nm. Elemental analyses were performed in the Microanalytical Laboratory of the Centre of Molecular and Macromolecular Studies PAS in Lodz.

4.2. Materials

Commercial 70% *m*-chloroperbenzoic acid (*m*-CPBA) was purchased from Sigma–Aldrich and the 1 M solution of tetrabutylammonium fluoride (TBAF) in THF from Fluka. The α-trifluoromethylated imino alcohols **3** were prepared according to published protocols [4].

4.3. Oxidation of trifluoromethylated imino alcohols 3a–h with *m*-CPBA—general procedure

To a solution of the corresponding imino alcohol **3** (1 mmol) in CH_2Cl_2 (2 mL), *m*-CPBA (1.1 mmol) was added, and the mixture was stirred for 2 h at room temperature. Then, the mixture was diluted with CH_2Cl_2 and washed with a saturated aqueous solution of Na_2CO_3 in order to remove the excess of *m*-CPBA and *m*-chlorobenzoic acid. The separated organic layers were collected and dried over anhydrous $MgSO_4$. After filtration, the solutions were evaporated to dryness. Purification of the crude products was achieved mainly by crystallisation, but in the case of **5c**–**5e**, preceding column chromatography was applied.

(Z)-N-Methyl-[(1R,2S)-2-(trifluoromethyl)bornan-2-ol-3-yliden]-amine N-oxide (**5a**). The pure product was obtained by crystallisation. Yield: 220 mg (82%). Colourless crystals, m.p. 248–250 °C (CH_2Cl_2/hexane); $[\alpha]_D^{25}$ +162.4 (*c* 0.010, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 0.98, 1.08, 1.13 (9H, 3s, $3CH_3$), 1.56–1.98 (4H, m, $2CH_2$), 2.63 (1H, d, $^3J_{H,H}$ = 4.4 Hz, CH), 3.70 (3H, s, CH_3N), 6.61 (1H, s, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ 9.5, 19.2, 20.9 ($3CH_3$), 22.4, 28.7 ($2CH_2$), 49.0 (CH), 50.7, 53.3 ($2C_q$), 52.3 (CH_3N), 81.1 (q, $^2J_{C,F}$ = 28.9 Hz, C_q), 124.9 (q, $^1J_{C,F}$ = 289.4 Hz, CF_3), 153.1 (C=N). ^{19}F NMR (188 MHz, $CDCl_3$): δ −67.1 (s, CF_3). IR (KBr): ν 3227*m* (br, OH), 1990*s*, 2964*s*, 2942*s*, 1642*s* (C=N), 1493*m*, 1447*m*, 1393*m*, 1374*m*, 1308*s*, 1258*vs*, 1233*s*, 1208*s*, 1173*vs*, 1119*vs*, 1070*m*, 1012*s*, 993*s*, 956*m*, 925*s*, 870*m*, 832*s*, 740*m*, 596*m* cm^{-1}. EI-MS *m*/*z* (rel. int.): 265 (59, M^+), 248 (40), 220 (13), 196 (13), 182 (100), 166 (23), 140 (12), 138 (16), 95 (31), 83 (15). Anal. Calcd for $C_{12}H_{18}F_3NO_2$ (265.29): C, 54.33; H, 6.84; N, 5.28. Found: C, 54.22; H, 6.67; N, 5.21.

(Z)-N-Ethyl-[(1R,2S)-2-(trifluoromethyl)bornan-2-ol-3-yliden]-amine N-oxide (**5b**). The pure product was obtained by crystallisation. Yield: 250 mg (89%). Colourless crystals, m.p. 147–149 °C (Et_2O); $[\alpha]_D^{25}$ +167.8 (*c* 0.010, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 0.96, 1.05, 1.10 (9H, 3s, $3CH_3$), 1.44 (3H, t, $^3J_{H,H}$ = 7.3 Hz, CH_3CH_2), 1.52–1.99 (4H, m, $2CH_2$), 2.64 (1H, d, $^3J_{H,H}$ = 4.5 Hz, CH), 3.87 (2H, q, $^3J_{H,H}$ = 7.3 Hz, CH_3CH_2N), 6.62 (1H, s, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ 9.5, 12.3, 19.2, 21.3 ($4CH_3$), 22.6, 28.7 ($2CH_2$), 50.6, 53.1 ($2C_q$), 51.7 (CH), 56.4 (CH_3CH_2N), 81.2 (q, $^2J_{C,F}$ = 28.8 Hz, C_q), 124.9 (q, $^1J_{C,F}$ = 290.3 Hz, CF_3), 151.8 (C=N). ^{19}F NMR (188, $CDCl_3$): δ −66.9 (s, CF_3). IR (KBr): ν 3267*m* (br, OH), 3016*m*, 2991*s*, 2963*s*, 2883*m*, 1620*m* (C=N), 1495*w*, 1458*m*, 1395*m*, 1375*m*, 1308*m*, 1261*s*, 1232*m*, 1172*vs*, 1159*vs*, 1128*s*, 1114*vs*, 1093*m*, 1025*m*, 1011*w*, 998*w*, 979*w*, 954*m*, 922*w*, 829*w*, 740*m*, 641*w* cm^{-1}. EI-MS *m*/*z* (rel. int.): 279 (54, M^+), 262 (41), 210 (15), 196 (100), 180 (19), 168 (11), 154 (11), 152 (12), 95 (27), 83 (11). Anal. Calcd for

$C_{13}H_{20}F_3NO_2$ (279.31): C, 55.90; H, 7.56; N, 5.01. Found: C, 55.95; H, 7.85; N, 5.01.

(Z)-N-Isopropyl-[(1R,2S)-2-(trifluoromethyl)bornan-2-ol-3-yliden]amine N-oxide (**5c**). The crude product was purified by column chromatography on silica gel using first CH_2Cl_2/hexane (2:1) and then CH_2Cl_2 with increasing amounts of ethyl acetate (0–5%) as eluents. The product was isolated as a yellowish oil. An analytically pure sample was obtained by crystallisation. Yield: 260 mg (82%). Colourless crystals, m.p. 40–43 °C (hexane); $[\alpha]_D^{25}$ +158.2 (*c* 0.2, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.00, 1.10, 1.14 (9H, 3s, $3CH_3$), 1.37–1.45 (6H, m, $(CH_3)_2CH$), 1.58–2.03 (4H, m, $2CH_2$), 2.75 (1H, d, $^3J_{H,H}$ = 4.5 Hz, CH), 4.27–4.40 (1H, m, $(CH_3)_2CHN$), 6.68 (1H, s, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ 9.6, 19.1, 20.0 ($3CH_3$), 19.4 (CH_2), 21.6, 22.9 (($CH_3)_2CH$), 28.8 (CH_2), 50.7, 53.0 ($2C_q$), 51.5 (CH), 60.7 (($CH_3)_2CH$), 81.6 (q, $^2J_{C,F}$ = 28.6 Hz, C_q), 125.2 (q, $^1J_{C,F}$ = 28.6 Hz, CF_3), 150.9 (C=N). ^{19}F NMR (188 MHz, $CDCl_3$): δ −66.8 (s, CF_3). IR (KBr): ν 3432*m* (br, OH), 2981*m*, 2941*m*, 2883*w*, 1611*m* (C=N), 1497*w*, 1455*m*, 1395*m*, 1378*m*, 1296*m*, 1261*s*, 1203*s*, 1183*s*, 1157*vs*, 1112*s*, 1076*m*, 1015*m*, 994*w*, 961*m*, 927*w*, 868*w*, 834*w*, 738*m*, 645*m* cm^{-1}. CI-MS (NH_3) *m*/*z* (rel. int.): 294 (100, $[M+1]^+$), 278 (30), 276 (14). HR-ESI-MS (NaI): Calcd for $C_{14}H_{22}F_3NO_2Na$: 316.1500; found: 316.1504.

(Z)-N-tert-Butyl-[(1R,2S)-2-(trifluoromethyl)bornan-2-ol-3-yliden]amine N-oxide (**5d**). The crude product was purified by column chromatography on silica gel using first a mixture of CH_2Cl_2/hexane (2:1) and then CH_2Cl_2 with increasing amounts of ethyl acetate (0–5%) as eluents. The product was isolated as a yellowish oil. An analytically pure sample was obtained by crystallisation. Yield: 290 mg (94%). Colourless crystals, m.p. 54–58 °C (hexane); $[\alpha]_D^{25}$ +154.5 (*c* 0.2, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.97, 1.07, 1.13 (9H, 3s, $3CH_3$), 1.55 (9H, s, $(CH_3)_3C$), 1.55–2.00 (4H, m, $2CH_2$), 3.06 (1H, d, $^3J_{H,H}$ = 4.8 Hz, CH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 9.6, 19.5, 21.8 ($3CH_3$), 22.7 (CH_2), 28.2 (($CH_3)_3C$), 28.6 (CH_2), 50.9, 52.0 ($2C_q$), 52.2 (CH), 71.0 (($CH_3)_3CN$), 83.2 (q, $^2J_{C,F}$ = 28.8 Hz, C_q), 125.3 (q, $^1J_{C,F}$ = 290.0 Hz, CF_3), 151.0 (C=N). ^{19}F NMR (188 MHz, $CDCl_3$): δ −66.2 (s, CF_3). IR (KBr): ν 3448*m* (br, OH), 2985*m*, 2942*m*, 2884*w*, 1582*w*, 1459*w*, 1395*w*, 1372*w*, 1293*w*, 1274*w*, 1257*m*, 1229*m*, 1200*m*, 1186*m*, 1164*vs*, 1151*vs*, 1125*s*, 1110*s*, 1008*w*, 983*w*, 960*w*, 833*w*, 731*w*, 656*w* cm^{-1}. CI-MS (NH_3) *m*/*z* (rel. int.): 309 (17), 308 (100, $[M+1]^+$), 252 (89). Anal. Calcd for $C_{15}H_{24}F_3NO_2$ (307.36): C, 58.62; H, 7.77. Found: C, 58.27; H, 7.72.

(Z)-N-Cyclohexyl-[(1R,2S)-2-(trifluoromethyl)bornan-2-ol-3-yliden]amine N-oxide (**5e**). The crude product was purified by column chromatography on silica gel using CH_2Cl_2/hexane (2:1) and then CH_2Cl_2 with increasing amounts of ethyl acetate (0–5%) as eluents. The product was isolated as a yellowish oil. An analytically pure sample was obtained by crystallisation. Yield: 310 mg (93%). Colourless crystals, m.p. 74–76 °C (hexane); $[\alpha]_D^{25}$ +168.0 (*c* 0.2, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.98, 1.08, 1.12 (9H, 3s, $3CH_3$), 1.15–1.40 (3H, m), 1.52–2.15 (11H, m), 2.72 (1H, d, $^3J_{H,H}$ = 4.7 Hz, CH), 3.84–3.98 (1H, m, CHN), 6.71 (1H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 9.6, 19.4, 21.6 ($3CH_3$), 23.0, 24.7, 28.8, 28.9, 29.9 ($7CH_2$), 50.6, 53.0 ($2C_q$), 51.4 (CH), 68.6 (CHN), 83.9 (q, $^2J_{C,F}$ = 28.6 Hz, C_q), 125.2 (q, $^1J_{C,F}$ = 290.0 Hz, CF_3), 150.9 (C=N). ^{19}F NMR (188 MHz, $CDCl_3$): δ −67.9 (s, CF_3). IR (KBr): ν 3432*m* (br, OH), 2997*m*, 2938*vs*, 2866*m*, 1607*m* (C=N), 1496*w*, 1461*s*, 1395*m*, 1372*w*, 1296*s*, 1260*vs*, 1170*vs*, 1156*vs*, 1189*s*, 1111*vs*, 1024*w*, 1005*w*, 962*s*, 928*w*, 836*w*, 739*w*, 652*m* cm^{-1}. CI-(NH_3) *m*/*z* (rel. int.): 335 (19), 334 (100, $[M+1]^+$), 316 (11). Anal. Calcd for $C_{17}H_{26}F_3NO_2$ (333.39): C, 61.24; H, 7.86. Found: C, 61.25; H, 7.86.

(Z)-N-[(1′R)-1′-Phenylethyl]-[(1R,2S)-2-(trifluoromethyl)bornan-2-ol-3-yliden]amine N-oxide (**5f**). The pure product was obtained by crystallisation. Yield: 290 mg (81%). Colourless crystals, m.p. 124–125 °C (Et_2O); $[\alpha]_D^{25}$ +131.5 (*c* 0.010, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.61, 0.85, 1.00 (9H, 3s, $3CH_3$), 1.52–1.97 (4H, m, $2CH_2$), 1.77 (3H, d, $^2J_{H,H}$ = 6.7 Hz, CH_3), 2.82 (1H, d, $^2J_{H,H}$ = 4.4 Hz, CH), 5.21 (1H, q, $^2J_{H,H}$ = 6.7 Hz, CH_3CH), 6.52 (1H, s, OH), 7.26–7.51 (5H, m, C_6H_5). ^{13}C NMR (50 MHz, $CDCl_3$): δ 9.5, 19.2, 19.6 ($3CH_3$), 20.9 (CH_3CH), 22.7, 28.7 ($2CH_2$), 51.1 (CH), 50.7, 53.0 ($2C_q$), 69.0 (CH_3CH), 81.5 (q, $^2J_{C-F}$ = 28.8 Hz, C_q), 125.1 (q, $^1J_{C,F}$ = 290.0 Hz, CF_3), 126.9, 128.5, 128.6 (5CH arom.), 137.8 (C_q arom.), 151.6 (C=N). ^{19}F NMR (188 MHz, $CDCl_3$): δ −66.6 (s, CF_3). IR (KBr): ν 3600−3100*w* (br, OH), 3014*m*, 2989*m*, 2957*m*, 2891*w*, 1771*w*, 1595*m*, 1495*m*, 1457*m*, 1441*w*, 1424*w*, 1399*w*, 1295*m*, 1263*s*, 1233*m*, 1174*s*, 1162*s*, 1149*vs*, 1127*w*, 1114*s*, 1056*m*, 1012*m*, 982*m*, 957*m*, 923*w*, 866*w*, 835*w*, 765*w*, 736*m*, 720*m*, 705*m*, 641*m* cm^{-1}. EI-MS *m*/*z* (rel. int.): 355 (0.8, M^+), 338 (0.3), 251 (0.7), 234 (0.6), 218 (0.4), 136 (1.3), 106 (10), 105 (100), 104 (4), 103 (5), 79 (6), 77 (6). HR-EI-MS: Calcd for $C_{19}H_{24}F_3NO_2$: 355.1759; found: 355.1758.

(Z)-N-Phenyl-[(1R,2S)-2-(trifluoromethyl)bornan-2-ol-3-yliden]-amine N-oxide (**5g**). The pure product was obtained by crystallisation. Yield: 300 mg (90%). Colourless crystals, m.p. 160–163 °C (CH_2Cl_2/hexane); $[\alpha]_D^{25}$ +58.78 (*c* 0.010, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.87, 1.10, 1.12 (9H, 3s, $3CH_3$), 1.62–1.95 (4H, m, $2CH_2$), 2.42 (1H, d, $^2J_{H,H}$ = 4.2 Hz, CH), 6.93 (1H, s, OH), 7.42–7.48 (5H, m, C_6H_5). ^{13}C NMR (50 MHz, $CDCl_3$): δ 9.5, 19.2, 21.1 ($3CH_3$), 22.7, 28.7 ($2CH_2$), 51.2, 53.2 ($2C_q$), 53.3 (CH), 81.5 (q, $^2J_{C,F}$ = 29.0 Hz, C_q), 125.0 (q, $^1J_{C,F}$ = 289.9 Hz, CF_3), 122.9, 129.2, 130.2 (5CH arom.), 145.2 (C_q arom.), 154.7 (C=N). ^{19}F NMR (188 MHz, $CDCl_3$): δ −67.0 (s, CF_3). IR (KBr): ν 3600−2880*w* (br, OH), 106*w*, 3077*w*, 3018*m*, 3002*s*, 2989*m*, 2977*s*, 2944*m*, 2926*m*, 2881*w*, 1887*w*, 1806*w*, 1606*m*, 1584*m*, 1489*s*, 1459*m*, 1401*m*, 1382*m*, 1320*m*, 1287*s*, 1267*vs*, 1233*m*, 1198*vs*, 1179*s*, 1164*vs*, 1150*vs*, 1117*s*, 1107*s*, 1073*m*, 1010*m*, 979*m*, 953*m*, 919*m*, 866*w*, 830*w*, 773*s*, 739*m*, 720*m*, 692*s*, 637*m* cm^{-1}. EI-MS *m*/*z* (rel. int.): 327 (63, M^+), 311 (22), 310 (38), 244 (72), 228 (13), 213 (22), 212 (18), 202 (12), 200 (18), 158 (10), 130 (100), 104 (65), 91 (27), 77 (59). Anal. Calcd for $C_{17}H_{20}F_3NO_2$ (327.35): C, 62.38; H, 6.16; N, 4.28. Found: C, 62.52; H, 5.89; N, 4.25.

(Z)-N-(4-Methoxyphenyl)-[(1R,2S)-2-(trifluoromethyl)bornan-2-ol-3-yliden]amine N-oxide (**5h**). The pure product was obtained by crystallisation. Yield: 320 mg (90%). Colourless crystals, m.p. 164–167 °C (CH_2Cl_2/hexane); $[\alpha]_D^{25}$ +69.50 (*c* 0.012, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.86, 1.08 (6H, 3s, $3CH_3$), 1.68–2.00 (4H, m, $2CH_2$), 2.45 (1H, d, $^2J_{H,H}$ = 4.0 Hz, CH), 3.81 (3H, s, CH_3O), 7.05 (1H, s, OH), 6.89–7.36 (4H, m, C_6H_4). ^{13}C NMR (50 MHz, $CDCl_3$): δ 9.5, 19.2, 21.0 ($3CH_3$), 22.7, 28.7 ($2CH_2$), 51.2, 53.0 ($2C_q$), 53.5 (CH), 55.4 (CH_3O), 81.50 (q, $^2J_{C,F}$ = 29.0 Hz, C_q), 125.1 (q, $^1J_{C,F}$ = 289.8 Hz, CF_3), 114.1, 124.2 (4CH arom.), 138.4, 154.0 ($2C_q$ arom.), 160.7 (C=N). ^{19}F NMR (188 MHz, $CDCl_3$): δ −68.1 (s, CF_3). IR (KBr): ν 3600−3450*w* (br, OH), 3119*w*, 3001*w*, 2987*w*, 2941*w*, 2846*w*, 1611*w*, 1599*m*, 1507*s*, 1459*w*, 1323*w*, 1285*w*, 1258*s*, 1198*m*, 1168*vs*, 1146*s*, 1110*s*, 1024*w*, 1009*w*, 977*w*, 954*w*, 917*w*, 845*m*, 812*w*, 732*w*, 608*w* cm^{-1}. EI-MS *m*/*z* (rel. int.): 357 (56, M^+), 341 (41), 340 (25), 274 (32), 258 (11), 257 (23), 243 (11), 242 (17), 230 (21), 188 (18), 161 (11), 160 (70), 135 (11), 134 (100), 124 (33), 123 (24), 122 (11), 120 (47), 109 (18), 108 (12), 107 (17), 95 (26), 92 (14), 77 (25). HR-EI-MS: Calcd for $C_{18}H_{22}F_3NO_2$: 357.1552; found: 357.1554. Anal. Calcd for $C_{18}H_{22}F_3NO_2$ (357.38): C, 60.49; H, 6.21; N, 3.92. Found: C, 60.41; H, 5.83; N, 3.90.

(Z)-N-Methyl-[(1R,2S)-2-(trifluoromethyl)-2-(trimethylsilyloxy)-bornan-3-yliden]amine N-oxide (**6**). The crude product was purified by column chromatography on silica gel using first CH_2Cl_2/hexane (3:2) and then CH_2Cl_2 with increasing amounts of ethyl acetate (0–50%) as eluents. The product was isolated as a yellowish oil. Yield: 270 mg (80%). An analytically pure sample was obtained by crystallisation. Colourless crystals, m.p. 74–76 °C (hexane); $[\alpha]_D^{25}$ +133.2 (*c* 0.008, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.18 (9H, s, $(CH_3)_3Si$), 0.93, 1.01, 1.09 (9H, 3s, $3CH_3$), 1.40–2.00 (4H, m, $2CH_2$), 2.60 (1H, $^3J_{H,H}$ = 4.4 Hz, CH), 3.68 (3H, s, CH_3N). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 1.9 (($CH_3)_3Si$), 10.7, 19.6, 21.9 ($3CH_3$), 23.8, 27.9 ($2CH_2$), 48.8, 55.9 ($2C_q$), 52.6 (CH), 81.4 (q, $^2J_{C,F}$ = 29.3 Hz, C_q),

124.6 (q, $^1J_{C,F}$ = 290.6 Hz, CF_3), 150.2 (C=N). ^{19}F NMR (188 MHz, $CDCl_3$): δ −64.9 (s, CF_3). IR (KBr): ν 3022*w* 3022*w*, 2988*w*, 2959*m*, 1632*w* (C=N), 1460*w*, 1393*w*, 1327*m*, 1263*s*, 1251*s*, 1179*vs*, 1141*vs*, 1106*m*, 1020*m*, 1011*m*, 963*w*, 898*m*, 869*m*, 845*s*, 760*w* cm^{-1}. CI-MS (NH_3) *m*/*z* (rel. int.): 338 (100, $[M+1]^+$, 322 (20). HR-ESI-MS (NaI): Calcd for $C_{15}H_{26}F_3NO_2SiN$: 360.1582; found: 360.1583.

4.4. Desilylation of nitrone 6

To a solution of nitrone **6** (337 mg, 1 mmol) in CH_2Cl_2 (1 mL), 2 mL (2 mmol) of a TBAF solution in THF were added and the mixture was stirred for 72 h at room temperature. Then the mixture was diluted with CH_2Cl_2 and washed with water. The separated organic layers were collected and dried over anhydrous $MgSO_4$. After filtration, the solutions were evaporated to dryness. The pure product was obtained by crystallisation. *(Z)-N-Methyl-[(1R,2S)-2-(trifluoromethyl)bornan-2-ol-3-yliden]amine N-oxide* (**5a**). Yield: 236 mg (89%). Colourless crystals, m.p. 246–249 °C (CH_2Cl_2/hexane); $[\alpha]_D^{25}$ +162.4 (*c* 0.010, $CHCl_3$).

4.5. Photo-isomerisation of nitrone 5a

A solution of **5a** (260 mg, 1 mmol) in methanol (100 mL) was stirred magnetically in a quartz flask, while a stream of argon was bubbled through the solution, which was irradiated with a high-pressure mercury lamp. After 1 h, the reaction was complete (TLC), and the solvent was evaporated in vacuo. The semi-solid residue was purified by column chromatography on silica gel using hexane with increasing amounts of CH_2Cl_2 (0–40%) as the eluent. Two main fractions containing the separated diastereoisomers 2-*exo*,3-*endo*- and 2-*exo*,3-*exo*-**7** were isolated in an overall yield of 182 mg (70%).

*(1R,2S,3S)-2-Hydroxy-2′-methyl-2-(trifluoromethyl)spiro[bornan-3,3′-oxaziridine] (2-exo,3-endo-***7**). Isolated as the less polar fraction. Yield: 70 mg (27%). Pure product was obtained by crystallisation. Colourless crystals, m.p. 107–108 °C (hexane); $[\alpha]_D^{25}$ −28.5 (*c* 0.2, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.97, 1.06, 1.15 (9H, 3s, $3CH_3$), 1.57–1.89 (4H, m, $2CH_2$), 1.95 (1H, d, $^2J_{H,H}$ = 4.2 Hz, CH), 1.93–1.97 (1H, m, CH), 2.79 (3H, s, CH_3N), 3.06 (1H, s, OH). ^{13}C NMR (50 MHz, $CDCl_3$): δ 9.8, 19.2, 21.6 ($3CH_3$), 21.1, 28.7 ($2CH_2$), 42.9 (CH), 44.6 (CH_3N), 48.0, 52.7 ($2C_q$), 80.3 (q, $^2J_{C,F}$ = 25.9 Hz, C_q), 93.4 (OCN); 124.7 (q, $^1J_{C,F}$ = 287.8 Hz, CF_3). ^{19}F NMR (188 MHz, $CDCl_3$): δ −71.3 (s, CF_3). IR (KBr): ν 3447*s* (br, OH), 3013*m*, 2994*m*, 2971*m*, 2937*m*, 2891*m*, 1636*w*, 1460*m*, 1432*m*, 1396*m*, 1387*m*, 1338*w*, 1289*s*, 1281*s*, 1242*w*, 1227*w*, 1167*vs*, 1151*s*, 1126*s*, 1111*m*, 1015*m*, 1000*m*, 973*m*, 953*m*, 924*w*, 854*m*, 811*w*, 710*m*, 621*w* cm^{-1}. CI-MS (NH_3) *m*/*z* (rel. int.): 267 (13), 266 (100, $[M+1]^+$). HR-ESI-MS (NaI): Calcd for $C_{12}H_{18}F_3NO_2Na$: 288.1187; found: 288.1187.

*(1R,2S,3R)-2-Hydroxy-2′-methyl-2-(trifluoromethyl)spiro[bornan- 3,3′-oxaziridine] (2-exo,3-exo-***7**). Isolated as the more polar fraction. Yield: 122 mg (43%). Pure product was obtained by crystallisation. Colourless crystals, m.p. 88–90 °C (hexane); $[\alpha]_D^{25}$ −73.5 (*c* 0.2, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.98, 1.08, 1.16 (9H, 3s, $3CH_3$), 1.45–1.95 (4H, m, $2CH_2$), 1.98–2.02 (1H, m, CH), 2.65 (1H, s, OH), 2.81 (3H, s, CH_3N). ^{13}C NMR (50 MHz, $CDCl_3$): δ 9.9, 19.5, 21.4 ($3CH_3$); 20.6, 28.5 ($2CH_2$); 42.7 (CH); 46.2 (CH_3N); 48.6, 52.7 ($2C_q$); 80.4 (q, $^2J_{C,F}$ = 26.5 Hz, C_q); 92.3 (OCN); 125.0 (q, $^1J_{C,F}$ = 287.7 Hz, CF_3). ^{19}F NMR (188 MHz, $CDCl_3$): δ −70.5 (s, CF_3). IR (KBr): ν 3490*s* (br, OH), 2983*m*, 2971*m*, 2938*m*, 1636*w*, 1467*w*, 1460*w*, 1435*w*, 1397*m*, 1389*m*, 1379*m*, 1281*s*, 1163*vs*, 1128*s*, 1122*s*, 1011*w*, 988*w*, 976*m*, 953*w*, 912*m*, 820*w*, 754*w*, 686*w* cm^{-1}. CI-MS (NH_3) *m*/*z* (rel. int.): 267 (12), 266 (100, $[M+1]^+$). HR-ESI-MS (NaI): Calcd for $C_{12}H_{18}F_3NO_2Na$: 288.1187; found: 288.1184.

4.6. X-ray crystal-structure determination of 5g

All measurements were performed on a Nonius KappaCCD area-detector diffractometer [14] using graphite-monochromated Mo Kα radiation (λ 0.71073 Å) and an Oxford Cryosystems Cryostream 700 cooler. The data collection and refinement parameters are given below [15] and a view of the molecule is shown in Fig. 1. Data reduction was performed with *HKL Denzo and Scalepack* [16]. The intensities were corrected for Lorentz and polarization effects, but not for absorption. Equivalent reflections were merged. The structures were solved by direct methods using *SIR92* [17] which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. The hydroxy H-atom was placed in the position indicated by a difference electron density map and its position was allowed to refine together with an isotropic displacement parameter. All remaining H-atoms were placed in geometrically calculated positions and refined by using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to $1.2U_{eq}$ of its parent C-atom ($1.5U_{eq}$ for the methyl groups). The refinement of the structures was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied. Neutral atom scattering factors for non-H-atoms were taken from Ref. [18], and the scattering factors for H-atoms were taken from Ref. [19] Anomalous dispersion effects were included in F_c [20]; the values for f' and f'' were those of Ref. [21]. The values of the mass attenuation coefficients are those of Ref. [22]. All calculations were performed using the *SHELXL97* [23] program.

Crystal data for **5g**: $C_{17}H_{20}F_3NO_2$, M = 327.34, crystallised from CH_2Cl_2/hexane, colourless, prism, crystal dimensions 0.15 mm × 0.18 mm × 0.28 mm, orthorhombic, space group $P2_12_12_1$, Z = 4, reflections for cell determination 2089, 2θ range for cell determination 4–55°, a = 7.2990(3) Å, b = 12.8005(5) Å, c = 16.8843(6) Å, V = 1577.5(1) Å^3, T = 160(1) K, D_X = 1.378 g cm^{-3}, μ(Mo Kα) = 0.113 mm^{-1}, scan type ϕ and ω, $2\theta_{(max)}$ = 55°, total reflections measured 22,221, symmetry independent reflections 2080, reflections with $I > 2\sigma(I)$ 1707, reflections used in refinement 2080, parameters refined 216; $R(F)$ [$I > 2\sigma(I)$ reflections] = 0.0479, $wR(F^2)$ [all data] = 0.1117 ($w = [\sigma(F_o^2) + (0.0633P)^2 + 0.0664P]^{-1}$, where $P = (F_o^2 + 2F_c^2/3)$, goodness of fit 1.107, final Δ_{max}/σ 0.001, $\Delta\rho$ (max; min) = 0.38; −0.33 e Å^{-3}, secondary extinction coefficient = 0.123(8).

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