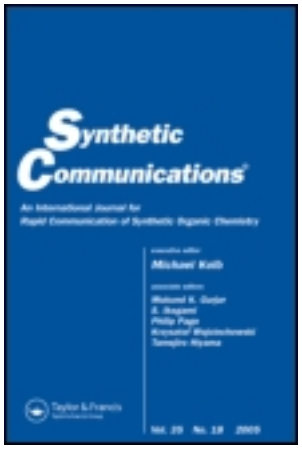

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Easy Access to cis-3-(Benzoxazol-2-yl)cyclopentanecarboxylic Acids from Camphorquinone and o-Aminophenols via an Unexpected Opening of Camphor Ring

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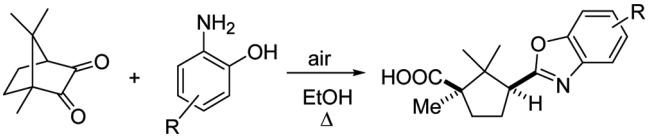
EASY ACCESS TO *cis*-3-(BENZOXAZOL-2-YL)CYCLOPENTANECARBOXYLIC ACIDS FROM CAMPHORQUINONE AND o-AMINOPHENOLS VIA AN UNEXPECTED OPENING OF CAMPHOR RING

Joanna Nowicka-Scheibe
West Pomeranian University of Technology, Szczecin, Institute of Chemistry and Environmental Protection, Szczecin, Poland

GRAPHICAL ABSTRACT



Abstract *An unexpected formation of* cis-*1,2,2-trimethyl-3-(benzoxazol-2-yl)cyclopentanecarboxylic acids was observed as the result of an oxidative C-C bond cleavage of the camphor ring in the intermediate imine during the condensation reactions between camphorquinone and o-aminophenols conducted under open air conditions.*

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Keywords Air oxidation; benzoxazole; caphoroquinone; condensation; o-aminophenols; ring opening

INTRODUCTION

The reactions of 1,2-diketones with amino alcohols were investigated by several research groups.[1] Depending on the molar ratio of the reagents used, structures of 1,2-diketones and N,O-binucleophiles or reaction conditions condensation reactions proceeding usually via Schiff bases lead to monocyclic oxazines or oxazolidines,[1] bicyclic,[2] or tricyclic[3,4] oxazino-oxazines or bisoxazolidines, belonging to the so-called propellanes.

In previous publications we reported a synthetic and structural study on propellanes derived from 1,2-cyclohexanedione and o-aminophenols and we demonstrated that the condensation reaction between 4-substituted 1,2-cyclohexanedione

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and substituted o-aminophenols yields, in a regio- and stereoselective manner, dibenzodioxadiaza[4.4.4]propellanes as single diastereoizomers (Scheme 1).[5]

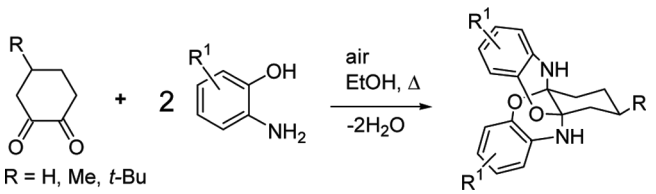
RESULTS AND DISCUSSION

In the present communication an unexpected formation of *cis*-1,2,2-trimethyl-3-(benzoxazol-2-yl)cyclopentanecarboxylic acids **4** in the reaction between camphoroquinone and a variety of substituted o-aminophenols is reported.

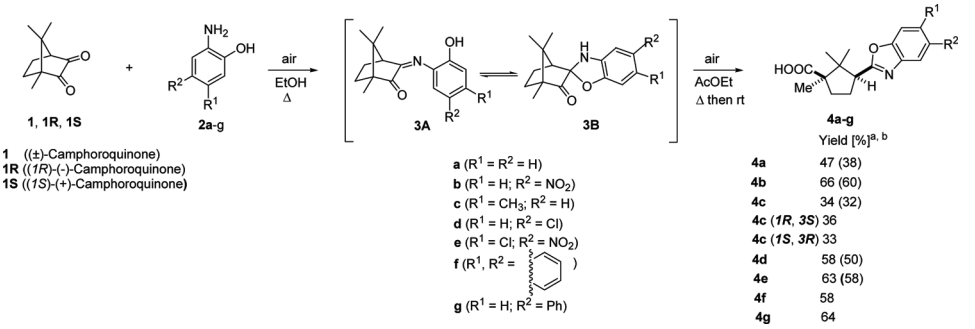
In the primary experiment performed in typical conditions (not air-protected reflux in EtOH solution) using 2-aminophenol (**2a**) and D,L-camphoroquinone (**1**) in 2:1 molar ratio, *cis*-1,2,2-trimethyl-3-(benzoxazol-2-yl)cyclopentanecarboxylic acid derivative (**4a**) was obtained in 47% yield after column chromatography (Scheme 2). Further experiments performed using D,L-camphoroquinone (**1**), enantiomerically pure isomers, and other derivatives of 2-aminophenols (**2b–e**) supported 3-(benzoxazol-2-yl)cyclopentanecarboxylic acid derivative formation in these conditions, although an influence of both factors such as substitution pattern in the o-aminophenol ring and different molar ratio of the reagents used on the yield of the product **4** was observed (Scheme 2). In general, an application of o-aminophenol with electron-withdrawing groups and using 1:2 molar ratio of reagents (**1**:**2a–g**) led to the better yields. Moreover, the twice-performed experiments revealed that optically active substrates **1R** and **1S** gave optically active products **4c** (***1R,3S***) ($[\alpha]_D = -29.33$) and **4c** (***1S,3R***) ($[\alpha]_D = +27.35$) in 36 and 33% yields, respectively.

In contrast to these results, a condensation performed in oxygen-free conditions (argon balloon) led to the regioselective formation of imine **3A**, which nevertheless was easily transformed to corresponding 3-(benzoxazol-2-yl)cyclopentanecarboxylic acid during purification in air conditions. These results indicated an oxidative process, in which aromatization leading to benzoxazole ring acts as a driving force for C-C bond cleavage of the camphor ring. This process starts from imine **3A**, which is formed regioselectively from the less hindered carbonyl group. The likely reaction pathway is shown in Scheme 2.

A synthesis of benzoxazoles from aldehydes and o-aminophenols via Schiff bases in oxidative conditions is well defined. In this approach 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ),[6] $PhI(OAc)_2$,[7] $ThClO_4$,[8] and $BaMnO_4$[9] were used as oxidants. Recently catalytic 4-metoxy-2,2,6,6-tetramethylpiperidine 1-oxyl (4-Me-TEMPO)[10] was used as well. There are also reports that benzoxazole can be formed from aldehydes under oxygen over carbon[11] or even under air.[12] Besides, Schiff bases derived from aldehydes or ketones were transformed into benzoxazoles under



Scheme 1. Synthesis of dibenzodioxadiaza[4.4.4]propellanes.



Scheme 2. Synthesis of **4a**–**g** in the condensation reaction of camphoroquinones **1** and o-aminophenols (**2a**–**g**). [a]Yield obtained by using 1:2 ratio of reagents (**1**:**2a**–**g**). [b]Yield obtained by using 1:1 ratio of reagents (**1**:**2a**–**e**) is given in the parentheses.

photochemical conditions.[13] Among the reactions studied under these conditions, the condensation between 1,2-dibenzoil and o-aminophenol proceeds with C-C bond cleavage toward 2-phenylbenzoxazole. However, the formation of benzoxazoles from cyclic 1,2-diones was hitherto unreported.

Because it was established that the transformation of intermediate imine **3A** to monocyclic acid **4** required oxidative conditions, the attempts to find the best oxidant to optimize the yield of **4** were taken. Various typical oxidants as H_2O_2, DDQ, SeO_2, and Oxone did not give positive results. The attempts resulted in a lot of by-products. It was impossible to isolate the main compound from the reaction mixture. An application of oxygen in the presence of activated carbon (Darco KB)[11] improved yields only slightly (**4c**, yield 36%).

A screening of common organic solvents [CH_3OH, EtOH, n-propyl and isopropyl alcohol, EtOAc, toluene, CH_3CN, EtOH with catalytic amount of P-toluenesulfonic acid (PTSA)] was also performed to find the best solvent and reaction time. Ethanol was the best solvent for imine formation, while ethyl acetate was good enough to form **4**. The best reaction times were 2 h under reflux in ethanol in an air atmosphere and 4 h under reflux in ethyl acetate followed by standing at room temperature for 3 days in an open flask. After this time, the products were purified on silica gel by using column chromatography (ethyl acetate–hexane 3:7).

All the products were characterized by ^{1}H NMR, ^{13}C NMR, infrared (IR) spectra, gas chromatography–mass spectrometry (GC/MS), electrospray ionization (ESI)–MS, and elemental analyses. The structures of unstable imines **3A** were confirmed by comparing ^{13}C NMR spectrum of crude **3A**(**b**) with ^{13}C NMR spectrum of referenced crude imine derived from D,L-camphoroquinone (**1**) and o-anisidine.[14] Characteristic ^{13}C NMR chemical shifts (205.5 ppm, 175.2 ppm, and 206.0 ppm, 175.2 ppm respectively for **3A**(**b**) and referenced imine) can be assigned to C=O and C=N. The structure of **4c** was determined by x-ray diffraction (Fig. 1).[15] Additionally, the ^{1}H, ^{15}N HMBC NMR were used as techniques for distinguishing benzoxazole ring or imine groups. By applying these methods, chemical shifts of nitrogen atoms (referenced to nitromethane) for compounds **4a**

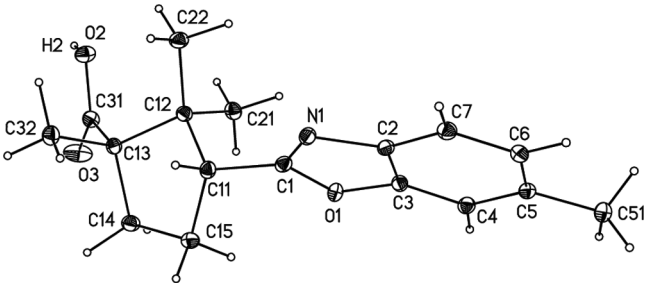


Figure 1. X-ray structure of **4c**.

and **4b** were detected at −136 ppm, indicating the nitrogen atom of benzoxazole.[16] The structures of **4a** and **b** and **4d**–**g** were proved by comparing their ^{13}C NMR spectra to the ^{13}C NMR spectra of **4c**.

To sum up, the condensation reactions of D,L-camphoroquinone, its enantiomerically pure antipodes, and a variety of substituted o-aminophenols conducted in unprotected conditions led to *cis*-1,2,2-trimethtyl-3-(benzoxazol-2-yl)cyclopentanecarboxylic acids. The obtained *cis*-bifunctionalizedcyclopentanes may be useful compounds as building blocks in drug discovery because benzoxazoles,[17] especially 2-cyclopentylbenzoxazoles,[18] were recognized as pharmacophores. Moreover, it is necessary to point out that easy access to both enantiomerically pure acids, possessing nonenolizable carboxyl groups, obtained from commercially available, enantiomerically pure camphoroquinones opens new possibilities in asymmetric synthesis (e.g., in the field of ligand design). These compounds could also expand the set of compounds applied as chiral derivatizing agents.

EXPERIMENTAL

Melting points were determined on a Boetius hot-stage apparatus. ^1H, ^{13}C NMR spectroscopic measurements were performed on a Bruker DPX 400 spectrometer equipped with a 5-mm 1H/BB inverse probehead, operating at 400.13 and 100.62 MHz. Purity and molecular mass determinations were carried out by GC-MS on a Hewlett-Packard instrument (model HP 6890) equipped with a mass detector HP 5973. The analytical procedure was developed on 30-m-long capillary column, 0.2 mm in diameter, with methyl-siloxane modified with phenyl groups (5% Ph, Me siloxane) in the 0.25-μm active phase layer. The ESI mass spectra were obtained on a Waters/Micromass (Manchester, UK) ZQ2000 mass spectrometer (single quadrupole type instrument, Z-spray, software Mass Lynx V3.5). The sample solutions were prepared in methanol. The concentration of **1** and **2** compounds was 1×10^{-4} M. The sample solutions were infused into the ESI source using a Harvard pump at a flow rate of 80 mL/min. The ESI source potentials were capillary 3 kV, lens 0.5 kV, extractor 4 V, and cone voltage 10 V. Nitrogen was used as the nebulizing and desolvating gas at flow rates of 100 and 300 L/h, respectively.

Silica gel (0.04–0.063 mm, Merck) was used for preparative column chromatography. Infrared (IR) spectra were taken with a Specord M80 instrument. Elemental analyses were performed on EuroEA 3000 series, EuroVector CHNS-O Elemental instrument.

The x-ray diffraction studies were performed on a Kuma KM4 CCD x-axis four-circle diffractometer equipped with an Oxford Cryosystem Cooler using graphite monochromatedMoKa radiation. The data were corrected for Lorentz and polarization effects as well as for absorption. The structure was solved by direct methods (SHELXS-97) and refined by the full-matrix least-squares methods using the SHELXL-97 program.[19] The crystal data and structure refinement are summarized in Table 1. Selected bond lengths (Å) and angles (°) are summarized in Table 2 and possible hydrogen bonds and short contacts in Table 3. Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 8252.

General Procedure for Synthesis of 4a–g

A solution of camphoroquinone (0.166 g, 0.001 mol) and corresponding 2-aminophenol (0.002 mol) in ethanol (10 mL) was refluxed for 2 h, and the solvent was removed under reduced pressure. The residue was dissolved in ethyl acetate and stirred under reflux for 4 h. The reaction mixture was left standing in an air atmosphere for 3 days. After this time, the solvent was removed, and the crude product was purified by column chromatography on silica gel with ethyl acetate/hexane (3:7) as a solvent and crystallized.

Data

Compound 4a, (1*RS*,3*SR*)-3-(benzoxazol-2-yl)-1,2,2-trimethylcyclopentanecarboxylic acid. White solid, mp 208–210 °C from n-hexane–ethyl acetate. IR (KBr pellet): $\nu = 3020$ (v br), 2972, 2650 (v br), 1692 (s), 1564 (m), 1456 (m), 1292 (m), 1246 (m), 1158 (m), 952 (w), 764 (w), 750 (m) cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$–DMSO-d_6 = 5:1) $\delta = 0.76$ (3 H, s, 1-CH_3), 1.34 (3 H, s, 2-CH_3), 1.35 (3 H, s, 2-CH_3), 1.63 (1 H, ddd, $J = 13.7$, 9.5, 4.2 Hz, C<u>H</u>H-5), 2.07–2.20 (1 H, m, C<u>H</u>H-4), 2.47–2.61 (1 H, m, CH<u>H</u>-4), 2.71 (1H, ddd, $J = 13.7$, 12.2, 6.8 Hz, CH<u>H</u>-5), 3.46 (1 H, t, $J = 9.8$ Hz, CH-3), 7.28–7.34 (2 H, m, C_6H_4), 7.50–7.55 (1 H, m, C_6H_4), 7.64–7.69 (1 H, m, C_6H_4); ^{13}C NMR (100.6 MHz, $CDCl_3$–DMSO-d_6 = 5:1): $\delta = 21.05$ (1-CH_3), 21.97, 22.44 (2 × 2-CH_3), 23.58 (CH_2-4), 32.33 (CH_2-5), 47.38 (C-2), 47.84 (CH-3), 55.73 (C-1), 110.29, 119.31, 123.96, 124.40, 140.90, 150.59 (C_6H_4), 167.64 (C=N), 177.53 (C=O); GC-MS (EI, 70 eV): $m/z = 273$ (69, $M^{+\cdot}$), 258 (12), 228 (100), 212 (14), 200 (11), 187 (33), 186 (33), 172 (16), 158 (21), 146 (83), 133 (60), 120 (12), 109 (55), 65 (10), 41 (11). Found: C, 70.20; H, 6.94; N, 5.06. $C_{16}H_{19}NO_3$ requires C, 70.31; H, 7.01; N, 5.12%.

Compound 4b, (1*RS*,3*SR*)-1,2,2-trimethyl-3-(5-nitrobenzooxazol-2-yl)cyclopentanecarboxylic acid. Yellow solid, mp 229–231 °C from n-hexane–ethyl acetate. IR (KBr pellet): $\nu = 3432$ (br), 3108 (w), 2972 (vbr), 1692 (vs), 1614 (s), 1562 (S), 1526 (vs), 1458 (m), 1440 (m), 1350 (s), 1264 (m), 1154 (m), 1122

(m), 962 (m), 896 (m), 824 (m), 736 (s), 692 (m) cm^{-1}; ^1H NMR (400.1 MHz, DMSO-d_6) $\delta = 0.67$ (3 H, s, 1-CH_3), 1.28 (3 H, s, 2-CH_3), 1.30 (3 H, s, 2-CH_3), 1.57 (1 H, ddd, $J = 13.6$, 9.6, 3.9 Hz, C<u>H</u>H-5), 2.08–2.20 (1 H, m, C<u>H</u>H-4), 2.36–2.48 (1 H, m, CH<u>H</u>-4), 2.59 (1 H, ddd, $J = 13.6$, 12.7, 6.8 Hz, CH<u>H</u>-5), 3.61 (1 H, t, $J = 9.8$ Hz, CH-3), 7.97 (1 H, d, $J = 9.0$ Hz, Ar), 8.30 (1 H, dd, $J = 9.0$, 2.3 Hz, Ar), 8.61 (1 H, d, $J = 2.3$ Hz, Ar), 12.40 (1 H, v br s, COOH); ^{13}C NMR (100.6 MHz, DMSO-$d_6 = 5$): $\delta = 21.11$ (1-CH_3), 21.81, 22.50 ($2 \times$ 2-CH_3), 23.35 (CH_2-4), 32.28 (CH_2-5), 47.35 (C-2), 47.45 (CH-3), 55.65 (C-1), 111.60, 115.55, 121.09, 141.11, 144.88, 154.21, 171.28 (Ar), 176.81 (C=O); ESI-MS $m/z = 318$. Found: C, 60.45; H, 5.77; N, 8.48. $C_{16}H_{18}N_2O_5$ requires C, 60.37; H,5.70; N, 8.80%.

Compound 4c, (1*RS*,3*SR*)-1,2,2-trimethyl-3-(6-methyl-benzooxazol-2-yl)cyclopentanecarboxylic acid. White solid, mp 188–190 °C from n-hexane–ethyl acetate. IR (KBr pellet): $\nu = 3432$ (br), 2968 (vbr), 1718 (vs), 1608 (m), 1562 (s), 1460 (m), 1242 (s), 1156 (m), 1116 (m), 864 (m), 810 (s), 734 (m), 692 (m) cm^{-1}; ^1H NMR (400.1 MHz, DMSO-d_6) $\delta = 0.63$ (3 H, s, 1-CH_3), 1.27 (3 H, s, 2-CH_3), 1.29 (3 H, s, 2-CH_3), 1.53 (1 H, ddd, $J = 13.5$, 9.6, 4.0 Hz, C<u>H</u>H-5), 2.02–2.13 (1 H, m, C<u>H</u>H-4), 2.34–2.48 (4 H, m, CH_3, CH<u>H</u>-4), 2.56 (1 H, ddd, $J = 13.5$, 12.2, 7.1 Hz, CH<u>H</u>-5), 3.50 (1 H, t, $J = 9.6$ Hz, CH-3), 7.16 (1 H, br d, $J = 7.7$ Hz, Ar), 7.50 (1 H, br s, Ar), 7.84 (1 H, d, $J = 8.1$ Hz, Ar), 12.29 (1 H, v br s, COOH); ^{13}C NMR (100.6 MHz, DMSO-d_6): $\delta = 21.07$ (1-CH_3), 21.30 (CH_3), 21.83, 22.53 ($2 \times$ 2-CH_3), 23.34 (CH_2-4), 32.24 (CH_2-5), 46.97 (C-2), 47.23 (CH-3), 55.49 (C-1), 110.71, 118.85, 125.39, 134.68, 138.58, 150.68, 166.98 (Ar), 176.89 (C=O); GC-MS (EI, 70 eV): $m/z = 287$ (84, M^+), 269 (23), 242 (100), 224 (17), 201 (83), 183 (20), 160 (89), 142 (73), 123 (74), 95 (12), 77 (27), 59 (4), 41 (32). Found: C, 71.28; H, 7.15, N, 4.34. $C_{17}H_{21}NO_3$ requires C, 71.06; H, 7.37; N, 4.87%.

Compound 4c (1R,3S), (1*R*,3*S*)-1,2,2-trimethyl-3-(6-methyl-benzooxazol-2-yl)cyclopentanecarboxylic acid. $[\alpha]_D = -29.33$. White solid, mp 188–190 °C from n-hexane–ethyl acetate. ^1H and ^{13}C NMR spectral data for this product were identical with those reported for **4c**.

Compound 4c (1S,3R), (1*S*,3*R*)-1,2,2-trimethyl-3-(6-methyl-benzooxazol-2-yl)cyclopentanecarboxylic acid. $[\alpha]_D = +27.35$. White solid, mp 187–191 °C from n-hexane–ethyl acetate. ^1H and ^{13}C NMR spectral data for this product were identical with those reported for **4c**.

Compound 4d, (1*RS*,3*SR*)-3-(5-chlorobenzooxazol-2-yl)-1,2,2-trimethyl-cyclopentanecarboxylic acid. Yellow solid, mp 209–211 °C from n-hexane–ethyl acetate. IR (KBr pellet): $\nu = 3436$ (br), 2968 (vbr), 1692 (vs), 1608 (w), 1558 (s), 1452 (s), 1376 (m), 1288 (m), 1260 (m), 1156 (m), 1122 (m), 1056 (m), 964 (m), 922 (m), 800 (s), 704 (m) cm^{-1}; ^1H NMR (400.1 MHz, DMSO-d_6) $\delta = 0.65$ (3 H, s, 1-CH_3), 1.26 (3 H, s, 2-CH_3), 1.27 (3 H, s, 2-CH_3), 1.55 (1 H, ddd, $J = 13.4$, 9.5, 3.3 Hz, C<u>H</u>H-5), 2.04–2.17 (1 H, m, C<u>H</u>H-4), 2.34–2.46 (1 H, m, CH<u>H</u>-4), 2.58 (1 H, ddd, $J = 13.4$, 12.2, 6.8 Hz, CH<u>H</u>-5), 3.54 (1 H, t, $J = 9.5$ Hz, CH-3), 7.41 (1 H, dd, $J = 8.6$, 2.0 Hz, Ar), 7.75 (1 H, d, $J = 8.6$ Hz, Ar), 7.84 (1 H, d, $J = 2.0$ Hz, Hz, Ar), 12.30 (1 H, v br s, COOH); ^{13}C NMR (100.6 MHz, DMSO-d_6): $\delta = 21.08$ (1-CH_3), 21.83, 22.51 ($2 \times$ 2-CH_3), 23.33 (CH_2-4), 32.26 (CH_2-5), 47.17 (C-2), 47.35 (CH-3), 55.56 (C-1), 112.09, 119.30, 124.92, 128.68, 142.09, 149.22, 169.44

(Ar), 176.83 (C=O); GC-MS (EI, 70 eV): $m/z = 307$ (37, M^+), 281 (1), 262 (9), 236 (3), 218 (2), 194 (16), 169 (13), 143 (38), 109 (100), 91 (35), 67 (28), 50 (26), 41 (33). Found: C, 62.60; H, 5.41; Cl, 11.06, N, 4,12. $C_{16}H_{18}ClNO_3$ requires C, 62.44; H, 5.89; Cl, 11.52; N, 4.55%.

Compound 4e, (1*RS*,3*SR*)-3-(6-chloro-5-nitro-benzooxazol-2-yl)-1,2, 2-trimethyl-cyclopentanecarboxylic acid. Yellow solid, mp 216–218 °C from n-hexane–ethyl acetate. IR (KBr pellet): $\nu = 3420$ (br), 2972 (vbr), 1690 (vs), 1608 (w), 1554 (vs), 1536 (vs), 1448 (vs), 1408 (w), 1344 (m), 1260 (m), 1146 (m), 1118 (m), 1004 (m), 960 (m), 882 (m), 836 (m) cm^{-1}; ^1H NMR (400.1 MHz, DMSO-d_6) $\delta = 0.66$ (3 H, s, 1-CH_3), 1.28 (3 H, s, 2-CH_3), 1.29 (3 H, s, 2-CH_3), 1.56 (1 H, ddd, $J = 13.6$, 9.6, 3.9 Hz, C<u>H</u>H-5), 2.07–2.20 (1 H, m, C<u>H</u>H-4), 2.33–2.46 (1 H, m, CH<u>H</u>-4), 2.58 (1 H, ddd, $J = 13.6$, 12.1, 7.1 Hz, CH<u>H</u>-5), 3.62 (1 H, t, $J = 9.5$ Hz, CH-3), 8.21 (1 H, s, Ar), 8.64 (1 H, s, Ar), 12.34 (1 H, v br s, COOH); ^{13}C NMR (100.6 MHz, DMSO-d_6): $\delta = 21.05$ (1-CH_3), 21.78, 22.44 (2 × 2-CH_3), 23.34 (CH_2-4), 32.26 (CH_2-5), 47.51 (C-2, CH-3), 55.64 (C-1), 109.13, 121.24, 121.68, 144.36, 144.56, 148.23, 173.35 (Ar), 176.71 (C=O); ESI-MS $m/z = 353$ $[M\text{-}H]^-$. Found: C, 54.76; H, 4.30; Cl, 9.89; N, 7.26%. $C_{16}H_{17}ClN_2O_5$ requires C, 54.48; H, 4.86; Cl, 10.05; N, 7.94%.

Compound 4f, (1*RS*,3*SR*)-1,2,2-trimethyl-3-naphtho[2,3-d]oxazol-2-yl-cyclopentanecarboxylic acid. Yellow solid, mp 223–225 °C from n-hexane–ethyl acetate. IR (KBr pellet): $\nu = 3412$ (vbr), 3040 (w), 2976 (vbr), 1692 (vs), 1650 (w), 1626 (m), 1568 (s), 1506 (m) 1444 (m), 1406 (s), 1310 (m), 1288 (s), 1248 (s), 1178 (m), 1118 (m), 956 (m), 868 (s), 742 (s) cm^{-1}; ^1H NMR (400.1 MHz, DMSO-d_6) $\delta = 0.70$ (3 H, s, 1-CH_3), 1.26 (3 H, s, 2-CH_3), 1.30 (3 H, s, 2-CH_3), 1.58 (1 H, ddd, $J = 13.2$, 9.6, 3.8 Hz, C<u>H</u>H-5), 2.14 (1 H, dtd, $J = 13.4$, 9.5, 6.9 Hz, C<u>H</u>H-4), 2.43–2.54 (1 H, m, CH<u>H</u>-4), 2.61 (1 H, ddd, $J = 13.2$, 12.1, 6.8 Hz, CH<u>H</u>-5), 3.59 (1 H, t, $J = 9.4$ Hz, CH-3), 7.48–7.56 (2 H, m, Ar), 8.02-8.10 (2 H, m, Ar), 8.18 (1 H, s, Ar), 8.26 (1 H, s, Ar), 12.30 (1 H, v br s, COOH); ^{13}C NMR (100.6 MHz, DMSO-d_6) $\delta = 21.14$ (1-CH_3), 21.80, 22.61 (2 × 2-CH_3), 23.31 (CH_2-4), 32.32 (CH_2-5), 47.21 (C-2), 47.49 (CH-3), 55.62 (C-1), 106.32, 116.61, 124.79, 125.51, 128.00, 128.42, 130.93, 131.07, 140.85, 149.29, 170.22 (Ar), 176.84 (C=O); GC-MS (EI, 70 eV): $m/z = 323$ (0), 295 (M-CO), 262 (28), 244 (23), 204 (17), 183 (14), 159 (7), 141 (5), 115 (17), 88 (4), 67 (3), 43 (17);

Found: C, 74.61; H, 6.40; N, 4.02%. $C_{20}H_{21}NO_3$ requires C, 74.28; H, 6.55; N, 4.33%.

Compound 4g, (1*RS*,3*SR*)-(1,2,2-trimethyl-3-(5-phenyl-benzooxazol-2-yl)-cyclopentanecarboxylic acid. White solid, mp 217–219 °C from n-hexane: ethyl acetate. IR (KBr pellet): $\nu = 3444$ (br), 2968 (vbr), 2336 (w), 1720 (vs), 1560 (s), 1470 (s). 1422 (m), 1380 (m), 1262 (m), 1210 (m), 1156 (m), 1112 (m), 956 (m), 820 (m), 760 (s), 696 (s) cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$: DMSO-$d_6 = 3{:}1$) (=0.78 (3 H, s, 1-CH_3), 1.34 (3 H, s, 2-CH_3), 1.36 (3 H, s, 2-CH_3), 1.63 (1 H, ddd, $J = 13.2$, 9.5, 3.5 Hz, C<u>H</u>H-5), 2.08–2.21 (1 H, m, C<u>H</u>H-4), 2.47–2.63 (1 H, m, CH<u>H</u>-4), 2.71 (1 H,td, $J = 13.2$, 6.6 Hz, CH<u>H</u>-5), 3.48 (1 H, t, $J = 9.5$ Hz, CH-3), 7.31–7.38 (1 H, m, C_6H_5), 7.45 (2 H, t, $J = 7.6$ Hz, C_6H_5), 7.54 (1 H, dt, J =ca. 8.4, 1.7 Hz, C_6H_3), 7.57–7.63 (3 H, m, C_6H_3, C_6H_5), 7.85 (1 H, br s, C_6H_3); ^{13}C NMR

(100.6 MHz, $CDCl_3$: DMSO-$d_6 = 3 : 1$): (=20.79 (1-CH_3), 21.67, 22.19 ($2 \times$ 2-CH_3), 23.29 (CH_2-4), 32.06 (CH_2-5), 47.11 (C-2), 47.58 (CH-3), 55.41 (C-1), 110.15, 117.31, 123.52, 126.84, 128.52, 137.24, 140.45, 141.34, 149.87 (C_6H_3, C_6H_4), 168.05 (C=N), 177.06 (C=O); GC-MS (EI, 70 eV): $m/z = 305$ (36, M-CO_2), 276 (39), 259 (21), 237 (27), 209 (100), 139 (59), 115 (9), 41 (24); Found: C, 75.68; H, 6.34; N, 3.92%. $C_{22}H_{23}NO_3$ requires C, 75.62; H, 6.63; N, 4.01.

All additional data (e.g., X-ray, ^1H, ^{13}C NMR data) are available as Supplementary Matarial online.

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