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Heterocyclically Bridged Tricyclic β-Lactames: A Simple Synthesis of 1,2,2a,8a-Tetrahydro-3-oxa-1-aza-cyclobuta[*b*]naphthalen-2-ones

A. Takó[1,*], **K.-H. Ongania**[1], and **K. Wurst**[2]

[1] Institut für Organische Chemie, Leopold-Franzens-Universität Innsbruck, A-6020 Innsbruck, Austria

[2] Institut für Anorganische, Allgemeine und Theoretische Chemie, Leopold-Franzens-Universität Innsbruck, A-6020 Innsbruck, Austria

Summary. The tricylic 3,4-bridged β-lactames **7** and **8** containing a hetero atom as 3-substituent of the azetidin-2-one ring were synthesized by intramolecular radical cyclization using *cis*-substituted 3-(2-bromo-aryloxy)-azetidine-2-ones **6** as precursors. These precursors were generated by stereospecific acid chloride–imine reaction from the corresponding substituted (2-bromophenoxy)-acetic acid chlorides **2** and imine **5**.

Keywords. β-Lactames, tricyclic; β-Lactames, 3-(2-bromo-aryloxy)-; Intramolecular radical reaction; 6-*exo-trig* Cyclization.

Heteroüberbrückte tricyclische β-Lactame: Ein einfacher Zugang zu 1,2,2a,8a-Tetrahydro-3-oxa-1-aza-cyclobuta[*b*]naphthalin-2-onen

Zusammenfassung. Die cis-substituierten 3-(2-Bromaryloxy)-azetidin-2-one **6**, dargestellt durch stereospezifische Säurechlorid/Imin-Reaktion aus den entsprechenden (2-Brom-phenoxy)-acetylchloriden **2** und den Iminen **5**, reagieren im Zuge einer intramolekularen radikalischen *exo-trig*-Reaktion zu den 3,4-heteroüberbrückten tricyclischen β-Lactamen **7** und **8**.

Introduction

Intramolecular radical cyclization reactions have emerged as a powerful synthetic tool for the construction of both carbocyclic and heterocyclic compounds [1]. The very high rates of cyclization of 2-(5-hexenyl)phenyl and related radicals has made aryl radical cyclizations a standard method for the preparation of benzo-fused 6-membered rings. Previously known tricylic 3,4-bridged azetidin-2-ones contain carbocyclic rings only [2–7]. In most cases their synthesis is limited to the [2 + 2] addition of cyclohexene or related derivatives to chlorosulfonyl isocyanate. The here presented heterocyclic bridge is unknown in connection with the described tricyclic ring system, the only related example being a bicyclus containing a lactone bridge [8]. Since the analogue procedure for the addition of chlorosulfonyl

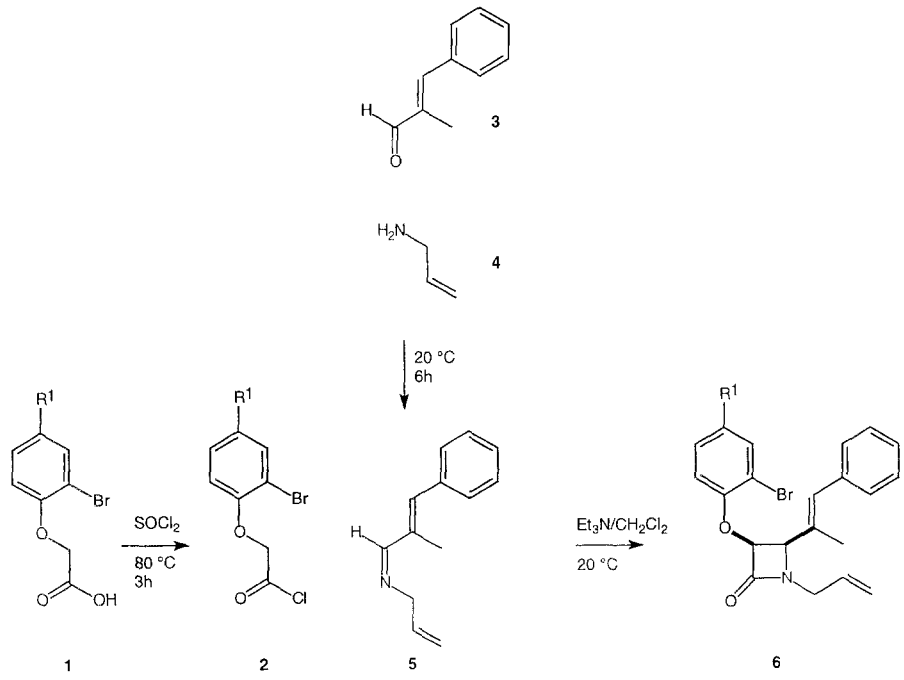
isocyanate to hetero-ene bonds has been described to fail [9], we have synthesized precursor models for the construction of this new class of compounds *via* intramolecular radical reaction. Suitable precursor lactames demand certain restrictions:

a) To be able to generate a six-membered ring, the azetidine-2-one must be *cis*-substituted in its 3- and 4-positions. To achieve this kind of substitution, the well known acid chloride–imine reaction is the most promising method [10].
b) The formation of the desired tricyclus requires that at least one of the two substituents contains another ring.
c) We decided to use the (2-bromophenoxy)-substituent in position 3 as radical donor and the 1-methyl-2-phenylvinyl substituent as radical acceptor in position 4 of the azetidin-2-one ring. The use of the chosen 4-substituent implies prochirality in the resulting precursor β-lactame. Hereby, a clear statement on the stereodifferentiation of the radical ring closure can be made.

In this communication we report on the synthesis of 1,2,2a,8a-tetrahydro-3-oxa-1-aza-cyclobuta[*b*]naphthalen-2-ones **7** and **8** by 6-*exo-trig* cyclisation. They represent a new class of polycyclic hetero-bridged β-lactames.

Results and Discussion

The β-lactames **6** required as educts for the following cyclization reaction have not been described in the literature. They were prepared in the usual manner by the acid chloride–imine reaction [11]; Scheme 1).

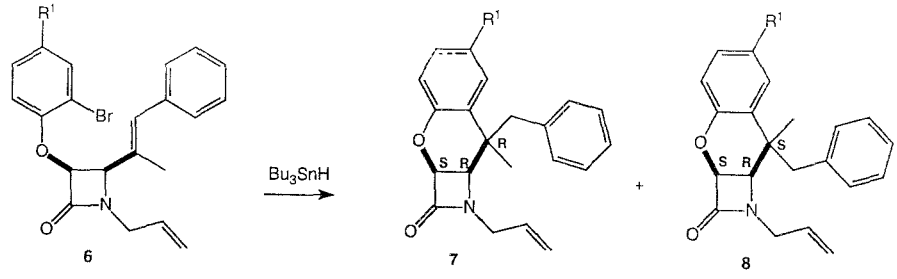


Scheme 1. Synthesis of precursor lactames **6** by acid chloride–imine reaction

The reactivity of substituted phenoxyacetic acid chlorides is high enough to allow reaction at room temperature. Thus, the synthesis of β-lactames using the acid chloride–imine reaction could be carried out using dichloromethane as solvent. The acid chlorides **2** smoothly react with imine **5** and triethylamine at 20°C diastereospecifically to (3*R*, 4*S*/3*S*, 4*R*)-azetidinones **6**. The relative stereochemistry of the resulting β-lactames **6** could easily be demonstrated to be *cis*-substituted using the vicinal coupling constant ($J_{3,4}$ = 4.8–5.0 Hz) of the β-lactam ring protons (*trans*-substitution would result in a coupling constant between 1 and 2 Hz [12]).

Using standard radical reaction conditions (tri-*n*-butyltin hydride, *AIBN*, benzene, 80°C), 1-allyl-3-(2-bromoaryloxy)-4-(1-ethyl-2-phenylvinyl)-azetidin-2-ones **6** react to build the two diastereomers **7** and **8** (Scheme 2, Table 1).

Primary generation of the 2-aryloxy radical in position 3 is followed by the regioselective reaction of this radical with the 4-(1-methyl-2-phenylvinyl)-substituent of the β-lactam. An *exo-trig* attack generates the more stable benzyl radical which is saturated by a hydrogen radical. The resulting product distribution shows a remarkable stereodifferentiation. Depending on the side of the radical attack relative to the double bond, one of two possible diastereomeres is formed. In the reaction described in this paper, regiospecific formation of the racemic (2a*S*, 8*R*, 8a*S*/2a*R*, 8*S*, 8a*R*) diastereomer **8** was preferred. Formation of a 7-ring – which would comply with the rules for ring closure – could not be observed [13]. Alkenylaryl radicals are known to have an increasing difference in strain energy between the transition states for *exo* and *endo* ring closure due to the presence of the aromatic ring [14]. The preferred formation of **8** from the intermediate phenyl radical cannot be easily explained. One possibility is that in the early transition state of the radical addition to the alkene, in which the distance between the reacting carbon atoms is about 2.3 Å, one of the possible conformations is preferred [15]. The proposed intermediate benzyl radical does not attack the 1-allyl



Scheme 2. Intramolecular radical cyclization reaction of precursor lactames **6**

Table 1. Product distribution of the radical cyclization reaction; all numbers represent isolated yields

Educts	R^1	Product A	Yield	Product B	Yield
6a	CH_3	**7a**	6%	**8a**	72%
6b	H	**7b**	6%	**8b**	76%

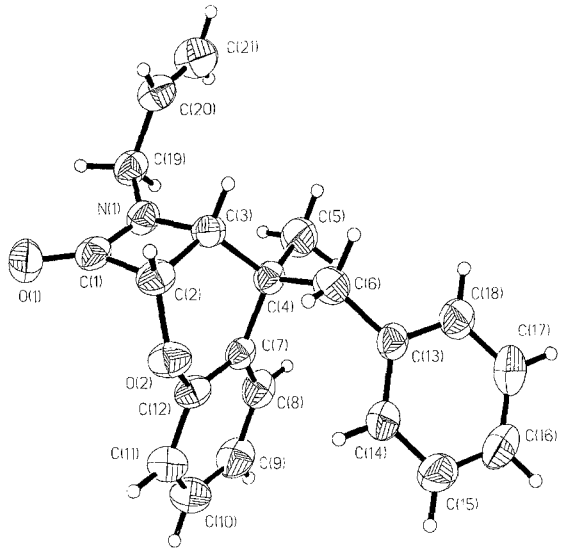


Fig. 1. X-ray crystal structure of (2a*S*, 8*R*,8a*S*)/(2a*R*,8*S*,8a*R*)-1-allyl-8-benzyl-8-methyl-1,2a,8,8a-tetrahydro-3-oxa-1-aza-cyclobuta[*b*]naphthalen-2-one (**8b**)

substituent which would result in the formation of a tetracyclus, bridging the lactam between positions 3 and 1.

The structure of the resulting products was determined using gradient supported homo- and heteronuclear correlation spectroscopy. The relative configuration of **8b** was proven by X-ray crystal structure determination of a single crystal, obtained by recrystallization of the product after chromatography (Fig. 1).

These examples, which are the first in a series of polycyclic β-lactames containing a heterocyclic bridge, show that intramolecular radical cyclization is a suitable tool for the synthesis of this hitherto unknown class of tricyclic β-lactames.

Experimental

NMR spectra were recorded with a Varian UNITY + 500 spectrometer. FTIR spectra were measured with a Mattson Galaxy Series FTIR 3000 instrument. Mass spectrometry data were received from a Finnigan MAT 95 equipment. All reagents and solvents were freshly distilled before use.

X-ray structure analysis of **8b**

$C_{21}H_{21}NO_2$ (319.4); orthorhombic, space group Pbca (Nr. 61); $a = 753.8(4)$, $(b) = 1885.4(9)$, $c = 2443.0(10)$ pm; V= 3.417(3) nm^3; $Z = 8$; $\mu = 0.079\,\text{mm}^{-1}$; F(000)= 1360; $\rho_{cal} = 1.242\,\text{g/cm}^3$; $T = 293$ K. The intensity data of a clear needle with the dimensions 0.3 $\times$0.3 $\times$ 0.9 mm were collected on a Siemens P4 diffractometer using graphite monochromatized MoK_α radiation ($\lambda = 71.073$ pm). Data were measured *via* ω-scans and corrected for *Lorentz* and polarization effects. A total of 2506 intensities (1867 unique, $R_{int} = 0.046$) were measured up to $2\theta_{max} = 42°$. The structure was solved by direct methods and refined on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters; hydrogen atoms were placed in calculated positions and treated as rigid groups. The final $wR(F^2)$ for 1139 reflections with $F_0 \geq 4\sigma(F_0)$ was 0.085, with a conventional $R(F)$ of 0.045 for 217 parameters [16, 17].

Procedure for the synthesis of substituted phenoxy acetic acid chlorides

(2-Bromo-4-methylphenoxy)-acetic acid (**1a**) and 2-bromophenoxy acetic acid (**1b**) were synthesized in the usual manner by reaction of the appropriately substituted 2-bromophenol with an equal amount of chloroacetic acid and 2 equivalents of NaOH. Workup and recrystallization of the resulting raw material from water yields 65% **1a** (m.p.: 144–145°C) and 67% **1b** (m.p.: 141–143°C).

(2-Bromo-4-methylphenoxy)-acetic acid chloride (**2a**) and 2-bromophenoxy acetic acid chloride (**2b**) were synthesized by boiling the acids with 3 equivalents of commercial grade thionyl chloride for 3 h, yielding 90–92% of pure acid chlorides **2a** (b.p.: 110°C at 0.04 mbar) and **2b** (b.p.: 91°C at 0.02 mbar, m.p.: 33–35°C). The acid chlorides were freshly distilled before used in the subsequent acid chloride–imine reaction.

Standard procedure for the synthesis of β-lactames via the acid chloride–imine reaction

10 mmol 2-methyl-3-phenylpropenal (**3**) and 10 mmol allylamine (**4**) were dissolved in 80 ml of dry benzene at 20°C. 5 g activated molecular sieve (diameter 4 Å) were added to remove the water. After the reaction was finished, as indicated by the formation of a clear solution and reaction control by NMR spectroscopy, the solvent was removed under reduced pressure. The total time required for the reaction was 6 h. The resulting imine **5** was used without further purification.

The β-lactames **6** were synthesized using the following standard procedure: 10 mmol crude imine **5** and 20 mmol triethylamine were dissolved in 200 ml dichloromethane under a nitrogen atmosphere. After preparing a solution of 13 mmol acid chloride **2** in 100 ml of dichloromethane, this solution was added dropwise to the imine/amine mixture over a period of 2 to 3 h at 20°C under vigorous stirring. After all acid chloride had been added, agitation was continued for another 14 h. After washing the reaction mixture with water several times and drying the organic phase, the solvent was removed under reduced pressure. The crude product was purified by chromatography or recrystallization.

1-Allyl-3-(2-bromo-4-methylphenoxy)-4-(1-methyl-2-phenylvinyl)-azetidin-2-one (**6a**)

Yield: 34%; $R_f = 0.49$ (CH_2Cl_2); FTIR ($CHCl_3$): $\bar{\nu} = 1755$ (C=O), 1493, 1252 (ArOC) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.01$ (s (d), 3H, C(CH_3)= CH-Ph), 2.26 (s, 3H, O-C_6H_3Br-CH_3), 3.60–3.68 (m, 1H, N-CH_2-CH=CH_2), 4.19–4.26 (m, 1H, N-CH_2-CH=CH_2), 4.53 (d, 1H, $J = 4.8$ Hz, PhO-CH-CH-C(CH_3)=), 5.25–5.30 (m, 2H, N-CH_2-CH=CH_2), 5.35 (d, 1 H, $J = 4.8$ Hz, PhO-CH-CH-C(CH_3)=), 5.78–5.91 (m, 1H, N-CH_2-CH=CH_2), 6.60 (s, 1H, C(CH_3)=CH-Ph), 7.03–7.47 (m, 8H, aromatic protons) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 15.26$ (C(CH_3)=CH-Ph), 20.14 (O-C_6H_3Br-CH_3), 43.54 (N-CH_2-CH=CH_2), 64.62 (PhO-CH-CH-C(CH_3)=), 82.87 (PhO-CH-CH-C(CH_3)=), 111.62 (quaternary aromatic C, Ph-Br), 119.26 (N-CH_2-CH=CH_2), 115.34, 126.86, 128.10, 128.90, 129.00, 133.61 (aromatic CH), 131.06 (C(CH_3)=CH-Ph), 130.78 (N-CH_2-CH=CH_2), 132.19 (CH-C(CH_3)=CH-Ph), 132.98 (O-C_6H_3Br-CH_3), 151.91 (O-C_6H_3Br-CH_3), 165.57 (C=O) ppm; MS-CI (180 eV): m/z (%) = 414 (30.9), 412 (27.8), 226 (100); MS-EI (70 eV): m/z (%) = 413, 411, 384, 353, 332 (21.6), 290, 249, 226 (100), 185 (17.6), 143 (34.5), 128 (36), 115 (18), 91, 63, 51; posFAB $(M+H)^+$: $C_{22}H_{23}BrNO_2$: calcd. 412.09122, found 412.09030; $C_{22}H_{23}$ $^{81}BrNO_2$: calcd. 414.0892, found 414.0916.

1-Allyl-3-(2-bromophenoxy)-4-(1-methyl-2-phenylvinyl)-azetidin-2-one (**6b**)

Yield: 42%; $R_f = 0.63$ (CH_2Cl_2/$H_3CCOOCH_2CH_3$ 9.5:0.5); FTIR ($CHCl_3$): $\bar{\nu} = 1757$ (C=O), 1477, 1248 (ArOC) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.97$ (s, 1H, CH_3), 3.58–3.66 (m, 1H, N-CH_2-CH=CH_2), 4.17–4.24 (m, 1H, N-CH_2-CH=CH_2), 4.51 (d, 1H, $J = 5.1$ Hz, PhO-CH-CH-C(CH_3)=), 5.23–5.28 (m, 2H, N-CH_2-CH=CH_2), 5.38 (d, 1H, $J = 5.1$ Hz, PhO-CH-CH-C(CH_3)=), 5.75–5.88

(m, 1H, N-CH_2-C*H*=CH_2), 6.57 (s, 1H, C(CH_3)=C*H*-Ph), 6.81–6.87 (m, 1H, aromatic proton), 7.20–7.49 (m, 8H, aromatic protons) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 15.29$ (C(*C*H_3)=CH-Ph), 43.61 (N-*C*H_2-CH=CH_2), 64.57 (PhO-CH-*C*H-C(CH_3)=), 82.66 (PhO-*C*H-CH-C(CH_3)=), 111.97 (quaternary C, Br-C_6H_4), 119.35 (N-CH_2-CH=*C*H_2), 115.43, 123.20, 126.89, 128.13, 128.51, 129.00, 131.18 (aromatic *C*H and C(CH_3)=*C*H-C_6-C_6H_5), 130.75 (N-CH_2-*C*H=CH_2), 132.06 (*C*(CH_3)=CH-C_6H_5), 136.90 (*C*$_6$H$_5$), 154.00 (O*C*$_6$H$_4$Br), 165.40 (C=O) ppm; MS-CI (180 eV): m/z (%) = 398 (69.9), 400 (72.8), 258 (35), 226 (32), 228 (28.2), 183 (31), 147 (57.3), 113 (36.9), 73 (100); MS-EI (70 eV): m/z (%) = 399, 368, 336, 318, (37.2), 276, 226 (90.5), 185 (34.7), 143 (100), 128 (89.1), 115 (46.6), 91 (229.3), 77 (27.1), 65 (13.2), 41 (92.3); posFAB $(M+H)^+$: $C_{21}H_{21}BrNO_2$: calcd. 398.07556, found 398.07504; $C_{21}H_{21}$ $^{81}BrNO_2$: calcd. 400.07357, found 400.07418.

Standard procedure for the radical induced reaction of 1-allyl-3-(2-bromoaryloxy)-4-(1-methyl-2-phenylvinyl)-azetidin-2-ones with Bu_3SnH/AIBN

A solution of 1 mmol of β-lactam **6** in 100 ml of dry benzene was refluxed for 1 h under a nitrogen atmosphere. Thin layer chromatography of the solution was used to prove the temperature stability of lactam **6**; all β-lactams were stable under the given reaction conditions. Subsequently, the solution was treated with 0.1 mmol *AIBN* as radical initiator and 1.5 mmol of tri-*n*-butyltin hydride, followed by continued heating to reflux under a nitrogen atmosphere. Reaction control was carried out every 12 h. When apparently no further reaction took place (after about 36 h), the reaction was again started by addition of 0.1 mmol *AIBN* and 1.5 mmol tri-*n*-butyltin hydride. After another 36 h, 0.1 more mmol *AIBN* were added, and heating was continued for another 24 h, bringing the total reaction time to 96 h. After cooling to 20°C the solvent was removed under reduced pressure and the raw product was fractionated by chromatography.

(2aS,8aR,8R)/(2aR,8aS,8R)-1-Allyl-8-benzyl-6,8-dimethyl-1,2a,8,8a-tetrahydro-3-oxa-1-aza-cyclobuta[b]naphthalen-2-one (**7a**)

Yield: 6% $R_f = 0.51$ (CH_2Cl_2/$H_3CCOOCH_2CH_3$ 9.5:0.5); ^{1}H NMR ($CDCl_3$): $\delta = 1.20$ (s, 3H, CH_3), 2.26 (s, 3H, Ph-CH_3), 2.95 (d, 1H, $J = 13.5$ Hz, benzylic CH_2), 3.33 (d, 1H, $J = 13.5$ Hz, benzylic CH_2), 3.84–3.91 (m, 1H, N-C*H*$_2$-CH=CH_2), 4.01 (d, 1H, $J = 5.0$ Hz, PhO-CH-C*H*-C(CH_3)-), 4.15–4.23 (m, 1H, N-C*H*$_2$-CH=CH_2), 5.07–5.23 (m, 2H, N-CH_2-CH=C*H*$_2$), 5.13 (d, 1H, $J = 5.0$ Hz, PhO-C*H*-CH-C(CH_3)–), 5.67–5.80 (m, 1H, N-CH_2-C*H*=CH_2), 6.93–7.29 (m, 8H, aromatic protons) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 21.00$ (Ph-CH_3), 22.82 (CH_3), 39.95 (quaternary C generated by ring closure), 40.90 (benzylic CH_2), 44.65 (N-*C*H_2-CH=CH_2), 63.96 (PhO-CH-*C*H-C(CH_3)), 81.03 (PhO-*C*H-CH-C(CH_3)), 118.15 (N-CH_2-CH=*C*H_2), 118.51, 126.04, 125.57, 128.80 (aromatic CH), 127.97, 130.84 (2 pairs of isochronic aromatic CH), 131.80 (quaternary aromatic C), 131.93 (N-CH_2-*C*H=CH_2), 132.61 (quaternary aromatic C), 136.59 (quaternary aromatic C), 150.47 (O*C*$_6$H$_4$), 166.01 (C=O) ppm; MS-CI (180 eV) m/z (%) = 334 (97.4), 113 (23.1), 97 (28.2), 73 (89.7), 71 (100); posFAB $(M+H)^+$: $C_{22}H_{24}NO_2$: calcd. 334.18070, found 334.18048.

(2a,S,8aR,8S)/(2aR,8aS,8R)-1-Allyl-8-benzyl-6,8-dimethyl-1,2a,8,8a-tetrahydro-3-oxa-1-aza-cyclobuta[b]naphthalen-2-on (**8a**)

Yield: 72%; $R_f = 0.43$ (CH_2Cl_2/$H_3CCOOCH_2CH_3$ 9.5:0.5); m.p.: 118–120°C (*n*-hexane); FTIR ($CHCl_3$): $\bar{\nu} = 1759$ (C=O), 1493, 1233 (ArOC) cm^{-1}; ^{1}H NMR: ($CDCl_3$): $\delta = 1.34$ (s, 3H, CH_3), 2.15 (s, 3H, Ph-CH_3), 2.61 (d, 1H, $J = 12.9$ Hz, benzylic C*H*$_2$), 2.97 (d, 1H, $J = 12.9$ Hz, benzylic CH_2), 3.49–3.56 (m, 1H, N-C*H*$_2$-CH=CH_2), 4.02 (d, 1H, $J = 5.1$ Hz, PhO-CH-C*H*-C(CH_3)–), 4.04–4.10 (m, 1H, N-C*H*$_2$-CH=CH_2), 5.01–5.17 (m, 2H, N-CH_2-CH=C*H*$_2$), 5.28 (d, 1H, $J = 5.1$ Hz, PhO-C*H*-CH-C(CH_3)–), 5.57–5.70 (m, 1H, N-CH_2-C*H*=CH_2), 6.50–7.14 (m, 8H, aromatic

protons) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 20.79$ (2 CH_3), 41.06 (quaternary C generated by ring closure), 43.99 (benzylic CH_2), 44.78 (N-*C*H_2-CH=CH_2), 65.40 (PhO-CH-*C*H-C(*C*H_3)), 80.24 (PhO-*C*H-CH-C(CH_3)), 118.89 (N-CH_2-CH=*C*H_2), 118.04, 126.35, 127.86, 129.03 (aromatic *C*H), 127.50, 130.56 (2 pairs of isochronic aromatic *C*H), 131.17 (N-CH_2-*C*H=CH_2), 129.49 (quaternary aromatic C), 132.34 (*C*$_6H_3$-CH_3), 136.12 (quaternary aromatic C), 149.46 (O*C*$_6H_3$), 166.00 (*C*=O) ppm; MS-CI (180 eV): m/z (%) = 334 (100); posFAB $(M+H)^+$: $C_{22}H_{24}NO_2$: calcd. 334.18070, found 334.18011.

(2aS,8aR,8R)/(2aR,8aS,8S)-1-Allyl-8-benzyl-8-methyl-1,2a,8,8a-tetrahydro-3-oxa-1-aza-cyclobuta[b]naphthalen-2-one (**7b**) $C_{21}H_{22}NO_2$

Yield: 6%; $R_f = 0.50$ (CH_2Cl_2/$H_3CCOOCH_2CH_3$ 9.5:0.5); FTIR ($CHCl_3$): $\bar{\nu} = 1755$ (C=O), 1485, 1265, 1227, 752 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.24$ (s, 3H, CH_3), 2.96 (d, 1H, $J = 13.5$ Hz, benzylic CH_2), 3.35 (d, 1H, $J = 13.5$ Hz, benzylic C*H*$_2$), 3.85–3.93 (m, 1H, N-C*H*$_2$-CH=CH_2), 4.03 (d, 1H, $J = 5.0$ Hz, PhO-CH-C*H*-C(CH_3)−), 4.15–4.22 (m, 1H, N-C*H*$_2$-CH=CH_2), 5.08–5.23 (m, 2H, N-CH_2-CH=C*H*$_2$), 5.16 (d, 1H, $J = 5.0$ Hz, PhO-C*H*-CH-C(CH_3)−), 5.65–5.80 (m, 1H, N-CH_2-C*H*=CH_2), 6.97–7.25 (m, 9H, aromatic protons) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 22.81$ (CH_3), 39.98 (quaternary C generated by ring closure), 40.90 (benzylic CH_2), 44.73 (N-*C*H_2-CH=CH_2), 64.04 (PhO-CH-*C*H-C(CH_3)), 80.99 (PhO-*C*H-CH-C(CH_3)), 118.28 (N-CH_2-CH=*C*H_2), 118.82, 123.28, 125.52, 126.57, 128.45 (aromatic CH), 127.98, 130.79 (2 pairs of isochronic aromatic CH), 131.86 (N-CH_2-*C*H=CH_2), 132.14, 136.53 (2 quaternary aromatic C), 152.82 (O*C*$_6H_4$), 165.79 (C=O) ppm; MS-CI (180 eV): m/z (%) = 320 (100); posFAB $(M+H)^+$: $C_{21}H_{22}NO_2$: calcd. 320.16505, found 320.16470.

(2aS,8aR,8S)/(2aR,8aR,8R)-1-Allyl-8-benzyl-8-methyl-1,2a,8,8a-tetrahydro-3-oxa-1-aza-cyclobuta[b]naphthalen-2-one (**8b**) $C_{21}H_{22}NO_2$

Yield: 76%; $R_f = 0.45$ (CH_2Cl_2/$H_3CCOOCH_2CH_3$ 9.5:0.5); m.p.: 115–118°C (*n*-Hexan); FTIR ($CHCl_3$): $\bar{\nu} = 1753$ (C=O), 1485, 1454, 1227, 760 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.37$ (s, 3H, CH_3), 2.60 (d, 1H, $J = 12.8$ Hz, benzylic CH_2), 3.01 (d, 1H, $J = 12.8$ Hz, benzylic CH_2), 3.52–3.60 (m, 1H, N-C*H*$_2$-CH=CH_2), 4.05 (d, 1H, $J = 5.1$ Hz, PhO-CH-C*H*-C(CH_3)−), 4.01–4.09 (m, 1H, N-C*H*$_2$-CH=CH_2), 5.00–5.17 (m, 2H, N-CH_2-CH=C*H*$_2$), 5.32 (d, 1H, $J = 5.1$ Hz, PhO-C*H*-CH-C(CH_3)−), 5.57–5.70 (m, 1H, N-CH_2-C*H*=CH_2), 6.60–7.24 (m, 9 H, aromatic protons) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 20.76$ (CH_3), 41.12 (newly built quaternary C), 43.83 (benzylic CH_2), 44.82 (N-*C*H_2-CH=CH_2), 65.70 (PhO-CH-*C*H-C(CH_3)), 80.26 (PhO-*C*H-CH-C(CH_3)), 118.89 (N-CH_2-CH=*C*H_2), 118.39, 123.08, 126.36, 127.42, 128.67 (aromatic *C*H), 127.55, 130.52 (2 pairs of isochronic aromatic CH), 131.14 (N-CH_2-*C*H=CH_2), 129.73 (quateranry aromatic C), 136.02 (quaternary aromatic C), 151.74 (O*C*$_6H_4$), 165.81 (C=O) ppm; MS-CI (180 eV): m/z(%) = 320 (100); posFAB $(M+H)^+$: $C_{21}H_{22}NO_2$: calcd. 320.16505, found 320.16482.

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