Synthesis of Optically Active 3-Amino-2,3-dihydrobenzopyran-4-ones by Ring Transformation of Aziridinecarboxamides

Karsten Woydowski, Jürgen Liebscher*

Institut für Chemie, Humboldt-Universität Berlin, Hessische Straße 1-2, 10115 Berlin, Germany

Fax +49(30)20938907; E-mail: liebscher@chemie.hu-berlin.de

Received 3 March 2000; revised 8 May 2000

Dedicated to Professor Richard Neidlein on the occasion of his 70th birthday

Abstract: Weinreb amides **1** of aziridinecarboxylic acids react with *o*-lithiated *O*-methoxymethylphenols **2** to 2-benzoylaziridines **3** which, after *O*-deprotection, undergo ring transformation by attack of the phenolic hydroxy group at 3-position of the aziridine ring affording optically active 3-aminodihydrobenzopyran-4-ones **5** under acidic conditions. Alternatively, 5-membered benzofuran-3-ones **6** and **7** can be obtained under basic conditions.

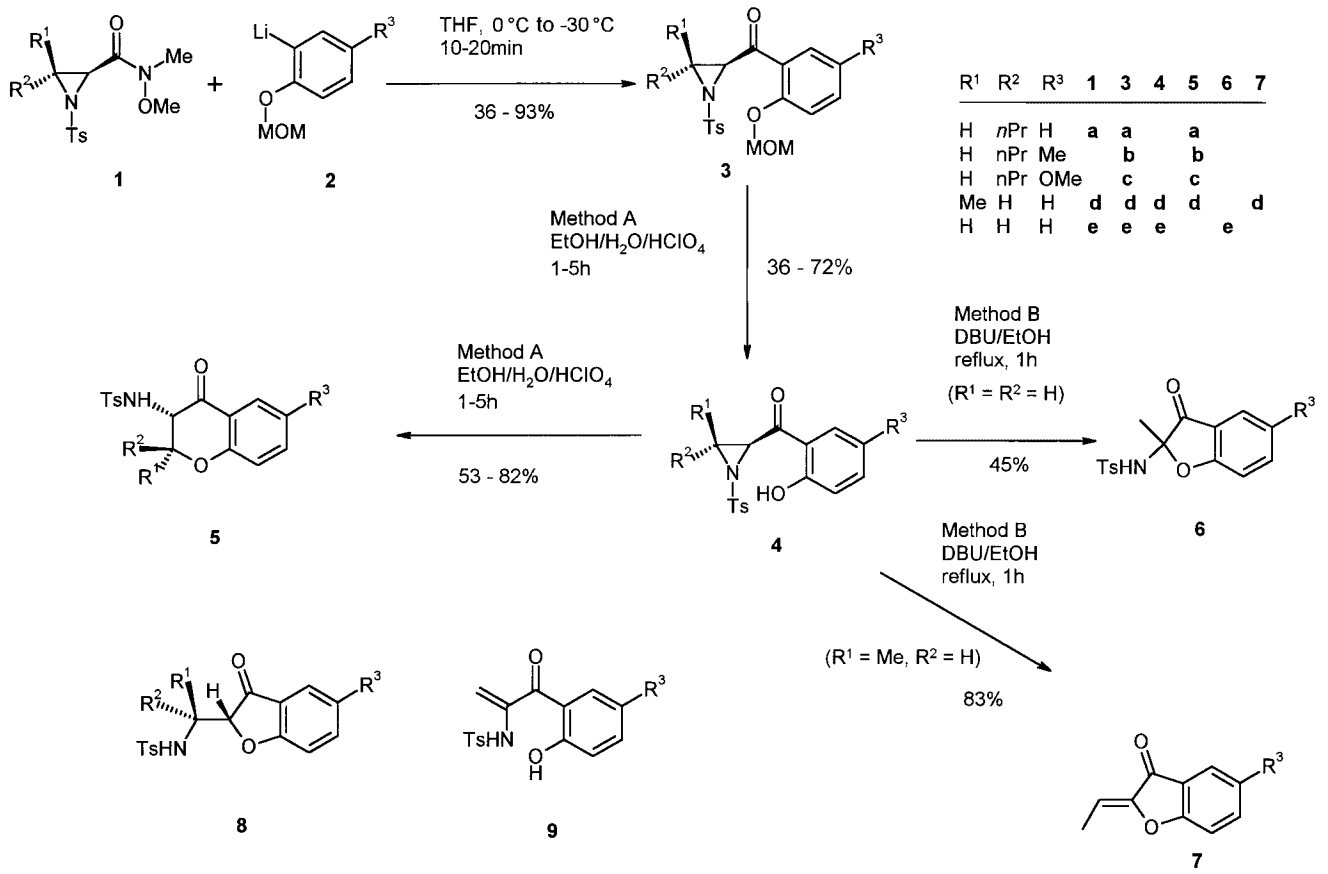
Key words: 2,3-dihydrobenzopyran-3-ones, aziridines, ring transformation, benzofuran-3-one, asymmetric synthesis

Ring transformation of chiral glycidic acid derivatives with binucleophiles turned out to be a useful methodology for the synthesis of optically active α-hydroxyalkyl or hydroxy 5-, 6-, and 7-ring heterocycles with a carbonyl carbon atom as ring atom.[1-6] For example, we developed a novel synthesis of enantiopure 3-hydroxy-2,3-dihydrobenzopyran-4-ones with 2-alkyl substituents by the reaction of Weinreb amides of oxiranecarboxylic acids (corresponding to **1** with O instead of TsN) with *O*-MOM-protected *o*-lithiated phenols **2** as C-C-O-building blocks.[1] The *o*-hydroxybenzoyloxiranes initially formed were *O*-deprotected under acidic conditions allowing a ring transformation by attack of the evolving phenolic hydroxy group at the ß-position of the starting oxirane ring as long as its substituents are in *trans* arrangement. When *cis*-oxiranecarboxamides were used as starting materials, an alternative attack at the α-position occurred resulting in the formation of 2-alkylidenebenzofuranones. Both types of products are alkyl analogues of naturally occurring flavonoids.

Corresponding ring transformations of optically active aziridinecarboxylic acid derivatives are rare.[7] We report here, first results in the synthesis of novel optically active 3-amino-2,3-dihydrobenzopyran-4-ones **4** by ring transformation of Weinreb amides **1** of aziridinecarboxylic acids with *o*-lithiated MOM-protected phenols **2**. 3-*trans*-Propyl, 3-*cis*-methyl and the 3-unsubstituted aziridines **1** were used as representative starting materials. The first could be obtained in enantiomerically pure form from Weinreb amides of the corresponding oxiranecarboxamides by ring opening with azide, Staudinger reaction of the resulting azidoalcohol with triphenylphosphine and final *N*-tosylation of the resulting aziridine according to Zwanenburg et al.[8] Compounds **1d** and **1e** were prepared from *N*-tosylated L-threonine or L-serine, respectively, by transformation to the corresponding Weinreb amide followed by Mitsunobu-conditions as reported for aziridine carboxylates.[9]

With these three Weinreb amides **1** in hand, we tried the ring transformation with *o*-lithiated *O*-MOM-protected phenols **2** (Scheme). The expected benzoylaziridines **3** were obtained in acceptable yields in the *trans*-series (**3a-3c**) and in the 3-unsubstituted case **3e**, while the *cis*-product **3d** was formed in modest yield (36%). This trend was also observed in the following ring transformation of the benzoylaziridines **3** into 3-tosylamino-benzopyrane-4-ones **5** by heating in $HClO_4$/EtOH/water (Method A), where the *O*-MOM protective group is split off and the appearing phenolic OH-group attacks the 3-position of the (*o*-hydroxy)benzoylaziridine **4**. Again, higher yields were obtained in the *trans*-series (Table). Remarkably, the 3-unsubstituted 2-(*o*-methoxymethoxybenzoyl)aziridine **3e** ($R^1 = R^2 = H$) resisted the transformation into the corresponding 3-aminobenzopyranone **5** and gave only the *O*-deprotected product **4e**. This demonstrates that substituents at position 3 of the aziridine ring exert an effect on the success of the ring transformation of **3** or **4** into **5**.

We also tried to isolate *o*-hydroxybenzoylaziridines **4** after shorter heating using Method A and to run the ring transformation under basic conditions (Method B). In these cases, however, the ring transformation resulted in the connection of the phenolic OH-group to position 2 of the starting 2-(*o*-hydroxybenzoyl)aziridine **4** rather than to position 3 thus forming either racemic 2-tosylaminobenzofuran-3-ones **6** or 2-alkylidenebenzofuran-3-ones **7**. The latter case resembles the reaction of the corresponding 3-alkyl-2-(*o*-hydroxybenzoyl)oxiranes. It is probably attributed to ß-elimination of tosylamide from the intermediate 2-(α-tosylaminoalkyl)-benzofuran-3-ones **8**, which could be isolated in our preliminary investigations of the reaction of **1a** with *O*-MOM-protected 1-naphthol. The formation of the 2-amino-benzofuran-3-one **6e** is unexpected since the phenolic O-atom and the tosylamino group are found at the same C-atom and analogous reactions were not observed in the *o*-hydroxybenzoyloxirane series.[1] The product **6e** could be formed by opening of the aziridine ring of the 2-(*o*-hydroxybenzoyl)aziridine **4** ($R^1 = R^2 = H$) by ß-elimination caused by attack of the base at position 3 of the aziridine ring. The resulting intermediates **9** would close the ring by addition of the phenolic OH-group to the enamine moiety or the corresponding imine. Intermediates structurally related to



Scheme

9 were proposed in the ring contraction of 3-amino-2-arylbenzopyran-4-ones to 2-aminobenzofuran-3-ones[10] resembling the transformation of **5** into **6**, which also has to be taken into consideration as another possible pathway to the 2-tosylaminobenzofuran-3-one **6e**.

All products **1**, **3**, **4**, **5**, and **6** are new. Their structure could be confirmed by spectroscopic methods, in particular by ^{1}H and ^{13}C NMR spectroscopy. The vicinal couplings of the protons in the 3-amino-dihydrobenzopyran-4-ones **5** clearly prove the relative configuration. The structure of the unexpected 2-aminobenzofuran-3-one **6e** is in agreement with the observation of a quaternary carbon atom at $\delta = 92.5$ ppm. No sign of the formation of diastereomers was found in the NMR-spectra of the crude products **3**, **4**, and **5**. Since we started from enantiopure starting materials **1** with two asymmetric carbon atoms, both of which cannot invert configuration at the same time, products **5** obtained must be enantiomerically pure.

The overall transformation of aziridine-2-carboxamides **1** into benzopyranones **5** represents the first asymmetric synthesis of 3-amino-2,3-dihydrobenzopyran-4-ones. Previously, only racemic products, mostly with 2-arylsubstituents (3-aminochromanones) or 2-unsubstituted compounds, had been prepared (*v. i.*). Some of them were further reduced to 3-amino-4-hydroxytetrahydrobenzopyranes exhibiting bronchiadilating and antispasmolytic properties.[11-13] The known racemic 3-amino-dihydrobenzopyran-4-ones were obtained by three principal routes. Thus the amino group was introduced into the benzopyrane-ring by Neber rearrangement,[11,13-17] nitrosation/reduction,[12,13,15-17] or nucleophilic substitution.[18-20] 3-Amino-dihydrobenzopyran-4-ones were further synthesised by ring formation of *o*-hydroxychalcones or corresponding bromo-adducts in the presence of amines and iodine,[21,22] trimethylsilylazide,[23] or azide in the presence of TFA.[24] Last, but not least, racemic 3-amino-dihydrobenzopyran-4-ones were accessible by ring transformation of 3-aryl-2-(*o*-hydroxybenzoyl)aziridines, which were obtained from chalcones or corresponding dibromides.[24,25] Although those ring transformations resemble the synthesis of our compounds **5** as far as the last step is concerned, important differences are found. Thus, compounds **5** are optically active and bear 2-alkyl rather than 2-aryl substituents. In light of the fact that *cis*-2-(*o*-hydroxybenzoyl)-3-phenylaziridine afforded mainly 2-benzylidene-benzofuran-3-one[25] (similar to **7**) rather than the 3-amino-2-phenylbenzopyran-4-one the transformation of the *cis*-aziridine **3d** into the *cis*-3-amino-2-methylbenzopyran-4-one **5d** is worth mentioning. Obviously, the 3-methyl-substituent in the 2-(*o*-hydroxybenzoyl)aziridine affects the mode of cyclisation as compared with 2-aryl-substituents favouring the attack of the phenolic hydroxy group at position 3 rather than at position 2 of the aziridine.

Table Starting Materials **1** and Products **3**, **4, 5**, **6** and **7**

	Yield (%)	Mp (°C)	R_f Solvent	$[\alpha]_D^{20}$ (*c*, $CHCl_3$)	^1H NMR ($CDCl_3$) δ (ppm), *J* (Hz)	^{13}C NMR ($CDCl_3$) δ (ppm), *J* (Hz)
1a	86	colourless oil	0.48 CH_2Cl_2/Me_2CO 95:5	+27.9	0.91 (t, 3 H, *J* = 7.4, CH_3), 1.45−2.15 (m, 4 H, $2CH_2$), 2.35 (s, 3 H, CH_3), 3.07 (m, 1 H, CH), 3.12 (s, 3 H, NCH_3), 3.68 (s, CH_3-O), 3.72 (d, 1 H, *J* = 3.9, CH), 7.23 (d, 2 H, *J* = 8.2, Aryl), 7.79 (d, 2 H, *J* = 8.2, Aryl)	13.7 (CH_3), 21.1 (CH_2), 21.6 (CH_3), 29.9 (CH_2), 32.5 (NCH_3), 41.7 (CH), 48.6 (CH), 62.0 (CH_3O), 127.6 (CH_{ar}), 129.6 (CH_{ar}), 137.1 (C_{ar}), 144.3 (C_{ar}), 162.0 (C=O)
1d	93	colourless oil	0.56 CH_2Cl_2/Me_2CO 95:5	−34.7	1.23 (d, 3 H, *J* = 5.7, CH_3), 2.37 (s, 3 H, CH_3) 3.08 (m, 1 H, CH), 3.12 (s, 3 H, CH_3-N), 3.65 (s, 3 H, CH_3-O), 3.74 (d, 1 H, *J* = 7.7, CH), 7.26 (d, 2 H, *J* = 8.2, Aryl), 7.80 (d, 2 H, *J* = 8.2, Aryl)	12.4 (CH_3), 21.7 (CH_3), 32.5 (CH_3-N), 40.0 (CH), 41.0 (CH), 61.8 (CH_3-O), 127.9 (CH_{ar}), 129.7 (CH_{ar}), 134.8 (C_{ar}), 144.7 (C_{ar}), 165.2 (CO)
1e	78	70−73 (C_6H_{14}/EtOAc 9:1)	0.53 CH_2Cl_2/Me_2CO 95:5	−8.5	2.38 (s, 3 H, CH_3), 2.57 (d, 1 H, *J* = 4.2, CH_2), 2.63 (d, 1 H, *J* = 6.9, CH_2)3.16 (s, 3 H, CH_3-N), 3.73 (s, 3 H, CH_3-O), 3.85 (m, 1 H, CH), 7.27 (d, 2 H, *J* = 8.2, Aryl), 7.78 (d, 2 H, *J* = 8.2, Aryl)	21.7 (CH_3), 31.9 (CH_2), 32.5 (CH_3-N), 33.1 (CH), 62.2 (CH_3-O), 128.2 (CH_{ar}), 129.8 (CH_{ar}), 134.2 (C_{ar}), 145.1 (C_{ar}), 166.1 (CO)
3a	58	colourless oil	0.76 CH_2Cl_2/Me_2CO 95:5		0.91 (t, 3 H, *J* = 7.4, CH_3), 1.46−2.12 (m, 4 H, $2CH_2$), 2.33 (s, 3 H, CH_3), 3.06 (m, 1 H, CH), 3.44 (s, 3 H, CH_3-O), 4.26 (d, 1 H, *J* = 4.2, CH), 5.21 (s, 2 H, CH_2), 6.93−7.76 (8H, Aryl)	13.7 (CH_3), 21.2 (CH_2), 21.6 (CH_3), 30.2 (CH_2), 49.7 (CH), 50.8 (CH), 56.6 (CH_3-O), 94.6 (CH_2), 114.8 (CH_{ar}), 116.2 (CH_{ar}), 121.9 (CH_{ar}), 127.3 (CH_{ar}), 127.4 (C_{ar}), 129.5 (CH_{ar}), 134.5 (CH_{ar}), 137.3 (C_{ar}), 144.1 (C_{ar}), 156.7 (C_{ar}), 194.3 (CO)
3b	53	colourless oil	0.49 C_5H_{12}/Et_2O 1:1		0.91 (t, 3 H, *J* = 7.4, CH_3), 1.48−2.10 (m, 4 H, $2CH_2$), 2.20 (s, 3 H, CH_3), 2.33 (s, 3 H, CH_3), 3.05 (m, 1 H, CH), 3.43 (s, 3 H, CH_3-O), 4.26 (d, 1 H, *J* = 4.2, CH), 5.18 (s, 2 H, CH_2), 7.03−7.77 (m, 7 H, Aryl)	13.7 (CH_3), 20.2 (CH_3), 21.2 (CH_2), 21.6 (CH_3), 49.7, 50.9 (CH), 56.5 (CH_3O), 94.6 (CH_2), 114.8 (CH_{ar}), 127.1 (C_{ar}), 127.3 (CH_{ar}), 129.5 (CH_{ar}), 130.6 (CH_{ar}), 131.4 (C_{ar}), 135.1 (CH_{ar}), 137.4 (C_{ar}), 144.1 (C_{ar}), 154.7 (C_{ar}), 194.4 (CO)
3c	63	colourless oil	0.72 C_5H_{12}/Et_2O 1:1		0.92 (t, 3 H, *J* = 7.4, CH_3), 1.44−2.12 (m, 4 H, $2CH_2$), 2.33 (s, 3 H, CH_3), 3.06 (m, 1 H, CH), 3.41 (s, 3 H, CH_3O), 3.70 (s, 3 H, CH_3O), 4.28 (d, 1 H, *J* = 4.1, CH), 5.03 (s, 2 H, CH_2), 6.76−7.76 (m, 7 H, Aryl)	13.8 (CH_3), 21.2 (CH_2), 21.6 (CH_3), 30.4 (CH_2), 50.2, 50.9 (CH), 55.8, 56.0 (CH_3O), 95.1 (CH_2), 112.7 (CH_{ar}), 114.6 (CH_{ar}), 117.6 (CH_{ar}), 123.3 (CH_{ar}), 126.8 (C_{ar}), 127.3 (CH_{ar}), 129.5 (CH_{ar}), 137.4 (C_{ar}), 151.0 (C_{ar}), 154.3 (C_{ar}), 193.2 (CO)
3d	36	colourless oil	0.76 C_5H_{12}/Et_2O 1:1		1.16 (d, 3 H, *J* = 5.8, CH_3), 2.36 (s, 3 H, CH_3), 3.22 (m, 1 H, CH), 3.45 (s, 3 H, CH_3-O), 4.24 (d, 1 H, *J* = 7.8, CH), 5.23 (dd, 2 H, *J* = 6.9, 8.6, CH_2), 6.85−7.82 (m, 8 H, Aryl)	12.2 (CH_3), 21.7 (CH_3), 41.8 (CH), 49.0 (CH), 56.7 (CH_3-O), 94.5 (CH_2), 114.6 (CH_{ar}), 122.0 (CH_{ar}), 127.3 (C_{ar}), 127.8 (CH_{ar}), 129.7 (CH_{ar}), 130.5 (CH_{ar}), 134.7 (CH_{ar}), 135.0 (C_{ar}), 144.6 (C_{ar}), 156.7 (C_{ar}), 192.1 (CO)
3e	72	colourless crystals	0.72 C_5H_{12}/Et_2O 1:1		2.50 (s, 3 H, CH_3), 2.74 (d, 1 H, *J* = 4.2, CH_2), 2.79 (d, 1 H, *J* = 7.0, CH_2), 3.62 (s, 3 H, CH_3O), 4.50 (dd, 1 H, *J* = 4.3, 7.0, CH), 5.43 (s, 2 H, CH_2), 7.09−7.94 (m, 8 H, Aryl)	21.7 (CH_3), 33.4 (CH_2), 41.4 (CH), 56.7 (CH_3O), 94.5 (CH_2), 114.8 (CH_{ar}), 121.9 (CH_{ar}), 127.2 (C_{ar}), 128.1 (CH_{ar}), 129.8 (CH_{ar}), 130.7 (CH_{ar}), 134.8 (CH_{ar}), 134.6 (C_{ar}), 144.9 (C_{ar}), 157.1 (C_{ar}), 193.7 (CO)
4d	75	colourless crystals	0.51 C_6H_{14}/Et_2O 11		1.15 (d, 3 H, *J* = 5.8, CH_3), 2.38 (s, 3 H, CH_3), 3.30 (m, 1 H, CH), 4.09 (d, 1 H, *J* = 7.6 Hz, CH), 6.85−7,85 (m, 8 H, Aryl), 11.62 (s, 1 H, OH)	12.7 (CH_3), 21.7 (CH_3), 41.3 (CH), 45.3 (CH), 118.7 (CH_{ar}), 119.0 (CH_{ar}), 115.4 (CH_{ar}), 128.0 ($2CH_{ar}$), 129.8 ($2CH_{ar}$), 129.9 (CH_{ar}), 137.4 (CH), 145.1 (C_{ar}), 162.6 (C_{ar}), 195.4 (=O)

Table (continued)

	Yield (%)	Mp (°C)	R_f Solvent	$[\alpha]_D^{20}$ (*c*, $CHCl_3$)	^1H NMR ($CDCl_3$) δ (ppm), *J* (Hz)	^{13}C NMR ($CDCl_3$) δ (ppm), *J* (Hz)
4e	75	colourless crystals	0.67 CH_2Cl_2/Me_2CO 95:5		2.37 (s, 3 H, CH_3), 2.70 (d, 1 H, *J* = 4.1, CH_2), 2.83 (d, 1 H, *J* = 7 Hz, CH_2), 4.14 (dd, 1 H, *J* = 4.1, *J* = 7.0, CH), 6.86–7.92 (m, 8 H, Aryl), 11.60 (s, 1 H, OH)	21.7 (CH_3), 32.7 (CH_2), 37.3 (CH), 118.6 (CH_{ar}), 119.0 (C_{ar}), 119.6 (CH_{ar}), 128.2 (CH_{ar}), 129.8 (CH_{ar}), 130.3 (CH_{ar}), 134.0 (C_{ar}), 137.7 (CH_{ar}), 145.4 (C_{ar}), 162.8 (C_{ar}), 195.9 (C=O)
5a[a]	80	131–32 (C_6H_{14}/EtOAc 7:3)	0.78 C_6H_{14}/AcOEt 7:3	+10.8	0.92 (t, 3 H, *J* = 7.4, CH_3), 1.18–2.14 (m, 4 H, $2CH_2$), 2.32 (s, 3 H, CH_3), 3.93 (m, 1 H, CH), 4.07 (m, 1 H, CH), 5.36 (d, 1 H, *J* = 6.4, NH), 6.87–7.73 (m, 8 H, Aryl)	13.8 (CH_3), 18.2 (CH_2), 21.6 (CH_3), 34.0 (CH_2), 59.6 (CH), 82.0 (CH), 117.8 (CH_{ar}), 119.1 (C_{ar}), 121.6 (CH_{ar}), 127.4 (CH_{ar}), 127.5 (CH_{ar}), 129.7 (CH_{ar}), 136.0 (C_{ar}), 136.8 CH_{ar}), 144.0 (C_{ar}), 161.5 (C_{ar}), 190.2 (CO)
5b	82	136–38 (C_6H_{14}/EtOAc 8:2)	0.74 CH_2Cl_2/Me_2CO 95:5	−15.9	0.92 (t, 3 H, *J* = 7.4, CH_3), 1.38–2.06 (m, 4 H, $2CH_2$), 2.18 (s, 3 H, CH_3), 2.33 (s, 3 H, CH_3), 3.89 (m, 1 H, CH), 4.02 (m, 1 H, CH), 5.33 (d, 1 H, *J* = 6.3, NH), 6.77–7.77 (m, 7 H, Aryl)	13.8 (CH_3), 18.3 (CH_2), 20.3, 21.6 (CH_3), 34.0 (CH_2), 59.7 (CH), 82.0 (CH), 117.6 (CH_{ar}), 118.6 (C_{ar}), 126.9 (CH_{ar}), 127.5 (CH_{ar}), 129.7 (CH_{ar}), 131.1 (C_{ar}), 135.7 (C_{ar}), 137.9 (CH_{ar}), 143.9 (C_{ar}), 159.6 (C_{ar}), 190.4 (CO)
5c	78	150–52 (C_6H_{14}/EtOAc 6:4)	0.69 CH_2Cl_2/Me_2CO 95:5	−37.9	0.91 (t, 3 H, *J* = 7.4, CH_3), 1.25–2.10 (m, 4 H, $2CH_2$), 2.33 (s, 3 H, CH_3), 3.66 (s, 3 H, CH_3O), 3.90 (m, 1 H, CH), 4.00 (m, 1 H, CH), 5.32 (d, 1 H, *J* = 6.4, NH), 6.80–7.73 (m, 7 H, Aryl)	13.8 (CH_3), 18.3 (CH_2), 21.6 (CH_3), 34.0 (CH_2), 55.8 (CH_3O), 59.8, 82.2 (CH), 107.6 (CH_{ar}), 118.8 (C_{ar}), 119.1 (CH_{ar}), 126.1 (CH_{ar}), 127.5 (CH_{ar}), 129.7 (CH_{ar}), 136.1 (C_{ar}), 143.9 (C_{ar}), 154.2 (C_{ar}), 156.3 (C_{ar}), 190.4 (CO)
5d	53	191–92 (C_6H_{14}/EtOAc 1:1)	0.80 C_6H_{14}/Et_2O 1:1	+192.0	1.24 (d, 3 H, *J* = 6.7, CH_3), 2.33 (s, 3 H, CH_3), 4.19 (m, 1 H, CH), 5.06 (m, 1 H, CH), 5.73 (d, 1 H, *J* = 2.8, NH), 6.84–7.73 (m, 8 H, Aryl)	11.9 (CH_3), 21.5 (CH_3), 58.5 (CH), 76.7 (CH), 118.6 (CH_{ar}), 118.9 (C_{ar}), 121.4 (CH_{ar}), 126.8 (CH_{ar}), 127.3 (CH_{ar}), 130.0 (CH_{ar}), 135.2 (C_{ar}), 137.2, (CH_{ar}), 144.1 (C_{ar}), 159.1, (C_{ar}), 188.1 (CO)
6e	45	150–51 (C_6H_{14}/EtOAc 6:4)	0.53 CH_2Cl_2/Me_2CO 95:5	±0	1.52 (s, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 6.15 (s, 1 H, NH), 6.83–7.67 (m, 8 H, Aryl)	21.6 (CH_3), 23.1 (CH_3), 92.5 (C), 113.0 (CH_{ar}), 119.3 (C_{ar}), 122.4 (CH_{ar}), 125.2 (CH_{ar}), 127.2 (CH_{ar}), 129.5 (CH_{ar}), 138.4, (CH_{ar}), 138.5 (C_{ar}), 143.8 (C_{ar}), 169.2 (C_{ar}), 196.9 (CO)
7d[b]	83					

[a] MS (70eV): *m/z* = 359 (M^+, 1), 204 (24), 121 (45), 43 (86), 18 (100).
[b] Known compound.[1]

In summary, our results demonstrate that the concept of ring transformation of oxirane carboxylic acids with binucleophiles can also be applied to their aza-analogues, i. e. to aziridine carboxylic acid derivatives as a new route to optically active amino-substituted heterocycles.

^1H and ^{13}C NMR spectra were recorded at 300 MHz and 75.5 MHz, respectively, on a BRUKER AC-300 with TMS as internal standard ($CDCl_3$). Optical rotation was determined with a PERKIN ELMER polarimeter 241. Silica gel (0.04–0.063 mm, MERCK) was used for preparative column chromatography. If not otherwise mentioned, chemicals were purchased from MERCK or ALDRICH. (2*S*,3*R*)-*N*-Methoxy-*N*-methyl-3-propyl-2-oxiranecarboxamide was prepared as reported before.[1]

(2*S*,3*R*)-*N*-Methoxy-*N*-methyl-1-(4-tosyl)-3-propyl-2-aziridinecarboxamide (1a)

NaN_3 (3.84, 60 mmol) and NH_4Cl (3.19 g, 60 mmol) were added to a solution of (2*S*,3*R*)-*N*-methoxy-*N*-methyl-3-propyl-2-oxiranecarboxamide[1] (3.45 g, 20 mmol) in MeOH (70 mL). After refluxing for 5 h, the mixture was concentrated under vacuum, combined with H_2O (70 mL) and extracted with EtOAc (3 × 30 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography ($CHCl_3$/MeOH, 9:1) providing the corresponding azido alcohol (3.3 g, mixtures of regioisomers, R_f = 0.52 and 0.38). This product (3.3 g, 15.3 mmol) was dissolved in MeCN (70 mL) and combined with PPh_3 (4.18 g, 15.9 mmol). The mixture was stirred at r.t. for 1 h, refluxed for 4 h, and concentrated. The $OPPh_3$ was filtered off and the solvent was completely evaporated. Flash chromatography ($CHCl_3$/MeOH, 9:1, R_f = 0.23) gave (2*S*,3*R*)-*N*-methoxy-*N*-methyl-3-propyl-2-aziridinecarboxamide (2.53 g, 14.7 mmol, 74% yield) which was dissolved in dry CH_2Cl_2 (30 mL). *p*-Tosyl chloride (2.93 mL, 15.4 mmol) and

Et_3N (2.14 mL, 15.4 mmol) were added under Ar and the mixture was stirred at r.t. for 12 h. Concentration under vacuum and purification by flash chromatography (CH_2Cl_2/Me_2CO, 95:5, R_f = 0.48) afforded **1a** (3.83 g, 86%).

(2*S*,3*S*)-*N*-Methoxy-*N*,3-dimethyl-1-(4-tosyl)-2-aziridinecarboxamide (1d)

HN(Me)OMe·HCl (0.82 g, 8.39 mmol) and Et_3N (1.18 mL, 8.39 mmol) were added to a suspension of L-*N*-tosylthreonine (2.33 g, 8.39 mmol) in dry CH_2Cl_2 (50 mL) under stirring. After cooling to 0 °C, DCC (1.73, 8.39 mmol) and DMAP (2 drops) were added under Ar and stirring was continued at r.t. for 15 h. The resulting mixture was diluted with Et_2O (50 mL) and the dicyclohexylurea was filtered off. Concentrating the filtrate and purifying by flash chromatography ($CHCl_3$/MeOH, 9:1, R_f = 0.23) provided the Weinreb amide of L-*N*-tosylthreonine (1.56 g, 4.95 mmol, 59% yield). This material was dissolved in dry CH_2Cl_2 (30 mL) and combined with PPh_3 (1.35 g, 5.2 mmol). A solution of DEAD (0.824 mL, 5.20 mmol) in CH_2Cl_2 (2 mL) was added dropwise under Ar at 0 °C and the mixture was stirred at r.t. for 15 h. Concentration and flash chromatography (CH_2Cl_2/Me_2CO, 95:5, R_f = 0.56) gave the final product **1d** (1.37 g, 93%).

(2*S*)-*N*-Methoxy-*N*-methyl-1-(4-tosyl)-2-aziridinecarboxamide (1e)

The same procedure was used as for **1d**. Intermediate Weinreb amide of L-*N*-tosylserine: (R_f = 0.22, $CHCl_3$/MeOH, 9:1, 43% yield; **1e** (R_f = 0.53, CH_2Cl_2/Me_2CO, 95:5, 78% yield).

***o*-Methoxymethoxybenzoylaziridines 3; General Procedure**

A solution of *t*-BuLi in pentane (1.6 M, 0.66 mL, 1.05 mmol) was added to a solution of the *O*-MOM-phenol corresponding to **2** (1 mmol) in dry THF (3 mL) at 0 °C under Ar. The mixture was stirred at 0 °C for 3 h. After cooling to −30 °C, a solution of the Weinreb amide **1** (1 mmol) in dry THF (1 mL) was added under stirring. Stirring was continued at 0 °C for 10 min (**1d**, **1e**) or 20 min (**1a**). After quenching with sat. NH_4Cl, the mixture was extracted with Et_2O (3 × approx. 10 mL). The combined organic phases were dried ($MgSO_4$), concentrated and purified by flash chromatography (CH_2Cl_2/Me_2CO, 95:5).

***o*-Hydroxybenzoylaziridines 4 and 3-(Tosylamino)dihydrobenzopyran-4-ones 5; General Procedure (Method A)**

70% $HClO_4$ (19 μL, 0.17 mmol) were added to a solution of benzoylaziridine **3** (0.5 mmol) in EtOH/H_2O (3 mL, 2:1). The mixture was refluxed (45 min for **4d**, 1 h for **4e**, 1.5 h for **5a**, **b**, **c**, 5 h for **5d**). After cooling to r.t., the mixture was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried with $MgSO_4$, concentrated and purified by flash chromatography (CH_2Cl_2/Me_2CO, 95:5)

Benzofuran-3-ones 6 and 7; General Procedure (Method B)

DBU (0.05 mmol) was added to a solution of the *o*-hydroxybenzoylaziridine **4** (0.5 mmol) in dry EtOH (3 mL). After refluxing for 1 h the solution was concentrated and submitted to flash chromatography (CH_2Cl_2/Me_2CO, 95:5).

Acknowledgement

We gratefully acknowledge financial support from the Deutsche Forschungsgemeinschaft and Fonds der Chemischen Industrie.

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Article Identifier:
1437-210X,E;2000,0,10,1444,1448,ftx,en;H01400SS.pdf