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Reactivity of chiral exocyclic *N*-acyliminium ions with aromatic derivatives

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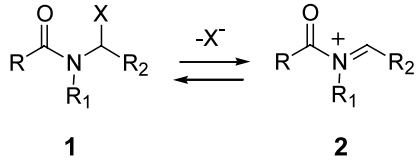
Abstract—Chiral *N*-acyliminium ions obtained from optically active *N*-[1-(phenylsulfonyl)alkyl]oxazolidin-2-ones at low temperature in the presence of titanium tetrachloride react with electron-rich aromatic compounds to afford the corresponding adducts in good yields and variable diastereoselectivities. Chemoselective cleavage of the oxazolidin-2-one ring with lithium/ammonia affords the corresponding benzylamines in enantioenriched form. The utilization of 4-benzyloxazolidin-2-one as a chiral auxiliary leads to intramolecular cyclization with exclusive formation of one diastereomer. The obtained tricyclic derivatives possess the core structure of some aza analogs of the anticancer drug podophyllotoxin.

1. Introduction

The synthetic utility of *N*-acyliminium ions as amidoalkylating agents[1] is attested by the increasing number of procedures that make use of these electrophilic intermediates for the synthesis of amino derivatives.[2] The reactivity of *N*-acyliminium ions can be suitably tuned by appropriate choice of the acyl moiety. Indeed, a carbamate group is more effective than an acyl group in stabilizing the positive charge on nitrogen.[3] The leaving group X in the amido derivative **1** also plays a fundamental role in shifting the equilibrium towards the formation of the iminium ion **2** (Scheme 1).[4]

The strongly electrophilic character of *N*-acyliminium ions permits the utilization of a wide range of nucleophiles such as allylsilanes,[5] enol derivatives,[6] and various organometallic reagents.[7] Aromatic derivatives can also be used for this purpose and the intramolecular addition of (hetero)aromatic groups to *N*-acyliminium ions represents a powerful procedure to build up polycyclic structures.[8] Direct addition of aromatic derivatives to *N*-acyliminium ions works efficiently only when electron-rich aromatics or heteroaromatic groups are used as nucleophiles.[9] Alternatively, different aromatic frameworks can be added to *N*-acyliminium ions by means of strong nucleophilic systems such as organometallic reagents.[10]



1 **2**

Scheme 1.

Recently, we have reported that chiral *N*-[1-(phenylsulfonyl)alkyl]imidazolidin-2-ones **3**[11] and *N*-[1-(phenylsulfonyl)alkyl]oxazolidin-2-ones **4**,**5**[12] react with Lewis acids such as $TiCl_4$ or $SnCl_4$ giving the corresponding *N*-acyliminium ions **6**, that upon reaction with different nucleophiles afford the corresponding addition products **7** (Scheme 2). Best results in terms of reactivity and diastereoselectivity can be obtained using imidazolidin-2-one derivatives **3**. However, this heterocyclic ring is resistant to cleavage, thus preventing the synthesis of primary amino derivatives in enantioenriched form.

In contrast, the oxazolidin-2-one ring is cleavable both under reductive conditions[12,13] or using trimethylsilyl iodide[14] but only allyltrimethylsilane adds efficiently to *N*-acyliminium ions derived from sulfones **4**,**5**. Herein, we report the utilization of optically active (phenylsulfonyl)alkyl oxazolidin-2-ones **4**,**5** as precursors of *N*-acyliminium ions in the reaction with aromatic derivatives.

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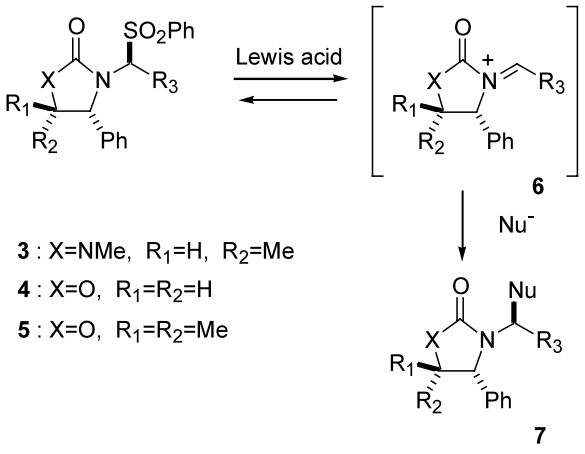
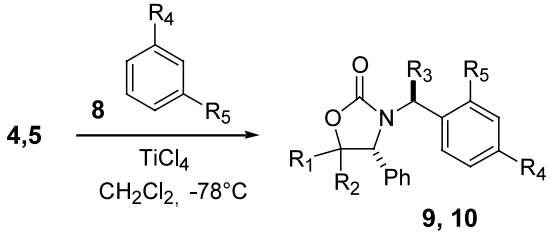


Scheme 2.



8a: R_4=OMe; R_5=H
8b: R_4=R_5=OMe

4a: R_3=*n*-C_7H_{15}

5a: R_3=Me_2CHCH_2
5b: R_3=Me
5c: R_3=Et
5d: R_3=Ph
5e: R_3=*n*-C_7H_{15}
5f: R_3=$BnOCH_2(CH_2)_3$

Scheme 3.

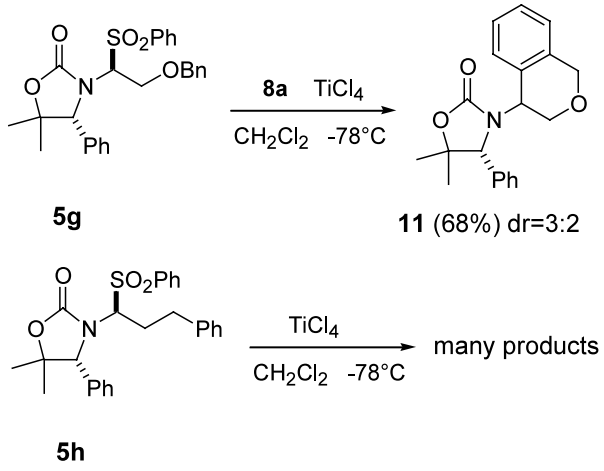
2. Results and discussion

2.1. Intermolecular addition of aromatic derivatives to chiral *N*-acyliminium ions

A preliminary survey on the reactivity of sulfone **4a** with different aromatic derivatives in the presence of $TiCl_4$ at −78°C clearly shows that only electron-rich rings add efficiently to the corresponding *N*-acyliminium ions (Scheme 3, Table 1, entry 1).

Indeed, benzene as well as moderately activated aromatics, e.g. isopropylbenzene fail to give any addition product. Disappointing results were also obtained using heteroaromatic compounds such as furan and *N*-methylindole that give unclean reaction mixtures from which the desired adducts are isolated only in low yields (15–25%). Conversely, anisole **8b** and 1,3-dimethoxybenzene **8b** react with sulfones 4,5 giving the corresponding adducts **9**,**10** in satisfactory yields with variable diastereoselectivities (Table 1). The best results are obtained with sulfone **5d** which contains a phenyl substituent (Table 1, entry 5). As expected, when a competitive intramolecular reaction can occur, this process usually prevails over the intermolecular addition. This is illustrated by the reaction of sulfone **5g** that in the presence of **8b** gives almost exclusively a product **11** arising from intramolecular attack of the benzyl moiety on the *N*-acyliminium ion intermediate in 68% yield (Scheme 4).

A similar cyclization has been attempted with sulfone **5h** under the usual conditions, but this derivative fails to undergo closure to the five-membered ring. This behavior has also been observed by DeNinno and co-workers on *N*-acyliminium ions derived from *N*-



Scheme 4.

Table 1. Synthesis of aryloxazolidin-2-ones **9**

Entry	Sulfone **4**,**5**	Aromatic **8**	Aryl derivative **9**,**10**					D.r.[a]	Yield[b] (%)
				R_1, R_2	R_3	R_4	R_5		
1	**4a**	**8a**	**9a**	H	*n*-C_7H_{15}	OMe	H	70:30	95
2	**5a**	**8a**	**10a**	Me	Me_2CHCH_2	OMe	H	85:15	71
3	**5b**	**8a**	**10b**	Me	Me	OMe	H	80:20	78
4	**5c**	**8a**	**10c**	Me	Et	OMe	H	70:30	65
5	**5d**	**8a**	**10d**	Me	Ph	OMe	H	95:5	73
6	**5e**	**8b**	**10e**	Me	*n*-C_7H_{15}	OMe	OMe	78:22	98
7	**5f**	**8b**	**10f**	Me	$BnO(CH_2)_4$	OMe	OMe	70:30	62

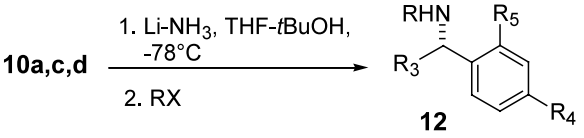
[a] Diastereomeric ratio was evaluated by ^1H NMR analysis.
[b] Yields of pure, isolated products.

acylhemiaminals.[9c] Cleavage of the oxazolidin-2-one ring of compounds **10** would afford the corresponding benzylamines in enantioenriched form. This cleavage is usually carried out in a reductive fashion using alkali metals in liquid ammonia, but these conditions seem incompatible with the presence of methoxy-substituted aromatic rings that would undergo to a Birch reduction.[15] However, Ojima and co-workers have demonstrated that cleavage of the oxazolidin-2-one proceeds much faster than the Birch reduction of aromatic derivatives.[16] Indeed, Li/NH_3 in THF/*t*-BuOH at −78°C cleaves the oxazolidin-2-one ring of compounds **10a**,**c**,**d** in about 10 min, while the methoxyphenyl ring remains unchanged during this time (Scheme 5).

Derivatives of benzylamines **12a**,**c**,**d** have been isolated in good yields and comparison of the specific rotation value of compounds **12c**,**d** with those reported in the literature allowed us to assign the absolute configuration of the major diastereomers of compounds **10c**,**d** as *S*.[17] This stereochemical outcome is in agreement with the observations made during the allylation of sulfones **4**,**5** with allyltrimethylsilane. Once again, the prevailing diastereomer seems to be produced by the attack of the nucleophile from the *re* face, assuming that the preferred configuration of the *N*-acyliminium ion intermediate is *E*.[18]

2.2. Intramolecular ring closure: synthesis of 4-desoxy-2-azapodophyllotoxin analogs

Podophyllotoxin **13** and structurally related lignans are known as anticancer agents but their pharmacological analogs have recently been prepared in order to provide new drugs endowed with higher potency and lower toxicity.[19]

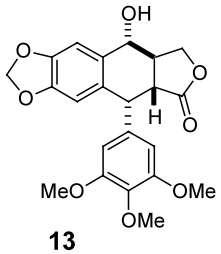


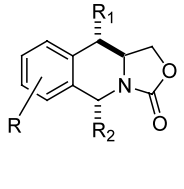
12a: (83%,e.e.=58%) R=MeOCO; R_3=*n*-C_7H_{15}; R_4=R_5=OMe

12c: (71%,e.e.=61%) R=Ac; R_3=Me; R_4=OMe; R_5=H

12d: (68%,e.e.=42%) R=H HCl; R_3=Et; R_4=OMe; R_5=H

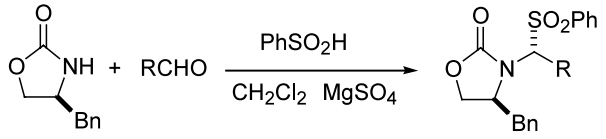
Scheme 5.





Various synthetic efforts have been directed toward the preparation of aza-analogs of podophyllotoxin **14**, which features an oxazolidin-2-one structure within a polycyclic framework.[20] The acid-catalyzed condensation between 4-benzyloxazolidin-2-ones and aldehydes represents a straightforward procedure to obtain the azapodophyllotoxin system,[20e] but this approach is restricted to the use of aromatic aldehydes. Since an *N*-acyliminium ion is probably involved in the cyclization step, the generation of this reactive intermediate from a suitable precursor at low temperature would allow efficient stereocontrol in the formation of the polycyclic structure. Furthermore, these conditions are consistent with the introduction of functionalized alkyl chains in the target molecule. Reaction of (*S*)-4-benzyl-1,3-oxazolidin-2-one **15** with aliphatic aldehydes **16** in the presence of benzenesulfinic acid gives an epimeric mixture of sulfones **17** in good yield (Scheme 6, Table 2).

The major diastereomer of compounds **17** has been isolated and the stereochemistry of the exocyclic stereocenter is assumed to be *R* in analogy with observations made for similar derivatives.[12] Generation of the corresponding *N*-acyliminium ion and intramolecular cyclization was carried out at −78°C under the usual conditions ($TiCl_4$, CH_2Cl_2). The cyclized products **18** were obtained as single stereoisomers in good yields (Scheme 7, Table 3).

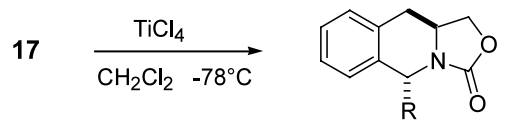


Scheme 6.

Table 2. Synthesis of sulfones **17** from oxazolidin-2-one **15**

Entry		Aldehyde **16**	**17**	d.r.[a]	Yield[b] (%)
1	**16a**	*n*-C_3H_7CHO	**17a**	75:25	98
2	**16b**	Me_2CHCH_2CHO	**17b**	70:30	86
3	**16c**	$PhCH_2CH_2CHO$	**17c**	65:35	75
4	**16d**	$Cl(CH_2)_5CHO$	**17d**	70:30	77
5	**16e**	$BnO(CH_2)_4CHO$	**17e**	80:20	65
6	**16f**	(*Z*)-$EtCH_2$=$CH(CH_2)_5CHO$	**17f**	80:20	85

[a] Diastereomeric ratio was evaluated by ^1H NMR analysis.
[b] Overall yields of pure, isolated products.



18

18a: R=*n*-C_3H_7

18b: R=Me_2CHCH_2

18c: R=$PhCH_2CH_2$

18d: R=$Cl(CH_2)_5$

18e: R=$BnOCH_2(CH_2)_3$

18f: R=(*Z*)-$EtCH_2{=}CH(CH_2)_5$

Scheme 7.

Table 3. Synthesis of tricyclic derivatives **18**

Entry	Sulfone **17**	**18**	Yield[a] (%)
1	**17a**	**18a**	98
2	**17b**	**18b**	78
3	**17c**	**18c**	80
4	**17d**	**18d**	95
5	**17e**	**18e**	65
6	**17f**	**18f**	66

[a] Yields of pure, isolated products.

$SnCl_4$ is also effective in promoting the ring closure but the yields obtained are invariably lower compared with the use of $TiCl_4$ as Lewis acid. It is worth noting that even though an *N*-acyliminium ion is postulated as a reactive intermediate in the formation of sulfones **17** we did not observe any cyclization at this stage. It is probable that the higher nucleophilicity of the benzenesulfinate anion compared with the aromatic ring favors the intermolecular addition over cyclization. However, an attempted allylation of sulfone **17b** using allyltrimethylsilane as previously described[12] failed and the tricyclic derivative **18b** was obtained as the main product. Formation of *N*-acyliminium ions from sulfones **17** promoted by $TiCl_4$ is rapid even at −78°C and this ensures short reaction times for the cyclization process (45 min) and prevents some unwanted side processes such as isomerisation of *Z* double bonds present in the substrate (Table 3, entry 6). The absolute configuration of the newly formed stereogenic center in compounds **18** has been confirmed as *S* by comparison with the spectroscopic data for an identical derivative obtained by Katritzky and co-workers using a related method based on benzotriazole chemistry.[21]

3. Conclusions

In summary, *N*-[1-(phenylsulfonyl)alkyl]oxazolidin-2-ones **4**,**5** react at −78°C with $TiCl_4$ giving the corresponding chiral *N*-acyliminium ions. These reactive intermediates add electron-rich aromatics in good yields and variable diastereoselectivities, affording aryl derivatives **9** and **10**. Rapid cleavage of the oxazolidin-2-one ring occurs at −78°C using Li/NH_3 giving benzylamines **12** without affecting the methoxyaromatic group also present in the molecule. Intramolecular cyclization is experienced when 4-benzyloxazolidin-2-one **15** is used as a chiral auxiliary in sulfones **17**. The obtained tricyclic derivatives **18** are structurally related to some aza analogs of podophyllotoxin, a cytotoxic metabolite endowed with anticancer properties.

4. Experimental

4.1. General

^1H NMR were performed at 300 MHz in $CDCl_3$ as solvent. ^{13}C NMR were performed at 75 MHz in $CDCl_3$ as solvent. Dichloromethane was dried by refluxing it over calcium hydride and then distilled. All chemicals used are available commercially. (Phenylsulfonyl)alkyloxazolidin-2-ones **4**,**5** were prepared using a previously reported method.[12] Enantiomeric ratio of compounds **12** was evaluated by GLC using a chiral column (30:70 dimethylpentylbetacyclodextrin-OV1701; 0.25 μ×0.25 mm i.d.; length 25 m, $\Delta T = 50$–180°C at 2°C/min); amine **12d** was converted into methyl carbamate before GLC analysis. Unless otherwise stated, characterization data for newly prepared compounds refer to the inseparable mixture of diastereomers. NMR data for the major diastereomer have been gathered from the spectra after chromatographic purification.

4.1.1. (4*R*)-5,5-Dimethyl-3-[1-(phenylsulfonyl)ethyl]-4-phenyloxazolidin-2-one, 5b. Mixture of 1′*S* and 1′*R* diastereomers (85:15); yield 95%; mp 130°C; $[\alpha]_D^{20} = -63.0$ (*c* 1.1, $CHCl_3$); IR (cm^{-1}, KBr) 1688; ^1H NMR (1′*S*) δ (ppm) 0.93 (s, 3H), 1.10 (d, 3H, $J = 7.3$ Hz), 1.64 (s, 3H), 4.96 (s, 1H), 5.42 (q, 1H, $J = 7.3$ Hz), 7.12–7.25 (m, 2H), 7.33–7.50 (m, 3H), 7.55–7.78 (m, 3H), 7.92–8.03 (m, 2H). ^{13}C NMR (1′*S*) δ (ppm) 13.1, 24.1, 29.0, 66.8, 70.0, 83.4, 126.4, 128.4, 129.1, 129.2, 129.6, 134.6, 137.4, 138.1, 157.3. Anal. calcd for $C_{19}H_{21}NO_4S$ (359.44) C, 63.49; H, 5.89; N, 3.90. Found C, 63.55; H, 5.93; N, 3.97%.

4.1.2. (4*R*)-5,5-Dimethyl-3-[1(phenylsulfonyl)propyl]-4-phenyloxazolidin-2-one, 5c. Mixture of 1′*S* and 1′*R* diastereomers (80:20); yield 79%; waxy solid; $[\alpha]_D^{20} = -45.5$ (*c* 1.5, $CHCl_3$); IR (cm^{-1}, neat) 1690; ^1H NMR (1′*S*) δ (ppm) 0.61 (t, 3H, $J = 7.3$ Hz), 1.00 (s, 3H), 1.21–1.42 (m, 1H), 1.55–1.60 (m, 1H), 1.63 (s, 3H), 4.98 (s, 1H), 5.12 (dd, 1H, $J = 3.7$, 9.9 Hz), 7.22–7.43 (m, 5H), 7.52–7.73 (m, 3H), 7.88–8.01 (m, 2H). ^{13}C NMR (1′*S*) δ (ppm) 11.1, 19.9, 24.4, 27.1, 67.2, 72.0, 83.5, 127.4, 128.9, 129.2, 129.4, 129.7, 134.5, 138.5, 138.2, 158.3. Anal. calcd for $C_{20}H_{23}NO_4S$ (373.47) C, 64.32; H, 6.21; N, 3.75. Found C, 64.38; H, 6.17; N, 3.80%.

4.1.3. (4*R*)-5,5-Dimethyl-3-[1-(phenylsulfonyl)phenylmethyl]-4-phenyloxazolidin-2-one, 5d. Mixture of 1′*S* and 1′*R* diastereomers (75:25); yield 60%; mp 80°C; $[\alpha]_D^{20} = -20.2$ (*c* 1.2, $CHCl_3$); IR (cm^{-1}, KBr) 1687; ^1H NMR (1′*S*) δ (ppm) 0.88 (s, 3H), 1.77 (s, 3H), 5.27 (s, 1H), 6.32 (s, 1H), 6.90–7.08 (m, 6H), 7.26–7.80 (m, 7H), 7.79–7.83 (m, 2H). ^{13}C NMR (1′*S*) δ (ppm) 24.1, 28.9,

29.9, 67.6, 83.7, 128.2, 128.4, 128.6, 128.9, 19.2, 129.3, 129.9, 130.7, 130.9, 134.4, 136.6, 137.6, 157.5. Anal. calcd for $C_{24}H_{23}NO_4S$ (421.51) C, 68.39; H, 5.50; N, 3.32. Found C, 68.35; H, 5.49; N, 3.37%.

4.1.4. (4*R*)-5,5-Dimethyl-3-[1-(phenylsulfonyl)-5-benzyl oxypentyl]-4-phenyloxazolidin-2-one, 5f. Mixture of 1′*S* and 1′*R* diastereomers (80:20); yield 65%; oil; $[\alpha]_D^{20} = -36.7$ (*c* 2.3, $CHCl_3$); IR (cm^{-1}, neat) 1688; ^1H NMR (1′*S*) δ (ppm) 1.00 (s, 3H), 1.07–1.38 (m, 4H), 1.50–1.60 (m, 2H), 1.64 (s, 3H), 3.05–3.18 (m, 2H), 4.34 (s, 2H), 4.98 (s, 1H), 5.16 (dd, 1H, *J* = 2.9, 10.2 Hz), 7.20–7.48 (m, 10H), 7.53–7.73 (m, 3H), 7.92–7.97 (m, 2H). ^{13}C NMR (1′*S*) δ (ppm) 23.1, 24.4, 25.9, 28.9, 29.1, 67.1, 69.6, 73.0, 74.9, 83.4, 127.8, 128.5, 128.7, 128.9, 129.1, 129.2, 129.3, 129.4, 129.7, 134.5, 137.5, 138.6, 158.2. Anal. calcd for $C_{29}H_{33}NO_5S$ (507.64) C, 68.61; H, 6.55; N, 2.76. Found C, 68.56; H, 6.58; N, 2.79%.

4.1.5. (4*R*)-5,5-Dimethyl-3-[1-(phenylsulfonyl)-2-benzyl oxyethyl]-4-phenyloxazolidin-2-one, 5g. Mixture of 1′*S* and 1′*R* diastereomers (85:15); yield 65%; mp 129°C; $[\alpha]_D^{20} = -44.2$ (*c* 1.5, $CHCl_3$); IR (cm^{-1}, KBr) 1688; ^1H NMR (1′*S*) δ (ppm) 0.96 (s, 3H), 1.72 (s, 3H), 3.37 (dd, 1H, *J* = 6.6, 10.6 Hz), 3.49 (dd, 1H, *J* = 5.9, 10.6 Hz), 3.80 (d, 1H, *J* = 10.7 Hz), 3.91 (d, 1H, *J* = 10.7 Hz), 5.03 (s, 1H), 5.49 (t, 1H, *J* = 6.6 Hz), 6.97–7.01 (m, 2H), 7.21–7.47 (m, 7H), 7.56–7.68 (m, 4H), 7.89–7.94 (m, 2H). ^{13}C NMR (1′*S*) δ (ppm) 24.4, 29.1, 65.0, 67.7, 72.8, 73.7, 83.5, 127.5, 127.9, 128.4, 128.6, 128.7, 128., 129.0, 129.4, 134.3, 136.9, 137.2, 139.0, 157.7. Anal. calcd for $C_{26}H_{27}NO_5S$ (465.56) C, 67.08; H, 5.85; N, 3.01. Found C, 67.02; H, 5.88; N, 2.97%.

4.2. General procedure for the preparation of aryl oxazolidin-2-ones 9 and 10

Sulfone **4**,**5** (2 mmol) was dissolved in CH_2Cl_2 (20 mL), and the solution was cooled at −78°C. $TiCl_4$ (4 mmol) was then added dropwise in 15 min and the temperature was kept at −78°C for 30 min. Aromatic derivative **8** (4 mmol) dissolved in CH_2Cl_2 (5 mL) was then added dropwise and after 1 h at −78°C the temperature was slowly raised to 0°C. The reaction mixture was then diluted with CH_2Cl_2 (20 mL) washed with brine (10 mL) and the organic phase was dried over $MgSO_4$. After removal of the solvent at reduced pressure the arylation product **9**,**10** obtained was purified by column chromatography (8:2 hexane–ethyl acetate).

4.2.1. (4*R*)-3-[1-(4-Methoxyphenyl)octyl]-4-phenyl oxazolidin-2-one, 9a. Mixture of 1′*S* and 1′*R* diastereomers (70:30); yield 95%; oil; $[\alpha]_D^{20} = -4.1$ (*c* 2.8, $CHCl_3$); IR (cm^{-1}, neat) 1695; ^1H NMR (1′S) δ (ppm) 0.84 (t, 3H, *J* = 6.8 Hz), 0.98–1.31 (m, 10H), 1.35–1.53 (m, 2H), 3.93 (s, 3H), 4.07 (dd, 1H, *J* = 6.2, 7.8 Hz), 4.28 (dd, 1H, *J* = 6.2, 8.9 Hz), 4.40 (dd, 1H, *J* = 7.8, 8.9 Hz), 4.98 (t, 1H, *J* = 8.0 Hz), 6.87 (d, 2H, *J* = 8.8 Hz), 7.11 (d, 2H, *J* = 8.8 Hz), 7.20–7.50 (m, 5H). Anal. calcd for $C_{24}H_{31}NO_3$ (381.51) C, 75.56; H, 8.19; N, 3.67. Found C, 75.61; H, 8.16; N, 3.71%.

4.2.2. (4*R*)-5,5-Dimethyl-3-[1-(4-methoxyphenyl)-3-methylbutyl]-4-phenyloxazolidin-2-one, 10a. Mixture of 1′*S* and 1′*R* diastereomers (85:15); yield 71%; mp 62°C; $[\alpha]_D^{20} = -24.6$ (*c* 1.0, $CHCl_3$); IR (cm^{-1}, KBr) 1693; ^1H NMR (1′*S*) δ (ppm) 0.67 (d, 3H, *J* = 5.9 Hz), 0.86 (d, 3H, *J* = 6.1 Hz), 0.88 (s, 3H), 1.15 (s, 3H), 1.26–1.60 (m, 3H), 3.84 (s, 4H, OMe+PhCHN), 5.12 (t, 1H, *J* = 7.3 Hz), 6.89 (2H, *J* = 8.8 Hz), 7.18 (d, 2H, *J* = 8.8 Hz), 7.30–7.59 (m, 5H). Anal. calcd for $C_{23}H_{29}NO_3$ (367.48) C, 75.17; H, 7.95; N, 3.81. Found C,75.24; H, 7.99; N, 3.79%.

4.2.3. (4*R*,1′*S*)-5,5-Dimethyl-3-[1-(4-methoxyphenyl)-ethyl]-4-phenyloxazolidin-2-one, 10b. Mixture of 1′*S* and 1′*R* diastereomers (80:20); yield 78%; oil; $[\alpha]_D^{20} = -45.5$ (*c* 1.5, $CHCl_3$); IR (cm^{-1}, neat) 1695; ^1H NMR (1′*S*) δ (ppm) 0.87 (s, 3H), 1.19 (d, 3H, *J* = 7.3 Hz), 1.23 (s, 3H), 3.84 (s, 3H), 4.28 (d, 1H, *J* = 7.7 Hz), 5.28 (q, 1H, *J* = 7.3 Hz), 6.89 (d, 2H, *J* = 8.8 Hz), 7.19 (d, 2H, *J* = 8.8 Hz), 7.22–7.45 (m 5H). Anal. calcd for $C_{20}H_{23}NO_3$ (325.40) C, 73.82; H, 7.12; N, 4.30. Found C, 73.76; H, 7.16; N, 4.26%.

4.2.4. (4*R*)-5,5-Dimethyl-3-[1-(4-methoxyphenyl)propyl]-4-phenyloxazolidin-2-one, 10c. Mixture of 1′*S* and 1′*R* diastereomers (70:30); yield 65%; oil; $[\alpha]_D^{20} = -42.6$ (*c* 0.7, $CHCl_3$); IR (cm^{-1}, neat) 1695. ^1H NMR (1′*S*) δ (ppm) 0.87 (s, 3H), 0.90 (t, 3H, *J* = 7.3 Hz), 1.16 (s, 3H), 203–2.28 (m, 1H), 2.32–2.55 (m, 1H), 3.83 (s, 3H), 4.21 (s, 1H), 4.91 (dd, 1H, *J* = 6.6, 9.2 Hz), 6.88 (d, 2H, *J* = 8.8 Hz), 7.14 (d, 2H, *J* = 8.8 Hz), 7.22–7.41 (m, 5H). ^{13}C NMR (1′*S*) δ (ppm): 11.2, 23.6, 25.2, 28.4, 55.0, 60.1, 69.0, 80.3, 113.4, 128.1, 128.2, 128.3, 128.4, 129.2, 131.5, 135.6, 137.9, 158.9. Anal. calcd for $C_{21}H_{25}NO_3$ (339.43) C, 74.31; H, 7.42; N, 4.13. Found C, 74.36; H, 7.45; N, 4.09%.

4.2.5. (4*R*)-5,5-Dimethyl-3-[1-(4-methoxyphenyl)-phenylmethyl]-4-phenyloxazolidin-2-one, 10d. Mixture of 1′*S* and 1′*R* diastereomers (95:5); yield 73%; oil; $[\alpha]_D^{20} = -51.7$ (*c* 3.0, $CHCl_3$); IR (cm^{-1}, neat) 1695; ^1H NMR (1′*S*) δ (ppm) 0.94 (s, 3H), 1.52 (s, 3H), 3.76 (s, 3H), 4.35 (s, 1H), 5.53 (s, 1H), 6.82 (d, 2H, *J* = 8.8 Hz), 7.08–7.30 (m, 12H). ^{13}C NMR (1′*S*) δ (ppm): 24.2, 28.7, 55.4, 62.5, 70.8, 81.4, 113.8, 127.2, 127.7, 128.0, 128.2, 128.4, 128.7, 129.1, 136.2, 138.8, 139.9, 158.9. Anal. calcd for $C_{26}H_{25}NO_3$ (387.47) C, 77.49; H, 6.50; N, 3.61. Found C, 77.45; H, 6.54; N, 3.60%.

4.2.6. (4*R*)-5,5-Dimethyl-3-[1-(2,4-dimethoxyphenyl)-octyl]-4-phenyloxazolidin-2-one, 10e. Mixture of 1′*S* and 1′*R* diastereomers (78:22); yield 98%; oil; $[\alpha]_D^{20} = -12.5$ (*c* 2.0, $CHCl_3$); IR (cm^{-1}, neat) 1695; ^1H NMR (1′*S*) δ (ppm) 0.77–0.90 (m, 5H), 1.01–1.20 (m, 8H), 1.22 (s, 3H), 1.41–1.62 (m, 2H), 3.66 (s, 3H), 3.80 (s, 3H), 3.84 (s, 3H), 5.23 (t, 1H, *J* = 7.7 Hz), 6.41 (dd, 1H, *J* = 2.6, 8.4 Hz), 6.47 (d, 1H, *J* = 2.6 Hz), 6.85 (d, 1H, *J* = 8.4 Hz), 7.29–7.43 (m, 5H). ^{13}C NMR (1′*S*) δ (ppm): 14.1, 22.4, 23.4, 26.6, 26.8, 28.8, 29.1, 29.3, 31.8, 52.1, 55.2, 80.8, 98.2, 103.5, 118.8, 126.8, 127.8, 128.0, 128.3, 128.8, 138.5, 157.7, 158.6, 160.5. Anal. calcd for $C_{27}H_{37}NO_4$ (439.59) C, 73.77; H, 8.48; N, 3.19. Found C, 73.73; H, 8.52; N, 3.15%.

4.2.7. (4*R*)-5,5-Dimethyl-3-[1-(2,4-dimethoxyphenyl)-5-benzyloxypentyl]-4-phenyloxazolidin-2-one, 10f. Mixture of 1′*S* and 1′*R* diastereomers (70:30); yield 62%; oil; $[\alpha]_D^{20}=-49.7$ (*c* 0.75, $CHCl_3$); IR (cm^{-1}, neat) 1695. ^1H NMR (1′*S*) δ (ppm) 0.86 (s, 3H), 1.22 (s, 3H), 1.30–1.80 (m, 6H), 3.35 (t, 2H, $J=6.2$ Hz), 3.78 (s, 3H), 3.82 (s, 3H), 4.14–4.35 (m, 2H), 4.42 (s, 1H), 5.18–5.38 (m, 1H), 6.35–6.70 (m, 2H), 6.86–6.92 (m, 1H), 7.24–7.53 (m, 9H), 7.96–8.05 (m, 1H). ^{13}C NMR (1′*S*) δ (ppm): 23.3, 25.7, 29.5, 31.5, 31.6, 52.1, 55.5, 64.9, 67.9, 70.3, 72.9, 81.0, 98.4, 103.7, 118.8, 127.8, 128.2, 128.4, 128.5, 128,6, 128.8, 129.0, 129.2, 129.3, 129.7, 132.9, 138.6, 157.9, 158.8, 160.7. Anal. calcd for $C_{31}H_{37}NO_5$ (503.63) C, 73.93; H, 7.41; N, 2.78. Found C, 73.98; H, 7.38; N, 2.81%.

4.2.8. (4*R*)-3-(3,4-Dihydro-1*H*-isochromen-4-yl)-5,5-dimethyl-4-phenyl-1,3-oxazolidin-2-one, 11. Mixture of diastereomers (3:2); yield 68%, oil; $[\alpha]_D^{20}=+18.7$ (*c* 1.5, $CHCl_3$); IR (cm^{-1}, neat) 1695; ^1H NMR δ (ppm) (diastereomer A) 0.88 (s, 3H), 1.50 (s, 3H), 3.46 (dd, 1H, $J=6.1$, 9.8 Hz), 4.21 (s, 1H), 4.46 (d, 1H, $J=$ 11.9 Hz), 4.63 (d, 1H, $J=11.3$ Hz), 5.18–5.38 (m, 2H), 7.12–7.40 (m, 9H). ^1H NMR δ (ppm) (diastereomer B) 0.89 (s, 3H), 1.54 (s, 3H), 3.26 (dd, 1H, $J=6.1$, 9.8 Hz), 4.21 (s, 1H), 4.58 (d, 1H, $J=$ 11.9 Hz), 4.63 (d, 1H, $J=11.3$ Hz), 5.18–5.38 (m, 2H), 7.12–7.40 (m, 9H). Anal. calcd for $C_{20}H_{21}NO_3$ (323.39) C, 74.28; H, 6.55; N, 4.33. Found C, 74.33; H, 6.54; N, 4.28%.

4.3. General procedure for the reductive cleavage of the oxazolidin-2-one ring

Aryl derivative **10** (2 mmol) was dissolved in a mixture of THF (80 mL) and *t*-BuOH (10 mL) and then Li shots (20 mmol) were added in one portion. After cooling at −78°C, NH_3 (100 mL) was condensed and the blue solution was stirred at this temperature for 10 min. The reaction mixture was then quenched by addition of solid NH_4Cl (2 g), warmed at room temperature and then the solvent was removed at reduced pressure. The residue was suspended in ethyl acetate (60 mL), washed with water (2×5 mL) and dried over Na_2SO_4. The crude amine obtained after evaporation of the solvent was converted into the corresponding derivative (see Scheme 5) by usual methods.

4.3.1. Methyl-1-(2,4-dimethoxyphenyl)octyl carbamate, 12a. Enantiomeric mixture (e.e. = 58%); yield 83%, oil, $[\alpha]_D^{20}=+5.3$ (*c* 3.7, $CHCl_3$); IR (cm^{-1}, neat) 3300, 1690; ^1H NMR δ ppm 0.87 (t, 3H, $J=6.2$ Hz), 1.21–1.38 (m, 10H), 1.71–1.86 (m, 2H), 3.63 (s, 3H), 3.79 (s, 3H), 3.81 (s, 3H), 4.68–4.85 (m, 1H), 5.54 (d, 1H, $J=9.9$ Hz), 6.42 (dd, 1H, $J=2.2$, 8.1 Hz), 6.46 (d, 1H, $J=2.2$ Hz), 7.07 (d, 1H, $J=8.1$ Hz). ^{13}C NMR δ ppm 14.1, 22.6, 26.6, 29.2, 29.3, 31.8, 35.7, 51.8, 53.6, 55.3, 55.4, 99.2, 103.9, 123.2, 129.1, 156.6, 158.1, 160.0. Anal. calcd for $C_{18}H_{29}NO_4$ (313.35) C, 68.99; H, 6.11; N, 4.47. Found C, 69.04; H, 6.06; N, 4.45%.

4.4. General procedure for the preparation of phenylsulfonyl derivatives 17

Oxazolidin-2-one **15** (5 mmol) was dissolved in dichloromethane (15 mL) and then benzenesulfinic acid (10 mmol), the appropriate aldehyde **16** (7.5 mmol) and anhydrous $MgSO_4$ (0.5 g) were sequentially added at room temperature. The mixture was stirred for 36 h at room temperature and then filtered over a short pad of Florisil. Removal of the solvent afforded the crude sulfone **17** which was purified by column chromatography (7:3 hexanes–ethyl acetate). The following data refer to the major diastereomer isolated as a pure compound.

4.4.1. (4*S*,1′*R*)-3-[1-(Phenylsulfonyl)butyl]-4-benzyl oxazolidin-2-one, 17a. Oil; $[\alpha]_D^{20}=+54.7$ (*c* 2.1, $CHCl_3$); IR (cm^{-1}, neat) 1695; ^1H NMR δ (ppm) 1.01 (t, 3H, $J=7.3$ Hz), 1.46–1.77 (m, 2H), 2.10–2.36 (m, 2H), 2.70 (dd, 1H, $J=11.4$, 12.8 Hz), 3.38 (dd, 1H, $J=3.7$, 13.2 Hz), 3.92 (q, 1H, $J=8.8$ Hz), 4.01 (dd, 1H, $J=$ 4.4, 9.1 Hz), 4.57–4.64 (m, 1H), 5.21 (dd, 1H, $J=5.1$–10.6 Hz), 7.58–7.88 (m, 9H), 7.93–7.98 (m, 1H). ^{13}C NMR δ (ppm): 13.4, 19.1, 27.7, 39.8, 55.1, 67.6, 74.4, 127.4, 128.6, 129.1, 129.2, 129.3, 129.5, 134.6, 135.3, 157.7. Anal. calcd for $C_{20}H_{23}NO_4S$ (373.47) C, 64.32; H, 6.21; N, 3.75. Found C, 64.26; H, 6.25; N, 3.81%.

4.4.2. (4*S*,1′*R*)-3-[1-(Phenylsulfonyl)-3-methylbutyl]-4-benzyloxazolidin-2-one, 17b. Oil; $[\alpha]_D^{20}=+35.6$ (*c* 2.2, $CHCl_3$); IR (cm^{-1}, neat) 1690; ^1H NMR δ (ppm) 0.97 (d, 3H, $J=6.2$ Hz), 1.03 (d, 3H, $J=6.2$ Hz), 1.72–1.91 (m, 1H), 1.98 (dt, 1H, $J=3.7$, 10.3 Hz), 2.23 (dt, 1H, $J=3.7$, 14.0 Hz), 2.65 (dd, 1H, $J=11.4$, 12.8 Hz), 3.39 (dd, 1H, $J=3.7$, 12.8 Hz), 3.87 (dd, 1H, $J=8.1$, 8.8 Hz), 4.00 (dd, 1H, $J=4.4$, 8.8 Hz), 4.57–4.64 (m, 1H), 5.29 (dd, $J=3.3$, 11.4 Hz), 7.21–7.43 (m, 5H), 7.55–7.78 (m, 4H), 7.93–7.98 (m, 1H). ^{13}C NMR δ (ppm): 20.9, 23.1, 24.6, 34.0, 39.8, 54.9, 67.5, 73.1, 127.4, 128.5, 129.1, 129.4, 134.5, 135.2, 136.6, 154.0. Anal. calcd for $C_{21}H_{25}NO_4S$ (387.49) C, 65.09; H, 6.50; N, 3.61. Found C, 65.14; H, 6.46; N, 3.66%.

4.4.3. (4*S*,1′*R*)-3-[1-(Phenylsulfonyl)-3-phenylpropyl]-4-benzyloxazolidin-2-one, 17c. Oil; $[\alpha]_D^{20}=+12.3$ (*c* 1.0, $CHCl_3$); IR (cm^{-1}, neat) 1691; ^1H NMR δ (ppm) 2.44–2.90 (m, 5H), 3.42 (dd, 1H, $J=3.7$, 9.9 Hz), 3.98 (q, 1H, $J=8.0$ Hz), 4.03 (dd, 1H, $J=4.4$, 8.9 Hz), 4.55–4.76 (m, 1H), 5.23 (dd, 1H, $J=4.1$, 10.7 Hz), 7.11–7.42 (m, 10H), 7.55–7.71 (m, 3H), 7.91–7.98 (m, 2H). ^{13}C NMR δ (ppm): 26.9, 32.7, 39.6, 56.3, 67.8, 75.6, 126.9, 127.5, 128.5, 128.8, 128.9, 129.1, 129.2, 129.3, 129.4, 129.5, 134.6, 135.4, 137.0, 139.3, 156.8. Anal. calcd for $C_{25}H_{25}NO_4S$ (435.54) C, 68.94; H, 5.79; N, 3.22. Found C, 68.89; H, 5.84; N, 3.26%.

4.4.4. (4*S*,1′*R*)-3-[1-(Phenylsulfonyl)-6-chlorohexyl]-4-benzyloxazolidin-2-one, 17d. Oil; $[\alpha]_D^{20}=+50.7$ (*c* 1.1, $CHCl_3$); IR (cm^{-1}, neat) 1688; ^1H NMR δ (ppm) 1.43–1.64 (m, 4H), 1.70–1.86 (m, 2H), 2.10–2.36 (m, 2H), 2.67 (dd, 1H, $J=11.3$, 12.8 Hz), 3.39 (dd, 1H, $J=3.7$, 12.8 Hz), 3.50 (t, 2H, $J=6.3$ Hz), 3.92 (q, 1H, $J=8.4$ Hz), 4.02 (dd, 1H, $J=4.4$, 8.8 Hz), 4.57–4.65 (m, 1H),

5.19 (dd, 1H, $J=4.4$, 10.6 Hz), 7.22–7.41 (m, 5H), 7.56–7.78 (m, 3H), 7.93–8.00 (m, 2H). Anal. calcd for $C_{22}H_{26}ClNO_4S$ (435.96) C, 60.61; H, 6.01; N, 3.21. Found C, 60.66; H, 5.97; N, 3.17%.

4.4.5. (4*S*,1′*R*)-3-[1-(Phenylsulfonyl)-5-benzyloxypentyl]-4-benzyloxazolidin-2-one, 17e. Oil; $[\alpha]_D^{20}=+42.6$ (c 1.8, $CHCl_3$); IR (cm^{-1}, neat) 1688; ^1H NMR δ (ppm) 1.40–1.95 (m, 6H), 2.10–2.42 (m, 2H), 2.70 (dd, 1H, $J=11.3$, 12.1 Hz), 3.34–3.44 (m, 1H), 3.47 (t, 2H, $J=5.9$ Hz), 3.91 (q, 1H, $J=8.2$ Hz), 4.06 (dd, 1H, $J=2.3$, 8.2 Hz), 4.45–4.70 (m, 1H), 5.19 (dd, 1H, $J=5.1$, 9.5 Hz), 7.10–7.41 (m, 10H), 7.49–7.73 (m, 3H), 7.93–8.05 (m, 2H). Anal. calcd for $C_{28}H_{31}NO_5S$ (493.62) C, 68.13; H, 6.33; N, 2.94. Found C, 68.18; H, 6.36; N, 2.99%.

4.4.6. (*Z*)(4*S*,1′*R*)-3-[1-(Phenylsulfonyl)-7-decenyl]-4-benzyloxazolidin-2-one, 17f. Waxy solid; $[\alpha]_D^{20}=+70.7$ (c 2.5, $CHCl_3$); IR (cm^{-1}, neat) 1688; ^1H NMR δ (ppm) 0.94 (t, 3H, $J=7.3$ Hz), 1.28–1.42 (m, 6H), 1.44–1.62 (m, 2H), 1.91–2.08 (m, 2H), 2.11–2.36 (m, 2H), 2.69 (dd, 1H, $J=11.8$, 12.4 Hz), 3.36 (dd, 1H, $J=4.0$, 13.5 Hz), 3.91 (q, 1H, $J=8.8$ Hz), 4.01 (dd, 1H, $J=4.0$, 8.8 Hz), 4.56–4.70 (m, 1H), 5.18 (dd, 1H, $J=3.7$, 11.0 Hz), 5.31–5.45 (m, 2H), 7.18–7.42 (m, 5H), 7.50–7.76 (m, 3H), 7.93–8.01 (m, 2H). ^{13}C NMR δ (ppm): 14.1, 32.1, 25.8, 28.6, 29.3, 32.4, 40.0, 41.6, 54.0, 67.8, 74.8, 127.6, 128.8, 129.2, 129.3, 129.5, 129.7, 129.8, 132.6, 135.5, 137.0, 158.4. Anal. calcd for $C_{26}H_{33}NO_4S$ (455.61) C, 68.54; H, 7.30; N, 3.07. Found C, 68.60; H, 7.26; N, 3.05%.

4.5. General procedure for the preparation of tricyclic derivatives 18

Sulfone **17** (2 mmol) was dissolved in CH_2Cl_2 (20 mL), and the solution was cooled at −78°C. $TiCl_4$ (3 mmol) was then added dropwise in 5 min and after 45 min at −78°C the reaction mixture was quenched with brine (10 mL). The aqueous phase obtained after separation was extracted with CH_2Cl_2 (3×10 mL) and the collected organic phase was dried over $MgSO_4$. After removal of the solvent at reduced pressure the tricyclic product **18** obtained was purified by column chromatography (7:3 hexane–ethyl acetate).

4.5.1. (5*R*,10a*S*)-5-Propyl-1,5,10,10a-tetrahydro[1,3]-oxazolo[3,4-b]isoquinolin-3-one, 18b. Yield 98%; mp 86°C; $[\alpha]_D^{20}=-146.4$ (c 2.0, $CHCl_3$) (lit.[21] mp 85–86°C; $[\alpha]_D^{20}=-148.6$); IR (cm^{-1}, KBr) 1692; ^1H NMR δ (ppm) 0.99 (t, 3H, $J=7.3$ Hz), 1.38–1.60 (m, 2H), 1.65–1.90 (m, 2H), 2.90–2.94 (m, 2H) 4.07 (dq, 1H, $J=2.9$, 7.7 Hz), 4.17 (dd, 1H, $J=3.0$, 8.4 Hz), 4.56 (dd, 1H, $J=8.1$, 8.8 Hz), 4.92 (dd, 1H, $J=4.0$, 9.2 Hz), 7.12–7.20 (m, 4H). ^{13}C NMR δ (ppm): 13.9, 19.4, 33.9, 39.4, 48.3, 52.6, 68.3, 126.8, 126.9, 129.4, 131.4, 136.3, 157.3 Anal. calcd for $C_{14}H_{17}NO_2$ (231.29) C, 72.70; H, 7.41; N, 6.06. Found C, 72.77; H, 7.46; N, 6.01%.

4.5.2. (5*R*,10a*S*)-5-(2-Methylpropyl)-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinolin-3-one, 18b. Yield 78%; oil; $[\alpha]_D^{20}=-100.7$ (c 3.0, $CHCl_3$); IR (cm^{-1}, neat) 1690; ^1H NMR δ (ppm) 0.96 (d, 3H, $J=6.6$ Hz), 1.14 (d, 3H, $J=6.2$ Hz), 1.51–1.95 (m, 3H), 2.88–2.93 (m, 2H), 4.07 (dq, 1H, $J=2.2$, 8.4 Hz), 4.16 (dd, 1H, $J=2.6$, 8.4 Hz), 4.53 (t, 1H, $J=8.1$ Hz), 4.98 (dd, 1H, $J=3.3$, 11.0 Hz), 7.08–7.21 (m, 4H). ^{13}C NMR δ (ppm) 21.6, 23.8, 25.1, 33.4, 46.9, 47.7, 51.1, 68.2, 126.7, 127.0, 129.4, 131.2, 136.9, 157.0. Anal. calcd for $C_{15}H_{19}NO_2$ (245.32) C, 73.44; H, 7.81; N, 5.71. Found C, 73.39; H, 7.80; N, 5.74%.

4.5.3. (5*R*,10a*S*)-5-(2-Phenylethyl)-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinolin-3-one, 18c. Yield 80%; oil; $[\alpha]_D^{20}=-109.3$ (c 4.0, $CHCl_3$); IR (cm^{-1}, neat) 1695; ^1H NMR δ (ppm) 2.01–2.38 (m, 2H), 2.73–2.96 (m, 4H), 3.97 (dq, 1H, $J=2.6$, 7.7 Hz), 4.12 (dd, 1H, $J=2.6$, 8.4 Hz), 4.35 (t, 1H, $J=8.4$ Hz), 5.01 (dd, 1H, $J=3.6$, 9.9 Hz), 7.08–7.39 (m, 9H). ^{13}C NMR δ (ppm) 32.6, 33.8, 38.7, 48.4, 52.9, 68.3, 126.1, 127.0, 127.1, 128.4, 128.6, 129.6, 131.6, 136.1, 141.7, 157.4. Anal. calcd for $C_{19}H_{19}NO_2$ (293.36) C, 77.79; H, 6.53; N, 4.77. Found C, 77.85; H, 6.49; N, 4.70%.

4.5.4. (5*R*,10a*S*)-5-(5-Chloropentyl)-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinolin-3-one, 18d. Yield 95%; oil; $[\alpha]_D^{20}=-85.1$ (c 2.0, $CHCl_3$); IR (cm^{-1}, KBr) 1691; ^1H NMR δ (ppm) 1.42–1.65 (m, 4H), 1.70–1.99 (m, 4H), 2.90–2.94 (m, 2H), 3.55 (t, 2H, $J=6.6$ Hz), 4.03–4.13 (m, 1H), 4.18 (dd, 1H $J=3.3$, 8.8 Hz), 4.57 (dd, 1H, $J=8.0$, 8.8 Hz), 4.90 (dd, 1H, $J=3.3$, 9.2 Hz), 7.09–7.26 (m, 4H). Anal. calcd for $C_{16}H_{20}ClNO_2$ (293.69) C, 65.41; H, 6.86; N, 4.72. Found C, 65.37; H, 6.90; N, 4.69%.

4.5.5. (5*R*,10a*S*)-5-(4-Benzyloxybutyl)-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinolin-3-one, 18e. Yield 65%; oil $[\alpha]_D^{20}=-55.7$ (c 3.0, $CHCl_3$); IR (cm^{-1}, neat) 1695; ^1H NMR δ (ppm) 1.48–1.87 (m, 4H), 1.89–2.12 (m, 2H), 2.85–2.92 (m, 2H), 3.50 (t, 2H, $J=6.2$ Hz), 4.04 (dq, 1H, $J=2.9$, 7.7 Hz), 4.14 (dd, 1H, $J=2.6$, 8.7 Hz), 4.32–4.38 (m, 1H), 4.47–4.56 (m, 2H), 4.90 (dd, 1H, $J=3.3$, 9.2 Hz), 7.08–7.60 (m, 8H), 8.02–8.06 (m, 1H). Anal. calcd for $C_{22}H_{25}NO_3$ (351.44) C, 75.19; H, 7.17; N, 3.99. Found C, 75.14; H, 7.20; N, 4.04%.

4.5.6. (*Z*)(5*R*,10a*S*)-5-(6-Nonenyl)-1,5,10,10a-tetrahydro[1,3]oxazolo[3,4-*b*]isoquinolin-3-one, 18f. Yield 66%; oil; $[\alpha]_D^{20}=-92.3$ (c 1.7, $CHCl_3$); IR (cm^{-1}neat) 1693; ^1H NMR δ (ppm) 0.96 (t, 3H, $J=7.0$ Hz), 1.21–1.57 (m, 6H), 1.62–1.80 (m, 2H), 1.83–2.09 (m, 4H), 2.89–2.93 (m, 2H), 4.07 (dq, 1H, $J=4.8$, 8.1 Hz), 4.16 (dd, 1H, $J=2.9$, 8.4 Hz), 4.55 (t, 1H, $J=8.1$ Hz), 4.90 (dd, 1H, $J=3.7$, 9.5 Hz), 5.30–5.45 (m, 2H), 7.07–7.25 (m, 4H). Anal. calcd for $C_{20}H_{27}NO_2$ (313.43) C, 76.64; H, 8.68; N, 4.47. Found C, 76.60; H, 8.71; N, 4.44%.

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