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Protoberberines from *Reissert*-Compounds VIII [1]. Oxazoloisoquinolines, New and Efficient Educts for the Synthesis of 8-Oxoprotoberberines

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Summary. Certain benzylated oxazoloisoquinolinones readily available from *Reissert* compounds provided an efficient access to 8-oxoprotoberberines in three steps. A series of these new precursors as well as several oxoprotoberberines were prepared and the scope and limitation of this procedure were investigated.

Keywords. Oxazoloisoquinolinones; X-ray crystal structure; 13a-Carboxy-8-oxo-protoberberines; 8-Oxoprotoberberines.

Introduction

We previously reported the reduction of 1-benzylated *Reissert* compounds giving oxazoloisoquinolines as the main products, which in turn could be readily transformed to 8-oxoprotoberberines [1] (general formulae **4**, **5**, **14**, and **15** in Schemes 2, 3, and 6).

As part of our continuing investigations in this area we have checked the uses of this pathway by synthesizing a series of new oxazoloisoquinolines **5** and several further 8-oxoprotoberberines **14** and **15**, which are known to possess biological activity [2]. In this paper we would like to present the results concerning these investigations.

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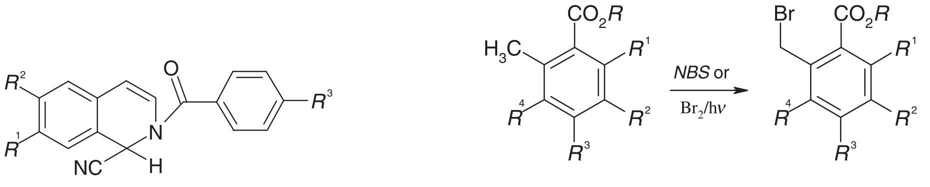
[a] Part of PhD thesis, LMU München, D

Results and Discussion

The required starting substances, *Reissert* compounds **1** and 2-(bromomethyl)benzoic acid esters **3** and **10** (Schemes 1 and 4), were synthesized according to standard procedures. Subsequent reaction of **1** and **3** as well as **1a** and **10**, according to an efficient general procedure, afforded the benzylated *Reissert* compounds **4** and **11** in good yields (52–90%; see Schemes 2 and 4).

The reduction of compounds **4** was performed by an approved method [1] leading to the desired oxazoloisoquinolines **5** summarized in Scheme 3. The yields were found to depend on the ester group of the benzyl moiety. Thus, the ethyl (or methyl) esters gave the best results; alkyl groups with larger steric demand caused decreasing yields. Therefore, all the following reductions were performed using the ethyl esters of the corresponding educts. In addition, it seemed that the substitution pattern in both the isoquinoline and benzyl fragments of **4** hardly influenced the reaction rate. Furthermore, according to Ref. [1] the by-products **6**–**9** could also be isolated (Scheme 3).

In this connection it should be noted, that the reduction of *Reissert* compounds **11**, lacking an *ortho* positioned carbalkoxy group, surprisingly did not take place in the same manner. Instead of the expected oxazoloisoquinolines the aldehydes **12** were preferably formed as the main products (Scheme 4). A possible explanation may be, that the formation of the intermediate *Reissert* salt, already containing the unsaturated target oxazoloisoquinoline skeleton [1] is favored by an intramolecular hydrogen bond between the ester and imino functions. However, this assumption is not in line with the result obtained on the reduction of the *o*-nitrobenzyl derivative **11d**. Although the NO_2-group is also capable to form a corresponding hydrogen



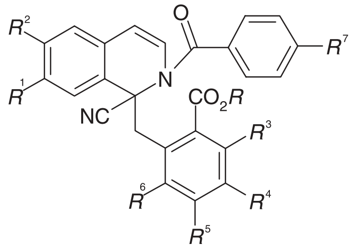
2 **3**

	*R*¹	*R*²	*R*³
1a	H	H	H
1b	H	H	*Me*
1c	H	H	O*Me*
1d	O*Me*	O*Me*	H
1e	O*Bn*	O*Me*	H
1f	O*Me*	O*Me*	*Me*
1g	O-CH$_2$-O		H

2,3	*R*	*R*¹	*R*²	*R*³	*R*⁴
a	*Me*	H	H	H	H
b	*Et*	H	H	H	H
c	*i-Pr*	H	H	H	H
d	*t-Bu*	H	H	H	H
e	*Et*	O*Me*	H	H	H
f	*Et*	H	O*Me*	O*Me*	H
g	*Et*	H	H	H	O*Me*
h	*Et*	O-CH$_2$-O		H	H
i[a]	*Et*	O*Me*	O*Me*	H	H

[a] **3**: Cl instead of Br

Scheme 1



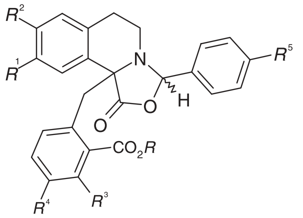
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	*R*
4a	H	H	H	H	H	H	H	*Me*
4b	H	H	H	H	H	H	H	*Et*
4c	H	H	H	H	H	H	H	*i-Pr*
4d	H	H	H	H	H	H	H	*t-Bu*
4e	H	H	H	H	H	H	*Me*	*Me*
4f	H	H	H	H	H	H	*Me*	*Et*
4g	H	H	H	H	H	H	O*Me*	*Me*
4h	O*Me*	O*Me*	H	H	H	H	H	*Me*
4i	O*Me*	O*Me*	H	H	H	H	H	*Et*
4j	O*Bn*	O*Me*	H	H	H	H	H	*Et*
4k	O-CH$_2$-O		H	H	H	H	H	*Et*
4l	H	H	O*Me*	H	H	H	H	*Et*
4m	H	H	H	O*Me*	O*Me*	H	H	*Et*
4n	H	H	H	H	H	O*Me*	H	*Et*
4o	O*Me*	O*Me*	O*Me*	H	H	H	*Me*	*Et*
4p	H	H	O-CH$_2$-O		H	H	H	*Et*
4q	O*Me*	O*Me*	O*Me*	O*Me*	H	H	H	*Et*
4r	O*Me*	O*Me*	O*Me*	O*Me*	H	H	*Me*	*Et*
4s	O*Me*	O*Me*	O-CH$_2$-O		H	H	H	*Et*
4t	O-CH$_2$-O		O*Me*	O*Me*	H	H	H	*Et*
4u	O-CH$_2$-O		O-CH$_2$-O		H	H	H	*Et*

Scheme 2

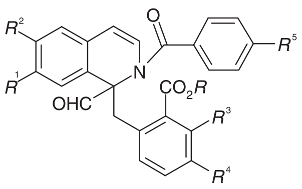
bond with the imino group, no formation of the desired oxazoloisoquinoline occurred.

Treating the oxazoloisoquinolines **5** with ethanolic potassium hydroxide according to Ref. [1] caused the generation of the new 8-oxoberbine carboxylic acids **13** in exellent yields (Scheme 5). Their structures were fully characterized by spectroscopic data and additionally confirmed by X-ray diffraction analysis of compound **13b** showing the *trans* configuration of the quinolizidine skeleton (Fig. 1).

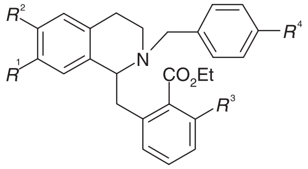
Finally, the carboxylic acids **13** were decarboxylated in an approved manner [1] affording the title compounds in good yields (84–94%). Thus, in the cases **13a**, **13b**, **13d**, and **13f** mixtures of the (±)-8-oxoprotoberberines **14a**–**d** (among others (±)-gusanlung D (**14c**) [3], (±)-8-oxodihydropalmatine (**14d**) [2, 4]) and 5,6-dihydrodibenzoquinolizin-8-ones **15a**–**d**, easily identified by their blue fluorescence at $\lambda = 365$ nm, were obtained. In the cases **13h** and **13i** the 8-oxodihydrodibenzoquinolizines (berberin-8-one, berlambine, (**15e**) [5, 6] and 8-oxocoptisine (**15f**) [7, 8]) were found to be the only products of the decarboxylation (Scheme 6).

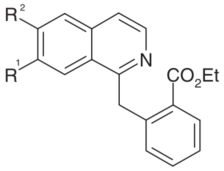


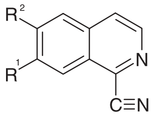
	*R*¹	*R*²	*R*³	*R*⁴	*R*⁵	*R*
5a	H	H	H	H	H	*Me*
5b	H	H	H	H	H	*Et*
5c	H	H	H	H	H	*i-Pr*
5d	H	H	H	H	H	*t-Bu*
5e	H	H	H	H	*Me*	*Me*
5f	H	H	H	H	*Me*	*Et*
5g	H	H	H	H	O*Me*	*Me*
5h	O*Me*	O*Me*	H	H	H	*Et*
5i	O*Bn*	O*Me*	H	H	H	*Et*
5j	O-CH$_2$-O		H	H	H	*Et*
5k	H	H	O*Me*	H	H	*Et*
5l	H	H	O-CH$_2$-O		H	*Et*
5m	O*Me*	O*Me*	O*Me*	O*Me*	H	*Et*
5n	O*Me*	O*Me*	O*Me*	O*Me*	*Me*	*Et*
5o	O*Me*	O*Me*	O-CH$_2$-O		H	*Et*
5p	O-CH$_2$-O		O*Me*	O*Me*	H	*Et*
5q	O-CH$_2$-O		O-CH$_2$-O		H	*Et*



	*R*¹	*R*²	*R*³	*R*⁴	*R*⁵	*R*
6a	H	H	H	H	H	*Me*
6b	H	H	H	H	H	*Et*
6c	H	H	H	H	*Me*	*Me*
6d	H	H	H	H	O*Me*	*Me*
6e	O*Me*	O*Me*	H	H	H	*Et*
6f	O*Bn*	O*Me*	H	H	H	*Et*
6g	O-CH$_2$-O		H	H	H	*Et*
6h	H	H	O*Me*	H	H	*Et*
6i	O*Me*	O*Me*	O*Me*	H	*Me*	*Et*
6k	O*Me*	O*Me*	O*Me*	O*Me*	*Me*	*Et*







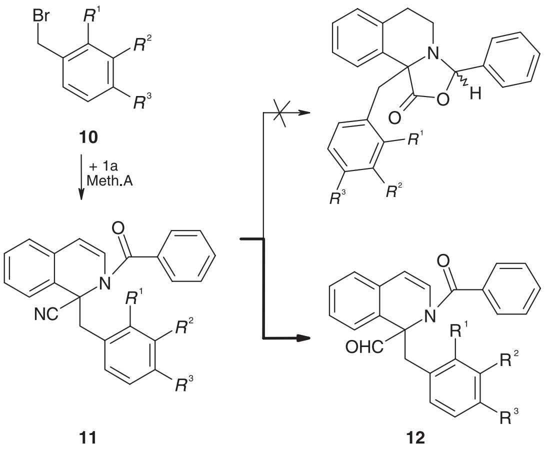
	*R*¹	*R*²	*R*³	*R*⁴
7a	H	H	H	H
7b	H	H	O*Me*	H
7c	O*Me*	O*Me*	O*Me*	CH$_3$

	*R*¹	*R*²
8a	O*Me*	O*Me*
8b	O-CH$_2$-O	

	*R*¹	*R*²
9a	O*Me*	O*Me*
9b	O*Bn*	O*Me*
9c	O-CH$_2$-O	

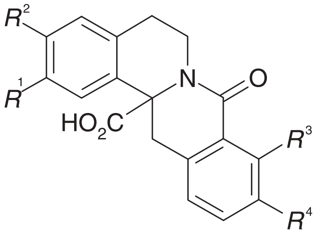
Scheme 3

In summary, we have shown the usefulness of the easily available 1-benzylated *Reissert* compounds as educts for the synthesis of 8-oxoberberines. This sequence represents a short route to the title compounds, which are of general interest because of their natural occurence and remarkable antitumor and antileukemic properties [2].



10,11,12	R^1	R^2	R^3
a	H	H	H
b	CH_3	H	H
c	Br	H	H
d	NO_2	H	H
e	-$(CH)_4$-		H
f	H	H	CO_2-*t-Bu*

Scheme 4



	R^1	R^2	R^3	R^4
13a	H	H	H	H
13b	O*Me*	O*Me*	H	H
13c	O*Bn*	O*Me*	H	H
13d	O-CH_2-O		H	H
13e	H	H	O*Me*	H
13f	O*Me*	O*Me*	O*Me*	O*Me*
13g	O*Me*	O*Me*	O-CH_2-O	
13h	O-CH_2-O		O*Me*	O*Me*
13i	O-CH_2-O		O-CH_2-O	

Scheme 5

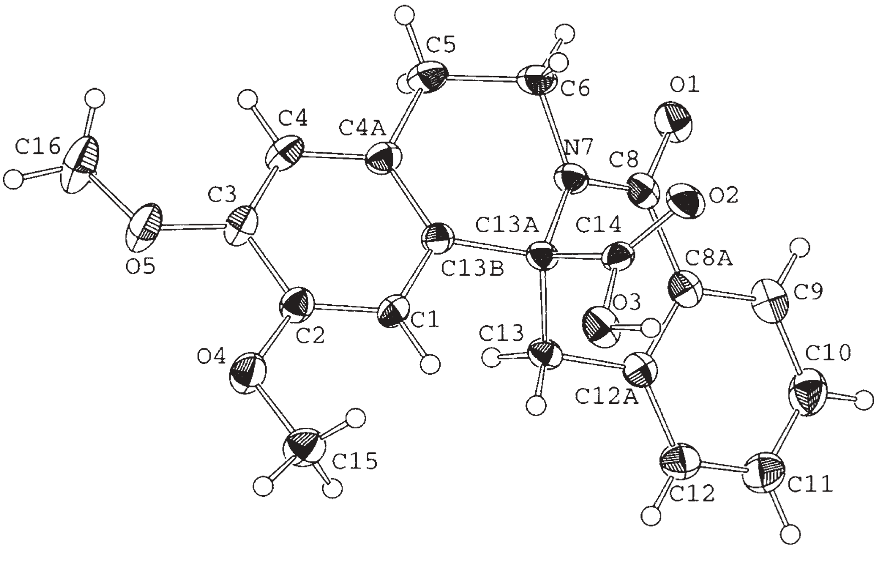
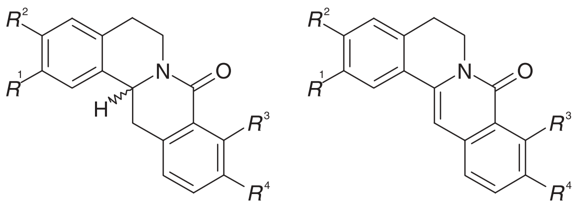


Fig. 1. Crystal structure of **13b**



14 **15**

14,15	R^1	R^2	R^3	R^4
a	H	H	H	H
b	O*Me*	O*Me*	H	H
c	O-CH_2-O		H	H
d	O*Me*	O*Me*	O*Me*	O*Me*
e	O-CH_2-O		O*Me*	O*Me*
f	O-CH_2-O		O-CH_2-O	

Scheme 6

Table 1. Crystallographic data of **13b**[a]

Formula	$C_{20}H_{19}NO_5$
Formula weight	353.37
Temperature (°K)	295
Color, shape	Pale yellow platelet
Crystal dimensions (mm)	$0.17 \times 0.43 \times 0.53$
Crystal system	monoclinic
Space group	*P21/c*
Cell dimensions:	
a/Å	11.064(4)
b/Å	11.1823(14)
c/Å	14.154(3)
β/°	101.87(2)
V/Å^3	1713.7 (7)
Radiaton	MoK_α ($\lambda = 0.71073$ Å)
Z	4
F(000)	744
μ/mm^{-1}	0.099
Density/$g\,cm^{-3}$	1.370
Reflections collected	2806
Independent reflections	2680 ($R_i = 0.0264$)
Observed reflections	2152 ($I > 2\sigma I$)
No. of parameters refined	237/0
R-values	
*R*1 ($2\sigma I$/all data)	0.0432/0.0574
*wR*2 ($2\sigma I$/all data)	0.1047/0.1139
Goodness of Fit	1.181
System used	SHELXS-86/SHELXL-93 [40]

[a] Further details of the crystal structure determination are available from Cambridge Crystallographic Data Center, 12 Union Road, GB Cambridge CB21EZ quoting the deposition number CCDC 159936 and the complete literature source (e-mail: deposit@ccdc.cam.ac.uk)

Experimental

Melting points are measured with a Reichert hot-stage microscope and are uncorrected. IR: Perkin Elmer FT-IR Paragon 1000 and Jasco FT-IR 410. NMR: Jeol GSX 400 and Jeol GSX 500 (^{1}H: 400 and 500 MHz, ^{13}C: 100 and 125 MHz, $CDCl_3$ (unless otherwise stated), *TMS* as internal reference). MS (70 eV): Hewlett Packard MS-Engine. Elemental analyses: Heraeus CHN-Rapid; the results are in good agreement with the calculated values. Thin layer chromatography (TLC): aluminum sheets Kieselgel 60 F_{254} (Merck), thickness of layer 0.2 mm. Flash chromatography (FC): ICN-SiliTech 32–36, 60 Å. Compounds **10a–10d** are commercial products. *Reissert* compound **1a** was prepared according to Ref. [9].

Reissert Compounds **1b–1g**; *General Procedure*

To a solution of the isoquinoline in 120 cm^3 of CH_2Cl_2 was added an aqueous solution of KCN and then dropwise under vigorous stirring and ice cooling the corresponding quantity of benzoyl chloride. Since the emulsion formed can warm up to boiling temperature the reaction flask should be equipped with a reflux condenser. Stirring was continued for 2 h under cooling and for 5 h at ambient temperature. The beige coloured emulsion was diluted with 150 cm^3 of CH_2Cl_2 and 200 cm^3 of brine. The organic layer was washed with 3 × 100 cm^3 of H_2O and dried with Na_2SO_4. After removing the solvent *in vacuo*, the residue was recrystallized from *Et*OH. The crystals were collected by filtration, washed with a small amount of *Et*OH, and dried at 60°C *in vacuo*. The melting points of **1b–1d** and **1g** are cited in Refs. [10–15] and are identical with those found; IR spectra were measured in KBr.

1,2-Dihydro-2-(4-methylbenzoyl)isoquinoline-1-carbonitrile (**1b**, [10])

Isoquinoline 63 mmol, KCN 126 mmol, *p*-toluic acid chloride 240 mmol; yield: 68%; IR: $\bar{\nu} = 1651$ (C=O) cm^{-1}; TLC (*n*-hexane:petroleum ether = 3:1): $R_f = 0.58$.

1,2-Dihydro-2-(4-methoxybenzoyl)isoquinoline-1-carbonitrile (**1c**, [11])

Isoquinoline 63 mmol, KCN 126 mmol, 4-methoxybenzoyl chloride 240 mmol; yield: 82%; IR: $\bar{\nu} = 1662$ (C=O) cm^{-1}; TLC (petroleum ether:*Et*O*Ac* = 3:2): $R_f = 0.50$.

2-Benzoyl-1,2-dihydro-6,7-dimethoxyisoquinoline-1-carbonitrile (**1d**, [12, 13])

6,7-Dimethoxyisoquinoline 61 mmol, KCN 126 mmol, benzoyl chloride 244 mmol; yield: 74%; IR: $\bar{\nu} = 2237$ (C≡N), 1660 (C=O) cm^{-1}; TLC (*n*-hexane:*Et*O*Ac* = 3:2): $R_f = 0.60$.

2-Benzoyl-7-benzyloxy-1,2-dihydro-6-methoxyisoquinoline-1-carbonitrile (**1e**, [14])

7-Benzyloxy-6-methoxyisoquinoline 50.1 mmol, KCN 180 mmol, benzoyl chloride 200 mmol; yield: 68%; IR: $\bar{\nu} = 2239$ (C≡N), 1650 (C=O) cm^{-1}; TLC (*n*-hexane:*Et*O*Ac* = 3:2): $R_f = 0.65$.

1,2-Dihydro-6,7-dimethoxy-2-(4-methylbenzoyl)isoquinoline-1-carbonitrile (**1f**, $C_{20}H_{18}N_2O_3$)

6,7-Dimethoxyisoquinoline 63 mmol, KCN 126 mmol, *p*-toluic acid chloride 240 mmol; yield: 75%; IR: $\bar{\nu} = 2239$ (C≡N), 1658 (C=O) cm^{-1}; TLC (*n*-hexane:EtOAc = 3:2): $R_f = 0.60$; MS (EI): m/z (%) = 334 ($M^{+\bullet}$, 13), 119 (100), 91 (74); ^{1}H NMR: $\delta = 7.43$ and 7.19 (2d, each $J = 7.9$ Hz, each 2H), 6.77 and 6.65 (2s, 5-H, 8-H), 6.55–6.44 (m, 3-H), 6.40 (s, 1-H), 5.90 (d, $J = 7.7$ Hz, 4-H), 3.85 and 3.84 (2s, 2 OCH_3), 2.34 (s, CH_3) ppm; ^{13}C NMR: $\delta = 168.90$, 150.32, 149.26, 142.69, 130.69, 129.65 (2C), 129.46, 129.34 (2C), 129.12, 124.79, 123.70, 116.75, 109.74, 108.77, 56.34, 56.20, 45.02, 21.66 ppm.

(Bromomethyl)arene Derivatives **3a–3h** *and* **10a–10f**, *General Procedures*

Method A: A mixture of the *o*-toluic acid esters **2** or 1-methylnaphthalene or *p*-toluic acid *t*-butylester [16], *N*-bromosuccinimide (*NBS*) and benzoyl peroxide was refluxed for 2 h. After cooling the solid was filtered off. The filtrate was washed with 2 × 50 cm^3 of H_2O, dried with Na_2SO_4 and evaporated under reduced pressure. The product thus obtained was purified by destillation or flash chromatography.

Method B: To a refluxing solution of **2** in dry benzene, irradiated with a 500 W lamp, was added dropwise a solution of Br_2 in the same solvent. After the addition was complete the mixture was heated under reflux for further 30 min without irradiation, after cooling to ambient temperature consecutively washed with 100 cm^3 of ice cold water, 100 cm^3 of saturated $NaHCO_3$ solution and again 100 cm^3 of H_2O, and dried with Na_2SO_4. The solvent was removed *in vacuo* and the products were purified by destillation or flash chromatography. Educts **2a** and **2b** are commercial products, **2c**–**2f**, **2h** and **2i** are described in Refs. [17–24]. The bromomethyl derivatives **10a**–**10d** are commercial products.

3-Methoxy-2-methyl-benzoic acid ethylester (**2g**, $C_{11}H_{14}O_3$)

A mixture of 2.0 g (12 mmol) of 3-methoxy-2-methyl-benzoic acid [25], 30 cm^3 of *Et*OH, and 2 cm^3 of conc. H_2SO_4 was refluxed for 12 h. After removing the solvent *in vacuo*, the oily residue was consecutively diluted with 10 cm^3 of ice cold H_2O and 20 cm^3 of Et_2O. The aqueous layer was extracted with 2 × 50 cm^3 of Et_2O, the combined organic phases were washed with 20 cm^3 of saturated $NaHCO_3$ solution and 20 cm^3 of H_2O, and dried with Na_2SO_4. After removing the solvent *in vacuo* a colourless oil was obtained, which was used for the next step without further purification. Yield: 2.3 g (99%); TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.70$; IR (film): $\bar{\nu} = 1726$ (CO_2R) cm^{-1}; MS (EI): m/z (%) = 194 ($M^{+\bullet}$, 39), 149 ($M^{+\bullet}$–OC_2H_5, 100), 91 (C_7H_7, 75); ^{1}H NMR: $\delta = 7.39$ (dd, $J = 7.9/3.1$ Hz, 6-H), 7.19 (br t, $J = 7.9$ Hz, 5-H), 6.96 (dd, $J = 7.9/0.9$ Hz, 4-H), 4.35 (q, $J = 7.1$ Hz, OCH_2), 3.83 (s, OCH_3), 2.42 (s, *Ph*-CH_3), 1.38 (t, $J = 7.1$ Hz, OC–CH_3) ppm.

2-(Bromomethyl)benzoic acid methylester (**3a**)

Method A, yield: 86%, bp 90–94°C/0.2 Pa [9]; TLC (*n*-hexane:*Et*O*Ac* = 3:2): $R_f = 0.80$.

2-(Bromomethyl)benzoic acid ethylester (**3b**)

Method A, yield: 93%, bp 98–100°C/0.16 Pa [9]; TLC (*n*-hexane:*Et*O*Ac* = 3:2): $R_f = 0.83$.

2-(Bromomethyl)benzoic acid isopropylester (**3c**)

Method A, yield: 82%, bp 107–109°C/0.15 Pa [26]; TLC (*n*-hexane:*Et*O*Ac* = 3:2): $R_f = 0.86$.

2-(Bromomethyl)benzoic acid t-butylester (**3d**, $C_{12}H_{15}BrO_2$)

Method A, yield: 78%; TLC (petroleum ether:$CHCl_3$ = 2:1): $R_f = 0.77$; IR (film): $\bar{\nu} = 1712$ (CO_2R), 704 (C–Br) cm^{-1}; MS (EI): m/z(%) = 215 ($M^{+\bullet}$–C_4H_9, 4), 213 ($M^{+\bullet}$–C_4H_9, 4), 133 (100), 105 (46), 77 (43); ^{1}H NMR: $\delta = 7.95$ (m, 6-H), 7.68–7.50 (m, 3-H, 4-H, 5-H), 5.35 (s, CH_2–Br), 1.63 (s, $C(CH_3)_3$) ppm.

2-(Bromomethyl)-6-methoxybenzoic acid ethylester (**3e**)

Method B, yield: 95% [27]; TLC (*n*-hexane:*Et*O*Ac* = 3:2): $R_f = 0.67$.

2-(Bromomethyl)-4,5-dimethoxybenzoic acid ethylester (**3f**)

Method B, yield: 53%, mp 78–81°C [20]; TLC (*n*-hexane:*Et*O*Ac* = 3:2): $R_f = 0.69$.

2-(Bromomethyl)-3-methoxybenzoic acid ethylester (**3g**, $C_{11}H_{13}BrO_3$)

Method B, yield: 81%; TLC (*n*-hexane:*Et*O*Ac* = 3:2): $R_f = 0.37$; MS (EI): m/z(%) = 274 ($M^{+\bullet}$, 5), 272 ($M^{+\bullet}$, 5), 193 (78), 165 (100), 77 (77); ^{1}H NMR: $\delta = 7.51$ (dd, $J = 8.0/1.1$ Hz, 6-H), 7.33 (t, $J = 8.0$ Hz, 5-H), 7.05 (dd, $J = 8.0/1.1$ Hz, 4-H), 5.05 (s, CH_2–Br), 4.40 (q, $J = 7.1$ Hz, OCH_2), 3.92 (s, OCH_3), 1.42 (t, $J = 7.1$ Hz, CH_3) ppm.

6-(Bromomethyl)-2,3-(methylenedioxy)benzoic acid ethylester (**3h**)

Method B, yield: 96%, mp 67°C [28]; TLC (*n*-hexane:*Et*O*Ac* = 3:2): $R_f = 0.76$.

6-(Chloromethyl)-2,3-dimethoxybenzoic acid ethylester (**3i**)

Educt is N-dimethoxybenzyl-N,N-dimethylamine; yield: 89%, bp 130°C/0.05 Pa [24]; TLC (*n*-hexane:*Et*O*Ac* = 3:2): $R_f = 0.65$.

1-(Bromomethyl)naphthalene (**10e**)

Method A, yield: 85%, colourless liquid [29]; TLC (*Et*O*Ac*:*n*-hexane = 3:1): $R_f = 0.78$; MS (EI): *m/z* (%) = 221 ($M^{+\bullet}$–H, 100), 219 ($M^{+\bullet}$–H, 100), 141 (63); ^{1}H NMR: $\delta = 8.10$ (m, 4-H), 7.82–7.77 (m, 3H), 7.57–7.33 (m, 3H), 4.90 (s, CH_2–Br) ppm.

*4-(Bromomethyl)benzoic acid t-*butylester (**10f**)

Method A, yield: 73%, colourless liquid [30]; TLC (petroleum ether:$CHCl_3$ = 2:1): $R_f = 0.70$; IR (film): $\bar{\nu} = 1713$ (CO_2R), 704 (C–Br) cm^{-1}; MS (CI): m/z (%) = 273 ($M^{+\bullet} + 1$, 12), 272 ($M^{+\bullet}$, 100), 271 ($M^{+\bullet} + 1$, 12), 269 ($M^{+\bullet}$, 98), 215 (29), 123 (67); ^{1}H NMR: $\delta = 7.90$ and 7.88 (2dd, each $J = 6.5/1.7$ Hz, 2-H, 6-H), 7.53 (dd, $J = 6.5/1.7$ Hz, 1H, 3-H/5-H), 7.34 (br d, $J = 6.2$ Hz, 1H, 3-H/5-H), 4.39 (s, CH_2–Br), 1.51 (s, $C(CH_3)_3$) ppm.

Benzylated Reissert Compounds **4** *and* **11**, *General Procedures*

Method A: According to Refs. [1, 9]; before extraction with benzene, the mixture was diluted with 20 cm^3 of H_2O. The products were dried *in vacuo* at 60°C.

Method B: A solution of the corresponding *Reissert* compound **1** in dry *DMF* was stirred for 30 min under N_2 at ambient temperature. After addition of NaH (60% dispersion in mineral oil) the reaction flask was equipped with a septum, and a solution of the appropriate benzyl halogenide **3** or **10** in *DMF* was added dropwise over *ca.* 15 min by a syringe under vigorous stirring. Stirring was continued for several hours and then the mixture was quenched cautiously with 800 cm^3 of ice/H_2O. The aqueous layer was extracted with 4×200 cm^3 of *Et*O*Ac* and the combined organic extracts were consecutively washed with 100 cm^3 of H_2O and 100 cm^3 of brine and dried with Na_2SO_4. Further workup was the same as described under Method A. For preparation and spectroscopic data of **4a**, **4b**, **4i**, and **4l** see Ref. [9].

2-[[2-Benzoyl-1-cyano-1,2-dihydroisoquinolin-1-yl]methyl]benzoic acid isopropylester (**4c**, $C_{28}H_{24}N_2O_3$)

Method A, **1a** 31.9 mmol, **3c** 33.9 mmol, cetrimonium bromide 69 mg, C_6H_6 100 cm^3, 50% NaOH solution 15 cm^3, 16 h; yield: 65%, mp 155–156°C; TLC (*n*-hexane:*EtOAc* = 3:1): $R_f = 0.55$; IR (KBr): $\bar{\nu} = 2240$ (C≡N), 1712, 1675 (C=O) cm^{-1}; MS (EI): *m/z* (%) = 305 (10), 218 (52), 105 (100); MS (CI): m/*z* (%) = 437 (100), 306 (74), 105 (49).

2-[[2-Benzoyl-1-cyano-1,2-dihydroisoquinolin-1-yl]methyl]benzoic acid t-butylester (**4d**, $C_{29}H_{26}N_2O_3$)

Method A, **1a** 20 mmol, **3d** 16.6 mmol, cetrimonium bromide 49 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 6 h; yield: 53%, mp 161–162°C; TLC (*n*-hexane:*EtOAc* = 3:1): $R_f = 0.70$; IR (KBr): $\bar{\nu} = 2241$ (C≡N), 1713, 1684 (C=O) cm^{-1}; MS (EI): *m/z* (%) = 218 (71), 105 (100), 84 (65); MS (CI): *m/z* (%) = 451 (14), 395 (100), 368 (51).

2-[[1-Cyano-1,2-dihydro-2-(4-methylbenzoyl)isoquinolin-1-yl]methyl]benzoic acid methylester (**4e**, $C_{27}H_{22}N_2O_3$)

Method A, **1b** 14.2 mmol, **3a** 17.5 mmol, cetrimonium bromide 50 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 4 h; yield: 74%; mp 176–177°C; TLC (*n*-hexane:*EtOAc* = 3:1): $R_f = 0.54$; IR (KBr): $\bar{\nu} = 1722$, 1665 (C=O) cm^{-1}; MS (EI): *m/z* (%) = 277 (5), 218 (29), 119 (100); MS (CI): *m/z* (%) = 423 (58), 278 (78), 119 (33).

2-[[1-Cyano-1,2-dihydro-2-(4-methylbenzoyl)isoquinolin-1-yl]methyl]benzoic acid ethylester (**4f**, $C_{28}H_{24}N_2O_3$)

Method A, **1b** 21.8 mmol and **3b** 24.7 mmol, cetrimonium bromide 53 mg, C_6H_6 60 cm^3, 50% NaOH solution 10 cm^3, 4 h; yield: 65%, mp 149°C; TLC (*n*-hexane:*EtOAc* = 3:1): $R_f = 0.59$; IR (KBr): $\bar{\nu} = 1721$, 1667 (C=O) cm^{-1}; MS (EI): *m/z* (%) = 291 (12), 218 (58), 119 (100); MS (CI): *m/z* (%) = 437 (71), 292 (92), 119 (100).

2-[[1-Cyano-1,2-dihydro-2-(4-methoxybenzoyl)isoquinolin-1-yl]methyl]benzoic acid methylester (**4g**, $C_{27}H_{22}N_2O_4$)

Method A, **1c** 13.4 mmol, **3a** 17.5 mmol, cetrimonium bromide 51 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 4 h; yield: 52%, mp 168–169°C; TLC (*n*-hexane:*EtOAc* = 3:1): $R_f = 0.54$; IR (KBr): $\bar{\nu} = 2242$ (C≡N), 1725, 1674 (C=O) cm^{-1}; MS (EI): *m/z* (%) = 277 (11), 218 (44), 135 (100); MS (CI): *m/z* (%) = 439 (100), 278 (41), 135 (38).

2-[[2-Benzoyl-1-cyano-1,2-dihydro-6,7-dimethoxyisoquinolin-1-yl]methyl]benzoic acid methylester (**4h**, $C_{28}H_{24}N_2O_5$)

Method A, **1d** 14 mmol, **3a** 17.1 mmol, cetrimonium bromide 50 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 4.5 h; yield: 90%, mp 162°C; TLC (*n*-hexane:*EtOAc* = 3:1): $R_f = 0.36$; IR (KBr): $\bar{\nu} = 1727$, 1672 (C=O) cm^{-1}; MS (EI): *m/z* (%) = 337 (53), 305 (59), 278 (100); MS (CI): *m/z* (%) = 469 (12), 338 (90), 105 (100).

2-[[2-Benzoyl-7-benzyloxy-1-cyano-1,2-dihydro-6-methoxyisoquinolin-1-yl]methyl]benzoic acid ethylester (**4j**, $C_{35}H_{30}N_2O_5$)

Method A, **1e** 12.6 mmol, **3b** 13 mmol, cetrimonium bromide 40 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 11 h; yield: 77%, mp 149°C; TLC (*n*-hexane:*EtOAc* = 1:1): $R_f = 0.48$; IR (KBr):

$\bar{\nu}=1717$, 1676 (C=O) cm^{-1}; MS (EI): m/z (%) = 427 (43), 354 (42), 91 (100); MS (CI): m/z (%) = 559 (2), 428 (13), 79 (100).

2-[[2-Benzoyl-1-cyano-1,2-dihydro-6,7-methylenedioxyisoquinolin-1-yl]methyl]benzoic acid ethylester (**4k**, $C_{28}H_{22}N_2O_5$)

Method B, **1g** 9.9 mmol, **3b** 12 mmol, *DMF* 50 cm^3, 60% NaH dispersion 390 mg, 1 h; yield: 67%, mp 144°C; TLC (*n*-hexane:*EtOAc* = 3:1): $R_f=0.44$; IR (KBr): $\bar{\nu}=2242$ (C≡N), 1714, 1668 (C=O) cm^{-1}; MS (EI): m/z (%) = 335 (19), 289 (57), 262 (100); MS (CI): m/z (%) = 467 (2), 336 (72), 105 (100).

2-[[2-Benzoyl-1-cyano-1,2-dihydroisoquinolin-1-yl]methyl]-4,5-dimethoxybenzoic acid ethylester (**4m**, $C_{29}H_{26}N_2O_5$)

Method A, **1a** 2 mmol, **3f** 1.9 mmol, cetrimonium bromide 10 mg, C_6H_6 30 cm^3, 50% NaOH solution 2.5 cm^3, 7 h; yield: 61%, mp 181°C; TLC (*n*-hexane:*EtOAc* = 3:1): $R_f=0.26$; IR (KBr): $\bar{\nu}=2240$ (C≡N), 1710, 1676 (C=O) cm^{-1}; MS (EI): m/z (%) = 305 (29), 278 (100), 105 (100); MS (CI): m/z (%) = 483 (100), 352 (100), 105 (29).

2-[[2-Benzoyl-1-cyano-1,2-dihydroisoquinolin-1-yl]methyl]-3-methoxy-benzoic acid ethylester (**4n**, $C_{28}H_{24}N_2O_4$)

Method A, **1a** 3.8 mmol, **3g** 4.2 mmol, cetrimonium bromide 50 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 17 h; yield: 64%, mp 164°C; TLC (*n*-hexane:*EtOAc* = 1:1): $R_f=0.43$; IR (KBr): $\bar{\nu}=2229$ (C≡N), 1714, 1677 (C=O) cm^{-1}; MS (EI): m/z (%) = 259 (16), 105 (100), 77 (23); MS (CI): m/z (%) = 453 (22), 322 (100), 105 (53).

2-[[1-Cyano-1,2-dihydro-6,7-dimethoxy-2-(4-methylbenzoyl)isoquinolin-1-yl]methyl]-6-methoxybenzoic acid ethylester (**4o**, $C_{31}H_{30}N_2O_6$)

Method B, **1d** 12 mmol, **3e** 13.5 mmol, *DMF* 100 cm^3, 60% NaH dispersion 480 mg, 1 h; yield: 70%, mp 168°C; TLC (*n*-hexane:*EtOAc* = 1:1): $R_f=0.41$; IR (KBr): $\bar{\nu}=2236$ (C≡N), 1718, 1676 (C=O) cm^{-1}; MS (EI): m/z (%) = 381 (5), 308 (100), 119 (29); MS (CI): m/z (%) = 382 (100), 336 (13), 119 (72).

6-[[2-Benzoyl-1-cyano-1,2-dihydroisoquinolin-1-yl]methyl]-2,3-methylenedioxybenzoic acid ethylester (**4p**, $C_{28}H_{22}N_2O_5$)

Method A, **1a** 3.8 mmol, **3h** 4.2 mmol, cetrimonium bromide 50 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 12 h; yield: 71%, mp 152°C; TLC (*n*-hexane:*EtOAc* = 3:1): $R_f=0.39$; IR (KBr): $\bar{\nu}=2231$ (C≡N), 1715, 1676 (C=O) cm^{-1}; MS (EI): m/z (%) = 335 (9), 262 (42), 105 (100); MS (CI): m/z (%) = 467 (33), 336 (58), 105 (100).

6-[[2-Benzoyl-1-cyano-1,2-dihydro-6,7-dimethoxyisoquinolin-1-yl]methyl]-2,3-dimethoxybenzoic acid ethylester (**4q**, $C_{31}H_{30}N_2O_7$)

Method B, **1d** 13.8 mmol, **3i** 14 mmol, *DMF* 100 cm^3, 60% NaH dispersion 550 mg, 1 h; yield: 71%, mp 135–136°C; TLC (*n*-hexane:*EtOAc* = 3:1): $R_f=0.37$; IR (KBr): $\bar{\nu}=2243$ (C≡N), 1709, 1674 (C=O) cm^{-1}; MS (EI): m/z (%) = 366 (13), 338 (100), 105 (19); MS (CI): m/z (%) = 366 (10), 338 (11), 105 (100).

6-[[1-Cyano-1,2-dihydro-6,7-dimethoxy-2-(4-methylbenzoyl)isoquinolin-1-yl]methyl]-2,3-dimethoxybenzoic acid ethylester (**4r**, $C_{32}H_{32}N_2O_7$)

Method B, **1f** 12.7 mmol, **3i** 13 mmol, *DMF* 100 cm^3, 60% NaH dispersion 508 mg, 1 h; yield: 72%, mp 155°C; TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.40$; IR (KBr): $\bar{\nu} = 2242$ ($C\equiv N$), 1714, 1663 (C=O) cm^{-1}; MS (EI): *m/z* (%) = 366 (10), 338 (100), 119 (52); MS (CI): *m/z* (%) = 557 (1), 412 (5), 195 (100).

6-[[2-Benzoyl-1-cyano-1,2-dihydro-6,7-methylenedioxyisoquinolin-1-yl]methyl]-2,3-dimethoxybenzoic acid ethylester (**4t**, $C_{30}H_{26}N_2O_7$)

Method B, **1g** 14.1 mmol, **3i** 14.3 mmol, *DMF* 100 cm^3, 60% NaH dispersion 550 mg, 1 h; yield: 74%, mp 161°C; TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.56$; IR (KBr): $\bar{\nu} = 2239$ ($C\equiv N$), 1709, 1673 (C=O) cm^{-1}; MS (EI): *m/z* (%) = 395 (2), 350 (12), 322 (100); MS (CI): *m/z* (%) = 396 (34), 322 (10), 105 (100).

6-[[2-Benzoyl-1-cyano-1,2-dihydro-6,7-methylenedioxyisoquinolin-1-yl]methyl]-2,3-methylenedioxybenzoic acid ethylester (**4u**, $C_{29}H_{22}N_2O_7$)

Method B, **1g** 7.1 mmol, **3h** mmol, *DMF* 50 cm^3, 60% NaH dispersion 283 mg, 1 h; yield: 63%, mp 167°C; TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.65$; IR (KBr): $\bar{\nu} = 2243$ ($C\equiv N$), 1712, 1675 (C=O) cm^{-1}; MS (EI): *m/z* (%) = 379 (16), 333 (16), 306 (100); MS (CI): *m/z* (%) = 511 (2), 380 (31), 105 (100).

2-Benzoyl-1-benzyl-1,2-dihydroisoquinoline-1-carbonitrile (**11a**)

Method A, **1a** 15.9 mmol, **10a** 16.3 mmol, cetrimonium bromide 47 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 5 h; yield: 92%, TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.55$; Ref. [31].

2-Benzoyl-1,2-dihydro-1-(2-methylbenzyl)isoquinoline-1-carbonitrile (**11b**)

Method A, **1a** 15.3 mmol, **10b** 15.6 mmol, cetrimonium bromide 44 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 3.5 h; yield: 88%; TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.56$; Ref. [31].

2-Benzoyl-1-(2-bromobenzyl)-1,2-dihydroisoquinoline-1-carbonitrile (**11c**, $C_{24}H_{17}BrN_2O$)

Method A, **1a** 15.3 mmol, **10c** 15.6 mmol, cetrimonium bromide 51 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 7 h; yield: 58%, mp 171°C; TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.63$; IR (KBr): $\bar{\nu} = 1660$ (C=O) cm^{-1}; MS (EI): *m/z* (%) = 105 (100), 77 (47); MS (CI): *m/z* (%) = 431 (1), 429 (1), 105 (24).

2-Benzoyl-1,2-dihydro-1-(2-nitrobenzyl)isoquinoline-1-carbonitrile (**11d**)

Method A, **1a** 15.3 mmol, **10d** 15.6 mmol, cetrimonium bromide 50 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 5.5 h; yield: 88%; TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.49$; Ref. [32].

2-Benzoyl-1,2-dihydro-1-(naphth-1-ylmethyl)isoquinoline-1-carbonitrile (**11e**, $C_{28}H_{20}N_2O$)

Method A, **1a** 15.3 mmol, **10e** 15.6 mmol, cetrimonium bromide 50 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 6 h; yield: 64%, mp 141°C; TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.49$; IR (KBr):

$\bar{\nu}=1669$ (C=O) cm^{-1}; MS (EI): m/z (%) = 400 (3), 268 (100), 259 (91); MS (CI): m/z (%) = 401 (100), 259 (80), 105 (78).

4-[[2-Benzoyl-1-cyano-1,2-dihydroisoquinolin-1-yl]methyl]benzoic acid t-butylester (**11f**, $C_{29}H_{26}N_2O_3$)

Method A, **1a** 15.9 mmol, **10f** 16.6 mmol, cetrimonium bromide 47 mg, C_6H_6 50 cm^3, 50% NaOH solution 7.5 cm^3, 6 h; yield: 42%, mp 160°C; TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f=0.71$; IR (KBr): $\bar{\nu}=1712$, 1677 (C=O) cm^{-1}; MS (EI): m/z (%) = 262 (59), 105 (100), 84 (89); MS (CI): m/z (%) = 451 (60), 395 (100), 368 (44).

Oxazoloisoquinolines **5** *and by-products* **6–9**

General procedure according to Ref. [1]. For isolation of the by-products **6–9** the reaction mixtures were concentrated *in vacuo* and the residues separated by flash chromatography; eluents were the same as indicated under TLC of compounds **5**. For yields and analytical data of compounds **5b** and **5h** as well as **6b** and **6e** see Ref. [1].

2-[(5,6-Dihydro-1-oxo-3-phenyloxazolo[4,3-a]isoquinolin-10b-yl)methyl]benzoic acid methylester (**5a**, $C_{26}H_{23}NO_4$)

4a 7.3 mmol, CH_3CO_2H 15 cm^3, CF_3CO_2H 27 cm^3, $NaBH_3CN$ 15.7 mmol, 1 h; yield: 45%, mp 128°C; IR (KBr): $\bar{\nu}=1785$, 1722 (C=O) cm^{-1}; MS (EI): m/z (%) = 369 (4), 310 (46), 264 (53), 149 (100); TLC (petroleum ether:*Et*O*Ac* = 3:1): $R_f=0.71$; ^{1}H NMR: $\delta=7.86$ (dd, $J=7.7/1.4$ Hz, 10-H), 7.81, 7.53, and 7.47 (3dd, each $J=7.6/1.5$ Hz, 3 arom H), 7.41–7.24 (m, 6 arom H), 7.17–7.12 (m, 7-H), 7.03–6.96 (m, 2 arom H), 5.67 (s, 3-H), 4.12 and 3.84 (AB, $J=14.0$ Hz, benzyl-CH_2), 3.72 (s, OCH_3), 3.29 (ddd, $J=14.3/12.9/4.3$ Hz, 5-H_a), 3.14 (ddd, $J=16.9/12.9/5.8$ Hz, 6-H_a), 2.84–2.75 (m, 5-H_b), 2.54 (dd, $J=16.9/4.3$ Hz, 6-H_b) ppm; ^{13}C NMR: $\delta=174.03$, 168.78, 136.91, 135.62, 133.61, 133.58, 132.97, 131.16, 130.01, 129.72, 129.50, 128.24, 127.82, 127.72, 127.05, 126.74, 90,80, 66.86, 51.79, 40.58, 37.18, 21.82 ppm.

2-[(5,6-Dihydro-1-oxo-3-phenyloxazolo[4,3-a]isoquinolin-10b-yl)methyl]benzoic acid isopropylester (**5c**, $C_{28}H_{27}NO_4$)

4c 6.9 mmol, CH_3CO_2H 15 cm^3, CF_3CO_2H 27 cm^3, $NaBH_3CN$ 15.7 mmol, 1 h; yield: 32%, mp 131–133°C; IR (KBr): $\bar{\nu}=1776$, 1705 (C=O) cm^{-1}; MS (EI): m/z (%) = 397 (5), 310 (100), 91 (15); TLC (petroleum ether:*Et*O*Ac* = 3:1): $R_f=0.78$; ^{1}H NMR: $\delta=7.87$ (dd, $J=7.8/1.5$ Hz, 10-H), 7.81 (dd, $J=7.7/1.6$ Hz, 1 arom H), 7.53 (dd, $J=7.7/1.2$ Hz, 1 arom H), 7.45 (dt, $J=7.7/1.6$ Hz, 1 arom H), 7.39–7.23 and 7.16–7.11 (2m, 7 + 2 arom H), 5.65 (s, 3-H), 5.08 (sept, $J=6.2$ Hz, 1 H), 4.20 and 3.79 (AB, $J=14.1$ Hz, benzyl-CH_2), 3.34 (ddd, $J=14.6/13.1/4.6$ Hz, 5-H_a), 3.13 (ddd, $J=16.9/13.1/6.1$ Hz, 6-H_a), 2.78 (ddd, $J=14.6/6.1/1.2$ Hz, 5-H_b), 2.53 (dt, $J=16.9/4.6$ Hz, 6-H_b), 1.29 and 1.04 (2d, $J=6.2$ Hz, 2 CH_3) ppm; ^{13}C NMR: $\delta=174.07$, 167.76, 137.05, 135.60, 133.61, 133.56, 133.48, 133.14, 131.02, 129.96, 129.72, 129.46, 128.35 (2C), 128.22 (2C), 127.76, 127.67, 127.01, 126.63, 90.80, 67.98, 66.88, 40.40, 37.11, 21.84, 21.80, 21.67 ppm.

2-[(5,6-Dihydro-1-oxo-3-phenyloxazolo[4,3-a]isoquinolin-10b-yl)methyl]benzoic acid t-butylester (**5d**, $C_{29}H_{29}NO_4$)

4d 6.7 mmol, CH_3CO_2H 15 cm^3, CF_3CO_2H 20 cm^3, $NaBH_3CN$ 15.7 mmol, 10 min; yield: 29%, mp 135°C; IR (KBr): $\bar{\nu}=1781$, 1699 (C=O) cm^{-1}; MS (EI): m/z (%) = 411 (8), 354 (12), 310 (100), 264 (76), 91 (60); TLC (petroleum ether:*Et*O*Ac* = 3:1): $R_f=0.88$; ^{1}H NMR: $\delta=7.86$ (d,

$J = 7.7$ Hz, 10-H), 7.84 and 7.53 (2d, $J = 8.1$ and 7.7 Hz, 2 arom H), 7.43 (t, $J = 7.7$ Hz, 1 arom H), 7.36–7.25 (m, 7 arom H), 7.13 (d, $J = 7.3$ Hz, 7-H), 7.00 (dd, $J = 8.1/0.9$ Hz, 2 arom H), 5.66 (s, 3-H), 4.26 and 3.75 (AB, $J = 14.1$ Hz, benzyl-CH_2), 3.40 (dt, $J = 14.8/4.7$ Hz, 5-H_a), 3.12 (dt, $J = 17.3/4.9$ Hz, 6-H_a), 2.82 (dd, $J = 14.8/4.9$ Hz, 5-H_b), 2.54 (dd, $J = 17.3/4.7$ Hz, 6-H_b), 1.46 (s, 3 CH_3) ppm.

2-[[5,6-Dihydro-3-(4-methylphenyl)-1-oxooxazolo[4,3-a]isoquinolin-10b-yl]methyl]benzoic acid methylester (**5e**, $C_{27}H_{25}NO_4$)

4e 7.1 mmol, CH_3CO_2H 15 cm^3, CF_3CO_2H 20 cm^3, $NaBH_3CN$ 15.7 mmol, 1 h; yield: 43%, mp 111–113°C; IR (KBr): $\bar{\nu} = 1776, 1717$ (C=O) cm^{-1}; MS (EI): m/z (%) = 383 (14), 324 (100), 105 (19), 84 (39); TLC (petroleum ether:*Et*O*Ac* = 4:1): $R_f = 0.73$; ^{1}H NMR: $\delta = 7.78$ (dd, $J = 7.8/1.9$ Hz, 10-H), 7.75 and 7.45 (2dd, each $J = 7.7/1.5$ Hz, 1 arom H), 7.39 and 7.29 (2dt, each $J = 7.7/1.5$ Hz, 2 arom H), 7.27–7.17 (m, 8-H, 9-H), 7.09–6.00 (m, 3 arom H), 6.86–6.81 (m, 2 arom H), 5.57 (s, 3-H), 4.03 and 3.79 (AB, $J = 14$ Hz, benzyl-CH_2), 3.68 (s, CH_3), 3.20 (ddd, $J = 14.4/13.1/4.5$ Hz, 5-H_a), 3.05 (ddd, $J = 16.8/13.1/5.7$ Hz, 6-H_a), 2.72 (ddd, $J = 14.4/5.7/1.3$ Hz, 5-H_b), 2.45 (dd, $J = 16.8/4.5$ Hz, 6-H_b), 2.28 (s, CH_3) ppm; ^{13}C NMR: $\delta = 173.06$, 167.76, 139.03, 135.98, 132.59, 132.50, 131.99, 131.88, 131.57, 130.11, 128.70, 128.44, 128.00 (2C), 127.23 (2C), 126.74, 126.70, 125.97, 125.66, 89.76, 65.84, 50.81, 39.51, 36.12, 20.76, 20.28 ppm.

2-[[5,6-Dihydro-3-(4-methylphenyl)-1-oxooxazolo[4,3-a]isoquinolin-10b-yl]methyl]benzoic acid ethylester (**5f**, $C_{28}H_{27}NO_4$)

4f 6.9 mmol, CH_3CO_2H 15 cm^3, CF_3CO_2H 27 cm^3, $NaBH_3CN$ 15.7 mmol, 1 h; yield: 47%, mp 139°C; IR (KBr): $\bar{\nu} = 1776, 1709$ (C=O) cm^{-1}; MS (EI): m/z (%) = 397 (9), 324 (100), 105 (18); TLC (petroleum ether:*Et*O*Ac* = 4:1): $R_f = 0.79$; ^{1}H NMR: $\delta = 7.87$–7.77 (m, 2 arom H), 7.51, (d, $J = 8.0$ Hz, arom H), 7.43 and 7.34 (2t, each $J = 8.0$ Hz, 2 arom H), 7.31–7.19 (m, 3 arom H), 7.11 (d, $J = 7.9$ Hz, 7-H), 7.09–7.01 and 6.91–6.83 (2m, each 2 arom H), 5.61 (s, 3-H), 4.29–4.06 (m, 3 H), 3.80 (d, $J = 14.0$ Hz, 1 H), 3.28 (dt, $J = 14.1/4.2$ Hz, 5-H_a), 3.09 (ddd, $J = 17.3/12.6/5.6$ Hz, 6-H_a), 2.76 (dd, $J = 14.1/5.6$ Hz, 5-H_b), 2.50 (dd, $J = 17.3/4.2$ Hz, 6-H_b), 2.32 (s, CH_3), 1.20 (t, $J = 7.2$ Hz, CH_3) ppm; ^{13}C NMR: $\delta = 174.02$, 168.29, 139.91, 136.93, 133.60, 133.49, 133.22, 133.02, 132.58, 130.97, 129.62, 129.41, 128.85, 128.37, 128.26, 127.68, 127.64, 126.91, 126.60, 90.72, 66.83, 60.60, 40.42, 37.06, 21.73, 21.22, 14.00 ppm.

2-[[5,6-Dihydro-3-(4-methoxyphenyl)-1-oxooxazolo[4,3-a]isoquinolin-10b-yl]methyl]benzoic acid methylester (**5g**, $C_{27}H_{25}NO_5$)

4g 6.8 mmol, CH_3CO_2H 15 cm^3, CF_3CO_2H 27 cm^3, $NaBH_3CN$ 15.7 mmol, 1 h; yield: 27%, mp 156°C; IR (KBr): $\bar{\nu} = 1783, 1707$ (C=O) cm^{-1}; MS (EI): m/z (%) = 399 (18), 340 (68), 121 (100); TLC (petroleum ether:*Et*O*Ac* = 4:1): $R_f = 0.68$; ^{1}H NMR: $\delta = 7.86$–7.79 (m, 2 arom H), 7.52 (dd, $J = 7.5/1.5$ Hz, 1 arom H), 7.45 and 7.35 (2dt, each $J = 7.5/1.5$ Hz, 2 arom H), 7.32–7.22 and 7.14–7.10 (2m, 2 + 1 arom H), 6.93 and 6.78 (2d, each $J = 8.8$ Hz, each 2 arom H), 5.62 (s, 3-H), 4.10 and 3.83 (AB, $J = 14.0$ Hz, benzyl-CH_2), 3.79 and 3.75 (2s, 2 CH_3), 3.26 (ddd, $J = 14.3/13.2/4.5$ Hz, 5-H_a), 3.15-3.03 (m, 6-H_a), 2.76 (ddd, $J = 14.3/5.8/1.1$ Hz, 5-H_b), 2.51 (dd, $J = 16.9/4.5$ Hz, 6-H_b) ppm.

2-[(9-Benzyloxy-5,6-dihydro-8-methoxy-1-oxo-3-phenyloxazolo[4,3-a]isoquinolin-10b-yl)methyl]benzoic acid ethylester (**5i**, $C_{35}H_{33}NO_6$)

4j 1.8 mmol, CH_3CO_2H 5 cm^3, CF_3CO_2H 9 cm^3, $NaBH_3CN$ 5.2 mmol, 15 min; yield: 30%, mp 168°C; IR (KBr): $\bar{\nu} = 1785, 1722$ (C=O) cm^{-1}; MS (EI): m/z (%) = 519 (9), 446 (10), 400 (14), 355 (21), 91

(100); TLC (*n*-hexane:*Et*O*Ac* = 1:1): $R_f = 0.85$; ^{1}H NMR: $\delta = 7.79$ and 7.56–7.52 (2m, 1 + 2 arom H), 7.46–7.24 and 7.07–7.02 (2m, 10 + 2 arom H), 6.59 and 5.63 (2s, 7-H and 3-H), 5.22 and 5.16 (2d, each $J = 12.0$ Hz, OBn), 4.24–4.04 (m, OCH_2), 4.04 and 3.64 (AB, $J = 14.0$ Hz, benzyl-CH_2), 3.89 (s, OCH_3), 3.23 (ddd, $J = 14.3/13.0/4.6$ Hz, 5-H_a), 3.04 (ddd, $J = 16.8/13.0/5.8$ Hz, 6-H_a), 2.74 (dd, $J = 14.3/5.8$ Hz, 5-H_b), 2.40 (dd, $J = 16.8/4.6$ Hz, 6-H_b), 1.19 (t, $J = 7.2$ Hz, CH_3) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 174.09$, 168.28, 149.44, 147.02, 136.95, 136.93, 135.69, 133.54, 133.29, 131.00, 129.97, 129.61, 128.54 (2C), 128.34 (2C), 128.22 (2C), 127.95, 127.85, 126.63, 126.45, 124.36, 112.81, 111.96, 90.74, 71.13, 66.39, 60.58, 56.02, 40.40, 37.22, 21.38, 14.06 ppm.

2-[(5,6-Dihydro-8,9-methylenedioxy-1-oxo-3-phenyloxazolo[4,3-a]isoquinolin-10b-ylethyl]benzoic acid ethylester (**5j**, $C_{28}H_{25}NO_6$)

4k 1.8 mmol, CH_3CO_2H 5 cm^3, CF_3CO_2H 9 cm^3, $NaBH_3CN$ 5.2 mmol, 1 h; yield: 37%, mp 134°C; IR (KBr): $\bar{\nu} = 1783$, 1716 (C=O) cm^{-1}; MS (EI): m/z (%) = 427 (12), 354 (100), 308 (6), 91 (10); TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.81$; ^{1}H NMR: $\delta = 7.81$ (dd, $J = 7.7/1.5$ Hz, arom H), 7.51 (dd, $J = 7.7/1.4$ Hz, arom H), 7.45 (dt, $J = 7.7/1.5$ Hz, arom H), 7.38–7.32 (m, 2 arom H), 7.32 (s, 10-H), 7.29–7.24 and 7.01–6.97 (2m, 2 + 2 arom H), 6.57 (s, 7-H), 5.97 and 5.94 (2d, each $J = 1.5$ Hz, OCH_2O), 5.62 (s, 3-H), 4.28–4.05 (m, OCH_2), 4.11 and 3.73 (AB, $J = 14.0$ Hz, benzyl-CH_2), 3.23 (ddd, $J = 14.5/13.1/4.7$ Hz, 5-H_a), 3.03 (ddd, $J = 16.8/13.1/5.8$ Hz, 6-H_a), 2.73 (ddd, $J = 14.5/5.8/1.1$ Hz, 5-H_b), 2.41 (dd, $J = 16.8/4.7$ Hz, 6-H_b), 1.19 (t, $J = 7.1$ Hz, CH_3) ppm; ^{13}C NMR: $\delta = 174.00$, 168.31, 147.42, 146.47, 136.89, 135.66, 133.41, 133.31, 131.02, 129.95, 129.68, 128.29 (2C), 128.21 (2C), 127.31, 126.66, 125.95, 108.66, 107.47, 101.08, 90.75, 66.88, 60.62, 40.46, 37.24, 22.09, 14.06 ppm.

6-[(5,6-Dihydro-1-oxo-3-phenyloxazolo[4,3-a]isoquinolin-10b-yl)methyl]-2-methoxy-benzoic acid ethylester (**5k**, $C_{28}H_{27}NO_5$)

4l 2.2 mmol, CH_3CO_2H 5 cm^3, CF_3CO_2H 9 cm^3, $NaBH_3CN$ 5.2 mmol, 1 h; yield: 29%, mp 152°C; IR (KBr): $\bar{\nu} = 1783$, 1716 (C=O) cm^{-1}; MS (EI): m/z (%) = 413 (4), 340 (100), 264 (19), 91 (16); TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.61$; ^{1}H NMR: $\delta = 7.82$ (dd, $J = 7.6/1.5$ Hz, 10-H), 7.39–7.33 and 7.32–7.22 (2m, 1 + 5 arom H), 7.19–7.14 (m, 2 arom H), 7.11 (dd, $J = 7.5/1.5$ Hz, arom H), 6.97 and 6.86 (2dd, each $J = 8.0/0.7$ Hz, 2 arom H), 5.70 (s, 3-H), 4.32–4.17 (m, OCH_2), 3.83 (s, OCH_3), 3.67 and 3.42 (AB, $J = 14.7$ Hz, benzyl-CH_2), 3.18–3.01 (m, 5-H_a and 6-H_a), 2.83–2.72 (m, 6-H_b), 2.51–2.39 (m, 5-H_b), 1.20 (t, $J = 7.2$ Hz, CH_3) ppm; ^{13}C NMR: $\delta = 174.54$, 168.19, 156.94, 135.62, 135.57, 133.67, 132.97, 130.13, 130.02, 129.60, 128.47 (2C), 128.30 (2C), 127.85, 127.45, 127.04, 125.88, 123.44, 110.02, 90.93, 66.03, 61.01, 56.21, 41.60, 37.48, 21.69, 14.03 ppm.

6-[(5,6-Dihydro-1-oxo-3-phenyloxazolo[4,3-a]isoquinolin-10b-yl)methyl]-2,3-methylenedioxy-benzoic acid ethylester (**5l**, $C_{28}H_{25}NO_6$)

4k 2.1 mmol, CH_3CO_2H 5 cm^3, CF_3CO_2H 9 cm^3, $NaBH_3CN$ 5.2 mmol, 1 h; yield: 45%, mp 147°C; IR (KBr): $\bar{\nu} = 1777$, 1710 (C=O) cm^{-1}; MS (EI): m/z (%) = 427 (9), 354 (100), 91 (12); TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.61$; ^{1}H NMR: $\delta = 7.81$ (d, $J = 7.7/1.5$ Hz, 10-H), 7.40–7.35 and 7.34–7.29 (2m, 1 + 2 arom H), 7.28–7.23 (m, 8-H and 9-H), 7.17–7.10 (m, 3 arom H), 6.94 and 6.85 (2d, each $J = 7.9$ Hz, 2 arom H), 6.05 and 6.02 (2d, each $J = 1.5$ Hz, OCH_2O), 5.68 (s, 3-H), 4.21 (dq, $J = 10.9/7.2$ Hz, OCH_2), 3.82 and 3.71 (2d, each $J = 14.1$ Hz, benzyl-CH_2), 3.20 (dt, $J = 13.1/4.9$ Hz, 5-H_a), 3.11 (dt, $J = 12.8/4.9$ Hz, 6-H_a), 2.85–2.78 (m, 5-H_b), 2.55–2.47 (m, 6-H_b), 1.19 (t, $J = 7.1$ Hz, CH_3) ppm; ^{13}C NMR: $\delta = 174.00$, 165,73, 147.23, 146.98, 135.75, 133.62, 132.91, 129.98, 129.42, 129.06, 128.26 (4C), 127.77, 127.66, 127.02, 126.33, 116.74, 109.96, 101.47, 90.82, 66.77, 60.89, 40.31, 37.39, 21.85, 14.02 ppm.

6-[(5,6-Dihydro-8,9-dimethoxy-1-oxo-3-phenyloxazolo[4,3-a]isoquinolin-10b-yl)methyl]-2,3-dimethoxybenzoic acid ethylester (**5m**, $C_{31}H_{33}NO_8$)

4q 1.8 mmol, CH_3CO_2H 5 cm^3, CF_3CO_2H 9 cm^3, $NaBH_3CN$ 5.2 mmol, 25 min; yield: 40%, mp 143°C; IR (KBr): $\bar{\nu} = 1782$, 1710 (C=O) cm^{-1}; MS (EI): m/z (%) = 430 (100), 322 (22), 105 (77); TLC (n-hexane:EtOAc = 3:1): $R_f = 0.52$; ^{1}H NMR: $\delta = 7.40$–7.34 and 7.32–7.26 (2m, 1 + 2 arom H), 7.29 (s, 10-H), 7.22–7.16 (m, 3 arom H), 6.92 (d, $J = 7.7$ Hz, arom H), 6.58 and 5.70 (2s, 7-H and 3-H), 4.21 (dq, $J = 10.7/7.2$ Hz, OCH_2), 3.94 and 3.91 (2s, 2 OCH_3), 3.89 (s, 2 OCH_3), 3.52 and 3.48 (AB, $J = 14.6$ Hz, benzyl-CH_2), 3.19–2.98 (m, 5-H_a and 6-H_a), 2.84–2.75 and 2.44–2.35 (2m, 5-H_b and 6-H_b), 1.19 (t, $J = 7.2$ Hz, CH_3) ppm; ^{13}C NMR: $\delta = 174.51$, 167.73, 151.73, 148.90, 148.13, 146.57, 135.67, 130.99, 130.06, 128.54, 128.26, 127.69, 126.98 (2C), 125.99 (2C), 124.54, 113.50, 111.61, 109.87, 90.90, 66.32, 61.42, 60.99, 56.14, 55.93 (2C), 40.53, 37.60, 21.42, 14.0 ppm.

6-[[5,6-Dihydro-8,9-dimethoxy-3-(4-methylphenyl)-1-oxooxazolo[4,3-a]isoquinolin-10b-yl]methyl]-2,3-dimethoxybenzoic acid ethylester (**5n**, $C_{32}H_{35}NO_8$)

4r 1.8 mmol, CH_3CO_2H 5 cm^3, CF_3CO_2H 9 cm^3, $NaBH_3CN$ 5.2 mmol, 25 min; yield: 37%, mp 141°C; IR (KBr): $\bar{\nu} = 1783$, 1709 (C=O) cm^{-1}; MS (EI): m/z (%) = 517 (5), 444 (100), 338 (9), 105 (12); TLC (n-hexane:EtOAc = 3:1): $R_f = 0.55$; ^{1}H NMR: $\delta = 7.28$–7.25 (m, 2 arom H), 7.17 (d, $J = 8.7$ Hz, arom H), 7.10–7.08 (m, 3 arom H), 6.91 (d, $J = 8.7$ Hz, arom H), 6.57 and 5.67 (2s, 7-H and 3-H), 4.22 (dq, $J = 10.8/7.1$ Hz, OCH_2), 3.94 and 3.92 (2s, 2 OCH_3), 3.87 (s, 2 OCH_3), 3.53–3.44 (m, benzyl-CH_2), 3.17–2.95 (m, 5-H_a and 6-H_a), 2.83–2.75 and 2.46–2.31 (2m, 5-H_b and 6-H_b), 2.34 (s, CH_3), 1.19 (t, $J = 7.2$ Hz, CH_3) ppm; ^{13}C NMR: $\delta = 174.56$, 167.72, 151.66, 148.77, 148.00, 146.45, 140.10, 135.56, 130.92, 128.94 (2C), 128.49 (2C), 127.72, 126.93, 125.97, 124.47, 113.39, 111.48, 109.77, 90.82, 66.32, 61.46, 61.42, 56.09, 55.90, 40.45, 37.51, 21.37, 21.31, 14.01 ppm.

6-[(5,6-Dihydro-8,9-dimethoxy-1-oxo-3-phenyloxazolo[4,3-a]isoquinolin-10b-yl)methyl]-2,3-methylenedioxybenzoic acid ethylester (**5o**, $C_{30}H_{29}NO_8$)

4s 1.9 mmol, CH_3CO_2H 5 cm^3, CF_3CO_2H 9 cm^3, $NaBH_3CN$ 5.2 mmol, 25 min; yield: 35%, mp 144°C; IR (KBr): $\bar{\nu} = 1779$, 1709 (C=O) cm^{-1}; MS (EI): m/z (%) = 487 (6), 414 (100), 91 (12); TLC (n-hexane:EtOAc = 1:1): $R_f = 0.78$; ^{1}H NMR: $\delta = 7.41$–7.36 and 7.35–7.30 (2m, 1 + 2 arom H), 7.24 (s, 10-H), 7.21–7.16 (m, 2 arom H), 6.93 and 6.84 (2d, each $J = 8.2$ Hz, 2 arom H), 6.56 (s, 7-H), 6.05 and 6.02 (2d, each $J = 1.3$ Hz, OCH_2O), 5.64 (s, 3-H), 4.19 (dq, $J = 10.7/7.2$ Hz, OCH_2), 3.93 and 3.88 (2s, 2 OCH_3), 3.78 and 3.71 (AB, $J = 14.1$ Hz, benzyl-CH_2), 3.14 (dt, $J = 13.2/5.0$ Hz, 5-H_a), 3.04 (dt, $J = 16.4/5.0$ Hz, 6-H_a), 2.84–2.75 and 2.44–2.35 (2m, 5-H_b and 6-H_b), 1.20 (t, $J = 7.2$ Hz, CH_3) ppm; ^{13}C NMR: $\delta = 174.30$, 165.80, 148.86, 148.06, 147.26, 146.98, 135.78, 130.03, 129.12, 128.32 (4C), 126.27, 126.00, 124.33, 116.74, 111.46, 110.08, 109.93, 101.48, 90.82, 66.35, 60.87, 56.07, 55.90, 40.12, 37.39, 21.40, 14.04 ppm.

6-[(5,6-Dihydro-8,9-methylenedioxy-1-oxo-3-phenyloxazolo[4,3-a]isoquinolin-10b-yl)methyl]-2,3-dimethoxybenzoic acid ethylester (**5p**, $C_{30}H_{29}NO_8$)

4t 1.9 mmol, CH_3CO_2H 5 cm^3, CF_3CO_2H 9 cm^3, $NaBH_3CN$ 5.2 mmol, 25 min; yield: 41%, mp 146°C; IR (KBr): $\bar{\nu} = 1778$, 1708 (C=O) cm^{-1}; MS (EI): m/z (%) = 487 (4), 414 (100), 322 (27), 105 (33), 91 (12); TLC (n-hexane:EtOAc = 1:1): $R_f = 0.81$; ^{1}H NMR: $\delta = 7.37$–7.32 and 7.31–7.24 (2m, 1 + 2 arom H), 7.29 (s, 10-H), 7.18–7.12 (m, 3 arom H), 6.91 (d, $J = 8.8$ Hz, arom H), 6.56 (s, 7-H), 5.97 and 5.94 (2d, each $J = 1.6$ Hz, OCH_2O), 5.66 (s, 3-H), 4.20 (dq, $J = 10.7/7.2$ Hz, OCH_2), 3.90 and 3.88 (2s, 2 OCH_3), 3.48 and 3.44 (AB, $J = 14.1$ Hz, benzyl-CH_2), 3.14–2.95 (m, 5-H_a and 6-H_a), 2.80–2.73 and 2.41–2.33 (2m, 6-H_b and 5-H_b), 1.17 (t, $J = 7.2$ Hz, CH_3) ppm; ^{13}C NMR: $\delta = 174.31$, 167.74, 151.76, 147.45, 146.79, 146.57, 135.62, 130.95, 130.05, 128.51 (2C), 128.24 (2C), 127.80, 127.32, 126.91, 125.81, 113.53, 108.73, 107.32, 101.48, 90.86, 66.68, 61.42, 60.99, 55.94, 40.60, 37.57, 22.09, 14.01 ppm.

6-[(5,6-Dihydro-8,9-methylenedioxy-1-oxo-3-phenyloxazolo[4,3-a]isoquinolin-10b-yl)methyl]-2,3-methylenedioxybenzoic acid ethylester (**5q**, $C_{29}H_{25}NO_8$)

4u 2.0 mmol, CH_3CO_2H 5 cm^3, CF_3CO_2H 9 cm^3, $NaBH_3CN$ 5.2 mmol, 45 min; yield: 49%, mp 171°C; IR (KBr): $\bar{\nu} = 1780$, 1702 (C=O) cm^{-1}; MS (EI): m/z (%) = 471 (10), 398 (100), 91 (12); TLC (*n*-hexane:*Et*O*Ac* = 1:1): $R_f = 0.55$; ^{1}H NMR: $\delta = 7.41$–7.35 and 7.35–7.28 (2m, 1 + 2 arom H), 7.29 (s, 10-H), 7.18–7.12 (m, 2 arom H), 6.92 and 6.85 (2d, each $J = 7.9$ Hz, 2 arom H), 6.56 (s, 7-H), 6.05, 6.02, 5.97, and 5.94 (4d, each $J = 1.4$ Hz, 2 OCH_2O), 5.64 (s, 3-H), 4.21 (dq, $J = 10.9/7.2$ Hz, OCH_2), 3.78 and 3.64 (AB, $J = 14.4$ Hz, benzyl-CH_2), 3.12 (dt, $J = 13.1/4.8$ Hz, 5-H_a), 3.02 (dt, $J = 16.4/4.8$ Hz, 6-H_a), 2.82–2.73 and 2.44–2.35 (2m, 5-H_b and 6-H_b), 1.20 (t, $J = 7.2$ Hz, CH_3) ppm; ^{13}C NMR: $\delta = 174.13$, 166.02, 147.46, 147.29, 147.04, 146.80, 135.75, 130.10, 129.04, 128.36 (4C), 127.39, 126.41, 125.73, 116.76, 110.04, 108.71, 107.47, 101.56, 101.17, 90.68, 66.69, 60.95, 40.00, 37.30, 22.09, 13.98 ppm.

Aldehydes **6** *2-[(2-Benzoyl-1-formyl-1,2-dihydroisoquinolin-1-yl)methyl]benzoic acid methylester* (**6a**, $C_{26}H_{21}NO_4$)

Yield: 16%, colourless solid, mp 113–115°C (*n*-hexane); IR (KBr): $\bar{\nu} = 1725$, 1658 (C=O) cm^{-1}; MS (CI): m/z (%) = 440 (6), 412 (100), 382 (28), 105 (54); TLC (petroleum ether:*Et*O*Ac* = 3:1): $R_f = 0.55$; ^{1}H NMR: $\delta = 9.59$ (s, CHO), 7.65–7.61 (m, 2 arom H), 7.56 (dd, $J = 7.7/1.5$ Hz, arom H), 7.53–7.49 and 7.48–7.41 (2m, 1 + 2 arom H), 7.29–7.24 and 7.19–7.16 (2m, 2 + 1 arom H), 7.14 (dd, $J = 7.7/1.3$ Hz, arom H), 7.08 (dt, $J = 7.7/1.5$ Hz, arom H), 6.93–6.88 (m, arom H), 6.66 (dd, $J = 7.7/1.3$ Hz, arom H), 6.22 and 5.19 (2d, each $J = 7.9$ Hz, 3-H and 4-H), 4.26 and 3.83 (AB, $J = 14.0$ Hz, benzyl-CH_2), 3.67 (s, OCH_3) ppm; ^{13}C NMR: $\delta = 191.22$, 170.19, 168.25, 136.56, 133.65, 132.77, 132.27, 131.45, 131.33, 130.50, 129.88, 128.95 (2C), 128.53 (2C), 127.72, 127.41, 127.25 (2C), 126.46 (2C), 125.58, 107.94, 72.42, 51.96, 37.95 ppm.

2-[[1-Formyl-1,2-dihydro-2-(4-methylbenzoyl)isoquinolin-1-yl]methyl]benzoic acid methylester (**6c**, $C_{27}H_{23}NO_4$)

Yield: 9%, colourless resin; IR (film): $\bar{\nu} = 1723$, 1657 (C=O) cm^{-1}; MS (CI): m/z (%) = 426 (24), 155 (49), 137 (100), 119 (38); TLC (petroleum ether:*Et*O*Ac* = 4:1): $R_f = 0.53$; ^{1}H NMR: $\delta = 9.50$ (s, CHO), 7.49–7.43 and 7.23–7.16 (2m, 3 + 4 arom H), 7.12–7.08 (m, arom H), 7.06 (dd, $J = 7.7/1.2$ Hz, arom H), 7.00 (dt, $J = 7.5/1.5$ Hz, arom H), 6.84–6.80 (m, arom H), 6.58 (dd, $J = 7.7/1.2$ Hz, arom H), 6.16 and 5.10 (2d, each $J = 7.9$ Hz, 2 arom H), 4.15 and 3.74 (AB, $J = 14.0$ Hz, benzyl-CH_2), 3.59 and 2.34 (2s, 2 CH_3) ppm.

2-[[1-Formyl-1,2-dihydro-2-(4-methoxybenzoyl)isoquinolin-1-yl]methyl]benzoic acid methylester (**6d**, $C_{27}H_{23}NO_5$)

Yield: 7%, colourless resin; IR (film): $\bar{\nu} = 1720$, 1655 (C=O) cm^{-1}; MS (CI): m/z (%) = 442 (49), 153 (100); TLC (petroleum ether:*Et*O*Ac* = 4:1): $R_f = 0.69$; ^{1}H NMR: $\delta = 9.55$ (s, CHO), 7.63–7.59 (m, 2 arom H), 7.53 (dd, $J = 7.8/1.5$ Hz, arom H), 7.29–7.25 and 7.19–7.12 (2m, 3 + 1 arom H), 7.06 (dt, $J = 7.8/1.5$ Hz, arom H), 6.97–6.93 and 6.91–6.88 (2m, 2 + 1 arom H), 6.62 (dd, $J = 7.8/1.1$ Hz, arom H), 6.27 and 5.18 (2d, each $J = 7.9$ Hz, 2 arom H), 4.23 and 3.79 (AB, $J = 14.3$ Hz, benzyl-CH_2), 3.86 (s, OCH_3), 3.66 (s, CH_3) ppm.

2-[(2-Benzoyl-7-benzyloxy-1-formyl-1,2-dihydro-6-methoxyisoquinolin-1-yl)methyl]benzoic acid ethylester (**6f**, $C_{35}H_{31}NO_6$)

Yield: 8%, colourless crystals, mp 176°C (*n*-hexane); IR (KBr): $\bar{\nu} = 1719$, 1659 (C=O) cm^{-1}; TLC (*n*-hexane:*Et*O*Ac* = 1:1): $R_f = 0.65$; ^{1}H NMR (CDCl$_3$): $\delta = 9.50$ (s, CHO), 7.65–7.28 (m, 11 arom H), 7.13 and 7.01 (2dt, $J = 7.6/1.2$ and $7.6/1.4$ Hz, 2 arom H), 6.75 (s, arom H), 6.44–6.40 (m, 2 arom H), 6.12 (d, $J = 7.9$ Hz, arom H), 5.11 and 5.07 (2d, each $J = 7.8$ Hz, OBn), 4.20 and 3.69 (AB, $J = 14.0$ Hz, benzyl-CH$_2$), 4.17–4.10 (m, OCH$_2$), 3.86 (s, OCH$_3$), 1.32 (t, $J = 7.0$ Hz, CH$_3$) ppm.

2-[(2-Benzoyl-1-formyl-1,2-dihydro-6,7-methylenedioxyisoquinolin-1-yl)methyl]benzoic acid ethylester (**6g**, $C_{28}H_{23}NO_6$)

Yield: 13%, colourless resin; IR (film): $\bar{\nu} = 1736$, 1691 (C=O) cm^{-1}; TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.62$; MS (CI): $m/z = 498$ (4), 470 (100), 105 (54); ^{1}H NMR: $\delta = 9.53$ (s, CHO), 7.63–7.58 (m, 2 arom H), 7.55 (dd, $J = 7.6/1.6$ Hz, arom H), 7.52–7.47 and 7.46–7.42 (2m, 1 + 2 arom H), 7.16 and 7.12 (2 dt, $J = 7.6/1.5$ and $7.6/1.6$ Hz, 2 arom H), 6.76 (dd, $J = 7./1.5$ Hz, arom H), 6.69 and 6.37 (2s, 2 arom H), 6.10 (d, $J = 7.8$ Hz, 1H), 6.02 and 5.96 (2d, each $J = 1.5$ Hz, OCH$_2$O), 5.04 (d, $J = 7{,}8$ Hz, 1H), 4.20–4.17 (m, OCH$_2$), 4.15 and 3.81 (AB, $J = 14.0$ Hz, benzyl-CH$_2$), 1.29 (t, $J = 7.2$ Hz, CH$_3$) ppm.

2-[(2-Benzoyl-1-formyl-1,2-dihydroisoquinolin-1-yl)methyl]-6-methoxybenzoic acid ethylester (**6h**, $C_{28}H_{25}NO_5$)

Yield: 16%, colourless oil; IR (film): $\bar{\nu} = 1726$, 1656 (C=O) cm^{-1}; TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.42$; MS (CI): $m/z = 456$ (26), 382 (81), 322 (100), 212 (91); ^{1}H NMR: $\delta = 9.54$ (s, CHO), 7.71–7.67 and 7.51–7.38 (2m, 2 + 3 arom H), 7.34–7.28, 7.23–7.20, and 6.94–6.91 (3m, 2 + 1 + 1 arom H), 6.81 (t, $J = 7.9$ Hz, arom H), 6.65 and 6.45 (2d, each $J = 7.9$ Hz, 2 arom H), 5.67 and 5.19 (2d, each $J = 7.8$ Hz, 2 arom H), 4.41 (dq, $J = 7.1/10.7$ Hz, OCH$_2$), 3.75 and 3.31 (AB, $J = 14.5$ Hz, benzyl-CH$_2$), 3.72 (s, OCH$_3$), 1.39 (t, $J = 7.1$ Hz, CH$_3$) ppm; ^{13}C NMR: $\delta = 191.67$, 170.78, 168.07, 155.71, 134.27, 133.95, 132.45, 131.21, 129.62 (2C), 129.03, 128.74, 128.62, 128.25 (2C), 127.61, 126.72, 126.51, 125.56, 125.49, 123.04, 108.94, 107.47, 72.13, 61.48, 55.76, 38.57, 14.17 ppm.

2-[[1-Formyl-1,2-dihydro-6,7-dimethoxy-2-(4-methylbenzoyl)isoquinolin-1-yl]methyl]-6-methoxybenzoic acid ethylester (**6i**, $C_{31}H_{31}NO_7$)

Yield: 22%, yellowish oil; IR (film): $\bar{\nu} = 1726$, 1622 (C=O) cm^{-1}; TLC (*n*-hexane:*Et*O*Ac* = 1:1): $R_f = 0.63$; MS (CI): $m/z = 530$ (100), 500 (12), 336 (55); ^{1}H NMR: $\delta = 9.49$ (s, CHO), 7.58 and 7.23 (2d, each $J = 8.2$ Hz, 2 + 2 arom H), 6.84 (t, $J = 8.2$ Hz, arom H), 6.72 (s, arom H), 6.66 (d, $J = 8.2$ Hz, arom H), 6.45 (s, arom H), 6.38 (d, $J = 7.9$ Hz, 1H), 5.78 (d, $J = 8.2$ Hz, arom H), 5.12 (d, $J = 7.9$ Hz, 1H), 4.39 (q, $J = 7.2$ Hz, OCH$_2$), 3.92 and 3.88 (2s, 2 OCH$_3$), 3.71 and 3.32 (AB, $J = 14.5$ Hz, benzyl-CH$_2$), 3.70 (s, OCH$_3$), 2.38 (s, CH$_3$), 1.38 (t, $J = 7.2$, CH$_3$) ppm.

6-[[1-Formyl-1,2-dihydro-6,7-dimethoxy-2-(4-methylbenzoyl)isoquinolin-1-yl]methyl]-2,3-dimethoxybenzoic acid ethylester (**6k**, $C_{31}H_{31}NO_7$)

Yield: 10%, yellowish resin; IR (film): $\bar{\nu} = 1731$, 1658 (C=O) cm^{-1}; TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.31$; MS (CI): $m/z = 560$ (16), 336 (16), 215 (100), 119 (39); ^{1}H NMR: $\delta = 9.50$ (s, CHO), 7.56 and 7.24 (2d, each $J = 8.2$ Hz, 2 + 2 arom H), 6.70 (s, arom H), 6.66 (d, $J = 8.6$ Hz, 5-H), 6.47 (s, 8-H), 6.37 (d, $J = 7.9$ Hz, 3-H), 5.99 and 5.17 (2d, $J = 8.6$ and 7.9 Hz, arom H and 4-H), 4.35 (q, $J = 7.2$ Hz, OCH$_2$), 3.91, 3.89, 3.76, and 3.72 (4s, 4 OCH$_3$), 3.62 and 3.30 (AB, $J = 14.8$ Hz, benzyl-CH$_2$), 2.40 (s, CH$_3$), 1.35 (t, $J = 7.2$ Hz, CH$_3$) ppm; ^{13}C NMR: $\delta = 192.38$, 170.59, 167.27, 151.20, 149.25, 148.44, 145.38, 141.70, 131.11, 129.53 (3C), 128.92 (2C), 127.15, 126.85, 125.87, 125.46, 118.56, 112.48, 109.79, 108.43, 107.07, 72.16, 61.33, 61.31, 56.23, 56.01, 55.87, 37.15, 21.56, 14.21 ppm.

2-[(2-Benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)methyl]benzoic acid ethylester (**7a**)

Yield: 3%, light yellow oil. Analytical and spectroscopic data were in line with those published in Ref. [1].

2-[(2-Benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)methyl]-6-methoxybenzoic acid ethylester (**7b**, $C_{27}H_{29}NO_3$)

Yield: 13%, colourless oil; TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.81$; IR (film): $\bar{\nu} = 1721$ (C=O) cm^{-1}; MS (CI): m/z (%) = 444 ($M^{+\bullet} + 29$, 10), 416 ($M^{+\bullet} + 1$, 100), 222 (51); ^{1}H NMR: $\delta = 7.25$–7.00 (m, 9 arom H), 6.87, 6.80, and 6.74 (3d, each $J = 8.3$ Hz, 3 arom H), 4.32 (q, $J = 7.1$ Hz, OCH$_2$), 3.96 (dd, $J = 9.0/5.0$ Hz, 1-H), 3.83 (s, OCH$_3$), 3.73 and 3.60 (AB, $J = 13.6$ Hz, N-benzyl-CH$_2$), 3.30 (dt, $J = 12.5/4.8$ Hz, 1H), 3.12 (dd, $J = 14.00/10.5$ Hz, 3-H$_a$), 3.00 (ddd, $J = 16.7/10.5/6.3$ Hz, 4-H$_a$), 2.90–2.78 (m, 3-H$_b$ + 1H), 2.52 (dd, $J = 16.7/4.1$ Hz, 4-H$_b$), 1.29 (t, $J = 7.1$ Hz, CH$_3$) ppm; ^{13}C NMR: $\delta = 168.62$ (C=O), 156.30, 139.62, and 138.62 (3s, 3C) 138.06 (s, C-4a), 134.12 (s, C-8a), 129.45 and 128.93 (2d, 2C), 128.64 (d, 2C), 128.31 (d, C-5), 127.91 (d, 2C), 126.57, 126.07, and 125.54 (3d, C-6, C-8, C-7), 124.62 (s, 1C), 123.59, 108.83, and 62.17 (3d, 2C, C-1), 60.99 and 57.74 (2t, OCH$_2$, N-CH$_2$), 55.96 (q, OCH$_3$), 41.79, 39.66, and 23.67 (3t, benzyl-CH$_2$, C-3, C-4), 14.20 (q, CH$_3$) ppm.

2-[[1,2,3,4-Tetrahydro-6,7-dimethoxy-2-(4-methylbenzyl)isoquinolin-1-yl]methyl]-6-methoxybenzoic acid ethylester (**7c**, $C_{30}H_{35}NO_5$)

Yield: 2%, colourless oil; TLC (*n*-hexane:*Et*O*Ac* = 1:1) $R_f = 0.79$; IR (film): $\bar{\nu} = 1716$ (C=O) cm^{-1}; MS (CI): m/z (%) = 490 ($M^{+\bullet} + 1$, 49), 296 (100); ^{1}H NMR: $\delta = 7.21$ (t, $J = 7.9$ Hz, arom H), 7.07 and 7.03 (2d, each $J = 7.8$ Hz, 4 arom H), 6.80 (d, $J = 7.9$ Hz, arom H), 6.69 (br d, $J = 7.9$ Hz, arom H), 6.58 and 6.21 (2s, 8-H, 5-H), 4.28 (q, $J = 7.2$ Hz, OCH$_2$), 3.93–3.86 (m, 1-H), 3.85 and 3.83 (2s, 2 OCH$_3$), 3.72 (d, $J = 13.5$ Hz, 1H, N-CH$_2$), 3.64 (s, OCH$_3$), 3.60 (d, $J = 13.5$ Hz, 1H, N-CH$_2$), 3.28–3.18 (m, 1H), 3.13 (dd, $J = 13.7/8.0$ Hz, 3-H$_a$), 2.97–2.87 (m, 4-H$_a$), 2.87–2.77 (m, 3-H$_b$ + 1H), 2.46–2.39 (m, 4-H$_b$), 2.32 (s, CH$_3$), 1.29 (t, $J = 7.2$ Hz, CH$_3$) ppm.

2-[(6,7-Dimethoxyisoquinolin-1-yl)methyl]benzoic acid ethylester (**8a**)

Yield: 13%, light yellow oil. Analytical and spectroscopic data were in line with those published in Ref. [1].

2-[(6,7-Methylenedioxyisoquinolin-1-yl)methyl]benzoic acid ethylester (**8b**, $C_{20}H_{17}NO_4$)

Yield: 5%, colourless oil; TLC (*n*-hexane:*Et*O*Ac* = 3:1) $R_f = 0.34$; ^{1}H NMR: $\delta = 8.30$ (d, $J = 5.7$ Hz, 3-H), 7.96 (dd, $J = 7.7/1.6$ Hz, arom H), 7.42 (s, 8-H), 7.38 (d, $J = 5.7$ Hz, 4-H), 7.32 (dt, $J = 7.7/1.8$ Hz, arom H), 7.26 (dt, $J = 7.7/1.6$ Hz, arom H), 7.06 (s, 5-H), 7.03–6.99 (m, arom H), 6.05 (s, OCH$_2$O), 4.96 (s, CH$_2$), 4.31 (q, $J = 7.1$ Hz, OCH$_2$), 1.30 (t, $J = 7.1$ Hz, CH$_3$) ppm.

6,7-Dimethoxyisoquinoline-1-carbonitrile (**9a**)

Yield: 15%, TLC (petroleum ether:*Et*O*Ac* = 3:1): $R_f = 0.48$ (blue fluorescent, $\lambda = 365$ nm); IR (KBr): $\bar{\nu} = 2227$ (CN) cm^{-1}; MS (EI): m/z (%) = 214 ($M^{+\bullet}$, 100), 199 (13), 184 (5); mp and ^{1}H NMR data were in line with those published in Ref. [33].

7-Benzyloxy-6-methoxyisoquinoline-1-carbonitrile (**9b**)

Yield: 52%; TLC (*n*-hexane:*Et*O*Ac* = 1:1): $R_f = 0.42$ (blue fluorescent, $\lambda = 365$ nm); mp and spectroscopic data were in line with those published in Ref. [34].

6,7-Methylenedioxyisoquinoline-1-carbonitrile (= [1,3]-Dioxolo[4,5-g]isoquinoline-1-carbonitrile, **9c**)

Yield: 25%, TLC (*n*-hexane:*Et*O*Ac* = 3:1): $R_f = 0.41$ (blue fluorescent, $\lambda = 365$ nm); IR (KBr): $\bar{\nu} = 2226$ (CN) cm^{-1}; mp, MS, and ^{1}H NMR data were in line with those published in Ref. [35].

The aldehydes **12** were prepared by the general procedure according to Ref. [1] starting from 0.6–0.7 mmol **11a–11e**/2.5 cm^3 of AcOH, 4.5 cm^3 of F_3CCO_2H, and 1.2–1.4 mmol of $NaCNBH_3$; reaction time: 45 min (**12a**, **12b**), 60 min (**12c–12e**).

2-Benzoyl-1-benzyl-1,2-dihydroisoquinoline-1-carbaldehyde (**12a**, $C_{24}H_{19}NO_2$)

Yield: 46%, mp 106°C (*n*-hexane); IR (KBr): $\bar{\nu} = 1726$, 1656 (C=O) cm^{-1}; MS (CI): m/z (%) = 354 (100), 324 (10), 262 (3), 105 (4); TLC (petroleum ether:*Et*O*Ac* = 3:1): $R_f = 0.70$; ^{1}H NMR: $\delta = 9.69$ (s, CHO), 7.55–7.44 and 7.32–7.25 (2m, 5 + 3 arom H), 7.18–7.12 and 7.11–7.05 (2m, 1 + 2 arom H), 6.97–6.93 (m, 5-H), 6.80–6.75 (m, 5-H + 2 arom H), 6.30 and 5.26 (2d, each $J = 7.9$ Hz, 3-H, 4-H), 3.83 and 3.30 (AB, $J = 13.9$ Hz, Ar–CH$_2$) ppm; ^{13}C NMR: $\delta = 191.67$ (d, CHO), 170.05 (s, CO), 135.89 and 133.51 (2s, 2C), 131.17 (d, 1C), 131.11 (s, C-4a), 130.35 (d, C-8), 128.87 (d, C-6/C-7), 128.68, 128.59, and 128.33 (3d, each 2C), 127.80, 127.75 (2d, 2C), 127.38 (s, C-8a), 126.82 (d, C-6/C-7), 126.74 (d, C-3), 126.58 (d, 1C), 125.50 and 107.58 (2d, C-5, C-4), 72.65 (s, C-1), 41.69 (t, Ar–CH$_2$) ppm.

2-Benzoyl-1,2-dihydro-1-(2-methylbenzyl)isoquinoline-1-carbaldehyde (**12b**, $C_{25}H_{21}NO_2$)

Yield: 24%, colourless resin; IR (KBr): $\bar{\nu} = 1730$, 1648 (C=O) cm^{-1}; TLC (petroleum ether:*Et*O*Ac* = 3:1): $R_f = 0.69$; ^{1}H NMR (CDCl$_3$): $\delta = 9.63$ (s, CHO), 7.56–7.44 and 7.31–7.22 (2m, 5 + 4 arom H), 7.18–7.12 and 7.11–7.05 (2m, 2 arom H), 6.97–6.93 (m, 5-H), 6.53 (d, $J = 7.7$ Hz, arom H), 6.25, 5.23 (2d, each $J = 7.9$ Hz, 3-H, 4-H), 3.92 and 3.30 (AB, $J = 13.9$ Hz, Ar–CH$_2$), 1.88 (s, CH$_3$) ppm.

2-Benzoyl-1-(2-bromobenzyl)-1,2-dihydroisoquinoline-1-carbaldehyde (**12c**, $C_{24}H_{18}BrNO_2$)

Yield: 32%, light yellow resin; IR (KBr): $\bar{\nu} = 1735$, 1659 (C=O) cm^{-1}; MS (CI): m/z (%) = 434 (100), 432 (98), 404 (12), 402 (12); TLC (petroleum ether:*Et*O*Ac* = 5:1): $R_f = 0.50$; ^{1}H NMR: $\delta = 9.59$ (s, CHO), 7.63–7.60 and 7.55–7.50 (2m, 1 + 2 arom H), 7.49–7.44 and 7.34–7.22 (2m, 2 + 3 arom H), 6.95–6.89 (m, 3 arom H), 6.79 (dt, $J = 7.6/1.6$ Hz, arom H), 6.43 (d, $J = 7.9$ Hz, 3-H), 6.24 (dd, $J = 7.6/1.6$ Hz, arom H), 5.22 (d, $J = 7.9$ Hz, 4-H), 4.12 and 3.37 (AB, $J = 14.4$ Hz, Ar–CH$_2$) ppm; ^{13}C NMR: $\delta = 191.36$, 170.38, 136.03, 133.74, 132.55, 132.40, 132.10, 131.57, 129.27, 129.22, 128.72, 128.32, 128.01, 127.68, 127.04, 126.41, 125.82, 125.77, 108.28, 71.65, 40.35 ppm.

2-Benzoyl-1,2-dihydro-1-(2-nitrobenzyl)isoquinoline-1-carbaldehyde (**12d**, $C_{24}H_{18}N_2O_4$)

Yield: 28%, light yellow resin; IR (KBr): $\bar{\nu} = 1731$, 1631 (C=O) cm^{-1}; MS (CI): m/z (%) = 399 (100), 369 (8), 105 (47); TLC (petroleum ether:*Et*O*Ac* = 5:1): $R_f = 0.65$; ^{1}H NMR: $\delta = 9.45$ (s, CHO), 7.56–7.35 and 7.23–7.03 (2m, 3 + 8 arom H), 6.84–6.81 (m, 5-H), 6.55 (dd, $J = 7.9/1.4$ Hz, arom H), 6.25 and 5.19 (2d, each $J = 7.9$ Hz, 3-H, 4-H), 4.17 and 3.57 (AB, $J = 14.1$ Hz, Ar–CH$_2$) ppm.

2-Benzoyl-1,2-dihydro-1-(naphth-1-ylmethyl)isoquinoline-1-carbaldehyde (**12e**, $C_{28}H_{21}NO_2$)

Yield: 12%, light yellow resin; TLC (petroleum ether:*Et*O*Ac* = 5:1): $R_f = 0.56$; ^{1}H NMR: $\delta = 9.63$ (s, CHO), 7.84–7.70 (m, 3H), 7.68–7.17 (m, 11H), 6.98 and 6.96 (2d, each $J = 7.1$ Hz, 2H), 5.62 and 4.83 (2d, each $J = 7.9$ Hz, 3-H, 4-H), 4.45 and 3.51 (AB, each $J = 14.5$ Hz, CH_2) ppm.

The 8-oxoprotoberberine carboxylic acids **13** were prepared by the general procedure according to Ref. [1] starting from 0.5–2.4 mmol of **5**; the crude product was dried *in vacuo* at ambient temperature and recrystallized. Analytical and spectroscopic data of the compounds **13a** and **13b** are listed in Ref. [1].

2-Benzyloxy-5,6,8,13-tetrahydro-3-methoxy-8-oxo-13aH-dibenzo[a,g]quinolizine-13a-carboxylic acid (**13c**, $C_{26}H_{23}NO_5$)

Yield: 88%, mp 231°C (*Et*O*Ac*); TLC ($CHCl_3$:CH_3OH = 9:1): $R_f = 0.47$; IR (KBr): $\bar{\nu} = 1719$, 1601 (C=O) cm^{-1}; MS (CI): m/z (%) = 414 (4), 386 (37), 384 (100), 374 (61), 282 (58); ^{1}H NMR (*DMSO*-d$_6$): $\delta = 13.16$ (s, CO_2H), 7.92 (d, $J = 7.7$ Hz, 9-H), 7.56–7.30 (m, 9 arom H), 6.86 (s, 4-H), 5.14 and 5.04 (AB, $J = 11.8$ Hz, benzyl-CH_2), 4.77 (dt, $J = 12.5/3.5$ Hz, 6-H_a), 3.86 (d, $J = 15.5$ Hz, 13-H_a), 3.80 (s, OCH_3), 3.23 (dt, $J = 12.5/8.0$ Hz, 6-H_b), 3.01 (d, $J = 15.5$ Hz, 13-H_b), 2.84 (m, 5-H_{ab}) ppm; ^{13}C NMR (*DMSO*-d$_6$): $\delta = 173.23$, 163.57, 148.89, 146.25, 136.90, 136.21, 132.10, 128.29 (2C), 128.15, 127.92 (2C), 127.87, 127.80, 127.59, 127.39, 127.08, 125.83, 112.13, 111.89, 70.43, 63.92, 55.35, 40.43, 37.19, 27.60 ppm.

5,6,8,13-Tetrahydro-2,3-methylenedioxy-8-oxo-13aH-dibenzo[a,g]quinolizine-13a-carboxylic acid (**13d**, $C_{19}H_{15}NO_5$)

Yield: 97%, mp 224°C (*Et*O*Ac*); TLC ($CHCl_3$:CH_3OH = 9:1): $R_f = 0.35$; IR (KBr): $\bar{\nu} = 1705$, 1635 (C=O) cm^{-1}; MS (EI): m/z (%) = 292 (7), 291 (9), 276 (16); ^{1}H NMR (*DMSO*-d$_6$): $\delta = 13.27$ (s, CO_2H), 7.91 (dd, $J = 7.5/1.3$ Hz, 9-H), 7.52 (dt, $J = 7.5/1.4$ Hz, 11-H), 7.43–7.35 (m, 10-H, 12-H), 7.25 (s, 1-H), 6.83 (s, 4-H), 6.05–6.02 (m, OCH_2O), 4.69 (dt, $J = 12.6/3.5$ Hz, 6-H_a), 3.89 (d, $J = 15.6$ Hz, 13-H_a), 3.30–3.20 (m, 6-H_b), 3.09 (d, $J = 15.6$ Hz, 13-H_b), 2.86–2.79 (m, 5-H_{ab}) ppm; ^{13}C NMR (*DMSO*-d$_6$): $\delta = 172.97$, 163.56, 146.64, 146.22, 135.97, 131.97, 128.71, 128.12, 127.54, 127.24, 127.18, 127.11, 108.22, 106.15, 101.10, 64.39, 41.03, 38.10, 28.25 ppm.

5,6,8,13-Tetrahydro-9-methoxy-8-oxo-13aH-dibenzo[a,g]quinolizine-13a-carboxylic acid (**13e**, $C_{19}H_{17}NO_2$)

Yield: 96%, mp 229°C (CH_3OH); TLC ($CHCl_3$:CH_3OH = 9:1): $R_f = 0.41$; IR (KBr): $\bar{\nu} = 1719$, 1618 (C=O) cm^{-1}; MS (EI): m/z (%) = 280 (26), 279 (27), 278 (56), 277 (45), 248 (34); ^{1}H NMR (*DMSO*-d$_6$): $\delta = 13.07$ (s, CO_2H), 7.72–7.68 (br d, $J = 7.6$ Hz, 1-H), 7.46–7.41 (m, 2-H, 3-H), 7.36–7.26 (m, 4-H, 11-H), 7.01 and 6.94 (2d, each $J = 7.9$ Hz, 12-H, 10-H), 4.68 (dt, $J = 12.7/4.2$ Hz, 6-H_a), 3.80 (s, OCH_3), 3.77 (d, $J = 15.7$ Hz, 13-H_a), 3.35–3.23 (m, 6-H_b), 3.05 (d, $J = 15.7$ Hz, 13-H_b), 2.98–2.83 (m, 5-H_{ab}) ppm; ^{13}C NMR (*DMSO*-d$_6$): $\delta = 172.93$, 161.32, 159.33, 138.63, 135.95, 132.59, 128.82, 127.39, 126.65, 125.82, 119.61, 116.94, 111.64, 55.74, 49.14, 42.08, 37.49, 28.54 ppm.

5,6,8,13-Tetrahydro-2,3,9,10-tetramethoxy-8-oxo-13aH-dibenzo[a,g]quinolizine-13a-carboxylic acid (**13f**, $C_{22}H_{23}NO_7$)

Yield: 95%, mp 218°C (*Et*O*Ac*); TLC ($CHCl_3$:CH_3OH = 9:1): $R_f = 0.23$; IR (KBr): $\bar{\nu} = 1709$, 1638 (C=O) cm^{-1}; MS (EI): m/z (%) = 428 (30), 414 (70), 370 (48), 369 (27), 368 (100); ^{1}H NMR (*DMSO*-d$_6$): $\delta = 13.03$ (s, CO_2H), 7.22 (s, 1-H), 7.18 and 7.08 (2d, each $J = 8.2$ Hz, 11-H, 12-H) 6.84 (s, 4-H), 4.69 (dt, $J = 12.9/4.2$ Hz, 6-H_a), 3.80 (s, OCH_3), 3.79–3.76 (m, 13-H_a, 2 OCH_3), 3.75

(s, OCH_3), 3.23 (ddd, $J = 12.9/10.1/4.9$ Hz, 6-H_b), 2.91 (d, $J = 15.1$ Hz, 13-H_b), 2.87–2.74 (m, 5-H_{ab}) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 173.69$, 162.12, 152.99, 148.99, 148.24, 147.43, 129.06, 127.64, 125.91, 122.73, 122.32, 115.88, 111.74, 109.69, 63.73, 60.64, 55.85, 55.72, 55.44, 41.51, 37.77, 28.00 ppm.

5,6,8,13-Tetrahydro-2,3-dimethoxy-9,10-methylenedioxy-8-oxo-13aH-dibenzo[a,g]quinolizine-13a-carboxylic acid (**13g**, $C_{21}H_{19}NO_7$)

Yield: 95%, mp 210°C (CH_3OH); TLC ($CHCl_3$:$CH_3OH = 9:1$): $R_f = 0.21$; IR (KBr): $\bar{\nu} = 1725$, 1622 (C=O) cm^{-1}; MS (EI): *m/z* (%) = 412 (39), 398 (12), 354 (60), 353 (29), 352 (100); ^{1}H NMR (*DMSO*-d_6): $\delta = 13.18$ (s, CO_2H), 7.23 (s, 1-H), 7.01 (d, $J = 7.6$ Hz, 12-H), 6.82 (s, 4-H), 6.81 (d, $J = 7.6$ Hz, 11-H), 6.15 and 6.08 (2s, OCH_2O), 4.72 (dt, $J = 12.9/4.0$ Hz, 13-H_a), 3.84 (d, $J = 15.6$ Hz, 6-H_a), 3.78 and 3.77 (2s, 2 OCH_3), 3.22–3.13 (m, 13-H_b), 2.93 (d, $J = 15.6$ Hz, 6-H_b), 2.85–2.78 (m, 5-H_{ab}) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 173.09$, 161.25, 148.31, 147.54, 147.42, 147.15, 129.07, 127.51, 125.81, 119.83, 111.87, 111.74, 111.14, 109.89, 101.91, 64.29, 55.78, 55.48, 40.57, 36.97, 27.88 ppm.

5,6,8,13-Tetrahydro-9,10-dimethoxy-2,3-methylenedioxy-8-oxo-13aH-dibenzo[a,g]quinolizine-13a-carboxylic acid (**13h**, $C_{21}H_{19}NO_7$)

Yield: 95%, mp 226°C (CH_3OH); TLC ($CHCl_3$:$CH_3OH = 9:1$): $R_f = 0.28$; IR (KBr): $\bar{\nu} = 1727$, 1616 (C=O) cm^{-1}; MS (EI): *m/z* (%) = 412 (39), 398 (100), 354 (69), 352 (100); ^{1}H NMR (*DMSO*-d_6): $\delta = 13.10$ (s, CO_2H), 7.21 (s, 1-H), 7.17 and 7.06 (2d, each $J = 8.4$ Hz, 12-H, 11-H), 6.82 (s, 4-H), 6.04–6.00 (m, OCH_2O), 4.57 (dt, $J = 12.9/4.4$ Hz, 6-H_a), 3.80 (s, OCH_3), 3.75–3.69 (m, OCH_3, 13-H_a), 3.44–3.23 (m, 6-H_b), 2.93 (d, $J = 15.2$ Hz, 13-H_b), 2.86–2.72 (m, 5-H_{ab}) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 173.00$, 161.55, 152.45, 148.93, 146.63, 146.24, 129.07, 128.86, 127.27, 122.81, 122.31, 115.90, 108.26, 106.03, 101.12, 64.04, 60.67, 55.87, 40.69, 37.26, 28.37 ppm.

5,6,8,13-Tetrahydro-2,3,9,10-di(methylenedioxy)-8-oxo-13aH-dibenzo[a,g]quinolizine-13a-carboxylic acid (**13i**, $C_{20}H_{15}NO_7$)

Yield: 98%, mp 218°C (*EtOAc*); TLC ($CHCl_3$:$CH_3OH = 9:1$): $R_f = 0.25$; IR (KBr): $\bar{\nu} = 1720$, 1636 (C=O) cm^{-1}; MS (EI): *m/z* (%) = 382 (41), 338 (80), 337 (42), 336 (100), 335 (36); ^{1}H NMR (*DMSO*-d_6): $\delta = 13.24$ (s, CO_2H), 7.23 (s, 1-H), 7.01 and 6.83–6.77 (2d, each $J = 8.0$ Hz, 12-H, 11-H), 6.80 (s, 4-H), 6.15, 6.09, and 6.02 (3s, 2 OCH_2O), 4.63 (dt, $J = 12.8/4.3$ Hz, 6-H_a), 3.79 (d, $J = 15.5$ Hz, 13-H_a), 3.25–3.14 (m, 6-H_b), 2.93 (d, $J = 15.5$ Hz, 13-H_b), 2.84–2.74 (m, 5-H_{ab}) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 172.86$, 161.23, 147.56, 147.09, 146.68, 146.25, 128.75, 127.77, 127.14, 119.78, 111.80, 111.03, 108.19, 106.22, 101.88, 101.11, 64.54, 41.23, 38.02, 28.30 ppm.

Tetra- and Dihydro-8H-dibenzoquinolizin-8-ones **14/15**, *General Procedure*

The acids **13** were decarboxylated by heating them to the melting temperature *in vacuo* (water pump). The products **14/15** were separated by FC.

5,6,13,13a-Tetrahydro-8H-dibenzo[a,g]quinolizin-8-one (Berbin-8-one, **14a***) and 5,6-Dihydro-8H-dibenzo[a,g]quinolizin-8-one* (**15a**)

From 500 mg (1.7 mmol) of **13a**; reaction time: 15 min; yields: **14a** 61%, **15a** 26%; for NMR and MS data see Ref. [1].

5,6,13,13a-Tetrahydro-2,3-dimethoxy-8H-dibenzo[a,g]quinolizin-8-one (2,3-Dimethoxy-berbin-8-one, **14b***) and 5,6-Dihyro-2,3-dimethoxy-8H-dibenzo[a,g] quinolizin-8-one* (**15b**)

From 300 mg (0.9 mmol) of **13b**; reaction time: 15 min; yields: **14b** 54%, **15b** 31%; for NMR and MS data see Ref. [1].

5,6,13,13a-Tetrahydro-2,3-methylenedioxy-8H-dibenzo[a,g]quinolizin-8-one (2,3-Methylenedioxyberbin-8-one, Gusanlung D, **14c***) and 5,6-Dihydro-2,3-methylenedioxy-8H-dibenzo[a,g]quinolizin-8-one* (**15c**)

From 150 mg (0.4 mmol) of **13d**; reaction time: 10 min; **14c**: yield: 27%; TLC (*Et*O*Ac*:*n*-hexane = 2:1): $R_f = 0.50$; ^{13}C NMR: $\delta = 158.67$, 146.77, 146.57, 137.24, 132.33, 131.81, 128.85, 128.60, 128.55, 127.37, 126.87, 108.81, 105.97, 101.00, 55.18, 38.49, 37.78, 29.61 ppm; mp, IR, MS, ^{1}H, and ^{13}C NMR data were in line with those published in Refs. [3, 36]; **15c**: yield: 58%; TLC (*Et*O*Ac*:*n*-hexane = 2:1): $R_f = 0.33$; MS (EI): m/z (%) = 291 ($M^{+\bullet}$, 66), 276 (100); ^{13}C NMR: $\delta = 162.10$, 148.71, 147.43, 137.40, 136.65, 132.27, 130.29, 127.94, 126.27, 126.01, 124.57, 123.73, 107.96, 105.06, 101.89, 101.48, 39.69, 28.57 ppm; mp, IR, and ^{1}H NMR data were in line with those published in Ref. [37].

5,6,13,13a-Tetrahydro-2,3,9,10-tetramethoxy-8H-dibenzo[a,g]quinolizin-8-one (Di-hydropalmatin-8-one, **14d***) and 5,6-Dihydro-2,3,9,10-tetramethoxy-8H-dibenzo[a,g] quinolizin-8-one (Oxypalmatine,* **15d***)*

From 240 mg (0.6 mmol) of **13f**; reaction time: 15 min; **14d**: yield: 47%; TLC (*Et*O*Ac*:*n*-hexane = 2:1): $R_f = 0.48$; IR (KBr): $\bar{\nu} = 1640$ (C=O) cm^{-1}; MS (EI): m/z (%) = 369 ($M^{+\bullet}$, 93), 368 (50), 354 (23), 192 (46), 178 (100), 163 (21); mp, ^{1}H and ^{13}C NMR data were in line with those published in Ref. [2]; **15d**: yield: 47%; TLC (*Et*O*Ac*:*n*-hexane = 2:1): $R_f = 0.32$; MS (EI): m/z (%) = 367 ($M^{+\bullet}$, 100), 352 (70), 338 (47), 324 (24), 308 (21), 280 (9); ^{13}C NMR: $\delta = 160.22$, 151.32, 150.05, 149.53, 148.37, 135.61, 132.37, 128.48, 122.32, 122.13, 119.33, 118.98, 110.45, 107.52, 100.87, 61.59, 56.85, 56.23, 56.01, 39.39, 28.22 ppm; mp and ^{1}H NMR data were in line with those published in Ref. [5].

5,6-Dihydro-9,10-dimethoxy-2,3-methylenedioxy-8H-dibenzo[a,g]quinolizin-8-one (Berberin-8-one, Oxyberberine, Berlambin, **15e***)*

From 200 mg (0.5 mmol) of **13h**; reaction time: 10 min; purification of the crude product by FC; yield: 81%; TLC (*Et*O*Ac*:*n*-hexane = 2:1): $R_f = 0.36$; IR (KBr): $\bar{\nu} = 1643$ (C=O) cm^{-1}; mp, MS, ^{1}H, and ^{13}C NMR data were in line with those published in Refs. [3, 5, 38].

5,6-Dihydro-2,3,9,10-di(methylenedioxy)-8H-dibenzo[a,g]quinolizin-8-one (Coptisin-8-one, **15f***)*

From 300 mg (0.78 mmol) of **13i**; reaction time: 30 min; purification of the crude product by FC (*n*-hexane:*Et*O*Ac* = 2:1); yield: 73%; TLC ($CHCl_3$:CH_3OH = 9:1): $R_f = 0.35$; mp, IR, MS, ^{1}H, and ^{13}C NMR data were in line with those published in Ref. [39].

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