Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2011, **9**, 538

www.rsc.org/obc

PAPER

Synthesis of 1-substituted 1,2,3,4-tetrahydrobenz[*g*]isoquinoline-5,10-diones†

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Received 6th July 2010, Accepted 15th September 2010
DOI: 10.1039/c0ob00391c

1,2-Disubstituted 1,2,3,4-tetrahydrobenz[*g*]isoquinoline-5,10-diones are prepared for the first time through an activated Pictet–Spengler reaction of the corresponding imines of 2-(1,4-dimethoxynaphth-2-yl)ethylamine in the presence of an acyl chloride and $AlCl_3$ followed by an oxidation with silver(II) oxide in nitric acid . Depending on the reaction conditions the *N*-trichloroacetyl protecting group could be cleaved off, converted to an *N*-methoxycarbonyl group or transformed to an *N*-(2-oxoacetamide) moiety. The synthesized 1,2-disubstituted 1,2,3,4-tetrahydrobenz[*g*]isoquinoline-5,10-diones constitute a new class of quinones, which has not been reported yet.

Introduction

Tetrahydroisoquinoline alkaloids have received much interest because of their tremendous structural diversity and broad spectrum of biological and pharmaceutical activities.[1] The most popular synthetic approaches towards isoquinolines are the Bischler–Napieralski reaction,[2] the Pomeranz–Fritsch reaction followed by reduction,[3] and the Pictet–Spengler reaction,[4] which often require electron-donating groups at the benzene ring for successful ring closure. On the other hand, quinones with annelated N-heterocycles constitute an important research area in organic synthesis due to the pronounced biological activities of several natural products. In recent decades, a whole range of antibiotics belonging to this family have been isolated. For instance, lemonomycin **1**, which was isolated from the fermentation broth of *Streptomyces candidus* (LL-AP191)[5,6] exhibited potent antibiotic activities against methicillin-resistant *Staphylococcus aureus* (MRSA), *Bacillus subtilis*, and vancomycin-resistant *Enterococcus faecium* (VREF) (Fig. 1).[7] The renieramycins, saframycins **2** and naphthyridinomycins are structurally related tetrahydroisoquinolines, and include potent cytotoxic agents that display a range of antitumor activities, antimicrobial activity, and other biological properties (Fig. 1).[8]

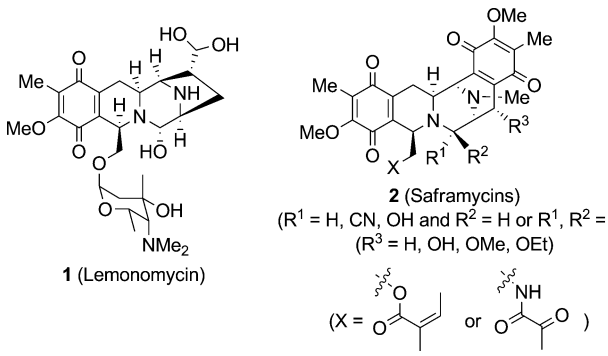

Fig. 1

Considering these interesting biological activities, the synthesis of 1-substituted 1,2,3,4-tetrahydrobenz[*g*]isoquinoline-5,10-diones was envisaged as a continuation of previous work in which an entry towards 2-substituted 1,2,3,4-tetrahydrobenz[*g*]isoquinoline-5,10-diones was developed.[9] Although several 1-substituted 1,2,3,4-tetrahydroisoquinolines have been synthesized, the synthesis of 1-substituted 1,2,3,4-tetrahydrobenz[*g*]isoquinoline-5,10-diones has been reported only once to the best of our knowledge.[10] In this patent, the reaction of 1,2,3,4-tetrahydroisoquinoline-5,8-diones with Brassard dienes is described. Haloacyl 1-substituted 1,2,3,4-tetrahydroisoquinolines have been found useful as antidotes for protecting crop plants from herbicide injury.[11]

Because of the availability of the previously reported 2-(1,4-dimethoxynaphth-2-yl)ethylamine,[9] a strategy for the synthesis of 1-substituted 1,2,3,4-tetrahydrobenz[*g*]isoquinoline-5,10-diones **3** was deployed based on the *N*-acyl-Pictet–Spengler reaction of the corresponding aldimine derived from **5**, followed by oxidative demethylation of the ring closed product **4** (Fig. 2).

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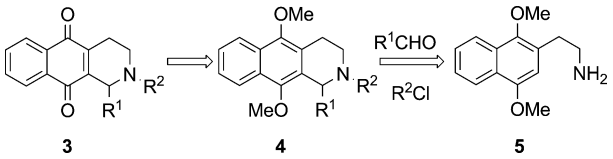
† Electronic supplementary information (ESI) available: Copies of ^{1}H NMR and ^{13}C NMR spectra for compounds **7c**, **7d**, **9**, **12a–e**, **13a**, **14**, **15**, **21**, **22**, **23a–c**, **24b**, **25–27**, **31** and **33**; UPLC chromatograms for **13a**, **14**, **21**, **22**, **12c**, **23a**, **23b**, **25**, **26**. See DOI: 10.1039/c0ob00391c



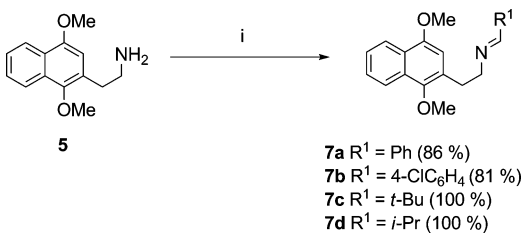
3 **4** **5**

Fig. 2

Results and discussion

The Pictet–Spengler reaction generally involves the cyclization of imines or iminium ions formed by the dehydration reaction of β-arylethyl amine derivatives with aldehydes.[4] The electrophilicity of the imine is of prime importance for the formation of the ring closed product and can be enhanced by protonation of the imine by means of strong Brønsted acids. But despite its wide application, this strategy is not suitable for acid-labile functional groups. The second strategy to enhance the electrophilic nature of the iminium intermediate is the application of the more electrophilic *N*-substituted iminium species such as *N*-acyliminium derivatives.[12]

For this purpose the imines **7a–d** were prepared *via* condensation of amine **5**[9] with aldehydes in dichloromethane under reflux in the presence of $MgSO_4$ (Scheme 1). In order to achieve a complete conversion of the β-naphthylethyl amine **5** to its corresponding imines **7** an excess of the volatile aldehydes pivaldehyde (**6c**) and isobutyraldehyde (**6d**) were used. In case of the reaction of **5** with non-volatile aromatic aldehydes **6a** and **6b** only one equivalent of the latter were added, giving rise to a 81–86% yield (^{1}H NMR). The addition of 2 equivalents of **6a** did not lead to any substantial increase of the yield, but caused purification problems of the imine **7a**.



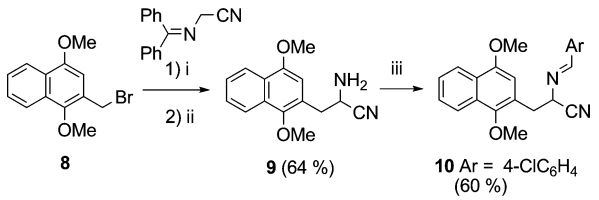
5

7a R^1 = Ph (86 %)
7b R^1 = 4-ClC_6H_4 (81 %)
7c R^1 = *t*-Bu (100 %)
7d R^1 = *i*-Pr (100 %)

Scheme 1 Synthesis of imines **7a–d**. *Reagents and conditions*: (i) 1 equiv. R^1CHO (**6a,b**) or 2 equiv. R^1CHO (**6c,d**), 3.3 equiv. $MgSO_4$ (anhyd.), CH_2Cl_2, reflux, 4 h (**6a,b**) or 2 h (**6c,d**).

2-Amino-3-(1,4-dimethoxynaphthalen-2-yl)propanenitrile (**9**) was synthesized according to a slightly modified literature procedure[13] by alkylation of 2-(diphenylmethyleneamino)-acetonitrile with 2-(bromomethyl)-1,4-dimethoxynapthalene (**8**)[14] under phase-transfer conditions, followed by hydrochloric acid hydrolysis of the intermediate alkylated imine. The corresponding imine of **9** and 4-chlorobenzaldehyde was prepared in dichloromethane under reflux in the presence of $MgSO_4$ (yield 60%, Scheme 2). Apart from unreacted 4-chlorobenzaldehyde no other products were detected in the crude reaction mixture, which could not be further purified and hence was used as such in the following step.

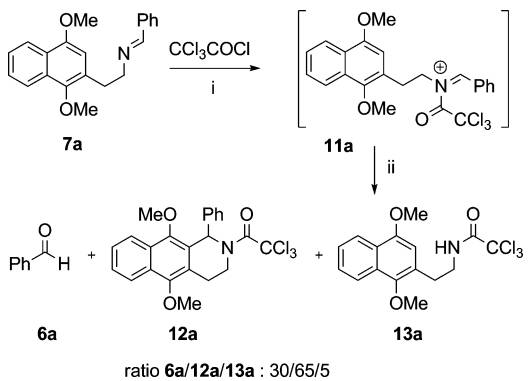
In a preliminary study, the cyclization of imine **7a** in the presence of acetyl, chloroacetyl, dichloroacetyl or trichloroacetyl chloride and a wide variety of Lewis acids ($AlCl_3$, $SnCl_4$, $SbCl_5$, $TiCl_4$, $BF_3{\cdot}Et_2O$, $BF_3{\cdot}THF$, AgOTf, $Sc(OTf)_3$) and solvents (1,2-



8 **9** (64 %) **10** Ar = 4-ClC_6H_4 (60 %)

Scheme 2 Synthesis of imine **10**. *Reagents and conditions*: (i) 0.9 equiv. 2-(diphenylmethyleneamino)acetonitrile, 6.4 equiv. NaOH (2.5 M), 0.05 equiv. TEBA, CH_2Cl_2, rt, 24 h; (ii) 1 equiv. HCl (1 M), THF, rt, 16 h; (iii) 1 equiv. ArCHO, 3.3 equiv. $MgSO_4$ (anhyd.), CH_2Cl_2, reflux, 4 h.

dichloroethane, CH_2Cl_2) was evaluated. The best yield of compound **12a** was obtained by reaction of **7a** with trichloroacetyl chloride in 1,2-dichloroethane in the presence of $AlCl_3$ (Scheme 3). In all cases, after workup of the reaction mixture, partial hydrolysis of the unreacted *N*-(trichloroacetyl)iminium ion intermediate **11a** was observed. Depending on the Lewis acid, solvent and the reaction conditions the ratio of **6a/12a/13a** varied from 85/0/15 to 30/65/5 (HPLC). Similar iminium ion hydrolyses in Pictet–Spengler reactions using metal chloride Lewis acids have been reported.[12g] Metal triflates, instead, have been reported to avoid this side reaction[12g] but neither the use of $Sc(OTf)_3$ nor AgOTf led to better **12a/13a** ratios. Fortunately, the *N*-trichloroacetyl amide **13a** could be separated from the ring-closed compound and benzaldehyde by means of flash chromatography. In order to confirm the structure of **13a**, this compound was synthesized in 57% yield by reaction of 2-(1,4-dimethoxynaphth-2-yl)ethylamine (**5**) with trichloroacetyl chloride (1.02 equiv.) in pyridine at room temperature for 2 h.



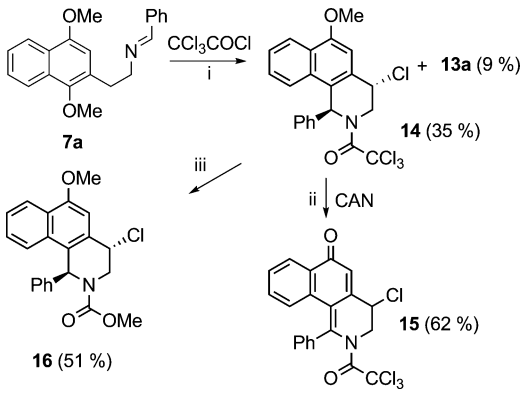
7a **11a** **6a** **12a** **13a**

ratio **6a/12a/13a** : 30/65/5

Scheme 3 Cyclization of imine **7a** in the presence of CCl_3COCl. *Reagents and conditions*: (i) 1.1 equiv. CCl_3COCl, 1,2-dichloroethane, rt, 0.5 h; (ii) 1 equiv. $AlCl_3$, reflux, 3 h.

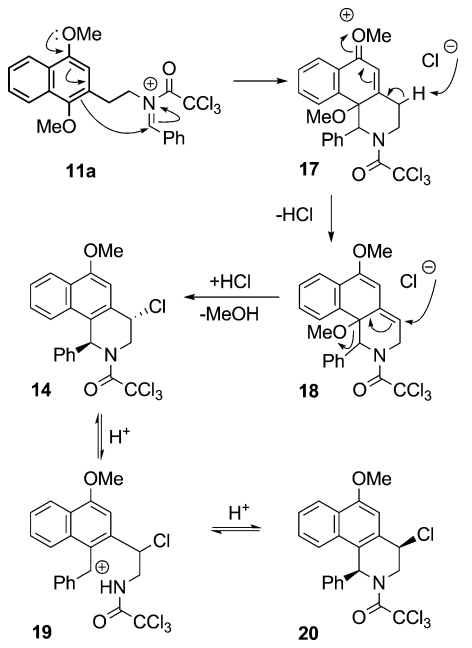
Remarkably, in the absence of any Lewis acid or in the presence of a weak Lewis acid like $BF_3{\cdot}Et_2O$, the formation of the ring-closed compound **12a** was not observed. Instead, after chromatography of the black tarry reaction mixture, the angular derivative **14** and the acyclic trichloroacetamide **13a** could be isolated in 35% and 9% yield, respectively (Scheme 4).

The structure of compound **14** was established on the basis of spectroscopic data. At room temperature the ^{1}H and ^{13}C NMR spectra of this compound contained two sets of signals, due to constrained rotation of the trichloroacetyl group. A variable-temperature NMR investigation was made to simplify the NMR spectra, and coalescence of signals was observed at 50 °C.



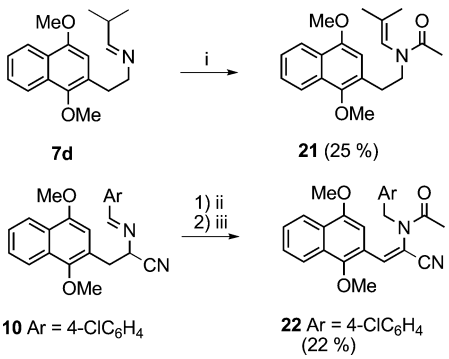
Scheme 4 Synthesis and transformations of compound **14**. *Reagents and conditions*: (i) 1.1 equiv. CCl_3COCl, 1,2-dichloroethane, rt, 0.5 h, then reflux, 3 h; (ii) 3.3 equiv. CAN, $MeOH/H_2O$ (10/1), rt, 2 h; (iii) 10 equiv. NaOH, $MeOH/H_2O$ (10/1), rt, 16 h.

This unexpected result occurs because of *ipso*-type electrophilic attack of the *N*-acyliminium cation **11a** to the carbon bearing the 1-methoxy group to form the resonance-stabilized **17**. This cation further stabilizes itself by loss of methanol and addition of chloride to the adjacent carbon to produce the angular tetrahydrobenzo[*h*]isoquinoline **14**. Based on the NMR analysis only one diastereomer is formed, and in view of the proposed mechanism the relative configuration of the heterocyclic substituents is assigned as *trans*. Under the present conditions an eventual epimerization of *cis*-substituted tetrahydrobenzo[*h*]isoquinoline **20** *via* an intermediate carbenium ion **19** cannot be excluded (Scheme 5).[15] Similar *ipso*-cyclizations with a displacement of a methoxy group on carbon have only been rarely reported. Upon Bischler–Napieralski reaction of (1,4-dimethoxynaphthalen-2-yl)ethylamides, in addition to the classical cyclization the formation of an angular derivative was observed, but this was not isolated pure or characterized.[16] Furthermore, the Fischer cyclisation of (1-methoxynaphthalen-2-yl)hydrazones has been reported to give rise to benzo[*e*]indoles,[17] and the treatment of 1-(2-(1-(1,4-dimethoxynaphthalen-2-yl)ethyl)phenyl)ethanol with *p*TsOH also led to an *ipso*-type displacement of methoxide.[18] The oxidative demethylation of **14** using cerium(IV) ammonium nitrate (CAN) in aqueous acetonitrile afforded compound **15** in 62% yield (Scheme 4). No rotameric phenomenon was observed in this case.



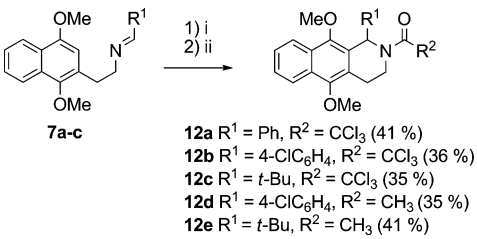
Scheme 5

The reaction of enolizable imine **7d** with acetyl chloride in the absence of a Lewis acid resulted in the formation of enamide **21**, which could not be cyclized successfully (Scheme 6). Treatment of the *N*-(arylidene)-1-cyano-2-naphthylethylamine **10** (Ar = 4-ClC_6H_4) with acetyl chloride in the presence of the strongly Lewis-acidic $AlCl_3$ did not result in a ring-closed product, but instead an acyclic enamide **22** was isolated in 22% yield after flash chromatography.



Scheme 6 Transformations of imines **7d** and **10**. *Reagents and conditions*: (i) 1.1 equiv. CH_3COCl, 1,2-dichloroethane, rt, 0.5 h, then reflux, 3 h; (ii) 1.1 equiv. CH_3COCl, 1,2-dichloroethane, 0.04 equiv. KI, rt, 0.5 h; (iii) 1 equiv. $AlCl_3$, reflux, 3 h.

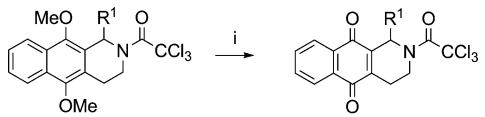
In view of the above-mentioned results, Pictet–Spengler reactions were limited to non-enolizable imines and to the use of $AlCl_3$ as Lewis acid. To avoid the formation of the side product **13a** and to improve the yield, the reaction procedure was further optimized by adding molecular sieves and a catalytic amount of potassium iodide[19] under argon atmosphere. Under these reaction conditions *N*-acyl-1,2,3,4-tetrahydrobenz[*g*]isoquinolines **12a–e** were obtained in moderate yields after flash chromatography (Scheme 7). The NMR spectra of the *N*-trichloroacetyl derivatives **12a–c** showed one set of signals while the signals in the NMR spectra of *N*-acetyl derivatives **12d** and **12e** were doubled. Presumably rotamers of the *N*-acetyl tetrahydrobenz[*g*]isoquinolines **12d** and **12e** exist in solution because of hindered rotation of the amide C–N bond. In order to simplify the ^1H NMR spectrum, compound **12e** was heated in an NMR tube in DMSO-d_6 to 75 °C but no



Scheme 7 Synthesis of compounds **12a–e**. *Reagents and conditions*: (i) 1.1 equiv. R^2COCl, 1,2-dichloroethane, 0.04 equiv. KI, rt, 0.5 h; (ii) 1 equiv. $AlCl_3$, reflux, 3 h.

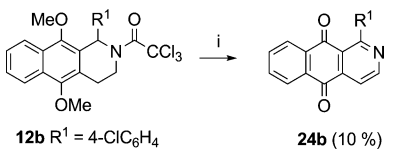
coalescence could be effected. Nevertheless, the composition of compound **12e** was confirmed by elemental analysis.

The oxidative demethylation of **12e** with CAN in aqueous acetonitrile gave rise to inseparable reaction mixtures. Analogous unselective oxidations of *N*-protected 5,10-dimethoxy-1,2,3,4-tetrahydrobenz[*g*]isoquinolines with CAN were observed earlier within our departments.[9] The oxidation of compounds **12a–c** to the corresponding quinones could be successfully accomplished by means of silver(II) oxide in 1,4-dioxane in the presence of nitric acid (6 M) as a co-oxidant (Scheme 8). In contrast with *N*-alkyl-1,2,3,4-tetrahydrobenz[*g*]isoquinoline-5,10-diones, which were not air-stable, these *N*-acyl-1,2,3,4-tetrahydrobenz[*g*]isoquinoline-5,10-diones **23a–c** could be stored at room temperature under air atmosphere without any noticeable degradation.[9] Of course, the electron-withdrawing trichloroacetyl group prevents these unsaturated heterocycles oxidizing.



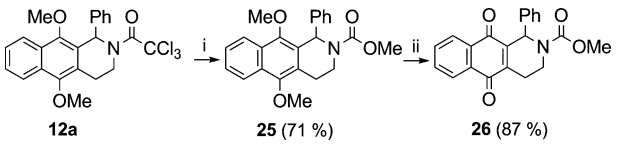
Scheme 8 Oxidation of compounds **12a–c**. *Reagents and conditions*: (i) 4 equiv. AgO, dioxane, 6 M HNO_3, 50 °C, 16 h.

Since trichloroacetamides can be deprotected under acidic hydrolytic conditions,[20–22] 1,2,3,4-tetrahydrobenz[*g*]isoquinoline **12b** was refluxed with 12 M HCl in methanol. After 8 h the reaction mixture was worked up, showing a 57% conversion of **12b** (^{1}H NMR) to a demethylated compound. After flash chromatography of the black tarry residue a 10% yield of the aromatized 2-azaanthraquinone **24b** was obtained (Scheme 9).



Scheme 9 Deprotection of compound **12b**. *Reagents and conditions*: (i) HCl 12 M, MeOH, reflux, 8 h.

The synthetic utility of the trichloroacetyl group was further explored by a reaction of compound **12a** with NaOH in aqueous methanol. Quite unexpectedly, instead of the *N*-deprotected compound, the product **25** of a haloform-type reaction was obtained in 71% yield (Scheme 10). In the ^{1}H NMR spectra of compound **25** at room temperature two sets of signals appeared, and the MeO-signal of the carboxylic ester even appeared as four singlets in a 19/25/31/25 ratio. The singlets of H-1 of these presumable carbamate rotamers merged at 50 °C while



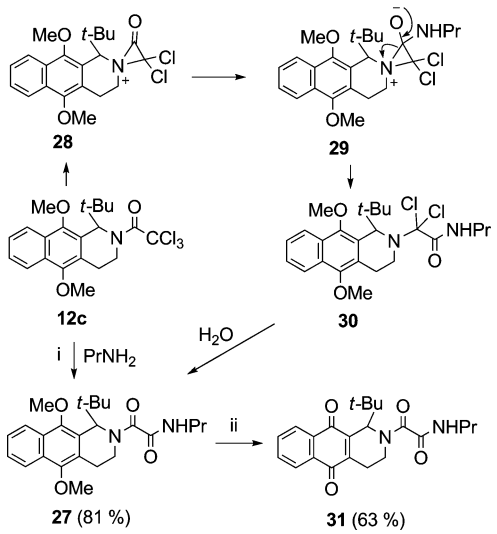
Scheme 10 Transformations of compound **12a**. *Reagents and conditions*: (i) 3 equiv. NaOH, MeOH/H_2O (10/1), reflux, 0.5 h; (ii) 4 equiv. AgO, dioxane, 6 M HNO_3, 50 °C, 16 h.

the COO*Me* singlets were reduced to two singlets (38/62 ratio). A possible explanation for the latter doubling may be a slow pyramidal inversion at nitrogen or rotamerism across the O═C–OMe single bond. For comparison, a detailed investigation of the amide rotamers of *N*-acetyl-5-benzyloxy-6,8-dimethoxy-1,3-*trans*-dimethyl-1,2,3,4-tetrahydroisoquinoline in toluene-d_8 revealed a convergence of the ^{1}H NMR signals at 57 °C.[23]

Most likely, the transformation of trichloroacetamide into the methylcarbamate occurs *via* a haloform-like displacement of the trichloromethyl group by methoxide. The intermediacy of a $[R_2N{=}C{=}O]^+$ cation, formed by base-induced β-elimination of chloroform (as has been reported for the reaction of secondary trichloroacetamides in basic medium with alcohols in the presence of CuCl and Bu_4NCl[22]) is less likely. The treatment of the angular *N*-trichloroacetyl tetrahydrobenz[*h*]isoquinoline **14** with NaOH in methanol also led to a *N*-methoxycarbonyl-protected analogue **16** (Scheme 4). Unfortunately, this compound completely decomposed upon standing at room temperature.

The oxidation of compound **25** to the targeted quinone derivative **26** was accomplished by silver(II) oxide in the presence of nitric acid. Also in this case, the COO*Me* protons displayed doubling in the ^{1}H NMR spectrum at 25 °C. Variable-temperature NMR experiments brought about coalescence of these signals at 50 °C, and more interestingly, extra doubling of the COO*Me* NMR signals into four singlets occurred at –30 °C, as was the case for compound **25** at room temperature.

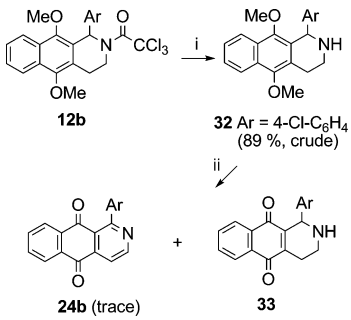
A reported one-pot synthesis of ureas by reaction of *N*-monosubstituted trichloroacetamides with morpholine,[24] or the analogous reactions of trichloroacetamides with carboxamides to form *N*-acylureas,[25] inspired us to examine the reaction of **12c** with an excess of propylamine. Instead of the expected propyl urea derivative and in contrast with the literature, the 2-oxoacetamide **27** was isolated in good yield (Scheme 11). The presence of the extra carbonyl function was confirmed by HRMS and ^{13}C NMR spectroscopy. The mechanism of this conversion may be interpreted as a Favorskii-type rearrangement, as reported for a comparable reaction of trichloromethanesulfinamides with



Scheme 11 Transformations of compound **12c**. *Reagents and conditions*: (i) excess $PrNH_2$, 50 °C, 21 h; (ii) 4 equiv. AgO, dioxane, 6 M HNO_3, 50 °C, 16 h.

morpholine in the presence of triethylamine.[26] This mechanism involves the formation of a three-membered cyclic intermediate **28**, with subsequent attack of propylamine on the carbonyl carbon atom, followed by ring-opening and hydrolysis of the CCl_2 moiety to give the observed product **27**. The spectroscopic analysis of compound **27** was hampered because of rotamerism in solution (25 °C). Unfortunately, variable-temperature NMR could not induce any coalescence at 45 °C. The corresponding quinone derivative **31** was obtained in 63% yield by the standard silver(II) oxide oxidation. The NMR spectra of this compound also displayed double sets of signals due to restricted rotation across the amide bond.

Finally, the cleavage of the trichloroacetyl group in **12b** was accomplished by means of NaOH in 5/1 acetonitrile/water under reflux (Scheme 12). Upon attempted chromatography on silica gel of this 1,2,3,4-tetrahydrobenz[*g*]isoquinoline degradation occurred, and therefore, in view of its high purity (NMR), it was used as such in the next step. After aqueous basic workup a complex reaction mixture was obtained in which compound **24b** could be distinguished as well as quinone **33** (tentatively). Unfortunately, the crude reaction mixture completely degraded upon attempted chromatography on silica gel.



Scheme 12 Transformations of compound **12b**. *Reagents and conditions*: (i) 5 equiv. NaOH, $MeCN/H_2O$ (5/1), reflux, 2 h; (ii) 4 equiv. AgO, dioxane, 6 M HNO_3, 50 °C, 16 h.

Conclusion

For the first time, the synthesis of *N*-acyl 1-substituted 1,2,3,4-tetrahydrobenz[*g*]isoquinolines **12a–e** has been achieved through an activated Pictet–Spengler reaction of the corresponding imine of 2-(1,4-dimethoxynaphth-2-yl)ethylamine in the presence of $AlCl_3$. In the absence of Lewis acids, a remarkable *ipso*-cyclisation with concomitant displacement of the methoxy group of the intermediate *N*-acyliminium ion is observed, leading to a tetrahydrobenzo[*h*]isoquinoline. The problematic ring closure is surprising in view of the fact that similar methoxy-substituted electron-rich phenethylamines are the textbook examples for Pictet–Spengler cyclizations, and therefore (*a priori*) no problems were expected with this method.

The *N*-trichloroacetyl group of the *N*-acyl-1,2,3,4-tetrahydrobenz[*g*]isoquinoline **12b** could be cleaved under the action of NaOH in acetonitrile, or converted to an *N*-methoxycarbonyl protecting group by means of NaOH in methanol. The reaction of *N*-trichloroacetyl-1,2,3,4-tetrahydrobenz[*g*]isoquinoline **12c** with propylamine unexpectedly gave rise to an 2-oxoacetamide. The *N*-acyl-, *N*-methoxycarbonyl- or *N*-(2-oxoacetamide)-1,2,3,4-tetrahydrobenz[*g*]isoquinolines **12a–c**, **25** and **27** were all oxidatively demethylated in good yields to the envisaged *N*-protected 1,2,3,4-tetrahydrobenz[*g*]isoquinoline-5,10-diones **23a–c**, **26** and **31** by silver(II) oxide in nitric acid.

Experimental

General experimental

^{1}H NMR spectra were recorded on a Bruker Avance DRX 250 spectrometer at 250 MHz, or a Bruker Avance II 500 spectrometer at 500 MHz with internal standard TMS. ^{13}C NMR spectra were recorded on a Bruker Avance DRX 250 spectrometer at 63 MHz, Bruker Avance II 500 spectrometer at 125 MHz with internal standard $CDCl_3$ (δ_C = 77). Coupling constants (*J* values) are reported in Hz. ^{13}C NMR assignments were made using DEPT spectra. Melting points were determined on a Büchi melting point apparatus B-540 and are uncorrected. GC-MS analyses were performed using an Intersience GC 8000 series gas chromatograph with a EC™-5 column (length: 30 m, internal diameter: 0.32 mm, film thickness: 0.25 μm). Products were injected in a split injector (250 °C); the inert carrier gas is helium. The mass spectrometer was a Fisons Instruments MD 800 using electron impact (70 eV) as ionization method. HRMS was measured with a VGQuattro II mass spectrometer. Elemental analyses were executed with Perkin Elmer Series II CHNS/O Analyzer 2400. UPLC analyses were obtained with an Acquity (Waters) with a reverse-phase C-18 column (Halo, 2.1 × 30 mm, 2.7 μm). The mobile phase (water/acetonitrile) contained 0.1% formic acid. The standard gradient consisted of a 1.5 min run from 5% to 95% acetonitrile at a flow of 0.6 ml/min with diode array UV detection. Infrared spectra were recorded with an Avatar 370 FT-IR apparatus (Thermo Nicolet), using the attenuated total reflection technology. Column chromatography was performed using Merck silica (diameter 40–63 μm). TLC-analysis was performed on glass-backed plates (Merck) coated with 0.2 mm silica $60F_{254}$.

Synthesis of 2-amino-3-(1,4-dimethoxynaphthalen-2-yl)propanenitrile 9

To a solution of 2-(diphenylmethyleneamino)acetonitrile (1.56 g, 7.09 mmol), 2-(bromomethyl)-1,4-dimethoxynapthalene (**8**, 2.2 g, 7.83 mmol) and TEBA (0.08 g, 0.35 mmol) in CH_2Cl_2 (20 ml), 2.5 M NaOH solution was added (20 ml). After 24 h of vigorous stirring, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 10 ml). The combined organic layers were washed with water (2 × 10 ml) and evaporated. The residue was solved in THF (30 ml) and 1 M HCl (7.8 ml) was added dropwise. After overnight stirring, the THF was evaporated, water was added and the organic material was taken into ether (3 × 10 ml). The aqueous layer was made alkaline by a saturated solution of $NaHCO_3$ and extracted with ether (3 × 25 ml). The combined extracts were dried (Na_2SO_4) and evaporated to afford the amine **9** (1.16 g, 64%) as a brown oil. δ_H (500 MHz; $CDCl_3$) 1.74 (2H, br s, NH_2), 3.21 (2H, dd, CH_2), 3.90 (3H, s, OCH_3), 3.99 (3H, s, OCH_3), 4.11 (1H, t, CHCN), 6.69 (1H, s, H-3), 7.47–7.56 (2H, m, H-6 and H-7), 8.01–8.03 (1H, m, H-8), 8.23–8.25 (1H, m, H-5); δ_C (125 MHz; $CDCl_3$) 36.3 (CH_2), 44.0 (CH), 55.7 (OCH_3), 62.1 (OCH_3), 105.4 (C-3), 121.8 (=CH), 121.9 (CN), 122.4 (=CH),

123.0 (=C_{quat}), 125.5 (=CH), 126.3 (=C_{quat}), 126.8 (=CH), 128.3 (=C_{quat}), 148.1 and 152.1 (2 × *C*–OMe). IR (ATR): ν = 1594, 1627, 2229 (CN), 2837, 2937, 3061, 3318, 3386 (NH_2) cm^{-1}. MS (ESI): *m/z* (%) = 257 (76) [M + H^+], 241 (12) [M – NH_2 + 1], 240 (100) [M – NH_2], 231 (12) [M – CN + 1], 230 (91) [M – CN].

Synthesis of imines 7a–d and 10

Typical procedure. To a mixture of **5** (0.50 g, 2.16 mmol) and anhydrous $MgSO_4$ (0.78 g, 6.50 mmol) in CH_2Cl_2 (10 ml), benzaldehyde (0.23 g, 2.17 mmol) was added (2 equivalents of aldehyde for imines **7c** and **7d**). After refluxing for 4 h (2 h for imines **7c** and **7d**), the reaction mixture was filtered and concentrated *in vacuo* to give the crude imine **7a** which was used in the next step without further purification. The conversion was 86% based on ^{1}H NMR analysis. Imines **7b** and **10** were also isolated as a mixture with the corresponding aldehyde.

***N*-Benzylidene-2-(1,4-dimethoxynaphthalen-2-yl)ethanamine 7a.** The crude reaction mixture contained 10–15% of benzaldehyde after washing with petroleum ether (to remove the non reacted amine **5**). Pale yellow oil. δ_H (250 MHz; $CDCl_3$) 3.22 (2H, t, *J* = 7.3 Hz, CH_2), 3.88 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 3.91–3.99 (2H, m, CH_2N), 6.67 (1H, s, H-3), 7.39–7.54 (5H, m, Ph), 7.69–7.73 (2H, m, H-6, H-7), 8.01–8.05 (1H, m, H-8), 8.17–8.21 (2H, m, H-5; s, HC=N). δ_C (63 MHz; $CDCl_3$) 31.7 (CH_2), 55.5 (OCH_3), 62.2 (OCH_3), 62.4 (CH_2N), 106.2 (C-3), 121.7 and 122.2 (C-5, C-8), 124.8 (C-6), 125.5 (=C_{quat}), 126.4 (C-7), 127.7 (= C_{quat}), 128.0 (=CH), 128.55 (=CH), 128.59 (=C_{quat}), 130.6 (=CH), 136.1 (=C_{quat}), 147.2 and 151.5 (2 × *C*–OMe), 161.5 (CH=N). IR (ATR): ν 1627, 1644 (C=N), 3062 cm^{-1}. MS (70 eV, *m/z* (%)): 320 (2) [M + 1], 319 (20) [M], 288 (100), 201 (49), 170 (26), 128 (21), 118 (60), 115 (20), 91 (92).

***N*-(4-Chlorobenzylidene)-2-(1,4-dimethoxynaphthalen-2-yl)ethanamine 7b.** Pale yellow oil. δ_H (250 MHz; $CDCl_3$) 3.21 (2H, t, *J* = 7.3 Hz, CH_2), 3.89 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 3.93–3.96 (2H, m, CH_2N), 6.64 (1H, s, H-3), 7.35–7.38 (2H, m, Ar), 7.50–7.53 (2H, m, H-6, H-9), 7.63–7.65 (2H, m, Ar), 8.01–8.03 (1H, m, H-8), 8.15 (1H, s, HC=N), 8.18–8.20 (1H, m, H-5). δ_C (63 MHz; $CDCl_3$) 31.7 (CH_2), 55.5 (OCH_3), 62.2 (OCH_3), 62.3 (CH_2N), 106.1 (C-3), 121.7 and 122.3 (C-5, C-8), 124.9 (C-6), 125.6 (=C_{quat}), 126.5 (C-7), 127.6 (=C_{quat}), 128.9 (=CH), 129.2 (=CH), 130.9 (=C_{quat}), 134.6 (=C_{quat}), 136.5 (=C_{quat}), 147.3 and 151.5 (2 × *C*–OMe), 160.1 (CH=N). IR (ATR): ν 1595, 1643 (C=N), 2836, 2935, 3066 cm^{-1}. MS (70 eV, *m/z* (%)): 355 (8) [M + 2], 353 (22) [M], 324 (30) [M – OMe + 2], 323 (17) [M – OMe + 1], 322 (87) [M – OMe], 202 (11), 201 (100), 186 (45), 171 (20), 170 (32), 154 (12), 152 (86), 128 (39), 127 (37), 125 (72), 115 (32), 89 (25).

***N*-(2,2-Dimethylpropylidene)-2-(1,4-dimethoxynaphthalen-2-yl)ethanamine 7c.** Colorless oil. δ_H (250 MHz; $CDCl_3$) 0.98 (9H, s, $(CH_3)_3C$), 3.08 (2H, t, *J* = 7.3 Hz, CH_2), 3.70 (2H, t, *J* = 7.3 Hz, CH_2), 3.89 (3H, s, OCH_3), 3.95 (3H, s, OCH_3), 6.64 (1H, s, H-3), 7.38 (1H, t, *J* = 1.1 Hz, HC=N), 7.39–7.54 (2H, m, H-6, H-7), 7.99–8.03 (1H, m, H-5), 8.17–8.21 (1H, m, H-8). δ_C (63 MHz; $CDCl_3$) 26.8 ($(CH_3)_3C$), 31.9 (CH_2), 35.9 ($(CH_3)_3C$), 55.6 (OCH_3), 61.8 (CH_2N), 62.1 (OCH_3), 106.3 (C-3), 121.7 and 122.2 (C-5, C-8), 124.7 and 126.4 (C-6, C-7), 125.5 (=C_{quat}), 127.7 (=C_{quat}), 128.6 (=C_{quat}), 147.3 and 151.4 (2 × *C*–OMe), 172.6 (CH=N). IR (ATR): ν 1595, 1664 (C=N), 2836, 2950 cm^{-1}. MS (70 eV, *m/z* (%)): 299 (63) [M], 268 (82), 200 (54), 185 (88), 170 (65), 127 (96), 115 (61), 98 (95), 69 (67), 56 (100).

***N*-(2-Methylpropylidene)-2-(1,4-dimethoxynaphthalen-2-yl)ethanamine 7d.** Colorless oil. δ_H (250 MHz; $CDCl_3$) 1.01 (6H, d, *J* = 6.8 Hz, $(CH_3)_2CH$), 2.38 (1H, m, $(CH_3)_2CH$), 3.09 (2H, t, *J* = 7.4 Hz, CH_2), 3.69 (2H, t, *J* = 7.4 Hz, CH_2N), 3.89 (3H, s, OCH_3), 3.96 (3H, s, OCH_3), 6.63 (1H, s, H-3), 7.41–7.44 (2H, m, H-6, H-7), 7.49 (1H, m, HC=N), 8.01 (1H, d, *J* = 8.3 Hz, H-8), 8.19 (1H, d, *J* = 8.3 Hz, H-5). δ_C (125 MHz; $CDCl_3$) 19.2 ($(CH_3)_2CH$), 31.9 (CH_2), 33.9 ($(CH_3)_2CH$), 55.6 (OCH_3), 61.8 (CH_2N), 62.1 (OCH_3), 106.3 (C-3), 121.7 and 122.2 (C-5, C-8), 124.8 and 126.4 (C-6, C-7), 125.6 (=C_{quat}), 127.7 (=C_{quat}), 128.6 (=C_{quat}), 147.3 and 151.5 (2 × *C*–OMe), 170.3 (CH=N). IR (ATR): ν 1596, 1669 (C=N), 2836, 2936, 2958 cm^{-1}. MS (70 eV, *m/z* (%)): 287 (48) [M + H^+ + 1], 286 (100) [M + H^+], 232 (81), 215 (43), 200 (33).

2-(4-Chlorobenzylideneamino)-3-(1,4-dimethoxynaphthalen-2-yl)propanenitrile 10. Brown oil. δ_H (250 MHz; $CDCl_3$) 3.36 (1H, dd, *J* = 13.4 Hz, *J* = 7.4 Hz, C*H*(H)), 3.50 (1H, dd, *J* = 13.4, 6.9 Hz, CH(*H*)), 3.88 (3H, s, OCH_3), 3.94 (3H, s, OCH_3), 4.96 (1H, dt, *J* = 7.2, 1.4 Hz, CHCN), 6.63 (1H, s, H-3), 7.38 (2H, d, *J* = 8.5 Hz), 7.43–7.56 (2H, m, H-6, H-7), 7.67 (2H, d, *J* = 8.5 Hz), 8.00–8.04 (1H, m, H-8), 8.19–8.24 (1H, m, H-5), 8.29 (1H, d, *J* = 1.3 Hz, HC=N). δ_C (63 MHz; $CDCl_3$) 35.8 (CH_2), 55.5 (OCH_3), 59.2 (CHCN), 62.3 (OCH_3), 106.0 (C-3), 117.9 (CN), 121.9 and 122.4 (C-5, C-8), 123.1 (=C_{quat}), 125.5 (C-6), 126.2 (=C_{quat}), 126.7 (C-7), 129.0 (=CH), 129.4 (=C_{quat}), 129.8 (=CH), 133.3 (=C_{quat}), 137.8 (=C_{quat}), 148.0 and 151.6 (2 × *C*–OMe), 162.0 (CH=N). IR (ATR): ν 1595, 1640 (C=N), 2837, 2933 cm^{-1}. MS (70 eV, *m/z* (%)): 380 (18) [M + 2], 379 (12) [M + 1], 378 (52) [M], 202 (13), 201 (100) [M – ArCH=NCHCN], 186 (27), 171 (12), 170 (21), 150 (12), 128 (19), 115 (16).

Reaction of imine 7a with CCl_3COCl without Lewis acid

A solution of trichloroacetyl chloride (0.28 g, 1.54 mmol) in 1,2-dichloroethane (1 ml) was added dropwise to a solution of imine **7a** (0.44 g, 1.38 mmol) in 1,2-dichloroethane (5 ml). The mixture was stirred at room temperature for 30 min and then heated to reflux for 3 h. After cooling, the reaction mixture was poured into water (20 ml), extracted with CH_2Cl_2 (3 × 20 ml), dried ($MgSO_4$) and evaporated. The products were isolated by column chromatography on silica gel.

2,2,2-Trichloro-1-(*trans*-4-chloro-6-methoxy-1-phenyl-3,4-dihydrobenzo[*h*]isoquinolin-2(1*H*)-yl)ethanone 14. Yield 0.225 g (35%). Colorless crystals, mp 204.6 – 205.2 °C (from EtOAc–Et_2O). R_f = 0.57 (petroleum ether/EtOAc: 2/1). δ_H (250 MHz, 25 °C, ratio minor:major = 1 : 2.2; $CDCl_3$) 3.51 (minor) and 3.91 (major) (1H, d, *J* = 15.0 Hz, C(*H*)H), 4.07 (3H, s, OCH_3), 4.99 (1H, d, *J* = 15.0 Hz, C(H)*H*)), 5.24 (minor) and 5.39 (major) (1H, br s, H-4), 6.82 (1H, s, H-5), 7.10–7.30 (5H, m, Ph), 7.40–7.65 (4H, m, H-8, H-9, H-10, H-1), 8.27–8.38 (1H, m, H-7). δ_H (250 MHz, 50 °C; $CDCl_3$) 3.20–3.95 (1H, br s, C(*H*)H), 4.08 (3H, s, OCH_3), 5.00 (1H, d, *J* = 15.0 Hz, C(H)*H*)), 5.33 (1H, br s, H-4), 6.84 (1H, s, H-5), 7.12–7.25 (5H, m, Ph), 7.40–7.51 (2H, m, H-8, H-9), 7.56 (1H, s, H-1), 7.62–7.66 (1H, m, H-10), 8.29–8.33 (1H, m, H-7). δ_C (63 MHz, 25 °C; $CDCl_3$) 46.8 (minor) and 47.0 (major) (C-3), 55.6 (minor) and 55.7 (major) (OCH_3), 56.3 (major) and 57.5 (minor) (C-1), 69.1 (minor) and 77.2 (major) (C-4), 86.8 (minor) and

93.0 (major) (CCl_3), 103.6 (major) and 104.8 (minor) (C-5), 121.5 (=C_{quat}), 122.6 (major) and 123.3 (minor) (=CH), 122.8 (=C_{quat}), 124.3 (=CH), 126.3 (=CH), 127.7 (=CH), 128.3 (=CH), 128.4 (=CH), 128.7 (=CH), 130.7 (minor) and 131.1 (major) (=C_{quat}), 138.0 (minor) and 139.5 (major) (=C_{quat}), 155.6 (C-6), 160.5 (C=O). ^{13}C NMR δ_C (125 MHz, 50 °C, $CDCl_3$) 47.2 (C-3), 55.7 (OCH_3), 57.5 (C-1), 93.2 (CCl_3), 103.9 (C-5), 121.8 (=C_{quat}), 122.7 (=CH), 124.2 (=C_{quat}), 126.3 (=CH), 127.8 (=CH), 128.3 (=CH), 128.7 (=CH), 131.0 (=C_{quat}), 139.5 (=C_{quat}), 155.8 (C-6), 160.5 (C=O). IR (ATR): ν 1589, 1628, 1666 (C=O), 2908, 2944, 3014, 3068 cm^{-1}. MS (ESI): *m/z* (%) = 472 (15) [M + H$^+$ + 4], 470 (26) [M + H$^+$ + 2], 468 (23) [M + H$^+$], 442 (27) [M – OCH_2 + H$^+$ + 4], 440 (100) [M – OCH_2 + H$^+$ + 2], 438 (86) [M – OCH_2 + H$^+$], 434 (30), 432 (32), 338 (43), 147 (30), 145 (68). Variable-temperature ^{1}H NMR (250 MHz, $CDCl_3$): 297 K (ratio 1 : 2.2), 313 K, 323 K; ^{13}C NMR (125 MHz, $CDCl_3$): 298 K, 323 K.

2,2,2-Trichloro-*N*-(2-(1,4-dimethoxynaphthalen-2-yl)ethyl)-acetamide 13a. Yield 0.05 g (9%). Colorless oil. R_f = 0.39 (petroleum ether/EtOAc : 2/1). δ_H (250 MHz, $CDCl_3$) 3.05–3.11 (2H, m, CH_2), 3.63–3.71 (2H, m, CH_2N), 3.92 (3H, s, OCH_3), 3.98 (3H, s, OCH_3), 6.58 (1H, s, H-3), 7.44–7.58 (3H, m, H-6, H-7, NH), 7.98–8.02 (1H, m, H-8), 8.20–8.25 (1H, m, H-5). δ_C (63 MHz, $CDCl_3$) 29.7 (CH_2N), 42.7 (CH_2), 55.7 (OCH_3), 61.9 (OCH_3), 92.5 (CCl_3), 105.3 (C-3), 121.6 (=CH), 122.4 (=CH), 125.3 (=CH), 125.9 (=C_{quat}), 126.0 (=C_{quat}), 126.9 (=CH), 128.4 (=C_{quat}), 147.1 and 152.3 (2 × *C*–OMe), 162.1 (C=O). IR (ATR): ν 1595, 1693 (C=O), 2836, 2936, 3068, 3333 (NH) cm^{-1}. MS (ESI): *m/z* (%) = 379 (25) [M + H$^+$ + 4], 378 (100) [M + H$^+$ + 2], 376 (95) [M + H$^+$], 348 (15) [M – OCH_3 + H$^+$ + 4], 346 (43) [M – OCH_3 + H$^+$ + 2], 344 (42) [M – OCH_3 + H$^+$], 232 (30), 199 (14), 183 (16).

Preparation of 2,2,2-trichloro-*N*-(2-(1,4-dimethoxynaphthalen-2-yl)ethyl)acetamide 13a

To a cooled (0 °C) solution of **5** (0.2 g, 0.86 mmol) in dry pyridine (1 ml), trichloroacetyl chloride (0.16 g, 0.88 mmol) was added dropwise. The reaction was stirred at room temperature for 2 h. Then, the mixture was poured into 2 M HCl (5 ml), extracted with CH_2Cl_2, dried ($MgSO_4$) and evaporated. The product was isolated by column chromatography (silica gel, petroleum ether/EtOAc : 2/1). Yield 185 mg (57%)

Oxidation of 3,4-dihydrobenzo[*h*]isoquinoline by CAN

To a cooled (0 °C) solution of **14** (0.12 g, 0.25 mmol) in acetonitrile (70 ml) was added dropwise a solution of CAN (0.46 g, 0.84 mmol) in water (7 ml). The reaction was stirred at room temperature for 2 h. Then the mixture was poured into brine, extracted with ethyl acetate, dried ($MgSO_4$) and evaporated. The product was purified by column chromatography. Yield 50 mg (62%).

4-Chloro-1-phenyl-2-(2,2,2-trichloroacetyl)-3,4-dihydrobenzo-[*h*]isoquinolin-6(2*H*)-one 15. Orange crystals, mp 210.0–211.0 °C (EtOAc). R_f = 0.27 (petroleum ether/EtOAc : 6/1). δ_H (250 MHz, $CDCl_3$) 3.68 (1H, m, C(*H*)H)), 4.94 (1H, d, *J* = 15.0 Hz, C(H)*H*)), 5.37 (1H, br s, H-4), 7.23 (1H, s, H-5), 7.32–7.60 (8H, m, Ph), 8.17–8.20 (1H, m, H-7). ^{13}C NMR δ_C (63 MHz, DMSO-d_6) 49.1 (C-3), 55.1 (C-4), 92.4 (CCl_3), 127.5 (=CH), 128.3 (=CH), 128.9 (=CH), 129.1 (=CH), 130.6 (=CH), 131.9 (=C_{quat}), 132.3 (=C_{quat}), 134.9 (=CH), 136.9 (=C_{quat}), 143.9 (=C_{quat}), 159.8 (CCl_3C=O), 176.9 (C=O). IR (ATR): ν 1595, 1708 (C=O), 1676 (NC=O), 2922 cm^{-1}. MS (ESI): no molecular ion.

Reaction of imine 7d with acetyl chloride

To a solution of imine **7d** (0.45 g, 1.58 mmol) in 1,2-dichloroethane (5 ml) a solution of acetyl chloride (0.14 g, 1.78 mmol) in 1,2-dichloroethane (1 ml) was added dropwise and the mixture was stirred at room temperature for 30 min and then heated to reflux for 3 h. After cooling the mixture was poured into water (20 ml), extracted with CH_2Cl_2 (3 × 20 ml), dried ($MgSO_4$) and evaporated. The product was purified by column chromatography. R_f = 0.37 (petroleum ether/EtOAc : 1/2). Pale yellow oil. Yield 0.13 g (25%).

***N*-(2-(1,4-Dimethoxynaphthalen-2-yl)ethyl)-*N*-(2-methylprop-1-enyl)acetamide (21).** ^{1}H NMR δ_H (250 MHz, $CDCl_3$) 1.63 and 1.74 (2 × 3H, 2×d, *J* = 1.3 Hz, (CH_3)$_2$C), 1.99 (3H, s, CH_3), 2.98–3.05 (2H, m, CH_2), 3.69–3.76 (2H, m, CH_2N), 3.89 (3H, s, OCH_3), 3.98 (3H, s, OCH_3), 5.84 (1H, m, =CH), 6.68 (1H, s, H-3), 7.40–7.55 (2H, m, H-6 and H-7), 7.99–8.03 (1H, m, H-8), 8.18–8.22 (1H, m, H-5).^{13}C NMR δ_C (63 MHz, $CDCl_3$) 17.5 (CH_3), 21.7 (CH_3), 22.0 (CH_3), 28.1 (CH_2), 47.9 (CH_2N), 55.6 (OCH_3), 61.9 (OCH_3), 105.5 (C-3), 121.6 (=CH), 122.2 (=CH), 124.3 (=CH), 124.8 (=CH), 125.5 (=C_{quat}), 126.4 (=CH), 126.9 (=C_{quat}), 128.5 (=C_{quat}), 135.5 (=C_{quat}), 147.2 and 151.7 (2 × *C*–OMe), 170.7 (C=O). IR (ATR): ν 1596, 1636 (C=O), 2847, 2935 cm^{-1}. MS (ESI): *m/z* (%) = 329 (13) [M + H$^+$ + 1], 328 (100) [M + H$^+$].

Reaction of imines 10, 7a–c with acyl chlorides

Typical procedure. To a solution of imine **10** (1.06 g, 2.8 mmol) in 1,2-dichloroethane (50 ml), KI (30 mg, 0.18 mmol) and molecular sieves (3 Å) were added. Then a solution of acetyl chloride (0.246 g, 3.08 mmol) in 1,2-dichloroethane (1 ml) was added dropwise and after stirring the mixture at room temperature for 30 min, anhydrous $AlCl_3$ (0.38 g, 2.8 mmol) was added and heating was applied to reflux for 3 h. After cooling, the mixture was filtered, poured into water and extracted by CH_2Cl_2 (3 × 20 ml). The combined extracts were washed by brine, dried ($MgSO_4$) and evaporated. The product was isolated by column chromatography. Yield 0.26 g (22%). Pale yellow crystals, mp 139.5–140.2 °C (CH_2Cl_2–Et_2O). R_f = 0.59 (petroleum ether/EtOAc : 1/2).

***N*-(4-Chlorobenzyl)-*N*-(1-cyano-2-(1,4-dimethoxynaphthalen-2-yl)vinyl)acetamide (22).** ^{1}H NMR δ_H (250 MHz, $CDCl_3$) 2.44 (3H, s, CH_3), 3.88 (3H, s, OCH_3), 3.98 (3H, s, OCH_3), 4.23 (2H, m, CH_2Ar), 6.85 (1H, s, H-3), 7.37–7.54 (4H, m, H-6, H-7, Ar), 7.73–7.77 (2H, m, Ar), 8.03–8.07 (1H, m, H-8), 8.15–8.20 (1H, m, H-5), 8.44 (1H, s, HC=).^{13}C NMR δ_C (63 MHz, $CDCl_3$) 14.5 (CH_3C=O), 26.1 (CH_2Ar), 55.5 (OCH_3), 62.3 (OCH_3), 105.8 (C-3), 121.9 (=CH), 122.2 (=CH), 124.9 (=CH), 125.7 (=C_{quat}), 126.4 (=CH), 126.6 (=C_{quat}), 128.6 (=C_{quat}), 129.0 (=CH), 129.4 (=CH), 134.0 (=C_{quat}), 134.8 (=C_{quat}), 136.9 (=C_{quat}), 147.0 (=C_{quat}), 149.0 (=C_{quat}), 151.4 (HC=), 151.7 (=C_{quat}), 158.2 (C=O). IR (ATR): ν 1560, 1596, 1613 (C=O), 2836, 2937, 2967, 2993, 3065 cm^{-1}. MS (ESI): *m/z* (%) = 423 (31) [M + H$^+$ + 2], 421 (100) [M + H$^+$].

2-(2,2,2-Trichloroacetyl)-5,10-dimethoxy-1-phenyl-1,2,3,4-tetrahydrobenzo[*g*]isoquinoline (12a). Scale of the reaction: 3.13 mmol imine **7a** (1.0 g). Colorless crystals, mp 143.3–144.3 °C

(Et_2O). R_f = 0.5 (petroleum ether/EtOAc : 6/1). Yield 0.6 g (41%). ^{1}H NMR δ_H (250 MHz, 24 °C, $CDCl_3$) 3.11–3.36 (2H, m, H-4), 3.49–3.62 (1H, m, NC(*H*)H), 3.79 and 3.93 (6H, 2×s, 2×OCH_3), 4.52–4.58 (1H, m, NC(H)*H*), 7.14–7.17 (2H, m, Ph), 7.25–7.29 (3H, m, Ph), 7.33 (1H, s, H-1), 7.47–7.59 (2H, m, H-7, H-8), 8.02–8.13 (2H, m, H-6, H-9).^{13}C NMR δ_C (63 MHz, 24 °C, $CDCl_3$) 23.3 (C-4), 41.0 (C-3), 54.6 (C-1), 61.2 (OCH_3), 62.1 (OCH_3), 93.4 (CCl_3), 122.2 (=CH), 122.7 (=CH), 123.2 (=C_{quat}), 124.3 (=C_{quat}), 125.9 (=CH), 126.4 (=C_{quat}), 127.2 (=C_{quat}), 127.89 (=CH), 127.95 (=CH), 128.0 (=C_{quat}), 128.6 (=CH), 140.4 (=C_{quat}), 149.3 and 149.7 (2×*C*–OMe), 160.0 (C=O). IR (ATR): ν 1670 (C=O), 2840, 2936 cm^{-1}. MS (ESI): *m*/*z* (%) = 468 (16) [M + H^+ + 4], 466 (53) [M + H^+ + 2], 464 (54) [M + H^+], 428 (10) [M – Cl], 405 (21), 404 (100), 225 (26), 200 (22). HRMS (ESI): *m*/*z* calcd for $C_{23}H_{20}Cl_3NO_3$ + H^+: 464.0582; found 464.0563. HMBC and HMQC were recorded for the correct assignment of the NMR signals.

2-(2,2,2-Trichloroacetyl)-5,10-dimethoxy-1-(4-chlorophenyl)-1,2,3,4-tetrahydrobenzo[*g*]isoquinoline (12b). Scale of the reaction: 1.2 mmol imine **7b** (0.41 g). Colorless crystals, mp 166.0–166.7 °C (Et_2O). R_f = 0.5 (petroleum ether/EtOAc : 6/1). Yield 0.21 g (36%). ^{1}H NMR δ_H (250 MHz, 22 °C, $CDCl_3$) 3.13–3.35 (2H, m, H-4), 3.43–3.56 (1H, m, NC(H)*H*), 3.81 and 3.93 (6H, 2×s, 2×OCH_3), 4.53–4.59 (1H, m, NC(*H*)H), 7.08–7.12 (2H, m, Ar), 7.23–7.27 (3H, m, Ar, H-1), 7.49–7.60 (2H, m, H-7, H-8), 8.01–8.13 (2H, m, H-6, H-9).^{13}C NMR δ_C (63 MHz, 23 °C, $CDCl_3$) 23.2 (C-4), 41.0 (C-3), 54.0 (C-1), 61.2 (OCH_3), 62.1 (OCH_3), 93.1 (CCl_3), 122.2 (=CH), 122.7 (=CH), 123.0 (=C_{quat}), 123.7 (=C_{quat}), 126.1 (=CH), 126.6 (=CH), 127.2 (=C_{quat}), 128.2 (=C_{quat}), 128.8 (=CH), 129.3 (=CH), 133.8 (=C_{quat}), 139.1 (=C_{quat}), 149.2 and 149.8 (2 × *C*–OMe), 160.0 (C=O). IR (ATR): ν 1669 (C=O), 2841, 2945, 2990 cm^{-1}. MS (ESI): *m*/*z* (%) = 502 (38) [M + H^+ + 4], 501 (46) [M + 4], 500 (73) [M + H^+ + 2], 499 (100) [M + 2], 498 (57) [M + H^+], 497 (86) [M], 464 (50) [M – Cl + 2], 462 (57) [M – Cl]. HRMS (ESI): *m*/*z* calcd for $C_{23}H_{19}Cl_4NO_3$ + H^+: 498.0192; found 498.0169.

2-(2,2,2-Trichloroacetyl)-5,10-dimethoxy-1-*tert*-butyl-1,2,3,4-tetrahydrobenzo[*g*]isoquinoline (12c). Scale of the reaction: 1.6 mmol imine **7c** (0.49 g). Colorless crystals, mp 177.5–178.3 °C (Et_2O). R_f = 0.58 (petroleum ether/EtOAc : 6/1). Yield 0.255 g (35%). ^{1}H NMR δ_H (250 MHz, 22 °C, $CDCl_3$) 1.07 (9H, s, $C(CH_3)_3$), 3.07–3.18 (1H, m, C(*H*)H), 3.29–3.44 (1H, m, C(H)*H*), 3.91 and 3.94 (6H, 2×s, 2×OCH_3), 4.00–4.16 (1H, m, NC(*H*)H), 4.66–4.77 (1H, m, NC(H)*H*), 6.06 (1H, s, H-1), 7.49–7.54 (2H, m, H-7, H-8), 8.03–8.12 (2H, m, H-6, H-9).^{13}C NMR δ_C (63 MHz, 24 °C, $CDCl_3$) 21.9 (C-4), 28.8 ($C(CH_3)_3$), 39.2 ($C(CH_3)_3$), 42.1 (C-3), 57.7 (C-1), 61.0 (OCH_3), 62.4 (OCH_3), 93.9 (CCl_3), 121.9 (=CH), 122.9 (=CH), 123.1 (=C_{quat}), 124.8 (=C_{quat}), 125.8 (=CH), 126.3 (=CH), 127.5 (=C_{quat}), 127.8 (=C_{quat}), 149.2 and 149.3 (2 × *C*–OMe), 160.4 (C=O). IR (ATR): ν 1663 (C=O), 2838, 2935, 2950, 2967, 2990 cm^{-1}. MS (ESI): *m*/*z* (%) = 448 (16) [M + H^+ + 4], 446 (49) [M + H^+ + 2], 444 (47) [M + H^+], 272 (36), 242 (9), 224 (100). HRMS (ESI): *m*/*z* calcd for $C_{21}H_{24}Cl_3NO_3$ + H^+: 444.0895; found 444.0912.

2-Acetyl-5,10-dimethoxy-1-(4-chlorophenyl)-1,2,3,4-tetrahydrobenzo[*g*]isoquinoline (12d). Scale of the reaction: 1.1 mmol imine **7b** (0.40 g). Colorless oil. R_f = 0.34 (petroleum ether/EtOAc : 1/2). Yield 0.155 g (35%). ^{1}H NMR δ_H (250 MHz, 24 °C, ratio minor/major : 1/3, $CDCl_3$) 2.23 (major) and 2.36 (minor) (3H, s, CH_3), 2.91–3.26 (2H, m, H-4), 3.51–3.78 (2H, m, H-3), 3.84 (major) and 3.86 (minor) (3H, s, OCH_3), 3.91 (major and minor) (3H, s, OCH_3), 6.51 (minor) and 7.35 (major) (1H, br s, H-1), 7.08–7.13 (2H, m, CH_{Ar}), 7.18–7.28 (2H, m, CH_{Ar}), 7.51–7.59 (2H, m, H-7, H-8), 8.04–8.13 (2H, m, H-6, H-9).^{13}C NMR δ_C (125 MHz, 24 °C, $CDCl_3$) 21.4 (minor) and 22.9 (major) (C-4), 21.8 (major) and 22.0 (minor) (CH_3), 39.0 (minor) and 41.0 (major) (C-3), 50.0 (major) and 54.9 (minor) (C-1), 61.6 and 62.3 (major, 2×OCH_3), 61.8 and 62.6 (minor, 2×OCH_3), 122.2 and 122.7 (major, =CH), 122.5 and 122.6 (minor, =CH), 123.9 (major) and 124.4 (minor) (=C_{quat}), 125.5 (=C_{quat}), 126.0 and 126.4 (major, =CH), 126.1 and 126.6 (minor, =CH), 127.0 (minor) and 127.4 (major) (=C_{quat}), 127.9 (=CH), 128.2 (major) and 128.6 (minor) (=C_{quat}), 128.4 and 128.8 (=CH), 133.0 (major) and 133.5 (minor) (=C_{quat}), 139.1 (minor) and 140.2 (major) (=C_{quat}), 148.1 and 149.7 (minor, 2 × *C*–OMe), 149.1 and 149.5 (major, 2 × *C*–OMe), 169.7 (major) and 170.1 (minor) (C=O). IR (ATR): ν 1637 (C=O), 2838, 2936 cm^{-1}. MS (ESI): *m*/*z* (%) = 398 (9) [M + H^+ + 2], 396 (25) [M + H^+], 300 (13), 293 (15), 292 (100). HRMS (ESI): *m*/*z* calcd for $C_{23}H_{22}ClNO_3$ + H^+: 396.1361; found 396.1343.

2-Acetyl-5,10-dimethoxy-1-*tert*-butyl-1,2,3,4-tetrahydrobenzo-[*g*]isoquinoline (12e). Scale of the reaction: 1.1 mmol imine **7c** (0.33 g). Colorless crystals, mp 147.5–147.7 °C (Et_2O-pentane). R_f = 0.35 (petroleum ether/EtOAc : 1/2). Yield 0.155 g (41%). ^{1}H NMR δ_H (250 MHz, 25 °C, ratio minor/major : 1/3, $CDCl_3$) 1.01 (major) and 1.04 (minor) (9H, s, $(CH_3)_3C$), 2.18 (major) and 2.34 (minor) (3H, s, CH_3), 3.07–3.20 (1H, m, C(*H*)H), 3.30–3.46 (1H, m, C(H)*H*), 3.58–3.70 (1H, m, NC(*H*)H), 3.82–4.00 (1H, m, NC(H)*H*), 3.88 (minor) and 3.89 (major) (3H, s, OCH_3), 3.91 (major) and 3.92 (minor) (3H, s, OCH_3), 5.22 (minor) and 6.18 (major) (1H, s, H-1), 7.48–7.54 (2H, m, H-7, H-8), 8.04–8.13 (2H, m, H-6, H-9).^{13}C NMR δ_C (63 MHz, 25 °C, $CDCl_3$) 20.8 (minor) and 21.8 (major) (C-4), 22.6 (minor) and 22.7 (major) (CH_3), 28.8 (major) and 28.9 (minor) ((CH_3)$_3$C), 38.2 (minor) and 42.8 (major) (C-3), 39.1 (major) and 39.7 (minor) ((CH_3)$_3$*C*), 54.2 (C-1), 59.9 and 61.3 (minor, 2×OCH_3), 61.7 and 62.3 (major, 2×OCH_3), 122.0 and 122.9 (major, =CH), 122.2 and 122.8 (minor, =CH), 124.1 (major) and 124.2 (minor) (=C_{quat}), 125.7 (=CH), 126.1 (major) and 126.2 (minor) (=CH), 126.5 (=C_{quat}), 127.5 (=C_{quat}), 127.8 (=C_{quat}), 148.8 and 149.3 (2 × *C*–OMe), 170.5 (minor) and 171.1 (major) (C=O). IR (ATR): ν 1639 (C=O), 2839, 2870, 2955 cm^{-1}. MS (ESI): no molecular ion was observed. Anal. calcd. for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97; N, 4.10. Found: C, 73.91; H, 8.00; N, 4.03. Variable temperature ^{1}H NMR (250 MHz, $CDCl_3$): 297 K, 321 K. ^{1}H NMR (250 MHz, DMSO-d_6): 297 K, 308 K, 318 K, 328 K, 338 K, 348 K. Signals became broader, but the ratio did not change substantially.

Oxidation of *N*-acyltetrahydro[*g*]isoquinolines 12

Typical procedure. To a mixture of **12a** (0.075 g, 0.16 mmol) and silver(II) oxide (0.08 g, 0.64 mmol) in 1,4-dioxane (5 ml) was added dropwise 6 M HNO_3 (0.7 ml), and the reaction was kept for 16 h at 50 °C. The reaction mixture was poured into a saturated solution of $NaHCO_3$ and extracted with Et_2O (3 × 20 ml). The combined ether extracts were dried ($MgSO_4$) and concentrated. The product was isolated by column chromatography. R_f = 0.70 (petroleum

ether/EtOAc : 2/1). Yellow crystals, mp 170.0–218.0 °C (Et_2O, decomposition). Yield 0.052 g (74%).

2-(2,2,2-Trichloroacetyl)-1-phenyl-1,2,3,4-tetrahydrobenzo[*g*]-isoquinoline-5,10-dione (23a). ^{1}H NMR δ_H (250 MHz, 24 °C, $CDCl_3$) 2.94–3.00 (2H, m, H-4), 3.33–3.47 (1H, m, NC(*H*)H), 4.57–4.64 (1H, m, NC(H)*H*), 7.00 (1H, s, H-1), 7.31–7.37 (5H, m, Ph), 7.71–7.80 (2H, m, H-7, H-8), 8.01–8.05 (1H, m, H-6), 8.12–8.16 (1H, m, H-9).^{13}C NMR δ_C (63 MHz, 25 °C, $CDCl_3$) 23.4 (C-4), 39.7 (C-3), 53.7 (C-1), 92.8 (CCl_3), 126.4 (═CH), 126.8 (═CH), 128.2 (═CH), 128.6 (═CH), 128.9 (═CH), 131.70 (═C_{quat}), 131.73 (═C_{quat}), 134.0 (═CH), 134.1 (═CH), 138.1 (═C_{quat}), 142.0 (═C_{quat}), 143.3 (═C_{quat}), 159.5 (C═O), 182.0 (C═O), 183.6 (C═O). IR (ATR): ν 1595, 1633 (C═O), 1654 (C═O), 1663 (C═O), 2850, 2919, 2950 cm^{-1}. MS (ESI): *m*/*z* (%) (with a lot of 'noise') = 438 (15) [M + H$^+$ + 4], 436 (80) [M + H$^+$ + 2], 434 (87) [M + H$^+$], 273 (100), 242 (29), 224 (90).

2-(2,2,2-Trichloroacetyl)-1-(4-chlorophenyl)-1,2,3,4-tetrahydrobenzo[*g*]isoquinoline-5,10-dione (23b). Scale of the reaction: 0.22 mmol **12b** (110 mg). Yellow crystals, mp 223.3–225.9 °C (CH_2Cl_2–Et_2O, decomposition). R_f = 0.77 (petroleum ether/EtOAc : 2/1). Yield 0.094 g (91%). ^{1}H NMR δ_H (250 MHz, 25 °C, $CDCl_3$) 2.94–2.99 (2H, m, H-4), 3.29–3.41 (1H, m, NC(H)*H*), 4.59–4.66 (1H, m, NC(*H*)H), 6.93 (1H, s, H-1), 7.32 (4H, s, Ar), 7.71–7.80 (2H, m, H-7, H-8), 8.01–8.05 (1H, m, H-6), 8.12–8.16 (1H, m, H-9).^{13}C NMR δ_C (63 MHz, 25 °C, $CDCl_3$) 23.3 (C-4), 39.7 (C-3), 53.1 (C-1), 92.7 (CCl_3), 126.5 (═CH), 126.8 (═CH), 129.2 (═CH), 129.5 (═CH), 131.6 (═C_{quat}), 134.1 (═CH), 134.2 (═CH), 134.6 (═C_{quat}), 136.7 (═C_{quat}), 141.5 (═C_{quat}), 143.5 (═C_{quat}), 159.5 (C═O), 181.9 (C═O), 183.5 (C═O). IR (ATR): ν 1593, 1639 (C═O), 1662 (C═O), 2896, 2939, 3065 cm^{-1}. MS (ESI): *m*/*z* (%) = no molecular ion.

2-(2,2,2-Trichloroacetyl)-1-*tert*-butyl-1,2,3,4-tetrahydrobenzo-[*g*]isoquinoline-5,10-dione (23c). Scale of the reaction: 0.24 mmol **12c** (106 mg). Yellow crystals, mp 216.7–218.8 °C (CH_2Cl_2–Et_2O, decomposition). R_f = 0.81 (petroleum ether/EtOAc : 2/1). Yield 0.08 g (81%). ^{1}H NMR δ_H (250 MHz, 24 °C, $CDCl_3$) 1.12 (9H, s, $C(CH_3)_3$), 2.80–3.04 (2H, m, H-4), 3.70–3.83 (1H, m, NC(H)*H*), 4.77–4.87 (1H, m, NC(*H*)H), 5.87 (1H, s, H-1), 7.71–7.80 (2H, m, H-7, H-8), 8.05–8.14 (2H, m, H-6, H-9).^{13}C NMR δ_C (63 MHz, 25 °C, $CDCl_3$) 22.8 (C-4), 29.5 ($C(CH_3)_3$), 37.9 ($C(CH_3)_3$), 41.6 (C-3), 56.0 (C-1), 93.3 (CCl_3), 126.1 (═CH), 126.9 (═CH), 131.5 (═C_{quat}), 132.2 (═C_{quat}), 133.7 (═CH), 134.0 (═CH), 142.4 (═C_{quat}), 144.4 (═C_{quat}), 159.7 (C═O), 182.8 (C═O), 183.6 (C═O). IR (ATR): ν 1595, 1628 (C═O), 1664 (C═O), 2873, 2954, 2976 cm^{-1}. MS (ESI): *m*/*z* (%) = 418 (26) [M + H$^+$ + 4], 416 (96) [M + H$^+$ + 2], 414 (100) [M + H$^+$], 379 (9) [M − Cl + 1], 378 (32) [M − Cl], 324 (18) [M − Cl–C_4H_9 + 2], 322 (32) [M − Cl– C_4H_9]. HRMS (ESI): *m*/*z* calcd for $C_{19}H_{18}Cl_3NO_3$ + H$^+$: 414.0425; found 414.0446.

Transformations of the *N*-trichloroacetyl group

Cleavage under acidic conditions. To a solution of compound **12b** (0.105 g, 0.26 mmol) in methanol (5 ml) 12 M HCl (1 ml) was added and the mixture was refluxed for 8 h. The mixture was rendered alkaline by 5% aqueous NaOH and extracted with ether (3 × 10 ml). The combined extracts were dried ($MgSO_4$) and evaporated. The product **24b** and unreacted compound **12b** were separated by column chromathography. R_f = 0.68 (petroleum ether/EtOAc : 1/1). Yield 0.005 g (10%, according to conversion). *1-(4-Chlorophenyl)benzo[g]isoquinoline-5,10-dione* (**24b**). Pale yellow crystals, mp 230.2–232.0 °C (CH_2Cl_2–Et_2O, decomposition). ^{1}H NMR δ_H (250 MHz, $CDCl_3$) 7.47 (4H, s, C_6H_4Cl), 7.82–7.86 (2H, m, H-6 and H-9), 8.15–8.20 (2H, m, d, *J* = 4.9 Hz, H-4 and H-8, overlap), 8.29–8.33 (1H, m, H-7), 9.08 (1H, d, *J* = 4.9 Hz, H-3). IR (ATR): ν 1593, 1668 (C═O), 1679 (C═O), 2849, 2917, 2955 cm^{-1}. MS (ESI): *m*/*z* (%) = 322 (33) [M + H$^+$ + 2], 321 (20) [M + H$^+$ + 1], 320 (100) [M + H$^+$].

Reactions with nucleophiles: MeOH/NaOH

To a solution of compound **12a** (0.33 g, 0.71 mmol) in methanol (5 ml) a solution of NaOH (0.1 g, 2.5 mmol) in water (1 ml) was added and the mixture was refluxed for 30 min. Methanol was evaporated and the residue was extracted with CH_2Cl_2 (3 × 10 ml). The combined extracts were dried ($MgSO_4$) and evaporated. The product was isolated by column chromatography. Yield 0.19 g (71%).

Methyl 3,4-dihydro-5,10-dimethoxy-1-phenylbenzo[*g*]isoquinoline-2(1*H*)-carboxylate (25). Colorless crystals, mp 139.9–140.6 °C (Et_2O). R_f = 0.57 (petroleum ether/EtOAc : 2/1). ^{1}H NMR δ_H (250 MHz, 22 °C, $CDCl_3$) 2.81–2.93 (1H, m, C(*H*)H), 3.04–3.21 (1H, m, C(H)*H*), 3.40–3.50 (1H, m, NC(*H*)H), 3.74 and 3.79 and 3.82 and 3.84 (3H, 4×s, CO_2CH_3), 3.89 (6H, s, OCH_3), 3.89–4.01 (1H, m, NC(H)*H*), 6.82 and 6.95 (1H, 2× br s, H-1), 7.18–7.26 (5H, m, Ph), 7.49–7.56 (2H, m, H-7 and H-8), 8.04–8.13 (2H, m, H-6 and H-9). ^{1}H NMR δ_H (250 MHz, 50 °C, $CDCl_3$) 2.78–2.90 (1H, m, C(*H*)H), 3.06–3.19 (1H, m, C(H)*H*), 3.40–3.51 (1H, m, NC(*H*)H), 3.78 and 3.80 (3H, 2×s, CO_2CH_3), 3.89 (6H, s, OCH_3), 3.80–3.95 (1H, m, NC(H)*H*), 6.90 (1H, br s, H-1), 7.15–7.24 (5H, m, Ph), 7.43–7.53 (2H, m, H-7 and H-8), 8.03–8.11 (2H, m, H-6 and H-9).^{13}C NMR δ_C (63 MHz, 24 °C, $CDCl_3$) 21.9 and 22.3 (C-4), 38.7 and 38.8 (C-3), 52.8 and 52.9 and 62.1 and 62.2 (CO_2CH_3), 53.1 and 53.2 (C-1), 61.5 (OCH_3), 122.16 and 122.26 (═CH), 122.6 and 122.7 (═CH), 124.6 (═C_{quat}), 125.7 (═CH), 126.1 (═CH), 126.3 (═C_{quat}), 127.2 and 127.3 (═CH), 128.3 (═CH), 141.5 and 141.6 (═C_{quat}), 148.4 and 148.8 (*C*–OMe), 149.4 and 149.5 (*C*–OMe), 156.1 and 156.6 (C═O). IR (ATR): ν 1684 (C═O), 2840, 2932, 2994 cm^{-1}. MS (ESI): *m*/*z* (%) = 378 (100) [M + H$^+$], 303 (15), 224 (7). Anal. Calcd for $C_{23}H_{23}NO_4$: C, 73.19; H, 6.14; N, 3.71. Found: C, 72.78; H, 6.02; N, 3.58.

Variable-temperature ^{1}H NMR (250 MHz, $CDCl_3$): 298 K, 303 K, 308 K, 313 K, 318 K, 323 K. HMQC was used for the assignment of the NMR signals.

Methyl *trans*-4-chloro-6-methoxy-1-phenyl-3,4-dihydrobenzo-[*h*]isoquinolin-2(1*H*)-carboxylate (16). The same reaction conditions were used as described above. Yield 0.015 g (51%) R_f = 0.55 (petroleum ether/EtOAc : 2/1). ^{1}H NMR δ_H (250 MHz, 25 °C, ratio minor/major = 1/1.7, $CDCl_3$) 3.53–3.61 (1H, m, C*H*(H)), 3.81 (major) and 3.94 (minor) (3H, 2×s, OCH_3), 4.05 (3H, s, OCH_3), 4.47 (major) and 4.65 (minor) (1H, 2×d, *J* = 15.0 Hz, CH(*H*)), 5.23–5.29 (1H, m, H-4), 6.76 (major) and 6.79 (minor) (1H, 2×s, H-5), 6.96 (minor) and 7.13 (major) (1H, 2×s, H-1), 7.12–7.26 (5H, m, Ph), 7.32–7.59 (3H, m, H-8, H-9, H-10),

8.24–8.29 (1H, m, H-7). No ^{13}C NMR could be recorded because of decomposition of this compound during the measurement.

Cleavage under basic conditions

To a solution of compound **12b** (0.095 g, 0.19 mmol) in acetonitrile (5 ml) a solution of NaOH (0.04 g, 0.1 mmol) in water (1 ml) was added and the mixture was refluxed for 2 h. The mixture was poured into water (20 ml) and extracted with CH_2Cl_2 (3 × 10 ml). The combined extracts were dried ($MgSO_4$) and evaporated. The product was used for the oxidation without purification. Pale yellow oil. Crude yield 0.06 g (89%). *1-(4-Chlorophenyl)-1,2,3,4-tetrahydro-5,10-dimethoxybenzo[g]isoquinoline* (**32**). ^1H NMR δ_H (250 MHz, $CDCl_3$) 2.08 (1H, br s, NH), 2.99–3.05 (4H, m, H-4, H-3), 3.58 (3H, s, OCH_3), 3.94 (3H, s, OCH_3), 5.55 (1H, s, H-1), 7.07–7.26 (4H, m, Ar), 7.41–7.53 (2H, m, H-7, H-8), 7.92–7.96 (1H, m, H-6), 8.08–8.11 (1H, m, H-9).^{13}C NMR δ_C (63 MHz, $CDCl_3$) 23.9 (C-4), 37.5 (C-3), 55.3 (C-1), 61.0 (OCH_3), 61.4 (OCH_3), 122.1 (═CH), 122.4 (═CH), 125.4 (═CH), 125.8 (═CH), 126.8 (═C_{quat}), 1126.9 (═C_{quat}), 127.8 (═C_{quat}), 128.3 (═CH), 129.1 (═C_{quat}), 129.4 (═CH), 132.7 (═C_{quat}), 143.2 (═C_{quat}), 148.9 and 149.6 (2 × *C*–OMe). IR (ATR): ν 1589, 2838, 2932, 3070, 3329 (NH) cm^{-1}. MS (ESI): *m/z* (%) = 356 (26) [M + H^+ + 2], 355 (18) [M + H^+ + 1], 354 (100) [M + H^+]. HRMS (ESI): *m/z* calcd for $C_{21}H_{20}ClNO_2$ + H^+: 354.1255; found 354.1237.

Reactions with nucleophiles: *n*-propylamine

To compound **12c** (0.1 g, 0.22 mmol), excess propylamine (1 ml) was added and the mixture was refluxed for 21 h. Then the mixture was evaporated, water (15 ml) was added and the organic material was extracted with CH_2Cl_2 (3 × 10 ml). The combined extracts were dried ($MgSO_4$) and evaporated. The product and unreacted compound **12c** were separated by column chromatography. R_f = 0.42 (petroleum ether/EtOAc : 1/1). Yield 0.06 g (81%, taking into account a conversion of 80%).

2-(1-*tert*-Butyl-3,4-dihydro-5,10-dimethoxybenzo[*g*]isoquinolin-2(1*H*)-yl)-2-oxo-*N*-propylacetamide (27). ^1H NMR δ_H (250 MHz, 24 °C, $CDCl_3$) 0.96–1.00 (3H, m, CH_3), 1.01 and 1.05 (9H, 2×s, $C(CH_3)_3$), 1.53–1.65 (2H, m, CH_2), 3.05–3.50 (4H, m, H-4, CH_2N), 3.71–3.80 (1H, m, NC(*H*)H), 3.89 and 4.00 (6H, 2×s, OCH_3), 4.26–4.50 (1H, m, NC(H)*H*), 6.09 and 6.84 (1H, 2×s, H-1), 7.21 and 7.41 (1H, 2×br s, NH), 7.48–7.52 (2H, m, H-7, H-8), 8.05–8.08 (2H, m, H-6, H-9).^{13}C NMR δ_C (63 MHz, 25 °C, $CDCl_3$) 10.1 and 11.3 (CH_3), 20.6 and 21.0 and 22.43 and 22.46 (C-4, CH_2), 28.6 and 28.7 ($C(CH_3)_3$), 39.0 and 39.5 ($C(CH_3)_3$), 40.2 and 41.1 and 41.2 and 41.7 (C-3, CH_2N), 55.5 and 57.8 (C-1), 61.3 (OCH_3), 62.1 and 62.5 (OCH_3), 122.0 (═CH), 122.8 and 123.0 (═CH), 123.5 and 123.9 (═C_{quat}), 125.4 and 125.5 (═C_{quat}), 125.6 and 125.7 (═CH), 126.09 and 126.11 (═CH), 127.2 and 127.3 (═C_{quat}), 127.9 (═C_{quat}), 148.9 and 149.0 (*C*–OMe), 149.2 (*C*–OMe), 161.96 and 162.06 (C═O), 163.2 (C═O). IR (ATR): ν 1614 (C═O), 1676 (C═O), 2875, 2920, 2961, 3307 (NH) cm^{-1}. MS (ESI): *m/z* (%) = 414 (18) [M + H^+ + 1], 413 (100) [M + H^+], 355 (10) [M – C_4H_{10}]. HRMS (ESI): *m/z* calcd for $C_{24}H_{32}N_2O_4$ + H^+: 413.2435; found 413.2443.

Variable-temperature ^1H NMR (250 MHz, $CDCl_3$): 298 K, 303 K, 308 K, 313 K, 318 K. No coalescence was observed.

Oxidation of compounds 25 and 27 with silver(II) oxide

An analogous procedure was used as described for the oxidation of **12**.

Methyl 3,4-dihydro-5,10-dioxo-1-phenylbenzo[*g*]isoquinolin-2(1*H*,5*H*,10*H*)-carboxylate (26). Scale of the reaction: 0.2 mmol **25** (100 mg). R_f = 0.47 (petroleum ether/EtOAc : 2/1). Yellow crystals, mp 196.5–197.2 °C (Et_2O). Yield 0.08 g (87%). ^1H NMR δ_H (250 MHz, 25 °C, $CDCl_3$) 2.78–3.07 (3H, m, NCH(*H*)C*H*$_2$), 3.75 and 3.83 (3H, 2×s, CO_2CH_3), 4.10–4.32 (1H, m, NC(*H*)H), 6.45 and 6.59 (1H, 2× br s, H-1), 7.26–7.31 (5H, m, Ph), 7.67–7.76 (2H, m, H-7 and H-8), 7.98–8.02 (1H, m, H-6), 8.11–8.14 (1H, m, H-9). ^1H NMR δ_H (250 MHz, 50 °C, $CDCl_3$) 2.84–2.92 (2H, m, CH_2), 3.00–3.12 (1H, m, NC(H)*H*)), 3.78 (3H, s, CO_2CH_3), 4.16–4.24 (1H, m, NC(H)*H*)), 6.51 (1H, br s, H-1), 7.25–7.30 (5H, m, Ph), 7.64–7.73 (2H, m, H-7 and H-8), 7.98–8.01 (1H, m, H-6), 8.09–8.13 (1H, m, H-9). ^1H NMR δ_H (250 MHz, −30 °C, $CDCl_3$) 2.72–3.15 (3H, m, NCH(*H*)C*H*$_2$), 3.75 and 3.77 and 3.86 and 3.87 (3H, 4×s, CO_2CH_3), 4.18–4.37 (1H, m, NC(*H*)H), 6.47 and 6.60 (1H, 2× br s, H-1), 7.29–7.42 (5H, m, Ph), 7.76–7.79 (2H, m, H-7 and H-8), 8.00–8.02 (1H, m, H-6), 8.14–8.17 (1H, m, H-9). ^{13}C NMR δ_C (63 MHz, 25 °C, $CDCl_3$) 22.7 and 23.0 (C-4), 35.1 and 35.5 (C-3), 52.6 (CO_2CH_3), 52.9 (C-1), 126.3 (═CH), 126.6 (═CH), 128.0 (═CH, br), 128.6 (═CH), 131.7 (═C_{quat}), 133.76 (═C_{quat}), 133.85 (═CH), 139.3 and 139.5 (═C_{quat}), 142.5 and 143.0 (═C_{quat}), 143.9 and 144.2 (═C_{quat}), 155.2 (C═O), 182.2 (C═O), 183.9 (C═O). IR (ATR): ν 1595, 1633 (C═O), 1661 (C═O), 1689 (C═O), 2884, 2954, 3007 cm^{-1}. MS (ESI): *m/z* (%) = 348 (100) [M + H^+], 272 (10), 224 (10).

Variable-temperature ^1H NMR (250 MHz, $CDCl_3$): 224 K, 234 K, 244 K; 245 K, 255 K, 265 K, 274 K, 284 K, 293 K, 303 K, 313 K, 323 K.

2-(1-*tert*-Butyl-3,4-dihydro-5,10-dioxobenzo[*g*]isoquinolin-2(1*H*,5*H*,10*H*)-yl)-2-oxo-*N*-propylacetamide (31). Scale of the reaction: 0.15 mmol **27** (60 mg). R_f = 0.40 (petroleum ether/EtOAc : 1/1). Yellow oil. Yield 0.035 g (63%). ^1H NMR δ_H (250 MHz, 24 °C, $CDCl_3$) 0.89–0.98 (3H, m, CH_3), 1.06 and 1.07 (9H, 2×s, $C(CH_3)_3$), 1.54–1.63 (2H, m, CH_2), 2.76–3.09 (2H, m, H-4), 3.22–3.33 (2H, m, CH_2N), 3.33–3.86 (1H, 2×m, NC(*H*)H), 4.58–5.02 (1H, 2×m, NC(H)*H*), 5.86 and 6.66 (1H, 2×s, H-1), 7.19 and 7.31 (1H, 2×br s, NH), 7.70–7.78 (2H, m, H-7, H-8), 8.07–8.13 (2H, m, H-6, H-9).^{13}C NMR δ_C (63 MHz, 25 °C, $CDCl_3$) 10.1 and 11.3 (CH_3), 20.8 and 21.4 and 22.5 and 22.9 (C-4, CH_2), 29.2 and 29.4 ($C(CH_3)_3$), 37.9 and 38.1 ($C(CH_3)_3$), 37.3 and 40.1 and 41.15 and 41.22 (C-3, CH_2N), 54.0 and 56.1 (C-1), 126.1 and 126.2 (═CH), 126.8 and 126.9 (═CH), 131.6 (═C_{quat}), 132.2 (═C_{quat}), 133.6 (═CH), 133.9 (═CH), 143.0 and 143.2 (═C_{quat}), 144.5 and 144.7 (═C_{quat}), 160.9 and 161.4 (C═O), 162.2 (C═O), 182.7 and 183.0 (C═O), 183.6 and 183.8 (C═O). IR (ATR): ν 1629 (C═O), 1662 (C═O), 2875, 2931, 2963, 3312 (NH) cm^{-1}. MS (ESI): *m/z* (%) = 384 (21) [M + H^+ + 1], 383 (100) [M + H^+], 228 (22). HRMS (ESI): *m/z* calcd for $C_{22}H_{26}N_2O_4$ + H^+: 383.1965; found 383.1941.

Acknowledgements

We gratefully acknowledge the Research Foundation – Flanders (FWO-Vlaanderen) and the Vrije Universiteit Brussel (HOA) for

financial support of this research. We thank Philippe Franck (UA) for the help with UPLC analyses.

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