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A New Synthesis of Benzo[*f*]isoindole-4,9-diones by Radical Alkylation and Bromomethylation of 1,4-Naphthoquinones

Jurgen Deblander,[a] Sam Van Aeken,[a] Jan Jacobs,[b] Norbert De Kimpe,[b] and Kourosch Abbaspour Tehrani*[a]

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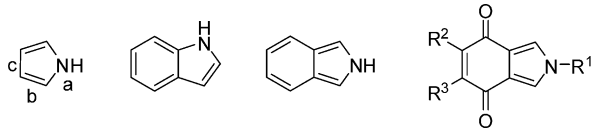
Two synthetic routes towards substituted benzo[*f*]isoindole-4,9-diones have been developed. One strategy relies on the synthesis of *N*-trifluoroacetyl-protected 2-(1-aminoalkyl)-1,4-naphthoquinones starting from 1,4-naphthoquinone and *N*-trifluoroacetyl-α-amino acids by a Kochi–Anderson oxidative decarboxylation method. Furthermore, it was demonstrated that 2-(1-aminoalkyl)-1,4-naphthoquinones are suitable precursors for the synthesis of 1-alkylbenzo[*f*]isoindole-4,9-diones by bromomethylation and subsequent *N*-deprotection. Further functionalization by *N*-alkylation and bromination resulted in completely and asymmetrically substituted benzo[*f*]isoindole-4,9-diones. The second synthesis is based on a reductive amination of 3-(bromomethyl)-1,4-dimethoxynaphthalene-2-carbaldehyde and subsequent oxidation.

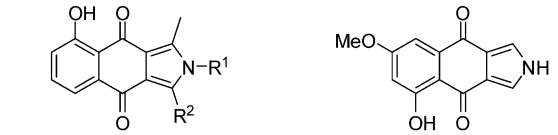
Introduction

Pyrroles and their derivatives are probably one of the most important classes of heterocyclic nitrogen compounds.[1] The electron-rich pyrrole moiety **1** can be found extensively in natural and synthetic substances,[2] either as a simple structural unit or as part of a more complex annulated system, for example, as indoles **2** and isoindoles **3**. These two families, which are a result of the fusion of benzene at the *b* or *c* bond of the pyrrole nucleus, respectively, are characterized by a high aromaticity index[3] and an increased stability in comparison with pyrrole.

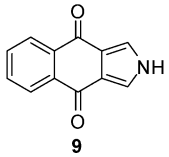


1 **2** **3** **4** $R^1 = R^2 = R^3 = H$; **5** $R^1 = Me$, $R^2 = Me$, $R^3 = OMe$ (*Reniera* indole)

Isoindole-4,7-diones **4**, which can be considered as quinonoid derivatives of **3**, are present in a number of natural products and exhibit a wide range of biological activities. An important example is the *Reniera* indole **5**, which has been isolated from the blue sponge *Reniera* sp. and exhibits a pronounced antimicrobial activity.[4] Bhimamycin C (**6**) and bhimamycin D (**7**), two related naphthoquinone-annulated pyrroles, which have been isolated from a terrestrial streptomycete,[5] are inhibitors of HIV-1 integrase,[6] display bioactivities against human ovarian cancer cell lines[7] and are EP4 receptor agonists in the treatment of pain.[8] Azamonosporascone (**8**) has been isolated from *Monosporascus cannonballus*, a fungus responsible for crop losses of water and musk melons.[9] 1,2,3-Triaryl-substituted benzo[*f*]isoindole-4,9-diones have also attracted attention as modulators of the Pin 1 class of peptidyl-prolyl *cis-trans* isomerases for the treatment of cancer.[10]



6 $R^1 = C_2H_4OH$, $R^2 = CH(OH)CH_3$ (bhimamycin C)
7 $R^1 = 2\text{-}COOHC_6H_5$, $R^2 = C(O)CH_3$ (bhimamycin D)
8 (azamonosporascone)



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Owing to the significant biological activity of benzo[*f*]-isoindole-4,9-dione analogues **9**, several pathways have been developed for their synthesis. The majority of these reaction strategies are based on a Huisgen-type cycloaddition of 1,3-dipoles such as azomethine ylides,[11] isoquinolinium or

[a] Laboratory of Organic Chemistry, Department of Applied Biological Sciences and Engineering, Faculty of Science and Bioengineering Sciences, Vrije Universiteit Brussel, Pleinlaan 2, 1050 Brussels, Belgium
[b] Department of Organic Chemistry, Faculty of Bioscience Engineering, Ghent University, Coupure Links 653, 9000 Ghent, Belgium
E-mail: Kourosch.Abbaspour.Tehrani@vub.ac.be
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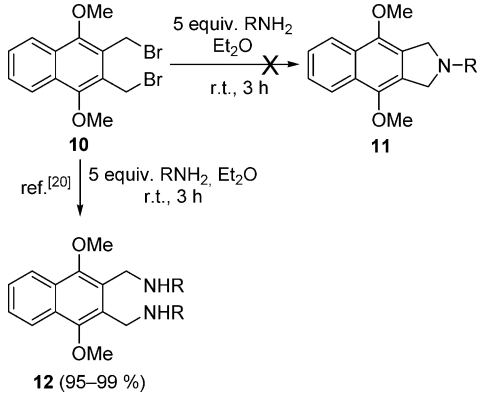
pyridinium[12] ylides and nitrile ylides[13] with 1,4-naphthoquinone. The condensation reaction of 2,5-dimethylpyrrole or 1,2,5-trimethylpyrrole with phthalic anhydride leads to 1,3-dimethyl- and 1,2,3-trimethylbenzo[*f*]isoindole-4,9-diones in 27–33% yields.[14] The Friedel–Crafts acylation of 1-butyl-2,5-dimethyl-1*H*-pyrrole-3,4-dicarbonyl dichloride with benzene, toluene and xylenes also yielded benzo[*f*]isoindole-4,9-diones in 33–88% yields.[15] A photochemical cycloaddition reaction of benzonitrile benzylide with 1,4-naphthoquinones resulted in the formation of 1,3-diphenyl-2*H*-benzo[*f*]isoindole-4,9-diones.[16] Multiply substituted benzo[*f*]isoindole-4,9-diones have been synthesized by the reaction of the rhodium complex of 3,4-bis(alkynoyl)pyrroles with acetylenes.[17] Other methods include the cyclocondensation of 2,3-diacetylenyl-1,4-naphthoquinones with hydrazine[18] and a particular rearrangement of 2-azaanthraquinones.[19]

Although these listed approaches are of great importance, very specifically substituted benzo[*f*]isoindole-4,9-diones or symmetrically substituted 1,3-analogues can only be synthesized by using elaborate synthetic pathways. Claessens et al. were the first to present a more general and efficient method for the preparation of 2-alkyl-2*H*-benzo[*f*]-isoindole-4,9-diones based on a ceric ammonium nitrate mediated oxidation of 2,3-bis(aminoalkyl)-1,4-dimethoxynaphthalenes.[20] As a continuation of this research two new syntheses of multiply substituted benzo[*f*]isoindole-4,9-diones have been developed.

Results and Discussion

The previously published strategy originated from the fact that the reaction of 2,3-bis(bromomethyl)-1,4-dimethoxynaphthalene (**10**) with primary amines resulted in the double substitution products **12** and not in the desired 4,9-dimethoxy-2,3-dihydro-1*H*-benzo[*f*]isoindoles **11** (Scheme 1).[20]

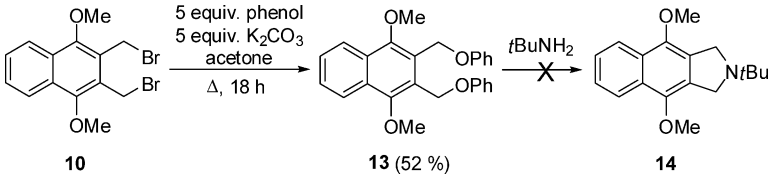


Scheme 1.

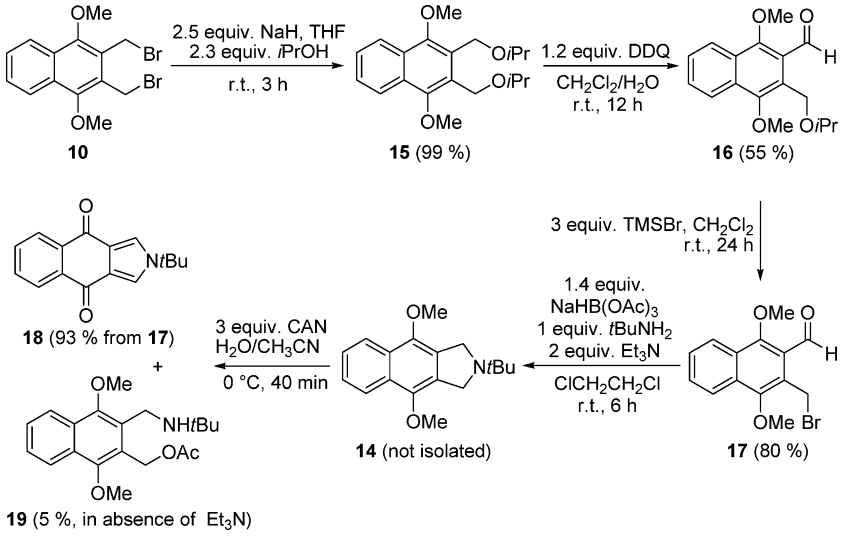
Therefore it was decided to replace the bromide leaving group by a group with moderate leaving-group ability. It was thought that the double replacement of the bromide in **10** by a phenoxy moiety would rule out the possibility of an S_N1-like substitution and would favour the formation of 4,9-dimethoxy-2,3-dihydro-1*H*-benzo[*f*]isoindoles **14**.[21]

Thus, the reaction of 2,3-bis(bromomethyl)-1,4-dimethoxynaphthalene (**10**) with excess phenol in acetone in the presence of potassium carbonate at reflux gave the bis-(phenoxylated) naphthalene **13** in 52% yield (Scheme 2). Different reaction conditions were applied to achieve substitution of the phenoxy leaving group. The reaction of bis-(phenoxylated) naphthalene **13** with 5 equiv. of *tert*-butylamine at reflux in THF for 24 h was unsuccessful. Changing the solvent to DMF or adding potassium carbonate was also unsuccessful, and the latter reaction performed in a sealed vessel under heating for 24 h also did not give any reaction. None of the reactions of compound **13** with *tert*-butylamine under different reaction conditions gave the desired 2,3-dihydro-1*H*-benzo[*f*]isoindole **14**.

Next, a desymmetrization strategy was developed to construct the 2,3-dihydro-1*H*-benzo[*f*]isoindole **14** (Scheme 3). By using a modified literature procedure,[22] 3-isopropoxymethyl-1,4-dimethoxynaphthalene-2-carbaldehyde (**16**) was prepared by substitution of both bromides of 2,3-bis(bromomethyl)-1,4-dimethoxynaphthalene (**10**) with sodium isopropoxide and subsequent oxidation of one isopropoxymethyl moiety to a formyl unit by using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in a dichloromethane/water biphasic system. Substitution of the remaining isopropoxy group of compound **16** by bromide was achieved by using 3 equiv. of bromotrimethylsilane in dichloromethane. With 3-(bromomethyl)-1,4-dimethoxynaphthalene-2-carbaldehyde (**17**) in hand, a reductive amination reaction was performed with *tert*-butylamine in the presence of sodium triacetoxyborohydride and triethylamine in 1,2-dichloroethane at room temperature, which immediately resulted in ring closure to yield 2,3-dihydro-1*H*-benzo[*f*]isoindole **14**. This compound proved to be unstable and was therefore used immediately without purification. In the last step, cerium(IV) ammonium nitrate (CAN) oxidation resulted in the target benzo[*f*]isoindole-4,9-dione **18** in an overall yield of 93% from compound **17**. The presence of triethylamine in the reductive amination step of compound **17** proved to be essential to avoid side-product formation. By omitting triethylamine from the reductive amination



Scheme 2.



Scheme 3.

step, in addition to 2-*tert*-butylbenzo[*f*]isoindole-4,9-dione (**18**), {3-[(*tert*-butylamino)methyl]-1,4-dimethoxy-2-naphthyl}methyl acetate (**19**) was also formed in a 1.5:1 ratio after CAN oxidation of the crude reaction mixture. Remarkably no oxidative demethylation of **19** occurred during the CAN treatment of this compound, which could be obtained in an analytically pure form by flash chromatography (Al_2O_3) and preparative HPLC. The mechanism of the ring-closing step probably involves a substitution of the bromide by *tert*-butylamine followed by an intramolecular reductive amination. Another possibility, in which a first equivalent of *tert*-butylamine is used in a reductive amination step and a second equivalent is consumed in a Michael-type substitution of the *ortho*-quinomethide formed by elimination of the benzylic bromide, is ruled out by the fact that no trace of 2,3-bis(*tert*-butylaminomethyl)naphthalene was observed and that yields higher than 50% were obtained. A third alternative, a reductive amination followed by an intramolecular substitution, may be rejected in light of the previous mechanistic considerations.[20]

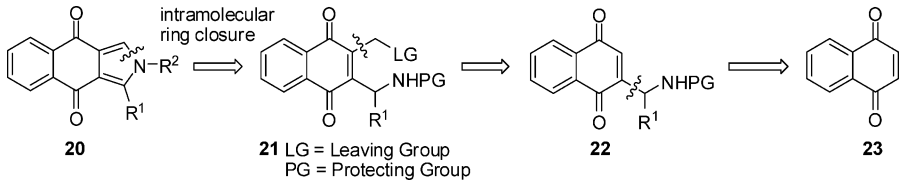
Although the *N*-substituted benzo[*f*]isoindole-4,9-dione **18** was successfully synthesized, the pathway followed was too lengthy and did not satisfy the requirement concerning the functionalization of C1 and/or C3. A new retrosynthetic strategy, using *N*-protected 2-(1-aminoalkyl)-1,4-naphthoquinones **22** as key intermediates, was proposed (Scheme 4). Amines of the type **22** display interesting biological activities, especially in the field of cancer research.[23]

As the key compounds **22** had to be prepared, preferably in one step, starting from the cheap and readily available 1,4-naphthoquinone (**23**), radical alkylation using α-amino acids as radical precursors was chosen. Among the radical-mediated syntheses,[24] the Barton method, in which a radical is generated from a photosensitive thiohydroxamic ester, seems to be the best method to date in terms of coupling efficiency, functional group compatibility and availability of the radical precursors.[25,26]

The Barton decarboxylation procedure has already been applied by Commandeur et al. in an unsuccessful attempt to generate 3-(aminoalkyl)-2-methylnaphthoquinones starting from *N*-Boc-alanine and *N*-Boc-β-alanine.[27] An alternative radical decarboxylation method,[27,28] based on the work of Kochi and Anderson,[29] resulted in the desired *N*-Boc-protected aminomethyl-functionalized quinone. A major advantage of this strategy is the fact that no radical precursors have to be prepared.

Although the Kochi–Anderson method, which is a silver-catalysed oxidative decarboxylation of acids by peroxydisulfate, seemed to be a very interesting procedure by which to prepare the key compounds **22**, it was reported that this method was not suitable for the addition of *N*-Boc-protected chiral α-amino acids to menadione.[27]

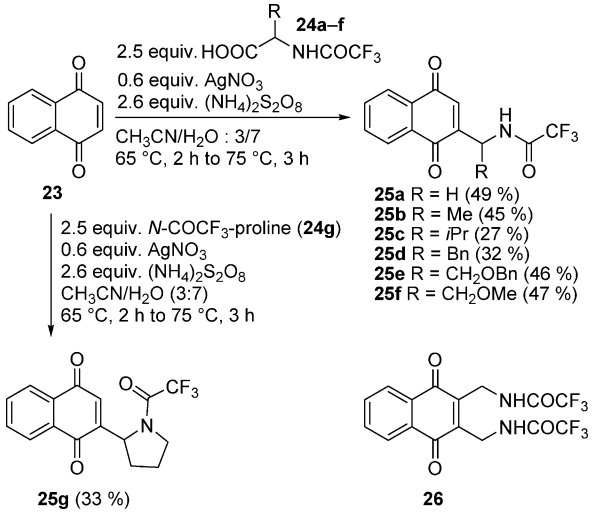
In an effort to circumvent this problem we wondered if the choice of the *N*-protecting group and the use of 1,4-naphthoquinone (**23**) instead of 2-methyl-1,4-naphthoquinone are decisive for the success of the radical addition



Scheme 4.

reaction. Based on the retrosynthetic analysis, it was decided to use *N*-trifluoroacetyl-protected α-amino acids. The trifluoroacetyl protecting group is highly stable under strongly acidic conditions, whereas its moderate steric hindrance offers the advantages of easy attachment and removal.[30] The *N*-trifluoroacetyl-protected α-amino acids were prepared by reaction of the corresponding α-amino acid with trifluoroacetic anhydride or with ethyl trifluoroacetate in combination with a base.[31]

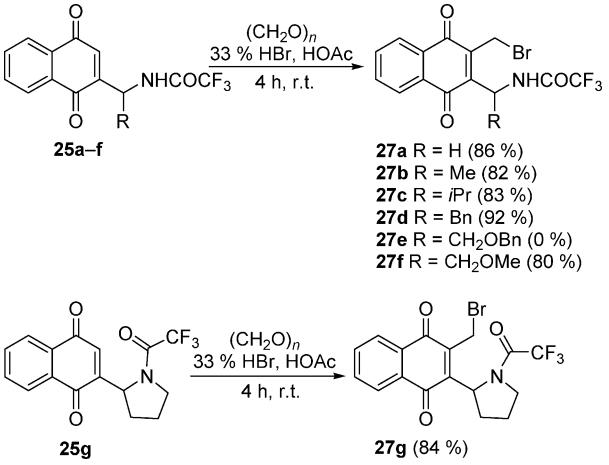
The radical addition was achieved by the reaction of 1,4-naphthoquinone (**23**) with 2.5 equiv. of the *N*-trifluoroacetyl-α-amino acid **24** and 0.3 equiv. of $AgNO_3$ in 30% aqueous acetonitrile at 65 °C. The best results were obtained if 1.3 equiv. of the radical initiator ammonium persulfate were added to the reaction mixture over 2 h. After stirring at 75 °C for 3 h, the reaction mixture was analysed by TLC or HPLC, and an additional 0.3 equiv. of $AgNO_3$ and 1.3 equiv. of ammonium persulfate were added (Scheme 5).



Scheme 5.

Although the yields obtained after flash chromatography were rather moderate, this strategy allows the preparation of a wide range of 2-(aminomethyl)-1,4-naphthoquinones **25**. It should be noted that after flash chromatography, 40–50% of the unconverted quinone **23** was also recovered. These results also indicate that the presence of an alkyl group generally has a small effect on the reactivity of the carbon radical. Only in one case, that is, the reaction of 1,4-naphthoquinone (**23**) with *N*-trifluoroacetylglycine (**24a**), was a double addition product **26** observed in 10% yield by HPLC–MS. This clearly demonstrates that the steric hindrance, induced by the α-substituent of the amino acid, plays an essential role in the outcome of the reaction. Because the retrosynthetic analysis in Scheme 4 necessitated the use of a base-labile *N*-protecting group, the radical coupling of *N*-Fmoc-glycine to 1,4-naphthoquinone was also evaluated under the above-mentioned reaction conditions. After a cumbersome flash-chromatographic procedure, Fmoc-protected 2-(aminomethyl)-1,4-naphthoquinone was isolated in 13% yield. The same coupling reaction of 1,4-naphthoquinone with *N*-Fmoc-alanine resulted in a complex mixture, which was not further investigated.

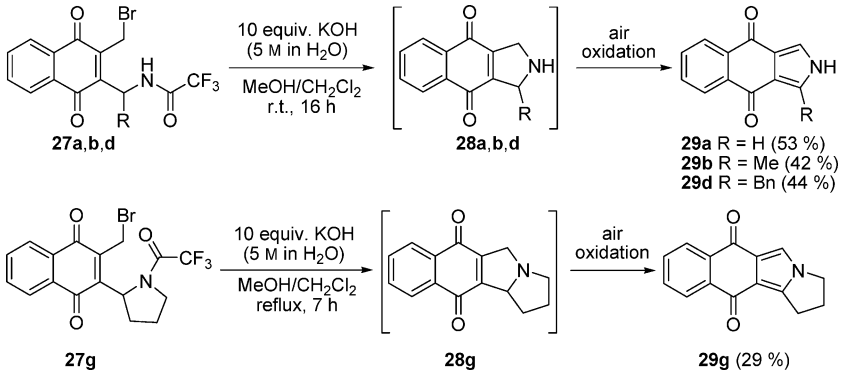
In a subsequent step, bromomethylation of **25a**–**g** was accomplished by reaction with excess paraformaldehyde and a concentrated solution of 33% HBr in acetic acid over 4 h to afford the asymmetrically bifunctionalized 1,4-naphthoquinones **27a**–**g** in 80–92% yields (Scheme 6). Although benzyl ethers are robust and stable to a wide range of acidic and basic conditions, the bromomethylation conditions proved to be too harsh for the benzyl ether **27e** and led to a complex reaction mixture.



Scheme 6.

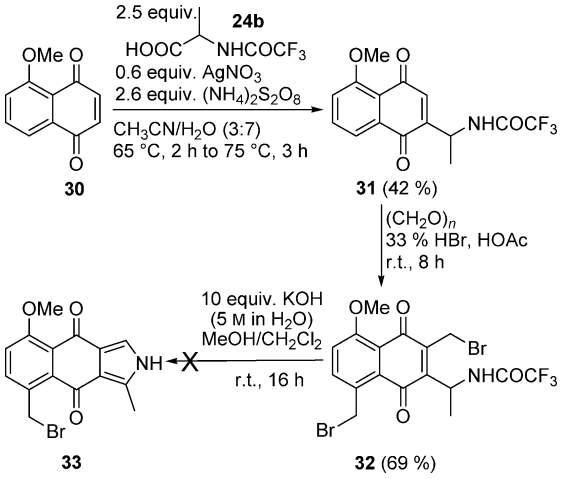
It was assumed that treatment of 3-(aminomethyl)-2-(bromomethyl)-1,4-naphthoquinone **27** with a base would result in the deprotection of the nitrogen atom and induce subsequent ring closure towards the envisioned products. The reactions of compounds **27a**,**b**,**d**,**g** with an excess of aqueous potassium hydroxide (5 M) in methanol/CH_2Cl_2 at room temperature indeed resulted in benzo[*f*]isoindole-4,9-diones **29a**,**b**,**d**,**g** in 29–53% yields after flash chromatography (Scheme 7). The intermediate 2,3-dihydrobenzo[*f*]isoindoles **28** are not stable and are oxidized spontaneously by air oxygen to the corresponding benzo[*f*]isoindole-4,9-diones **29**.[11b,20] Although the intramolecular ring closure, which is a 5-*exo*-tet reaction, is favoured, the reaction of **27f** (R = CH_2OMe) with aqueous potassium hydroxide in MeOH/CH_2Cl_2 did not result in the desired ring-closed product; instead a complex mixture was obtained. Most likely, the intermediate 2,3-dihydrobenzo[*f*]isoindole, if formed at all, undergoes elimination of MeOH under the strongly basic conditions and thus triggers other degradation reactions.

In an attempt to synthesize *peri*-substituted benzo[*f*]isoindole-4,9-diones **32**, the radical aminoalkylation of 5-methoxy-1,4-naphthoquinone (**30**) with *N*-trifluoroacetylalanine was performed. One regioisomer (**31**) was formed and isolated in 42% yield after flash chromatography. Not completely unexpectedly, the reaction of **31** with paraformaldehyde and HBr resulted in double bromomethylation (Scheme 8). It was not possible to effect a single bromo-



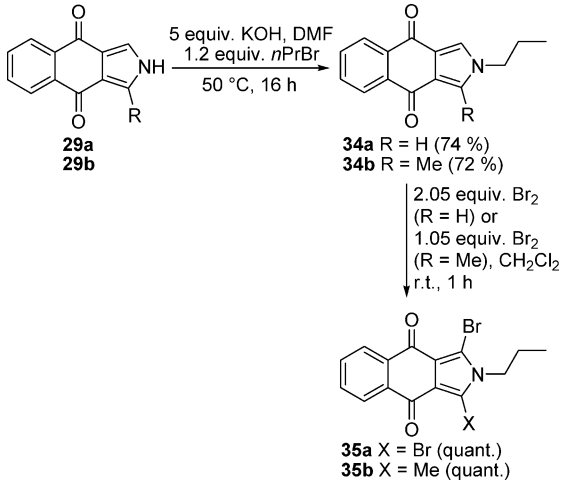
Scheme 7.

methylation because under the rather harsh conditions required for the introduction of a bromomethyl group at the 3-position of **31**, the 8-position of compound **31** also started to react. The correct regiochemistry of the aromatic bromomethyl and aminomethyl moiety in compound **32** was determined by NOESY. A cross-peak was observed between the CH_2 group at the 8-position and the CH_3CH group at the 2-position. In the other possible regioisomer, that is, *N*-trifluoroacetyl-2-(1-aminoethyl)-3,5-bis(bromomethyl)-8-methoxy-1,4-naphthoquinone, a cross-peak between the OCH_3 group and the CH_3CH group at the 2-position would have to appear, which was not the case. By extension, the structure of compound **31** was assigned as *N*-trifluoroacetyl-2-(1-aminoethyl)-5-methoxy-1,4-naphthoquinone. Unfortunately, the final potassium hydroxide induced ring closure only led to inseparable reaction mixtures.



Scheme 8.

To functionalize the pyrrole unit of benzo[*f*]isoindole-4,9-dione **29a** (R = H), the *N*-alkylation of **29a** was performed by treatment of the isoindole in the presence of potassium carbonate with bromopropane in DMF at 90 °C for 15 h in accordance with a literature method.[32] After flash chromatography of the very impure reaction mixture, 2-propyl-2*H*-benzo[*f*]isoindole-4,9-dione (**34a**) was obtained in 43% yield. The reaction conditions were optimized by using an excess of potassium hydroxide instead of potassium carbonate at only 50 °C for 16 h, which led to **34a** in 74% yield. This optimized procedure was also used for the synthesis of the dialkylated 1-methyl-2-propyl-2*H*-benzo[*f*]isoindole-4,9-dione (**34b**) in 72% yield. Bromination of compounds **34b** and **34a** with 1 or 2 equiv. of bromine in dichloromethane at room temperature for 1 h resulted in a complete substitution of the pyrrole unit (Scheme 9). The selective monobromination of 2-propyl-2*H*-benzo[*f*]isoindole-4,9-dione (**34a**) with 1 equiv. of bromine was not possible under these reaction conditions. The brominated benzo[*f*]isoindole-4,9-diones **35a**,**b** were obtained in 100% yield and may be interesting substrates for transition-metal-catalysed coupling reactions.



Scheme 9.

Conclusions

N-Trifluoroacetyl-protected 2-(1-aminoalkyl)-1,4-naphthoquinones have been synthesized for the first time by a procedure based on the Kochi–Anderson oxidative decarboxylation method starting from 1,4-naphthoquinone and *N*-trifluoroacetyl-α-amino acids. Furthermore, it has been demonstrated that 2-(1-aminoalkyl)-1,4-naphthoquinones are suitable precursors for the synthesis of 1-alkylbenzo[*f*]-isoindole-4,9-diones by a bromomethylation and subse-

quent *N*-deprotection. Further functionalization by *N*-alkylation and bromination resulted in completely and asymmetrically substituted benzo[*f*]isoindole-4,9-diones.

Experimental

General Experimental Methods: GC–MS analyses were performed by using an Interscience GC 8000 series gas chromatograph with a EC^{TM}-5 column (length: 30 m, internal diameter: 0.32 mm, film thickness: 0.25 μm). Products were injected into a split injector (250 °C); the inert carrier gas was helium. Mass spectra were measured with a Fisons MD 800 instrument by using electron impact (70 eV) as the ionization method. HRMS data were obtained with a QTof Micro mass spectrometer (positive ion mode). Under standard measurement conditions the sample was dissolved in CH_3CN/H_2O (1:1) containing 0.1% formic acid. High-resolution ^1H (250 MHz) and ^{13}C NMR (63 MHz) spectra were recorded in $CDCl_3$, [D_6]DMSO, CD_3OD, CD_3CN or CD_2Cl_2 with a Bruker Avance DRX 250 spectrometer. Chemical shifts are reported in ppm downfield from TMS. ^{13}C NMR assignments were made by analysis of DEPT, HMQC, HMBC, 2D COSY and 2D NOESY spectra. Infrared spectra were recorded with an Avatar 370 FT-IR apparatus (Thermo Nicolet). Unless otherwise stated, the IR spectra were recorded by using attenuated total reflection technology. Flash chromatography was performed by using Merck silica (diameter: 40–63 μm). TLC analysis was performed on glass-backed plates (Merck) coated with 0.2 mm silica with UV indicator 60_{F254}. Preparative HPLC was performed by using a Gilson HPLC instrument (332 PUMP) and a Gilson UV detector (UV/Vis-156) with a reversed-phase Discovery BIO wide-pore C_{18} column (length: 25 cm, internal diameter: 21.2 mm, particle size: 10 μm) using a MeCN/H_2O gradient containing 0.1% trifluoroacetic acid. Melting points (m.p.) were determined with a melting point apparatus with a temperature gradient of 1 °C/min and are not corrected.

General Method for the Synthesis of *N*-Trifluoroacetyl-Protected Amino Acids 24a–f: Triethylamine (3.1 mL, 22 mmol) was added to a suspension of α-amino acid (22 mmol) in methanol (11 mL). After stirring for about 5 min, ethyl trifluoroacetate (3.3 mL, 28 mmol) was added, and the resulting mixture was stirred at room temperature for about 16 h. The solvent was removed under reduced pressure, and the resulting residue was dissolved in water (50 mL), acidified with concentrated aqueous hydrochloric acid (4 mL) and stirred for 15 min. The mixture was then extracted with ethyl acetate (2 × 30 mL), and the organic layers were combined. The combined organic layers were washed with brine, dried ($MgSO_4$), and the solvent was removed under reduced pressure to provide a solid, which was washed with hexane and dried to provide the desired *N*-trifluoroacetyl amino acid **24a**–**f**.

Spectroscopic data have been reported for *N*-trifluoroacetylglycine (**24a**),[31c,31e,33] *N*-trifluoroacetylalanine (**24b**),[31a,31f] *N*-trifluoroacetylvaline (**24c**),[33,34] *N*-trifluoroacetylphenylalanine (**24d**),[33,35] *N*-trifluoroacetyl-*O*-benzylserine (**24e**)[31d] and *N*-trifluoroacetylproline (**24g**).[31b] Spectroscopic data for *N*-trifluoroacetyl-*O*-methylserine (**24f**): Yield: 94%. ^1H NMR (250 MHz, [D_6]DMSO): δ = 3.25 (s, 3 H, OMe), 3.66 [dd, J = 10.2, 4.5 Hz, 1 H, CH(*H*)], 3.70 [dd, J = 10.2, 7.3 Hz, 1 H, C*H*(H)], 4.51 (td, J = 7.5, 4.5 Hz, 1 H, CH), 9.80 (br. d, J = 7.7 Hz, 1 H, NH), 13.1 (br. s, 1 H, OH) ppm. ^{13}C NMR (63 MHz, [D_6]DMSO): δ = 52.7 (CH), 58.1 (OMe), 70.0 (CH_2), 115.8 (q, J = 288.0 Hz, CF_3), 156.5 (q, J = 36.6 Hz, *C*OCF_3), 169.7 (COOH) ppm. IR (ATR): $\tilde{\nu}$ = 3218, 1743, 1698, 1561, 1158, 1118, 1044, 898, 807, 668 cm^{-1}.

Synthesis of 1,4-Dimethoxy-2,3-bis(phenoxymethyl)naphthalene (13): A solution of 2,3-bis(bromomethyl)-1,4-dimethoxynaphthalene (**10**; 1.00 g, 2.7 mmol) in acetone (10 mL) was added to a solution containing phenol (1.25 g, 13.5 mmol) and potassium carbonate (1.85 g, 13.5 mmol) in acetone (10 mL). The reaction mixture was heated at reflux for 18 h. The solvent was evaporated in vacuo, and the residue was redissolved in dichloromethane. The organic solution was washed with water and brine and dried ($MgSO_4$). Evaporation of the solvent yielded 1,4-dimethoxy-2,3-bis(phenoxymethyl)naphthalene (**13**), which was purified by recrystallization (petroleum ether/ethyl acetate) to give off-white crystals (0.56 g, 52%). M.p. 124.3 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.98 (s, 6 H, 2 MeO), 5.37 (s, 4 H, 2 CH_2), 6.93–7.02 (m, 6 H, 6 CH_{ar}), 7.24–7.30 (m, 4 H, 4 CH_{ar}), 7.56–7.61 (m, 2 H, 2 CH_{ar}), 8.14–8.19 (m, 2 H, 2 CH_{ar}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 62.06 (2 MeO), 63.97 (2 CH_2), 114.93 (4 CH_{ar}), 121.09 (2 CH_{ar}), 123.10 (2 CH_{ar}), 125.39 (2 C_{quat}), 127.12 (2 CH_{ar}), 129.36 (2 C_{quat}), 152.61 (2 C_{quat}), 158.92 (2 C_{quat}) ppm. IR (ATR): $\tilde{\nu}_{max}$ = 1355 cm^{-1}. MS (ES$^+$): *m*/*z* (%) = 307 (100) [M – PhO]$^+$.

Synthesis of 2-*tert*-Butyl-2*H*-benzo[*f*]isoindole-4,9-dione (18)

Synthesis of 2,3-Bis(isopropoxymethyl)-1,4-dimethoxynaphthalene (15): 2-Propanol (0.707 g, 12 mmol) was added dropwise to a solution of 2,3-bis(bromomethyl)-1,4-dimethoxynaphthalene (**10**; 2 g, 5.35 mmol) and sodium hydride (0.334 g, 13.9 mmol) in tetrahydrofuran (12 mL). The mixture was stirred at room temperature for 3 h and then quenched with water. The ethyl acetate extract was washed with water and brine and dried ($MgSO_4$). After evaporation in vacuo, a yellow oil (1.84 g, 99%) was obtained, which was used without purification in the next step. An analytically pure sample was obtained by silica gel column chromatography (EtOAc/cyclohexane, 1:9; R_f = 0.28). ^1H NMR (250 MHz, $CDCl_3$): δ = 1.28 (d, J = 6.1 Hz, 12 H, 4 CH_3), 3.81 (sept, J = 6 Hz, 2 H, 2 CH), 3.98 (s, 6 H, 2 OMe), 4.82 (s, 4 H, 2 CH_2), 7.47–7.55 (m, 2 H, 2 CH_{ar}), 8.09 (dd, J = 3.3, 6.4 Hz, 2 H, 2 CH_{ar}) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 22.3 (4 CH_3), 61.7 (2 CH_2), 63.5 (2 OMe), 71.8 (2 CH), 122.8 (2 CH_{ar}), 126.4 (2 CH_{ar}), 127.1 (2 C_{quat}), 129.0 (2 C_{quat}), 152.0 (2 C_{quat}) ppm. IR (ATR): $\tilde{\nu}_{max}$ = 1353, 1122, 1076, 1046, 1019, 772 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 332 (48) [M]$^+$, 272 (57), 257 (31), 214 (47), 229 (100), 215 (99), 186 (57), 171 (56), 143 (31), 128 (48), 115 (50). HRMS (ESI): calcd. for $C_{20}H_{28}O_4$ + H^+ 333.2060; found 333.2089.

Synthesis of 3-(Isopropoxymethyl)-1,4-dimethoxynaphthalene-2-carbaldehyde (16): 2,3-Dichloro-4,5-dicyano-1,4-naphthoquinone (DDQ; 1.336 g, 5.89 mmol) was added to a solution of 2,3-bis(isopropoxymethyl)-1,4-dimethoxynaphthalene (**15**; 1.836 g, 5.35 mmol) in dichloromethane/water (10:1; 75 mL). The reaction was monitored to completion by TLC. After completion, the reaction mixture was washed with a saturated sodium hydrogen carbonate solution and brine, and afterwards dried with $MgSO_4$ and concentrated in vacuo. Purification with silica gel column chromatography (EtOAc/cyclohexane, 1:9; R_f = 0.15) gave a colourless oil (0.848 g, 55%). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.25 (d, J = 6.1 Hz, 6 H, 2 CH_3), 3.82 (sept, J = 6.1 Hz, 1 H, CH), 3.98 and 4.05 (2 s, 2 × 3 H, 2 OMe), 4.98 (s, 2 H, CH_2), 7.57–7.67 (m, 2 H, 2 CH_{ar}), 8.14 and 8.21 (2 d, J = 8.3 Hz, 2 × 1 H, CH_{ar}), 10.70 (s, 1 H, CHO) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 22.1 (2 CH_3), 60.6 (CH_2), 63.6 (OMe), 64.9 (OMe), 72.1 (CH), 123.1 (CH_{ar}), 123.4 (CH_{ar}), 124.9 (C_{quat}), 125.7 (C_{quat}), 127.2 (CH_{ar}), 128.8 (C_{quat}), 129.5 (CH_{ar}), 131.6 (C_{quat}), 151.9 (C_{quat}), 158.5 (C_{quat}), 191.6 (CHO) ppm. IR (ATR): $\tilde{\nu}_{max}$ = 1688, 1350, 1051, 959, 776 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 288 (18) [M]$^+$, 245 (86), 230 (61), 215 (53), 213

(58), 199 (46), 189 (40), 186 (100), 143 (42), 127 (79), 114 (89). $C_{17}H_{20}O_4$ (288.34): calcd. C 70.81, H 6.99; found C 68.59, H 7.22.

Synthesis of 3-(Bromomethyl)-1,4-dimethoxynaphthalene-2-carbaldehyde (17): Bromotrimethylsilane (2.20 g, 14.35 mmol) was added dropwise to a solution of 3-(isopropoxymethyl)-1,4-dimethoxynaphthalene-2-carbaldehyde (**16**; 1.038 g, 4.8 mmol) in dichloromethane (50 mL). The reaction mixture was stirred at room temperature overnight and then washed with a saturated sodium hydrogen carbonate solution and dried ($MgSO_4$). Concentration in vacuo gave a white solid (1.812 g, 80%), which was used without further purification. An analytically pure sample was obtained by silica gel column chromatography (EtOAc/cyclohexane, 1:6; R_f = 0.30). M.p. 105–106 °C. It was impossible to obtain a suitable mass spectrum because the analyses of the compound by EI (GC/MS) and by ESI (positive and negative) gave no signal. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.98 and 4.01 (2 s, 2×3 H, 2 OMe), 5.20 (s, 2 H, CH_2), 7.52–7.66 (m, 2 H, 2 CH_{ar}), 8.04 (dd, J = 0.5, 7.7 Hz, 1 H, CH_{ar}), 8.14 (dd, J = 0.5, 8.1 Hz, 1 H, CH_{ar}), 10.63 (s, 1 H, CHO) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 22.8 (CH_2), 60.7 (OMe), 63.7 (OMe), 120.6 (C_{quat}), 121.4 (CH_{ar}), 121.5 (CH_{ar}), 123.8 (C_{quat}), 125.9 (CH_{ar}), 126.9 (C_{quat}), 127.9 (CH_{ar}), 129.7 (C_{quat}), 149.9 (C_{quat}), 159.2 (C_{quat}), 189.3 (CHO) ppm. IR (ATR): $\tilde{\nu}_{max}$ = 1679, 1404, 1351, 1047, 956, 777, 724 cm^{-1}. $C_{14}H_{13}BrO_3$ (309.16): calcd. C 54.39, H 4.24; found C 54.58, H 4.27.

Synthesis of 2-*tert*-Butyl-4,9-dimethoxy-2,3-dihydro-1*H*-benzo[*f*]isoindole (14): Triethylamine (0.0462 g, 0.46 mmol), sodium triacetoxyborohydride (0.067 g, 0.32 mmol) and *tert*-butylamine (0.0166 g, 0.23 mmol) were added successively to a solution of 3-(bromomethyl)-1,4-dimethoxynaphthalene-2-carbaldehyde (**17**; 0.070 g, 0.23 mmol) in 1,2-dichloroethane (3 mL). The reaction mixture was stirred under argon at room temperature and monitored to completion by HPLC. After 6 h, the reaction mixture was quenched with a saturated sodium hydrogen carbonate solution, extracted with ethyl acetate and dried ($MgSO_4$). After filtration and removal of the solvent in vacuo, a black solid was obtained, which was used as such in the subsequent reaction step because the compound proved to be unstable. Any attempt to purify the compound by column chromatography or by crystallization only led to further degradation. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.37 [s, 9 H, $C(CH_3)_3$], 3.96 (s, 6 H, OMe), 4.47 (s, 4 H, 2 CH_2), 7.46–7.50 (m, 2 H, 2 CH_{ar}), 8.09 (dd, J = 3.3, 6.3 Hz, 2 H, 2 CH_{ar}) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 25.6 (3 CH_3), 43.5 (C_{quat}), 49.8 (2 CH_2), 61.2 (2 OMe), 122.0 (2 CH_{ar}), 125.8 (2 CH_{ar}), 128.7 (2 C_{quat}), 146.2 (2 C_{quat}), 175.4 (2 C_{quat}) ppm. MS (EI, 70 eV): m/z = 286 [M + 1]$^+$.

Synthesis of 2-*tert*-Butyl-2*H*-benzo[*f*]isoindole-4,9-dione (18): The above-obtained crude product **14** (0.064 g, 0.22 mmol) was dissolved in a mixture of acetonitrile/water (2:1; 3 mL) and cooled to 0 °C, after which cerium(IV) ammonium nitrate (0.369 g, 0.067 mmol) was added. The reaction mixture was stirred for 1 h and then quenched with water, extracted with ethyl acetate and dried ($MgSO_4$). After filtration and removal of the solvent in vacuo, the residue was purified by flash chromatography on aluminium oxide (EtOAc/petroleum ether, 1:4; R_f = 0.10) to provide a yellow powder (0.052 g, 93%). M.p. 172–173 °C. The NMR spectroscopic data of **18** were in accordance with data reported in the literature.[20]

{3-[(*tert*-Butylamino)methyl]-1,4-dimethoxynaphthalen-2-yl}methyl Acetate (Trifluoroacetate Salt) (19): This compound was obtained by rinsing the aluminium oxide of the above-mentioned chromatographic separation with CH_2Cl_2/MeOH (98:2). These combined washings were concentrated in vacuo and purified by preparative HPLC to remove traces of **18**. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.27 [s, 9 H, $C(CH_3)_3$], 2.10 [s, 3 H, $C(O)CH_3$], 3.95 and 4.00 (2 s, 2×3 H, 2 OMe), 4.09 (br. s, 2 H, CH_2N), 5.50 (s, 2 H, CH_2O), 7.50–7.60 (m, 2 H, 2 CH_{ar}), 8.03–8.14 (m, 2 H, 2 CH_{ar}) ppm (NH_2^+ signal was not visible). ^{13}C NMR (63 MHz, $CDCl_3$): δ = 8.97 [$C(CH_3)_3$], 20.3 [$C(O)CH_3$], 28.9 [$C(CH_3)_3$], 37.4 (CH_2N), 58.2 (CH_2O), 62.1 (OCH_3), 62.7 (OCH_3), 121.8 (CH_{ar}), 122.2 (CH_{ar}), 123.4 (C_{quat}), 125.8 (C_{quat}), 126.3 (2 CH_{ar}), 151.1 and 152.5 (2 OMe), 170.1 [$C(O)CH_3$] ppm (CF_3, COO^- and two C_{quat} signals could not be distinguished). IR (ATR): $\tilde{\nu}_{max}$ = 719, 775, 968, 1019, 1197, 1224, 1357, 1685, 1736 cm^{-1}. MS (ES$^+$): m/z (%) = 346 (100) [M + H]$^+$, 304 (20), 286 (52), 273 (38).

General Procedure for the Preparation of *N*-Trifluoroacetyl-Protected 2-(1-Aminoalkyl)-1,4-naphthoquinones 25 and 31: *N*-Trifluoroacetyl-protected amino acid **24** (2.5 equiv.) and silver nitrate (0.3 equiv.) were added to a stirred solution of 1,4-naphthoquinone **23** or **29** (6 mmol) in 30% aq. CH_3CN. The mixture was heated to 65 °C, and a solution of ammonium persulfate (1.3 equiv.) in 30% aq. CH_3CN was added dropwise over 2 h. Subsequently, the mixture was stirred at 75 °C for 3 h. After TLC or HPLC analysis, an additional amount of silver nitrate (0.3 equiv.) and ammonium persulfate (1.3 equiv.) in 30% aq. CH_3CN were added dropwise over 2 h. After being stirred at 75 °C for an additional 3 h, the reaction mixture was cooled to room temperature and extracted with dichloromethane. The organic extracts were washed with brine, dried ($MgSO_4$) and the solvents evaporated in vacuo. The crude product was purified by flash chromatography on silica gel.

***N*-Trifluoroacetyl-2-(aminomethyl)-1,4-naphthoquinone (25a):** Yield: 49%. R_f = 0.18 (EtOAc/cyclohexane, 1:4). M.p. 146.2–147.1 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.48 (d, J = 6.3 Hz, 2 H, CH_2), 6.93 (s, 1 H, 3-H), 7.03 (br. s, 1 H, NH), 7.73–7.84 (m, 2 H, 6-H and 7-H), 8.05–8.16 (m, 2 H, 5-H and 8-H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 39.2 (CH_2), 115.7 (q, J = 287.7 Hz, CF_3), 126.5 and 126.6 (C-5 and C-8), 131.7 and 132.0 (C_{quat}), 134.1 and 134.5 (C-6 and C-7), 135.9 (C-3), 143.8 (C_{quat}), 157.2 (q, J = 37.1 Hz, $COCF_3$), 184.4 (C=O), 185.1 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3316, 1709, 1660, 1536, 1300, 1157, 995, 922, 777 cm^{-1}. MS (ES): m/z (%) = 284 (100) [M + H]$^+$. HRMS (ESI): calcd. for $C_{13}H_8F_3NO_3$ + H$^+$ 284.0529; found 284.0522; Δ = 2.4 ppm.

***N*-Trifluoroacetyl-2-(1-aminoethyl)-1,4-naphthoquinone (25b):** Yield: 45%. R_f = 0.23 (EtOAc/cyclohexane, 1:4). M.p. 167.8–168.7 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.60 (d, J = 7.1 Hz, CH_3), 5.11 [dq (pseudo-quint), J = 7.2 Hz, 1 H, CH], 6.87 (s, 1 H, 3-H), 7.26 (br. s, 1 H, NH + $CHCl_3$), 7.75–7.82 (m, 2 H, 6-H and 7-H), 8.07–8.13 (m, 2 H, 5-H and 8-H) ppm. ^{13}C NMR (63 MHz, [D$_6$]DMSO): δ = 19.0 (CH_3), 43.4 (CHN), 115.7 (q, J = 288.4 Hz, CF_3), 125.6 and 126.2 (C-5 and C-8), 131.3 and 131.6 (C_{quat}), 133.0 (C-3), 134.3 (C-6 and C-7), 150.2 (C_{quat}), 155.5 (q, J = 36.8 Hz, $COCF_3$), 183.4 (C=O), 184.5 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3298, 1696, 1661, 1593, 1549, 1334, 1167, 987, 782 cm^{-1}. MS (ES): m/z (%) = 298 (100) [M + H]$^+$. HRMS (ESI): calcd. for $C_{14}H_{10}F_3NO_3$ + H$^+$ 298.0685; found 298.0679; Δ = 2.0 ppm.

***N*-Trifluoroacetyl-2-[(1-amino-2-methyl)propyl]-1,4-naphthoquinone (25c):** Yield: 27%. R_f = 0.39 (EtOAc/cyclohexane, 1:3). M.p. 129.8–130.7 °C. Over a period of 12 h this compound started to decompose in $CDCl_3$. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.06 and 0.93 [2 d, J = 6.7 Hz, 2×3 H, $CH(CH_3)_2$], 2.22–2.31 [m, 1 H, $CH(CH_3)_2$], 4.59 [dd (pseudo-t), J = 9.3 Hz, 1 H, HCN], 6.85 (s, 1 H, 3-H), 7.43–7.47 (br. s, 1 H, NH), 7.77–7.82 (m, 2 H, 6-H and 7-H), 8.06–8.12 (m, 2 H, 5-H and 8-H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.2 (CH_3), 20.1 (CH_3), 31.8 [$CH(CH_3)_2$], 58.8 (CHNH), 115.7 (q, J = 288.1 Hz, CF_3), 126.4 and 126.8 (C-5 and

C-8), 131.7 and 132.0 (C_{quat}), 134.1 and 134.5 (C-6 and C-7), 137.0 (C-3), 145.9 (C_{quat}), 156.9 (q, J = 37.2 Hz, *C*OCF$_3$), 184.4 (C=O), 185.5 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3315, 2965, 1698, 1659, 1592, 1550, 1204, 1151, 929, 779, 718, 699 cm^{-1}. MS (ES): *m*/*z* (%) = 326 (100) [M + H]$^+$, 284 (47), 213 (55). HRMS (ESI): calcd. for $C_{16}H_{14}F_3NO_3$ + H$^+$ 326.0999; found 326.0997; Δ = 0.6 ppm.

***N*-Trifluoroacetyl-2-(1-amino-2-phenylethyl)-1,4-naphthoquinone (25d):** Yield: 32%. R_f = 0.13 (EtOAc/cyclohexane, 1:6). M.p. 178.0–179.2 °C. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 3.18 [dd, J = 9.9, 7.6 Hz, 1 H, CH(*H*)], 3.22 [dd, J = 9.9, 7.6 Hz, 1 H, C*H*(H)], 5.20 [dt (pseudo-q), J = 7.7 Hz, 1 H, CH], 6.59 (s, 1 H, 3-H), 7.11–7.20 (m, 2 H, CH$_{ar}$), 7.23–7.30 (m, 3 H, CH$_{ar}$), 7.45 (br. d, J = 8.8 Hz, 1 H, NH), 7.75–7.84 (m, 2 H, 6-H and 7-H), 8.01–8.08 (m, 1 H, 8-H or 5-H), 8.09–8.17 (m, 1 H, 5-H or 8-H) ppm. ^{13}C NMR (63 MHz, CDCl$_3$): δ = 40.5 (CH$_2$), 53.4 (CH), 115.6 (q, J = 287.8 Hz, CF$_3$), 126.4, 126.8 and 127.5 (C_{quat}), 129 (C-5 and C-8), 131.7 and 132.0 (C_{quat}), 134.2 and 134.5 (C-6 and C-7), 135.5 (C_{quat}), 136.3 (C-3), 145.6 (C_{quat}), 156.5 (q, J = 37.6 Hz, *C*OCF$_3$), 184.2 (C=O), 185.4 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3290, 1701, 1658, 1593, 1562, 1168, 967, 913, 775 cm^{-1}. MS (ES): *m*/*z* (%) = 374 (50) [M + H]$^+$, 261 (100). HRMS (ESI): calcd. for $C_{20}H_{14}F_3NO_3$ + H$^+$ 374.1004; found 374.0979; Δ = 5.0 ppm.

***N*-Trifluoroacetyl-2-[1-amino-2-(benzyloxy)ethyl]-1,4-naphthoquinone (25e):** Yield: 46%. R_f = 0.31 (EtOAc/cyclohexane, 1:4). M.p. 103–104 °C. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 3.77 [dd, J = 10.0, 4.5 Hz, 1 H, CH(*H*)], 3.79 [dd, J = 10.0, 4.5 Hz, 1 H, C*H*(H)], 4.50 (s, 2 H, CCH$_2$), 5.29 (dt, J = 8.0, 4.4 Hz, 1 H, CH), 6.81 (s, 1 H, 3-H), 7.17–7.27 (m, 5 H, CH$_{ar}$), 7.30–7.35 (br. s, 1 H, NH), 7.73–7.77 (m, 2 H, 6-H and 7-H), 8.04–8.07 (m, 2 H, 5-H and 8-H) ppm. ^{13}C NMR (63 MHz, CDCl$_3$): δ = 49.7 (CH), 69.0 [CH(*C*H$_2$)], 73.3 (CH$_2$), 115.6 (q, J = 287.7 Hz, CF$_3$), 126.3, 126.7 and 128.2 (C_{quat}), 127.9 and 128.6 (C-5 and C-8), 131.8 and 131.9 (C_{quat}), 134.0 and 134.3 (C-6 and C-7), 135.7 (C-3), 136.8 (C_{quat}), 145.2 (C_{quat}), 156.7 (q, J = 37.7 Hz, *C*OCF$_3$), 184.3 (C=O), 184.5 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3280, 1698, 1661, 1560, 1206, 1168, 113, 1083, 780 cm^{-1}. No suitable MS could be recorded by EI or ESI (positive or negative). $C_{21}H_{16}F_3NO_4$ (403.36): calcd. C 62.53, H 4.00, N 3.47; found C 62.76, H 4.04, N 3.43.

***N*-Trifluoroacetyl-2-(1-amino-2-methoxyethyl)-1,4-naphthoquinone (25f):** Yield: 47%. R_f = 0.24 (EtOAc/cyclohexane, 1:3). M.p. 143.7–44.6 °C. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 3.36 (s, 3 H, OCH$_3$), 3.72 (d, J = 4.4 Hz, 2 H, CH$_2$), 5.31 (dt, J = 7.7, 4.4 Hz, 1 H, CH), 6.82 (s, 1 H, 3-H), 7.31 (br. d, J = 7.4 Hz, 1 H, NH), 7.76–7.79 (m, 2 H, 6-H and 7-H), 8.07–8.14 (m, 2 H, 5-H and 8-H) ppm. ^{13}C NMR (63 MHz, CDCl$_3$): δ = 49.4 (CH), 59.2 (OCH$_3$), 71.8 (CH$_2$), 115.6 (q, J = 286.0 Hz, CF$_3$), 126.4 and 126.7 (C-5 and C-8), 131.9 and 132.0 (C_{quat}), 134.1 and 134.3 (C-6 and C-7), 135.7 (C-3), 145.1 (C_{quat}), 156.7 (q, J = 36.2 Hz, CO), 184.3 (C=O), 184.6 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3247, 3083, 1717, 1662, 1562, 1185, 1152, 1089, 923, 782, 700 cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{12}F_3NO_4$ + H$^+$ 328.0797; found 328.0810; Δ = 3.9 ppm.

***N*-Trifluoroacetyl-2-(2-pyrrolidinyl)-1,4-naphthoquinone (25g):** Yield: 33%. R_f = 0.32 (EtOAc/cyclohexane, 1:3). M.p. 115.5–116.3 °C. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.87–2.13 (m, 3 H, NCHC*H*$_2$C*H*$_2$), 2.36–2.51 (m, 1 H, NCHC*H*$_2$C*H*$_2$), 3.76–3.96 (m, 2 H, NCH$_2$), 5.33 (dd, J = 8.7, 3.6 Hz, 1 H, CH), 6.53 (s, 1 H, 3-H), 7.72–7.81 (m, 2 H, 6-H and 7-H), 8.03–8.14 (m, 2 H, 5-H and 8-H) ppm. ^{13}C NMR (63 MHz, CDCl$_3$): δ = 24.3 (NCH$_2$*C*H$_2$), 30.8 (NCH*C*H$_2$), 47.6 (NCH$_2$), 57.6 (NCH), 116.1 (q, J = 287.6 Hz, CF$_3$), 126.2 and 126.6 (C-5 and C-8), 131.9 (C_{quat}), 132.1 (C-3), 132.8 (C_{quat}), 134.0 and 134.1 (C-6 and C-7), 148.3 (C_{quat}), 155.5 (q, J = 37.3 Hz, *C*OCF$_3$), 184.2 (C=O), 184.7 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 2984, 1689, 1661, 1593, 1448, 1186, 1150, 965, 778, 760, 703 cm^{-1}. MS (ES): *m*/*z* (%) = 324 (100) [M + H]$^+$. HRMS (ESI): calcd. for $C_{16}H_{12}F_3NO_3$ + H$^+$ 324.0847; found 324.0834; Δ = 4.5 ppm.

***N*-Trifluoroacetyl-2-(1-aminoethyl)-5-methoxy-1,4-naphthoquinone (31):** Yield: 42%. R_f = 0.25 (EtOAc/cyclohexane, 2:3). M.p. 170.5–171.5 °C. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.58 (d, J = 7.0 Hz, 3 H, CH$_3$), 4.03 (s, 3 H, OCH$_3$), 5.05 [dq (pseudo-quint), J = 7.4 Hz, 1 H, CHN], 6.80 (s, 1 H, 3-H), 7.30–7.37 (m, 1 H, 7-H), 7.45 (br. d, J = 8.0 Hz, 1 H, NH), 7.70–7.74 (m, 2 H, 6-H and 8-H) ppm. ^{13}C NMR (63 MHz, CDCl$_3$): δ = 20.9 (CH$_3$), 48.5 (NCH), 56.7 (OCH$_3$), 115.8 (q, J = 288.0 Hz, CF$_3$), 118.3 (C-7), 119.3 (C-6 or C-8), 119.9 (C_{quat}), 133.4 (C-3), 134.1 (C_{quat}), 135.8 (C-6 or C-8), 149.1 (C_{quat}), 156.5 (q, J = 37.4 Hz, CO), 160.3 (*C*OMe), 184.6 (C=O), 184.9 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3292, 1723, 1650, 1587, 1308, 1213, 1182, 1142, 946, 725 cm^{-1}. MS (ES): *m*/*z* (%) = 328 (100) [M + H]$^+$. HRMS (ESI): calcd. for $C_{15}H_{12}F_3NO_4$ + H$^+$ 328.0791; found 328.0803; Δ = 3.7 ppm.

General Procedure for the Preparation of *N*-Trifluoroacetyl-Protected 2-(1-Aminoalkyl)-3-(bromomethyl)naphthalene-1,4-diones (27): Paraformaldehyde (50 mmol, 1.5 g) and a solution of 33% HBr in acetic acid (10 mL) were added to a stirred mixture of *N*-trifluoroacetyl-protected 2-(1-aminoalkyl)naphthalene-1,4-diones **25** (1 mmol) in acetic acid (5 mL). The mixture was stirred at room temperature for 4 h, then water (20 mL) was added, and the aqueous solution was extracted with dichloromethane. The organic extracts were washed with water, dried (MgSO$_4$) and the solvents evaporated in vacuo. Flash chromatography on silica gel gave the desired compound **27**.

***N*-Trifluoroacetyl-2-(aminomethyl)-3-(bromomethyl)-1,4-naphthoquinone (27a):** Yield: 86%. R_f = 0.22 (EtOAc/cyclohexane, 1:6). M.p. 116–117 °C. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 4.59 (d, J = 6.4 Hz, 2 H, CH$_2$N), 4.77 (s, 2 H, CH$_2$Br), 7.22–7.28 (m, 1 H, NH + CHCl$_3$), 7.77–7.81 (m, 2 H, 6-H and 7-H), 8.06–8.10 (m, 1 H, 8-H or 5-H), 8.12–8.16 (m, 1 H, 5-H or 8-H) ppm. ^{13}C NMR (63 MHz, CDCl$_3$): δ = 20.2 (CH$_2$Br), 36.3 (CH$_2$N), 115.6 (q, J = 287.6 Hz, CF$_3$), 126.5 and 127.1 (C-5 and C-8), 131.4 and 131.6 (C_{quat}), 134.4 and 134.7 (C-6 and C-7), 140.5 (C_{quat}), 144.6 (C_{quat}), 157.4 (q, J = 37.6 Hz, *C*OCF$_3$), 182.2 (C=O), 185.3 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3303, 1695, 1661, 1291, 1179, 1154, 984, 732 cm^{-1}. MS (ES): *m*/*z* (%) = 376/378 (15) [M + H]$^+$, 296 (100). HRMS (ESI): calcd. for $C_{14}H_9BrF_3NO_3$ + H$^+$ 375.9791; found 375.9783; Δ = 2.1 ppm.

***N*-Trifluoroacetyl-2-(1-aminoethyl)-3-(bromomethyl)-1,4-naphthoquinone (27b):** Yield: 82%. R_f = 0.31 (EtOAc/cyclohexane, 1:6). M.p. 142.5–143.5 °C. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.67 (d, J = 7.0 Hz, CH$_3$), 4.75 and 4.59 (2 d, J = 9.9 Hz, 2 × 1 H, CH$_2$Br), 5.41 [dq (pseudo-quint), J = 7.2 Hz, 1 H, CH], 7.64–7.71 (br. s, 1 H, NH), 7.75–7.80 (m, 2 H, 6-H and 7-H), 8.05–8.13 (m, 2 H, 5-H and 8-H) ppm. ^{13}C NMR (63 MHz, CDCl$_3$): δ = 19.5 (CH$_3$), 20.2 (CH$_2$Br), 45.3 (CHN), 115.7 (q, J = 287.6 Hz, CF$_3$), 126.6 and 127.0 (C-5 and C-8), 131.3 and 131.9 (C_{quat}), 134.4 and 134.6 (C-6 and C-7), 142.7 and 144.1 (C_{quat}), 156.6 (q, J = 37.4 Hz, *C*OCF$_3$), 182.0 (C=O), 182.4 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3438, 1721, 1667, 1525, 1329, 1292, 1168, 1151, 938, 726 cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{11}BrF_3NO_3$ + H$^+$ 389.9947; found 389.9944; Δ = 0.7 ppm.

***N*-Trifluoroacetyl-2-(1-amino-2-methylpropyl)-3-(bromomethyl)-1,4-naphthoquinone (27c):** Yield: 83%. R_f = 0.17 (EtOAc/cyclohexane, 1:3). M.p. 165.5–166.4 °C. ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.96 (d, J = 6.8 Hz, 3 H, CH$_3$), 1.14 (d, J = 6.5 Hz, 3 H, CH$_3$), 2.40–2.55 [m, 1 H, C*H*(CH$_3$)$_2$], 4.71 and 4.69 (2 d, J = 10.0 Hz, 2 × 1 H, CH$_2$Br), 4.85 [dd (pseudo-t), J = 9.8 Hz, 1 H, CHN], 7.37 (br. d,

J = 9.2 Hz, 1 H, NH), 7.75–7.84 (m, 2 H, 6-H and 7-H), 8.05–8.10 (m, 1 H, 8-H or 5-H), 8.13–8.18 (m, 1 H, 5-H or 8-H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.6 and 20.1 [CH(CH_3)$_2$], 20.5 (CH_2Br), 31.9 [CH(CH$_3$)$_2$], 56.0 (NCH), 115.7 (q, J = 287.9 Hz, CF_3), 126.6 and 127.1 (C-5 and C-8), 131.6 and 131.7 (C_{quat}), 134.3 and 134.7 (C-6 and C-7), 143.5 and 144.2 (C_{quat}), 157.0 (q, J = 37.4 Hz, COCF$_3$), 182.0 (C=O), 185.8 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3212, 2968, 1671, 1684, 1592, 1556, 1292, 1189, 1138, 726 cm^{-1}. MS (ES): m/z (%) = 418/420 (30) [M + H]$^+$, 338 (100). HRMS (ESI): calcd. for $C_{17}H_{15}BrF_3NO_3$ + H$^+$ 418.0260; found 418.0255; Δ = 1.2 ppm.

***N*-Trifluoroacetyl-2-(1-amino-2-phenylethyl)-3-(bromomethyl)-1,4-naphthoquinone (27d):** Yield: 92%. R_f = 0.26 (EtOAc/cyclohexane, 1:6). M.p. 203.4–204.2 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.27 [dd, J = 14.2, 6.6 Hz, 1 H, CCH(H)], 3.30 [dd, J = 14.2, 7.9 Hz, 1 H, CCH(H)], 4.52 and 4.53 (2 d, J = 10.3 Hz, 2 × 1 H, CH_2Br), 5.48 [dt (pseudo-q), J = 8.0 Hz, 1 H, CH], 7.22–7.35 (m, 5 H, CH_{ar} + $CHCl_3$), 7.58 (br. d, J = 9.2 Hz, 1 H, NH), 7.78–7.85 (m, 2 H, 6-H and 7-H), 8.11–8.17 (m, 2 H, 5-H and 8-H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.2 (CH_2Br), 39.6 (CHCH_2), 51.3 (CH), 115.6 (q, J = 287.7 Hz, CF_3), 126.7, 127.1 and 127.5 (C_{quat}), 128.9 and 129.2 (C-5 and C-8), 131.4 and 131.8 (C_{quat}), 134.5 and 134.8 (C-6 and C-7), 135.9 (C_{quat}), 143.0 and 143.5 (C_{quat}), 156.7 (q, J = 37.5 Hz, COCF$_3$), 181.9 (C=O), 185.9 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3322, 1716, 1653, 1665, 1295, 1181, 1153, 727, 698 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{15}BrF_3NO_3$ + H$^+$ 466.0260; found 466.0269; Δ = 2.0 ppm.

***N*-Trifluoroacetyl-2-(1-amino-2-methoxyethyl)-3-(bromomethyl)-1,4-naphthoquinone (27f):** Yield: 80%. R_f = 0.31 (EtOAc/cyclohexane, 1:3). M.p. 157–158 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.41 (s, 3 H, OCH_3), 3.69 [dd, J = 9.9, 6.0 Hz, 1 H, CH(H)OMe], 3.94 [dd, J = 9.9, 7.9 Hz, 1 H, CH(H)OMe], 4.69 and 4.67 (2 d, J = 9.9 Hz, 2 × 1 H, CH_2Br), 5.57 (ddd, J = 8.3, 8.3, 6.2 Hz, 1 H, CH), 7.68 (br. d, J = 8.6 Hz, 1 H, NH), 7.78–7.82 (m, 2 H, 6-H and 7-H), 8.08–8.11 (m, 1 H, 8-H or 5-H), 8.14–8.17 (m, 1 H, 5-H or 8-H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 18.0 (CH_2Br), 46.8 (CH), 56.7 (OCH_3), 69.8 (CH_2O), 113.3 (q, J = 287.7 Hz, CF_3), 124.4 and 124.7 (C-5 and C-8), 139.0 and 129.4 (C_{quat}), 132.1 and 132.4 (C-6 and C-7), 138.7 and 142.6 (C_{quat}), 154.7 (q, J = 37.7 Hz, COCF$_3$), 179.5 (C=O), 183.4 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3229, 3060, 1702, 1671, 1631, 1550, 1291, 1185, 1147, 1119, 1080, 921, 725, 669 cm^{-1}. No suitable MS could be recorded by EI or ESI (positive or negative).

***N*-Trifluoroacetyl-2-(2-pyrrolidinyl)-3-(bromomethyl)-1,4-naphthoquinone (27g):** Yield: 84%. R_f = 0.25 (EtOAc/cyclohexane, 1:9). M.p. 152.1–152.6 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.02–2.37 (m, 3 H, CHCH_2CH_2N), 2.45–2.55 (m, 1 H, CHCH_2CH_2N), 3.97–4.19 (m, 2 H, NCH_2), 4.84 and 4.62 (2 d, J = 9.9 Hz, 2 × 1 H, CH_2Br), 5.15 (t, J = 8.3 Hz, 1 H, CH), 7.70–7.78 (m, 2 H, 6-H and 7-H), 7.99–8.05 (m, 1 H, 8-H or 5-H), 8.08–8.14 (m, 1 H, 5-H or 8-H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.7 (NCH_2CH_2), 26.0 (CH_2Br), 29.6 (CHCH_2), 48.1 (NCH_2), 58.3 (CH), 116.0 (q, J = 287.2 Hz, CF_3), 126.5 and 126.7 (C-5 and C-8), 131.4 and 132.2 (C_{quat}), 134.1 (C-6 and C-7), 144.0 and 145.0 (C_{quat}), 155.4 (q, J = 36.9 Hz, COCF$_3$), 182.1 (C=O), 183.4 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1680, 1663, 1589, 1295, 1456, 1445, 1295, 1239, 1176, 1143, 954, 799, 758, 727, 710 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{13}BrF_3NO_3$ + H$^+$ 416.0104; found 416.0109; Δ = 1.2 ppm.

***N*-Trifluoroacetyl-2-(1-aminoethyl)-3,8-bis(bromomethyl)-5-methoxy-1,4-naphthoquinone (32):** Yield: 69%. R_f = 0.19 (EtOAc/cyclohexane, 3:7). M.p. 112.9–113.9 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.64 (d, J = 7.0 Hz, 3 H, CH_3), 4.04 (s, 3 H, OCH_3), 4.72 and 4.56 (2 d, J = 10.0 Hz, 2 × 1 H, C^{3}CH_2Br), 5.02 and 5.00 (2 d, J = 10.0 Hz, 2 × 1 H, C^{8}CH_2Br), 5.36 (dq, J = 9.0, J = 7.0 Hz, 1 H, NCH), 7.32 (d, J = 8.9 Hz, 1 H, 6-H), 7.64 (d, J = 8.8 Hz, 1 H, NH), 7.75 (d, J = 8.9 Hz, 1 H, 7-H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.5 (CH_3), 20.4 (CH_2Br), 32.1 (CH_2Br), 45.2 (NCH), 56.7 (OCH_3), 116.7 (q, J = 287.7 Hz, CF_3), 118.3 (C-6), 121.2 and 130.3 (C_{quat}), 132.0 (C-8), 139.6 (C-7), 144.2 and 145.7 (C_{quat}), 156.6 (q, J = 37.5 Hz, COCF$_3$), 183.9 (C=O), 184.7 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3270, 1698, 1653, 1560, 1259, 1186, 1158, 1035, 881, 727 cm^{-1}. No suitable MS could be recorded by EI or ESI (positive or negative).

General Procedure for the Synthesis of Benzo[*f*]isoindole-4,9-diones 29: A 5 M KOH solution (10 equiv.) was added to a solution of *N*-trifluoroacetyl-protected 2-(1-aminoalkyl)-3-(bromomethyl)-1,4-naphthoquinone **27** (100 mg) in methanol/dichloromethane (1:1, 20 mL) at 0 °C under N_2. The cooling bath was removed, and the mixture was stirred at room temperature for 20 h. In the next step, the solvent was removed under vacuum, and water (15 mL) was added to the residue. After extraction with dichloromethane (1×) and ethyl acetate (1×), the combined organic layers were dried ($MgSO_4$) and the solvents evaporated in vacuo. Purification by flash chromatography on silica gel afforded benzo[*f*]isoindole-4,9-diones **29**.

2*H*-Benzo[*f*]isoindole-4,9-dione (29a): Yield: 53%. The NMR spectroscopic data were in accordance with the data reported in the literature.[36]

1-Methyl-2*H*-benzo[*f*]isoindole-4,9-dione (29b): Yield: 42%. R_f = 0.24 (EtOAc/cyclohexane, 3:2). M.p. 241.2–241.8 °C. ^{1}H NMR (250 MHz, CD_3OD): δ = 2.60 (s, 3 H, CH_3), 7.42 (s, 1 H, 3-H), 7.71–7.75 (m, 2 H, 6-H and 7-H), 8.14–8.18 (m, 2 H, 5-H and 8-H) ppm (NH was not visible). ^{13}C NMR (63 MHz, [D$_6$]DMSO): δ = 12.3 (CH_3), 116.8 (C_{quat}), 121.4 (C-3), 121.6 (C_{quat}), 126.2 (C-5 and C-8), 132.9 and 133.1 (C-6 and C-7), 135.1 and 135.6 (C_{quat}), 136.8 [C(CH$_3$)], 179.3 (C=O), 179.8 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3225, 2399, 1641, 1532, 1336, 932, 713 cm^{-1}. MS (ES): m/z (%) = 212 (100) [M + H]$^+$. HRMS (ESI): calcd. for $C_{13}H_9NO_2$ + H$^+$ 212.0706; found 212.0702; Δ = 1.9 ppm.

1-Benzyl-2*H*-benzo[*f*]isoindole-4,9-dione (29d): Yield: 44%. R_f = 0.16 (EtOAc/cyclohexane, 1:3). ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 4.51 (s, 2 H, CH_2), 7.26–7.36 (m, 5 H, CH_{ar}), 7.39 (s, 1 H, CHN), 7.70–7.75 (m, 2 H, 6-H and 7-H), 8.21–8.26 (m, 2 H, 5-H and 8-H), 8.84 (br. s, 1 H, NH) ppm. ^{13}C NMR (126 MHz, CD_2Cl_2): δ = 33.3 (CH_2), 120.5 (CH), 127.0 and 127.1 and 127.5 (C_{ar}), 129.3 and 129.4 (C-5 and C-8), 133.1 and 133.3 (C-6 and C-7), 136.0, 136.6 and 137.5 (C_{quat}), 138.8 (C_{quat}), 180.7 (C=O), 181.2 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3213, 1643, 1528, 1359, 1242, 930, 710 cm^{-1}. MS (ES): m/z (%) = 288 (100) [M + H]$^+$. HRMS (ESI): calcd. for $C_{19}H_{13}NO_2$ + H$^+$ 288.1019; found 288.1012; Δ = 2.4 ppm.

Synthesis of 2,3-Dihydro-1*H*-benzo[*f*]pyrrolo[2,1-*a*]isoindole-6,11-dione (29g): A 5 M aqueous KOH solution (10 equiv.) was added to a solution of *N*-trifluoroacetyl-2-(2-pyrrolidinyl)-3-(bromomethyl)-1,4-naphthoquinone (**27g**; 100 mg, 0.241 mmol) in methanol/dichloromethane (1:1; 20 mL) at 0 °C under N_2. The cooling bath was removed, and the mixture was heated at reflux for 7 h. In the next step, the solvent was removed under vacuum, and water (15 mL) was added to the residue. After extraction with dichloromethane and ethyl acetate, the combined organic layers were dried ($MgSO_4$) and the solvents evaporated in vacuo. Purification by flash chromatography on silica gel afforded the benzo[*f*]isoindole-4,9-dione **29g** in 29% yield. R_f = 0.21 (EtOAc/cyclohexane, 1:1). M.p. 219.2–219.7 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.67 (quint, J = 7.1 Hz, 2 H, NCH_2CH_2), 3.21 (t, J = 7.3 Hz, 2 H, NCCH_2),

4.10 (t, J = 7.2 Hz, 2 H, NCH_2), 7.36 (s, 1 H, 5-H), 7.65–7.72 (m, 2 H, 8-H and 9-H), 8.21–8.26 (m, 2 H, 7-H and 10-H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 24.9 (NCH_2CH_2), 27.4 ($NCCH_2$), 47.1 (NCH_2), 114.0 (C_{quat}), 117.7 (CH), 126.7 and 126.9 (C-7 and C-10), 132.7 and 132.9 (C-8 and C-9), 135.6, 136.7 and 143.9 (C_{quat}), 180.3 (C=O), 180.6 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 3119, 2959, 1652, 1528, 1222, 988, 719 cm^{-1}. MS (ES): m/z (%) = 238 (100) [M + H]$^+$. HRMS (ESI): calcd. for $C_{15}H_{11}NO_2 + H^+$ 238.08630; found 238.08639; Δ = 3.8 ppm.

***N*-Alkylation. Synthesis of 2-Propyl-2*H*-benzo[*f*]isoindole-4,9-dione (34a) and 1-Methyl-2-propyl-2*H*-benzo[*f*]isoindole-4,9-dione (34b):** Synthesis of **34a** as an example. Compound **29a** (50 mg, 0.25 mmol) was added to a suspension of KOH (70 mg, 1.25 mmol) in DMF (5 mL) . After stirring the solution for 1 h, 1-bromopropane (43 mg, 0.35 mmol) was added. The reaction mixture was then heated and stirred at 50 °C overnight. The resulting suspension was poured into water and extracted with dichloromethane. The combined organic layers were washed with water, dried with anhydrous $MgSO_4$ and filtered, and the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (EtOAc/cyclohexane, 1:3; R_f = 0.16) to obtain 44 mg (74%) of **34a**.

2-Propyl-2*H*-benzo[*f*]isoindole-4,9-dione (34a): The NMR spectroscopic data were in accordance with data reported in the literature.[20]

1-Methyl-2-propyl-2*H*-benzo[*f*]isoindole-4,9-dione (34b): Yield: 72%. R_f = 0.24 (EtOAc/cyclohexane, 3:2). M.p. 172.4–173.4 °C. ^1H NMR (250 MHz, [D$_6$]DMSO): δ = 0.85 (t, J = 7.3 Hz, 3 H, CH_2CH_3), 1.72 (sext, J = 7.3 Hz, 2 H, CH_2CH_3), 2.58 (s, 3 H, CH_3), 3.94 (t, J = 7.3 Hz, 2 H, NCH_2), 7.67 (s, 1 H, 3-H), 7.73–7.77 (m, 2 H, 6-H and 7-H), 8.04–8.09 (m, 2 H, 5-H and 8-H) ppm. ^{13}C NMR (63 MHz, [D$_6$]DMSO): δ = 10.6 (CH_3), 10.7 (CH_2CH_3), 23.0 (CH_2CH_3), 47.9 (NCH_2), 117.2 and 120.4 (C_{quat}), 125.1 (CH), 126.1 and 126.2 (C-5 and C-8), 133.0 and 133.2 (C-6 and C-7), 134.8 and 135.5 (C_{quat}), 137.0 [C(CH_3)], 178.9 (C=O), 179.6 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1645, 1538, 1261, 1224, 953, 711 cm^{-1}. MS (ES): m/z (%) = 254 (100) [M + H]$^+$. HRMS (ESI): calcd. for $C_{16}H_{15}NO_2 + H^+$ 254.1103; found 254.1113; Δ = 3.9 ppm.

Bromination. Synthesis of 1-Bromo-3-methyl-2-propyl-2*H*-benzo[*f*]isoindole-4,9-dione (35b) and 1,3-Dibromo-2-propyl-2*H*-benzo[*f*]isoindole-4,9-dione (35a): Synthesis of **35b** as an example. A solution of bromine (33 mg, 0.21 mmol) in dichloromethane (5 mL) was added dropwise to **34b** (51 mg, 0.2 mmol) in dichloromethane (5 mL). The reaction mixture was stirred at room temperature for 1 h. Evaporation of the solvent under vacuum gave **35b** (66 mg) in 100% yield.

1-Bromo-3-methyl-2-propyl-2*H*-benzo[*f*]isoindole-4,9-dione (35b): Yield: 100%. M.p. 133–134 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.01 (t, J = 7.4 Hz, 3 H, CH_2CH_3), 1.78 (sext, J = 7.6 Hz, 2 H, CH_2CH_3), 2.73 (s, 3 H, CH_3), 3.98 (t, J = 7.3 Hz, 2 H, NCH_2), 7.65–7.71 (m, 2 H, 6-H and 7-H), 8.19–8.27 (m, 2 H, 5-H and 8-H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 11.1 (CH_3), 11.9 (CH_2CH_3), 23.2 (CH_2CH_3), 46.7 (NCH_2), 107.6 (C_{quat}), 118.8 and 119.3 (C_{quat}), 126.6 and 126.7 (C-5 and C-8), 133.0 (C-6 and C-7), 135.4 and 135.6 (C_{quat}), 137.6 (C_{quat}), 179.0 (C=O), 180.2 (C=O) ppm. IR (ATR): $\tilde{\nu}$ = 1649, 1510, 1248, 1227, 1062, 968, 712 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{14}BrNO_2 + H^+$ 332.0281; found 332.0282; Δ = 0.3 ppm.

1,3-Dibromo-2-propyl-2*H*-benzo[*f*]isoindole-4,9-dione (35a): Yield: 100%. M.p. 127.5–128.5 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.04 (t, J = 7.4 Hz, 3 H, CH_2CH_3), 1.85 (sext, J = 7.6 Hz, 2 H, CH_2CH_3), 4.18 (t, J = 7.6 Hz, 2 H, NCH_2), 7.70–7.76 (m, 2 H, 6-H and 7-H), 8.24–8.31 (m, 2 H, 5-H and 8-H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 11.0 (CH_3), 23.0 (CH_2CH_3), 48.8 (NCH_2), 108.6 (2 C_{quat}), 120.6 (2 C_{quat}), 127.0 (C-5 and C-8), 133.4 (C-6 and C-7), 135.0 (2 C_{quat}), 178.1 (2 C=O) ppm. IR (ATR): $\tilde{\nu}$ = 2923, 1656, 1593, 1491, 1356, 1230, 996, 715 cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{11}Br_2NO_2 + H^+$ 395.9229; found 395.9248; Δ = 4.8 ppm.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR spectra of compounds **14**–**19**, **24e**, **25a**–**g**, **27a**–**d**,**f**,**g**, **29a**,**b**,**d**,**g**, **31**, **32**, **34a**,**b** and **35a**,**b**.

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