Synthesis of 1,2,7,7a-Tetrahydro-1a*H*-cyclopropa[*b*]quinoline-1a-carboxylic Acid Derivatives, Doubly Constrained ACC Derivatives, by a Remarkable Cyclopropanation Process

Zsolt Szakonyi,[†,‡] Ferenc Fülöp,[‡] Dirk Tourwé,[§] and Norbert De Kimpe*[,†]

Department of Organic Chemistry, Faculty of Agricultural and Applied Biological Sciences, Ghent University, Coupure Links 653, B-9000 Ghent, Belgium, Institute of Pharmaceutical Chemistry, University of Szeged, H-6701, Szeged, POB 121, Hungary, and Organic Chemistry Department, Vrije Universiteit Brussel, Pleinlaan 2, B-1050 Brussels, Belgium

norbert.dekimpe@rug.ac.be

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Reaction of *N*-benzoyl-1,2,3,4-tetrahydroquinoline-2-carboxylic acid with acetic anhydride resulted in 1*H*,3*H*,5*H*-oxazolo[3,4-*a*]quinolin-3-one derivative **13**. Different cyclopropanation processes were applied to **13**, but only diazomethane in the presence of water furnished the hitherto unknown methyl 1,2,7,7a-tetrahydro-1a*H*-cyclopropa[*b*]quinoline-1a-carboxylate **14**, which can be considered as a doubly constrained 1-aminocyclopropane-1-carboxylic acid system. The mechanism of the cyclopropanation was studied in detail. The new ACC ester **14** was transformed into fused tetracyclic hydantoin derivatives, which comprised a new type of heterocyclic system.

Introduction

Cyclopropane amino acids and their derivatives are of broad interest as biological probes, enzyme inhibitors, and conformationally constrained analogues of native amino acids.[1−4] Since the cyclopropane ring introduces a steric constraint into the amino acid, the chemical reactivity of the functional groups changes. The simplest of such compounds, 1-aminocyclopropane-1-carboxylic acid (**1**), is known to be the biochemical precursor of the plant hormone ethylene in a process catalyzed by the ethylene-forming enzyme.[5] Substances that inhibit the ethylene-forming enzyme would allow effective control of the growth of plants and, therefore, be of the greatest importance in agriculture.[6−8]

The cyclopropane ring exhibits a certain "unsaturated character", which results in a restriction of the torsion angles about the $C_\alpha-C{=}O$ bond to small values, due to conjugation of the carbonyl group with the ring.[9,10] Insertion of a conformationally constrained amino acid into a peptide can cause significant changes in the conformation, which in turn may affect the ability of the peptide to fit to a receptor. Recently, we described the synthesis of 3,4-methano-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (**2**), a new doubly constrained analogue of phenylalanine, as a combination of 1-aminocyclopropane-1-carboxylic and 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid.[11] As a continuation of this search for novel constrained amino acid derivatives, our present aim was to synthesize the hitherto unknown methyl 2,3-methano-1,2,3,4-tetrahydroquinoline-2-carboxylate (**3**) (Figure 1) and its derivatives as a combination of 1-aminocyclopropane-1-carboxylic acid and 1,2,3,4-tetrahydroquinoline-2-carboxylic acid moieties. Tetrahydroquinolines, such as their 2-carboxylic acid derivatives, are also at the center of interest since they have strong affinities for the glycine binding site of the NMDA receptor.[12−14] Over-excitation of this receptor plays an important role in neuronal cell death during ischaemic or hypoxic conditions such as stroke or epilepsy.[15,16] 1,2,3,4-Tetrahydroquinoline-2-carboxylic acid derivatives may serve as building blocks of pharmacologically active dipeptides,[17,18] and some of them also have explicit antihypertensive effects.[19]

* To whom correspondence should be addressed. Tel: 32 9 264 59 51. Fax: 32 9 264 62 43.
† Ghent University.
‡ University of Szeged.
§ Vrije Universiteit Brussel.

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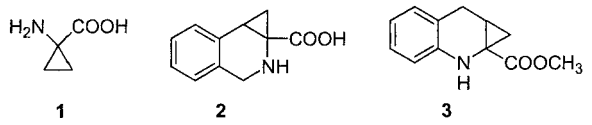

1 2 3

Figure 1.

To synthesize the title compound **3**, two important problems had to be solved: the preparation of a very unstable 1,4-dihydroquinoline-1-carboxylic acid and/or its derivatives as possible starting materials for the cyclopropanation process, the latter being the second problem, involving a compound bearing an electron-attracting carboxylic function adjacent to the double bond.

Results and Discussion

Methyl 1,2,3,4-tetrahydroquinoline-2-carboxylate **5** was prepared by a literature method, starting from commercially available quinaldinic acid **4** (Scheme 1).[12,13] The catalytic hydrogenation of **4** over platinum oxide under hydrogen at atmospheric pressure and ambient temperature resulted in the corresponding tetrahydro acid derivative, which was converted without isolation to the amino ester **5** in an overall yield of 80%. First, we attemped to prepare the N-protected methyl 2,3-dihydroquinoline-2-carboxylate **6** by selective oxidation of **5** via N-chlorination with *tert*-butyl hypochlorite and subsequent dehydrochlorination with triethylamine,[20] followed by protection of the nitrogen with methyl chloroformate (Scheme 1).

Instead of the expected compound **6**, a mixture containing several chlorinated components was obtained. After purification of the mixture by column chromatography, it was found that the main component was the starting material **5**, which was accompanied by methyl 6-chloro-, 8-chloro-, and 6,8-dichloro-1,2,3,4-tetrahydroquinoline-2-carboxylates **7**−**9** and methyl 6,8-dichloroquinoline-2-carboxylate **10**, which were isolated and identified by ^{1}H and ^{13}C NMR and LRMS spectroscopy. When 2 equiv of *tert*-butyl hypochlorite in dry CH_2Cl_2 were used at 0 °C for 1 h, in addition to **10**, methyl 6,8-dichloro-1,2,3,4-tetrahydroquinoline-2-carboxylate **9** was isolated as the main component in 65% isolated yield. Application of *N*-chlorosuccinimide as an N-chlorination agent[11,21] led to similar results; N-chlorination was not observed, as such reaction products probably rearranged to ring-chlorinated products.

Zecchini and Paradisi reported an unexpected cyclization of *N*-acyl-1,2,3,4-tetrahydroquinoline-2-carboxylic acids as an alternative pathway of the Dakin−West reaction.[18] The 1*H*,3*H*,5*H*-oxazolo[3,4-*a*]quinoline derivatives formed that were described appeared to us to be excellent starting materials for the synthesis of cyclopropane-fused tetrahydroquinoline derivatives.

Acylation of methyl 1,2,3,4-tetrahydroquinoline-2-carboxylate **5** with benzoyl chloride in pyridine, followed by alkaline hydrolysis of the ester group, resulted in *N*-benzoyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylic acid **12**. Treatment of amide **12** with acetic anhydride afforded 1*H*,3*H*,5*H*-oxazolo[3,4-*a*]quinoline derivative **13** in good yield (Scheme 2). The mechanism of the cyclization has been discussed in detail in the literature.[18]

The attempted cyclopropanation of compound **13** with dimethylsulfoxonium methylide, generated from trimethylsulfoxonium iodide with NaH in DMSO, failed.[22] Application of diazomethane, prepared by a literature method,[23] as a cyclopropanation agent for 48 h during stirring at room temperature led to the unexpected formation of methyl 1,2,7,7a-tetrahydro-1a*H*-cyclopropa[*b*]quinoline-1a-carboxylate **14** and benzaldehyde (Scheme 2). The reaction was monitored by ^{1}H NMR spectroscopy (disappearance of the olefinic H-3 signal). When Pd(II) acetate was used as a catalyst in an effort to reduce the reaction time,[24] only the fast decomposition of diazomethane was observed.

The suggested reaction pathway is shown in Scheme 3. It is presumed that the first step is a slow hydrolysis of oxazolidone **13** to the corresponding acid derivative **15**, followed by rapid esterification and cyclopropanation and finally decomposition of intermediate **16** to amino ester **14** and benzaldehyde. It must be mentioned that alternative reaction pathways are also possible as shown in Scheme 4. When compound **13** was stirred with a dried ethereal solution of diazomethane, no reaction was observed, pointing to the necessity of the presence of water in the cyclopropanation process. After **13** had been stirred for a few days in water-saturated diethyl ether solution, quinaldic acid and benzoic acid were identified in the reaction mixture.

The hydrolysis of amino ester **14** to the corresponding amino acid was attempted by several methods, but regardless of whether acidic or basic conditions were applied, only numerous decomposition products were obtained. Boc or Cbz protection of the nitrogen also failed, probably because of the steric hindrance and the strong electron-withdrawing character of the aromatic ring and the ester group.

Since hydantoins are typical heterocyclic derivatives of α-amino acids that are of importance both chemically and pharmacologically, it was decided to synthesize some of these compounds. When amino ester **14** was reacted with different isocyanates, urea derivatives **20a**−**c** were obtained (Scheme 5).

No reaction occurred when the corresponding thiocyanates were used. Urea derivatives **20a**−**c** were converted to hydantoins **21a**−**c** by base-catalyzed ring closure, resulting in a new heterocyclic system.[25]

Experimental Section

^{1}H and ^{13}C NMR, DEPT, and COSY spectra were recorded at 270 and 67.9 MHz, with the exception of compound **14**, for which the ^{1}H NMR spectrum was recorded at 500 MHz. IR spectra were measured with an FT-IR spectrometer. Electron impact (EI) mass spectra were obtained at 70 eV. Melting points are uncorrected. Chromatographic separations were performed on Merck Kieselgel 60 (230−400 mesh ASTM). Reactions were monitored with Merck Kieselgel 60 F_{254}-precoated TLC plates (0.25 mm thickness). All chemicals and solvents were used as supplied. Methyl 1,2,3,4-tetrahydroquinoline-2-carboxylate **5** was prepared by hydrogenation of

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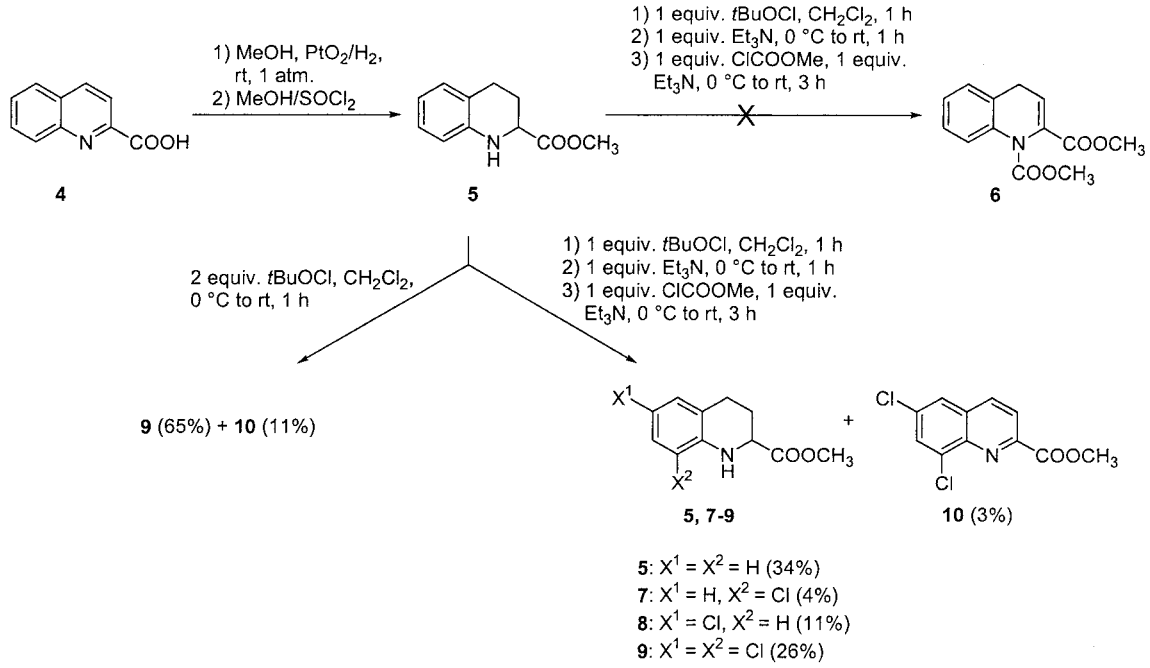
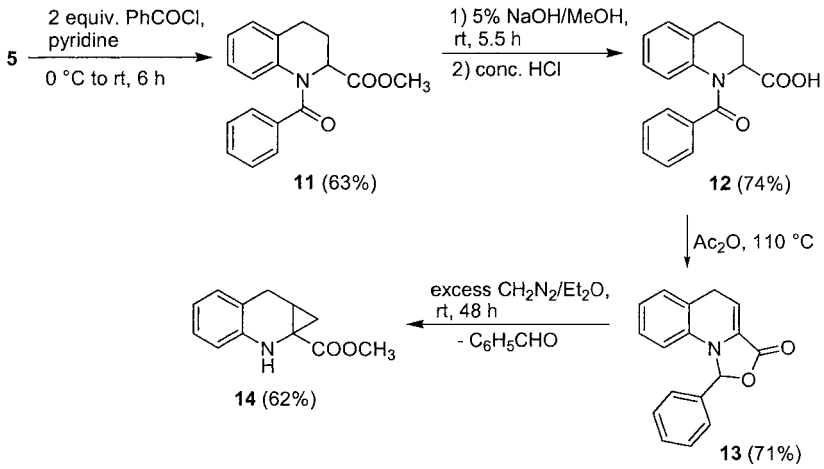
Scheme 1



Scheme 2

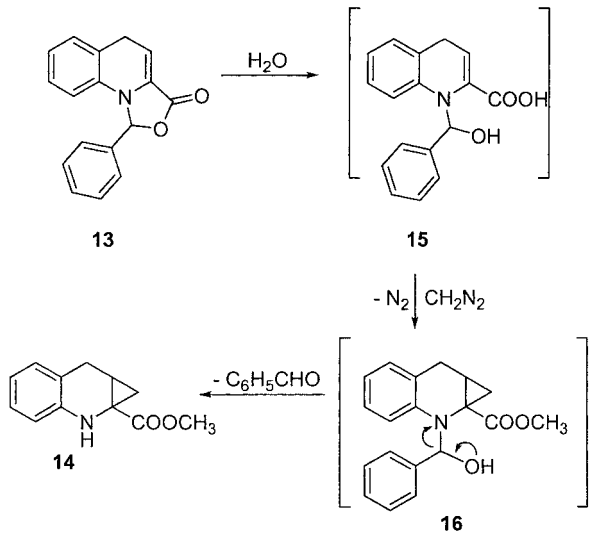


quinaldic acid in methanol over platinum oxide under normal pressure of hydrogen followed by esterification with methanol according to a literature method.[12]

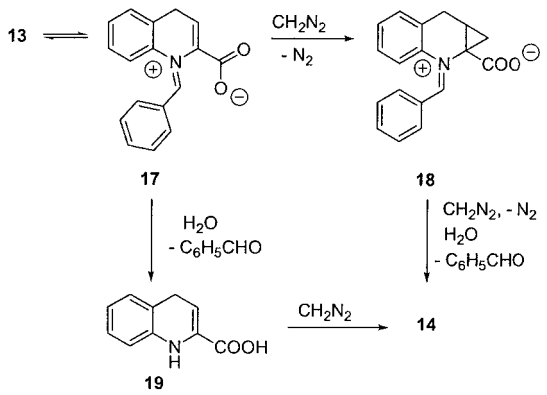
Reaction of Methyl 1,2,3,4-Tetrahydroquinoline-2-carboxylate (5) with *tert*-Butyl Hypochlorite. Method A. To a stirred solution of 0.38 g (2 mmol) of compound **5** in 6 mL of dry CH_2Cl_2 was added 0.22 g (2 mmol) of *tert*-butyl hypochlorite, dissolved in 2 mL of CH_2Cl_2, dropwise at 0 °C under a N_2 atmosphere. The temperature was allowed to rise to room temperature, and after the solution was stirred for 1 h, 0.20 g (2 mmol) of Et_3N, dissolved in 2 mL of dry CH_2Cl_2, was added dropwise at 0 °C. After being stirred for 3 h at room temperature, the mixture was poured in a separatory funnel containing 50 mL of $CHCl_3$ and was washed with 1 M HCl solution (10 mL) and water (2 × 10 mL). The organic phase was dried ($MgSO_4$) and evaporated, and the resulting crude product was purified by flash chromatography on silica gel (eluent: petroleum ether/EtOAc = 9:1) furnishing the starting material **5** (34%) and compounds **7**−**10** (**7**, 4%; **8**, 11%; **9**, 26%; **10**, 3%).

Method B. To a stirred solution of 3.82 g (20 mmol) of compound **5** in 60 mL of dry CH_2Cl_2 was added 4.34 g (40 mmol) of *tert*-butyl hypochlorite, dissolved in 30 mL of CH_2Cl_2, dropwise at 0 °C under a N_2 atmosphere. The temperature was allowed to rise to room temperature, and after being stirred for 1 h, the solution was poured in a separatory funnel and extracted with ice-cold 5% $NaHCO_3$ solution (2 × 30 mL) and water (2 × 20 mL). The organic phase was dried

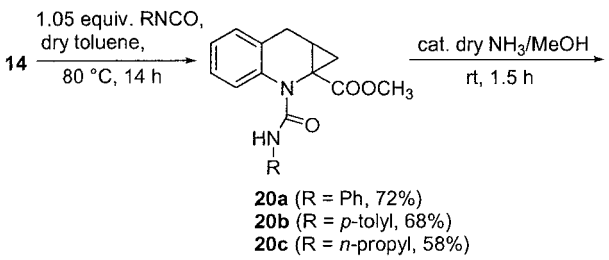
Scheme 3



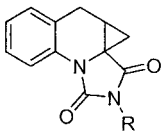
Scheme 4



Scheme 5



20a (R = Ph, 72%)
20b (R = *p*-tolyl, 68%)
20c (R = *n*-propyl, 58%)



21a (R = Ph, 80%)
21b (R = *p*-tolyl, 78%)
21c (R = *n*-propyl, 85%)

($MgSO_4$) and evaporated, and the crude product was purified by flash chromatography on silica gel (eluent: petroleum ether/EtOAc = 9:1), furnishing compounds **9** (65%) and **10** (11%).

Methyl 8-chloro-1,2,3,4-tetrahydroquinoline-2-carboxylate (7): mp 47−49 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.99−2.09 (m, 1 H, CH_2CH_2CH), 2.25−2.31 (m, 1 H, CH_2CH_2CH), 2.77−2.84 (m, 2 H, $ArCH_2$), 3.79 (s, 3 H, $COOCH_3$), 4.09−4.17 (m, 1 H, CH), 4.9 (br s, 1 H, NH), 6.56 (t, 1 H, J = 7.7 Hz, ArH), 6.87 (d, 1 H, J = 7.5 Hz, ArH), 7.11 (d, 1 H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 20.6 (C-3), 26.1 (C-4), 51.9 ($COOCH_3$), 55.2 (C-2), 120.8, 138.1, 142.3 (C_q, aromatic), 113.9, 127.6, 128.9 (CH, aromatic), 172.8 ($COOCH_3$); IR (KBr, cm^{-1}) 3380, 1724, 1475; LRMS (70 eV, *m*/*z*) 225 (M^+, 32), 189 (33), 166 (100), 132 (32). Anal. Calcd for $C_{11}H_{12}ClNO_2$: C, 58.54; H, 5.36; N, 6.21. Found: C, 58.69; H, 5.47; N, 6.45.

Methyl 6-chloro-1,2,3,4-tetrahydroquinoline-2-carboxylate (8): mp 46−48 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.93−2.05 (m, 1 H, CH_2CH_2CH), 2.17−2.29 (m, 1 H, CH_2CH_2CH), 2.67−2.77 (m, 2 H, $ArCH_2$), 3.77 (s, 3 H, $COOCH_3$), 4.02 (dd, 1 H, J = 4.0, 8.1 Hz, CH), 6.5 (d, 1 H, J = 7.9 Hz, ArH), 6.92 (s, 1 H, overlapped, ArH), 6.94 (dd, 1 H, J = 8.1, 2.0 Hz, ArH); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 24.2 (C-3), 25.6 (C-4), 52.4 ($COOCH_3$), 53.7 (C-2), 121.9, 122.0, 141.5 (C_q, aromatic), 115.6, 126.9, 128.7 (CH, aromatic), 173.5 ($COOCH_3$); IR (KBr, cm^{-1}) 3390, 2927, 1734, 1492, 1222; LRMS (70 eV, *m*/*z*) 225 (M^+, 11), 166 (100). Anal. Calcd for $C_{11}H_{12}ClNO_2$: C, 58.54; H, 5.36; N, 6.21. Found: C, 58.32; H, 5.51; N, 6.14.

Methyl 6,8-dichloro-1,2,3,4-tetrahydroquinoline-2-carboxylate (9): mp 44−45 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.97−2.05 (m, 1 H, CH_2CH_2CH), 2.23−2.27 (m, 1 H, CH_2CH_2-CH), 2.73−2.80 (m, 2 H, $ArCH_2$), 3.79 (s, 3 H, $COOCH_3$), 4.09−4.15 (m, 1 H, CH), 4.9 (br s, 1 H, NH), 6.86 (d, 1 H, J = 1.9 Hz, ArH), 7.11 (d, 1 H, J = 2.1 Hz, ArH); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 23.8 (C-3), 25.7 (C-4), 52.6 ($COOCH_3$), 53.5 (C-2), 118.6, 121.0, 122.8, 137.9 (C_q, aromatic), 126.6, 127.2 (CH, aromatic), 172.9 ($COOCH_3$); IR (KBr, cm^{-1}) 3435, 1722, 1452, 1140; LRMS (70 eV, *m*/*z*) 259 (M^+, 24), 200 (100), 165 (22), 164 (24). Anal. Calcd for $C_{11}H_{11}Cl_2NO_2$: C, 50.79; H, 4.26; N, 5.38. Found: C, 50.43; H, 4.35; N, 5.14.

Methyl 6,8-dichloroquinoline-2-carboxylate (10): mp 193−195 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 4.09 (s, 3 H, $COOCH_3$), 7.82 (d, 1 H, J = 2.3 Hz), 7.90 (d, 1 H, J = 2.3 Hz), 8.26 (d, 1 H, J = 8.6 Hz), 8.29 (d, 1 H, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 53.4 ($COOCH_3$), 122.8, 125.4, 131.2, 137.0 (CH, aromatic), 130.7, 134.1, 136.0, 141.5, 148.6 (C_q, aromatic), 165.4 ($COOCH_3$); IR (KBr, cm^{-1}) 1722, 1452, 1139, 868; LRMS (70 eV, *m*/*z*) 255 (M^+, 14), 197 (100), 161 (19). Anal. Calcd for $C_{11}H_7Cl_2NO_2$: C, 51.59; H, 2.76; N, 5.47. Found: C, 51.93; H, 3.05; N, 5.17.

Methyl *N*-Benzoyl-1,2,3,4-tetrahydroquinoline-2-carboxylate (11). To a stirred solution of 4.97 g (26.0 mmol) of amino ester **5** was added 7.31 g (52.0 mmol) of benzoyl chloride dropwise at 0 °C. After standing for 6 h in a dark place at room temperature, the mixture was poured into 300 mL of cold water and extracted with EtOAc (3 × 100 mL). The organic phase was washed with 2 M HCl solution (2 × 50 mL), water (50 mL), and 10% $NaHCO_3$ solution (2 × 50 mL), dried ($MgSO_4$), and evaporated in vacuo. The crude product was purified by flash chromatography on silica gel (eluent: petroleum ether/EtOAc = 9:1), furnishing 4.83 g (63%) of pure compound **11**: mp 101−105 °C (lit.[18] mp 108−109 °C); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.83−1.93 (m, 1 H, CH_2CH_2CH), 2.55−2.69 (m, 1 H, CH_2CH_2CH), 2.73−2.82 (m, 2 H, $ArCH_2$), 3.72 (s, 3 H, $COOCH_3$), 5.13 (t, 1 H, J = 8.2 Hz, CH), 6.62 (d, 1 H, J = 7.9 Hz, ArH), 6.85 (t, 1 H, J = 7.8 Hz, ArH), 6.98 (t, 1H, J = 7.4 Hz, ArH), 7.13−7.34 (m, 6 H, ArH); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 26.1 (C-3), 28.6 (C-4), 52.2 (C-2), 56.1 ($COOCH_3$), 124.7, 126.0, 127.1, 127.8, 128.8, 130.4, 135.1 (CH, aromatic), 126.2, 132.6, 138.3 (C_q, aromatic), 170.2 ($COOCH_3$), 172.1 (CON); IR (KBr, cm^{-1}) 1750, 1637, 1423; LRMS (70 eV, *m*/*z*) 295 (M^+, 79), 236 (68), 130 (28), 105 (100), 77 (64).

***N*-Benzoyl-1,2,3,4-tetrahydroquinoline-2-carboxylic Acid (12).** A 2.51 g (8.5 mmol) portion of **11** was dissolved in a 5% solution of NaOH in MeOH. After being stirred for 5.5 h at room temperature, the solution was evaporated to dryness, and the residue was dissolved in 50 mL of water. The aqueous solution was extracted with EtOAc (2 × 20 mL), acidified with concentrated HCl, and extracted with Et_2O (3 × 30 mL). The Et_2O phase was dried ($MgSO_4$) and evaporated in vacuo, resulting in 1.76 g (74%) of compound **12**: mp 178−180 °C (lit.[18] mp 180−181 °C); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.0−2.2 (m, 1 H), 2.6−2.9 (m, 3 H), 5.12 (t, 1 H, J = 8.6 Hz), 6.59 (d, 1 H, J = 7.7 Hz, ArH), 6.86 (dt, 1 H, J = 7.6, 1.3 Hz, ArH), 7.01 (dt, 1 H, J = 7.6, 1.0 Hz, ArH), 7.1−7.5 (m, 6 H, ArH); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 26.2 (C-3), 28.3 (C-4), 56.5 (C-2), 125.3, 126.3, 126.5, 127.3, 128.0, 129.1, 130.8, (CH, aromatic), 133.1, 134.6, 138.0 (C_q, aromatic); 171.2 (COO); 176.2 (CON); IR (KBr, cm^{-1}) 1715, 1643; LRMS (70 eV, *m*/*z*) 282 (M + 1$^+$, 15), 281 (M^+, 77), 236 (30), 132 (100), 105 (90).

1-Phenyl-1*H*,3*H*,5*H*-oxazolo[3,4-*a*]quinolin-3-one (13). A 2.81 g (1 mmol) portion of **12** was dissolved in 50 mL of acetic anhydride, and the solution was stirred for 1 h under N_2 at 110 °C. The solution was then evaporated to dryness, and the residue was dissolved in $CHCl_3$ (100 mL) and washed with $NaHCO_3$ solution (5%, 2 × 30 mL) and water (50 mL). The organic phase was dried ($MgSO_4$) and evaporated in vacuo, and the crude product was purified by flash chromatography on silica gel (eluent: petroleum ether/EtOAc = 9:1), furnishing 1.85 g (71%) of pure compound **13**: mp 105−108 °C (lit.[18] mp 111−112 °C); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 3.71−3.99 (m, 2 H, $ArCH_2$), 5.80 (dd, 1 H, J = 3.3, 5.3 Hz, CH_2CH=C), 6.38 (d, 1 H, J = 7.6 Hz, ArH), 6.38 (s, 1 H, NCHO), 6.9−7.1 (m, 3 H, ArH), 7.5−7.7 (m, 5 H, ArH); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 28.1 ($ArCH_2$), 90.7 (CH), 101.5 (CH=C), 112.2 (CH=*C*), 123.3, 127.2, 127.3, 128.2, 128.5, 129.1, 130.5 (CH, aromatic), 119.5, 135.2, 137.7 (C_q, aromatic), 162.9 (CO); IR (KBr, cm^{-1}) 1784, 1494, 1229, 739; LRMS (70 eV, *m*/*z*) 264 (M + 1$^+$, 12), 263 (M^+, 56), 157 (23), 129 (100), 102 (14).

Methyl 1,2,7,7a-Tetrahydro-1a*H*-cyclopropa[*b*]quinoline-1a-carboxylate (14). A 1.30 g (5 mmol) portion of **13**

was dissolved in 50 mL of an ethereal solution of CH_2N_2, and the solution was stirred for 48 h at room temperature. When the reaction was complete (checked by ^{1}H NMR), the solution was evaporated to dryness and the yellow residual oil was purified by Kugelrohr distillation (110 °C air bath, 0.05 mmHg), which resulted in 0.61 g (62%) of pure compound **14** as a yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.27 (dd, 1 H, J = 4.8, 6.7 Hz, cyclopropane CH_2), 1.34 (dd, 1 H, J = 4.6, 9.5 Hz, cyclopropane CH_2), 2.15−2.18 (m, 1 H, CH), 2.91 (d, 1 H, J = 16.1 Hz, ArCH_2), 3.16 (dd, 1 H, J = 5.5, 16.1 Hz, ArCH_2), 3.77 (s, 3 H, $COOCH_3$), 6.62 (d, 1 H, J = 7.9 Hz, ArH), 6.72 (t, 1 H, J = 7.3 Hz, ArH), 6.97 (d, 1 H, J = 7.4 Hz, ArH), 7.02 (t, 1 H, J = 7.5 Hz, ArH); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 18.2 (cyclopropane CH_2), 23.2 (CH), 26.4 (ArCH_2), 40.2 (C_q), 52.2 ($COOCH_3$), 115.0, 119.5, 127.1, 129.2 (CH, aromatic), 118.9, 141.5 (C_q, aromatic), 173.6 (COO); IR (liquid film, NaBr, cm^{-1}) 3392, 2954, 1725, 1441, 909, 734; LRMS (70 eV, *m*/*z*) 204 (M + 1$^+$, 69), 144 (100). Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.76; H, 6.59; N, 6.71.

Methyl *N*-(Phenylaminocarbonyl)-1,2,7,7a-tetrahydro-1a*H*-cyclopropa[*b*]quinoline-1a-carboxylate (20a). A 0.172 g (0.9 mmol) portion of amino ester **5** and 0.106 g (0.95 mmol) of phenyl isocyanate were dissolved in 5 mL of dry toluene, and the solution was stirred overnight at room temperature. Evaporation to dryness, followed by chomatographic purification on silica gel (eluent: petroleum ether/EtOAc = 2:1, R_f 0.35), resulted in 0.21 g (72%) of compound **20a**: mp 143−146 °C; ^{1}H NMR (C_6D_6, 270 MHz) δ 1.04 (t, 1H, J = 5.8 Hz, cyclopropane CH_2), 1.80 (dd, 1H, J = 15.2, 6.9 Hz, ArCH_2), 1.88−2.0 (m, 1H, CH), 2.1−2.2 (m, 1H, cyclopropane CH_2), 2.58 (dd, 1H, J = 15.0, 7.8 Hz, ArCH_2), 3.20 (s, 3H, $COOCH_3$), 6.8−7.1 (m, 6H, ArH), 7.16 (s, 1H, NH), 7.45 (d, 2H, J = 7.9 Hz, ArH), 7.55 (d, 1H, J = 7.9 Hz, ArH); ^{13}C NMR (C_6D_6, 67.9 MHz) δ 27.8 (cyclopropane CH_2), 31.3 (ArCH_2), 32.1 (CH), 43.4 (C_q), 53.3 ($COOCH_3$), 120.3, 124.3, 125.0, 126.1, 128.6, 129.7, 130.3 (CH, aromatic), 136.4, 140.6, 141.6 (C_q, aromatic), 153.9 (NCONH), 173.4 ($COOCH_3$); IR (KBr, cm^{-1}) 3296, 1728, 1656; LRMS (70 eV, *m*/*z*) 322 (M$^+$, 17), 203 (100), 175 (50), 143 (55). Anal. Calcd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.42; H, 6.01; N, 8.41.

Methyl *N*-(*p*-Tolylaminocarbonyl)-1,2,7,7a-tetrahydro-1a*H*-cyclopropa[*b*]quinoline-1a-carboxylate (20b). A 0.255 g (1.33 mmol) portion of amino ester **5** and 0.16 g (1.4 mmol) of *p*-tolyl isocyanate were dissolved in 10 mL of dry toluene, and the solution was stirred overnight at 80 °C. Evaporation to dryness, followed by chromatographic purification on silica gel (eluent: petroleum ether/EtOAc = 2:1, R_f 0.4), resulted in 0.31 g (68%) of compound **20b**: mp 103−105 °C; ^{1}H NMR (C_6D_6, 270 MHz) δ 1.02 (t, 1H, J = 5.9 Hz, cyclopropane CH_2), 1.78 (dd, 1H, J = 7.1, 15.3 Hz, ArCH_2), 1.90 (m, 1H, CH), 2.06 (s, 3H, ArCH_3), 2.17 (dd, 1H, J = 4.9, 8.6 Hz, cyclopropane CH_2), 2.57 (dd, 1H, J = 7.8, 15.3 Hz, ArCH_2), 3.20 (s, 3H, $COOCH_3$), 6.83−7.03 (m, 6H, ArH + NH), 7.40 (d, 2H, J = 8.6 Hz, ArH), 7.57 (d, 1H, J = 7.9 Hz, ArH); ^{13}C NMR (C_6D_6, 67.9 MHz) δ 20.7 (ArCH_3), 26.6 (cyclopropane CH_2), 30.2 (ArCH_2), 31.0 (CH), 42.3 (C_q), 52.2 ($COOCH_3$), 119.4, 127.7, 128.0, 128.4, 128.6, 129.6 (CH, aromatic), 123.9, 124.9, 132.5, 135.3 (C_q, aromatic), 152.9 (NCONH), 172.4 ($COOCH_3$); IR (KBr, cm^{-1}) 3414, 1728, 1677, 1520, 1320; LRMS (70 eV, *m*/*z*) 337 (M + 1$^+$, 22), 203 (100), 175 (61), 143 (57). Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.05; H, 6.17; N, 8.56.

Methyl 2-Propylaminocarbonyl-1,2,7,7a-tetrahydro-1a*H*-cyclopropa[*b*]quinoline-1a-carboxylate (20c). A 0.16 g (0.84 mmol) portion of amino ester **5** and 0.075 g (0.88 mmol) of propyl isocyanate were dissolved in 5 mL of dry toluene, and the solution was stirred overnight at 80 °C. Evaporation to dryness, followed by chromatographic purification on silica gel (eluent: petroleum ether/EtOAc = 2:1, R_f 0.28), resulted in 0.140 g (58%) of compound **20c**: mp 103−106 °C; ^{1}H NMR (C_6D_6, 270 MHz) δ 0.73 (t, 3H, J = 7.3 Hz, $CH_2CH_2CH_3$), 1.04 (t, 1H, J = 5.9 Hz, cyclopropane CH_2), 1.23−1.36 (m, 2H, $CH_2CH_2CH_3$), 1.83 (dd, 1H, J = 6.9, 14.9 Hz, ArCH_2), 1.91−2.02 (m, 1H, CH), 2.11 (dd, 1H, J = 4.9, 8.6 Hz, cyclopropane CH_2), 2.63 (dd, 1H, J = 7.9, 15.2 Hz, ArCH_2), 3.04−3.7 (m, 2H, $CH_2CH_2CH_3$), 3.22 (s, 3H, $COOCH_3$), 4.88 (t, 1H, J = 5.3 Hz, NH), 6.83−7.11 (m, 3H, ArH), 7.86 (d, 1H, J = 7.9 Hz, ArH); ^{13}C NMR (C_6D_6, 67.9 MHz) δ 11.4 ($CH_2CH_2CH_3$), 23.7 ($CH_2CH_2CH_3$), 26.6 (cyclopropane CH_2), 30.3 (ArCH_2), 31.2 (CH), 42.0 (C_q), 42.5 ($CH_2CH_2CH_3$), 52.1 ($COOCH_3$), 124.3, 127.7, 128.0, 128.4 (CH, aromatic), 134, 7, 141.1 (C_q, aromatic), 155.4 (NCONH), 172.6 ($COOCH_3$); IR (KBr, cm^{-1}) 3359, 2958, 1742, 1652; LRMS (70 eV, *m*/*z*) 289 (M + 1$^+$, 10), 203 (100), 176 (53), 143 (49). Anal. Calcd for $C_{16}H_{20}N_2O_3$: C, 66.65; H, 6.99; N, 9.72. Found: C, 66.32; H, 7.25; N, 9.49.

2-Phenyl-4a,5-dihydro-1*H*,4*H*-cyclopropa[*e*]imidazo-[1,5-*a*]quinoline-1,3(2*H*)-dione (21a). A 0.17 g (0.53 mmol) portion of urea **20a** was dissolved in 10 mL of MeOH, and 5 drops of methanol containing 25% of dry NH_3 was added to the solution. The reaction was complete after being stirred for 1.5 h at room temperature (TLC monitoring). The solution was evaporated to dryness, and the resulting crystalline product was recrystallized from EtOAc/petroleum ether to yield 0.125 g (80%) of **21a**: mp 162−163 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.58 (t, 1H, J = 5.9, cyclopropane CH_2), 1.67 (dd, 1H, J = 5.9, 9.6 Hz, cyclopropane CH_2), 2.42−2.49 (m, 1H, CH), 3.15 (d, 1H, J = 16.2 Hz, ArCH_2), 3.26 (dd, 1H, J = 4.0, 16.5 Hz, ArCH_2), 7.1−7.5 (m, 8H, ArH), 7.93 (d, 1H, J = 8.3 Hz, ArH); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 15.0 (cyclopropane CH_2), 22.3 (CH), 27.1 (ArCH_2), 44.5 (C_q), 121.0, 125.1, 126.3, 127.9, 128.2, 129.1, 130.0 (CH, aromatic), 123.9, 131.8, 132.0 (C_q, aromatic), 152.0 (NCON), 171.1 (NCOC$_q$); IR (KBr, cm^{-1}) 3467, 1772, 1722, 1404; LRMS (70 eV, *m*/*z*) 290 (M$^+$, 51), 262 (26), 156 (13), 143 (100). Anal. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.52; H, 5.23; N, 9.49.

2-(*p*-Tolyl)-4a,5-dihydro-1*H*,4*H*-cyclopropa[*e*]imidazo-[1,5-*a*]quinoline-1,3(2*H*)-dione (21b). Starting from 0.12 g (0.36 mmol) of **20b**, the procedure used was similar to that for the preparation of **21a** from **20a**: yield 78%, mp 143−144 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.61 (dd, 1H, J = 5.9, 9.8 Hz, cyclopropane CH_2), 1.69 (dd, 1H, J = 5.9, 9.6 Hz, cyclopropane CH_2), 2.40 (s, 3H, ArCH_3), 2.43−2.51 (m, 1H, CH), 3.18 (d, 1H, J = 15.5 Hz, ArCH_2), 3.29 (dd, 1H, J = 4.3, 15.5 Hz, ArCH_2), 7.08−7.39 (m, 7H, ArH), 7.93 (d, 1H, J = 8.3 Hz, ArH); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 15.2 (cyclopropane CH_2), 21.4 (CH_3), 22.5 (CH), 27.3 (ArCH_2), 44.7 (C_q), 121.2, 126.4, 125.3, 128.2, 130.0, 130.3 (CH, aromatic), 124.1, 129.3, 132.3, 138.5 (C_q, aromatic), 152.5 (NCON), 171.5 (NCOC$_q$); IR (KBr, cm^{-1}) 1773, 1718, 1406, 1146; LRMS (70 eV, *m*/*z*) 305 (M$^+$, 24), 144 (100), 116 (21). Anal. Calcd for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.20. Found: C, 74.62; H, 5.59; N, 8.91.

2-Propyl-4a,5-dihydro-1*H*,4*H*-cyclopropa[*e*]imidazo-[1,5-*a*]quinoline-1,3(2*H*)-dione (21c). Starting from 0.08 g (0.28 mmol) of **20c**, the procedure used was similar to that for the preparation of **21a** from **20a**: yield 85%; mp 80−81 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.98 (t, 3H, J = 7.4 Hz, $CH_2CH_2CH_3$), 1.42−1.53 (m, 1H, cyclopropane CH_2), 1.58 (dd, 1H, J = 5.9, 9.6 Hz, cyclopropane CH_2), 1.61−1.81 (m, 2H, $CH_2CH_2CH_3$), 2.33−2.41 (m, 1H, CH), 3.13 (dd, 1H, J = 1.5, 16.5 Hz, ArCH_2), 3.21 (dd, 1H, J = 4.0, 16.5 Hz, ArCH_2), 3.59−3.65 (m, 2H, $CH_2CH_2CH_3$), 7.04−7.31 (m, 3H, ArH), 7.89 (d, 1H, J = 8.3 Hz, ArH); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ 11.3 ($CH_2CH_2CH_3$), 14.5 ($CH_2CH_2CH_3$), 21.6 (cyclopropane CH_2), 21.7 ($CH_2CH_2CH_3$), 27.0 (CH), 40.8 (ArCH_2), 44.4 (C_q), 120.8, 124.8, 127.9, 130.0 (CH, aromatic), 123.7, 132.2 (C_q, aromatic), 153.3 (NCON), 172.2 (NCOC$_q$); IR (KBr, cm^{-1}) 2930, 1760, 1710, 1416; LRMS (70 eV, *m*/*z*) 256 (M$^+$, 57), 170 (4), 143 (100), 128 (20). Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.55; H, 6.62; N, 10.65.

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