

Novel Oxidation of Substituted Pyrrolidines by *N*-Bromosuccinimide; Rapid Synthesis of Pyrrolo[2,1-*a*]isoquinolines

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Abstract: A new method for converting 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolines into 5,6-dihydropyrrolo[2,1-*a*]isoquinolines by the use of *N*-bromosuccinimide as an oxidant is presented.

Key words: azomethine ylides, cycloadditions, oxidation, pyrroles

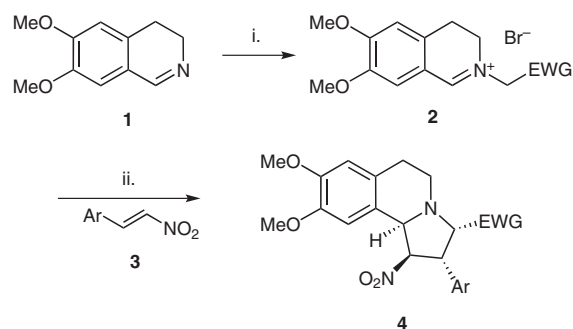
The biological importance of pyrrole-containing natural products, such as heme, chlorophyll, and vitamin B₁₂ and a large number of alkaloids has stimulated extensive research on the synthesis and reactivity of pyrrole derivatives.² There are many methods for the synthesis of these important heterocycles, including the 1,3-dipolar cycloaddition of azomethine ylides to alkynes, followed by aromatization of the intermediate pyrrolines.³ However, the preparation of pyrroles by dehydrogenation of pyrrolidines has found little application due to lack of general methods and the forcing conditions required in most cases.⁴

The development of a method that allows this reaction under essentially mild and neutral conditions should heighten the synthetic potential of this conversion. In this paper we report our results on the direct conversion of one type of pyrrolidine into the corresponding pyrrole in excellent yields using *N*-bromosuccinimide under mild conditions.⁵

Considerable interest has been shown in substituted pyrrolo[2,1-*a*]isoquinolines due to their diverse biological activity. Since the discovery of the potent cytotoxic and topoisomerase I inhibitor activity of lamellarine alkaloids,⁶ a number of new synthetic strategies have been developed based on, e.g. intramolecular oxidative biaryl coupling,⁷ thermal reactions of 4-isoxazoline derivatives (obtained by cycloaddition of 3,4-dihydroisoquinoline *N*-oxides with alkynes),⁸ intramolecular Heck reactions,⁹ and cyclization of 1- or 2-benzylisoquinolines.^{10,11}

As a continuation of our research programme in this field¹² we have decided to study the dehydrogenation of 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolines **4**, which were prepared by 1,3-dipolar cycloaddition of azomethine ylides derived from dihydroisoquinolinium salts previously studied in detail by us.¹³ The dipoles pro-

duced by dehydrohalogenation reacted with a wide range of dipolarophiles e.g. maleimides, maleates, nitro olefins etc. Accordingly, the reaction of **1** with methyl bromoacetate or phenacyl bromides, in anhydrous diethyl ether, gave the quaternary salts **2**. Reaction of isoquinolinium salts **2** with triethylamine at ambient temperature in the presence of the appropriate dipolarophiles **3** gave stereoselectively the corresponding *anti-endo* cycloadducts **4** in high yield (Scheme 1). Alternatively, several of these cycloadducts could be prepared directly from **1** using a one-step method described by us (for characterization see Table 2).^{13g}



Scheme 1 Reagents and conditions: (i) EWG-CH₂Br, Et₂O, r.t.; (ii) Et₃N, EtOH, r.t.

After several unsuccessful exploratory experiment using various oxidizing agents (e.g., MnO₂, DDQ, H₂O₂, KMnO₄) we decided to use *N*-bromosuccinimide,¹⁴ which is most frequently used for the oxidation of sulfides to sulfoxides¹⁵ and alcohols to carbonyl compounds.¹⁶ This reagent was useful for the direct transformation of aldehydes into acid bromides¹⁷ or nitriles.¹⁸ However, there are few reports on the oxidation of heterocyclic compounds with *N*-bromosuccinimide; the oxidation of indoles to isatins,¹⁹ 2,3-dihydrobenzofurans to benzofurans,²⁰ and isoxazoline to isoxazole²¹ has been accomplished by *N*-bromosuccinimide. In addition to some two-step processes (halogenation with NBS; dehydrohalogenation by a base),²² in one case a 3,4-dihydroisoquinoline derivative was aromatized in refluxing carbon tetrachloride in the presence of *N*-bromosuccinimide.²³

Table 1 5,6-Dihydropyrrolo[2,1-*a*]isoquinolines **5** Obtained

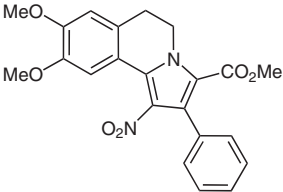
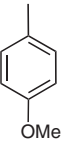
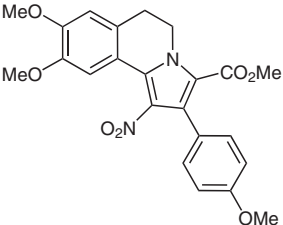
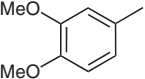
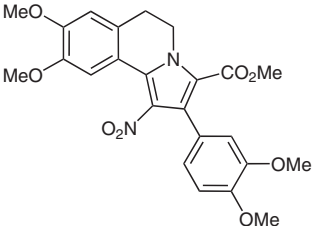
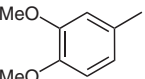
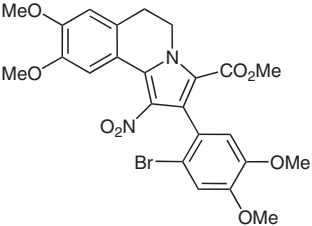
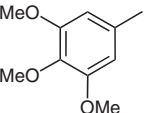
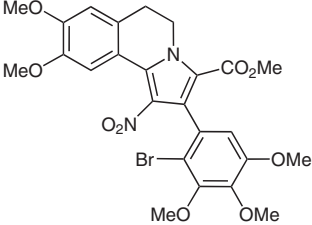
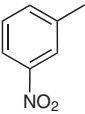
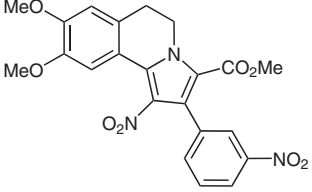
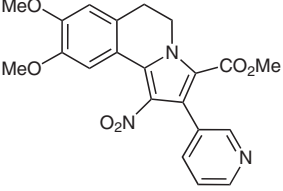
Entry	Cycloadduct ^a	EWG	Ar	Temp	Product ^b	Yield (%)
1	4a ^{13g}	CO ₂ Me		r.t.	5a 	72
2	4b ^{13g}	CO ₂ Me		r.t.	5b 	70
3	4c ^{13g}	CO ₂ Me		0 °C	5c 	81
4	4d ^{13g}	CO ₂ Me		0 °C to r.t.	5d 	77
5	4e ^{13g}	CO ₂ Me		0 °C	5e 	60
6	4f ^{13g}	CO ₂ Me		r.t.	5f 	81
7	4g ^{13g}	CO ₂ Me		r.t.	5g 	86

Table 1 5,6-Dihydropyrrolo[2,1-*a*]isoquinolines **5** Obtained (continued)

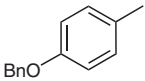
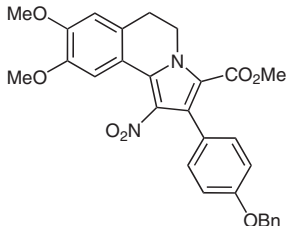
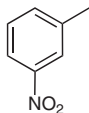
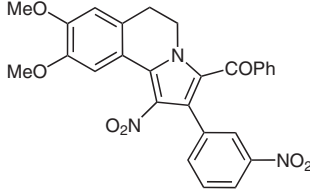
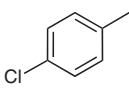
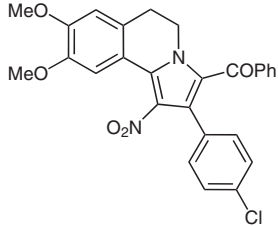
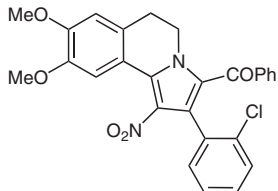
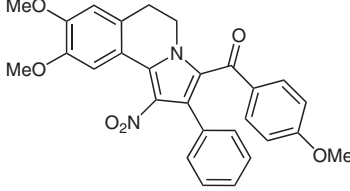
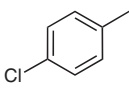
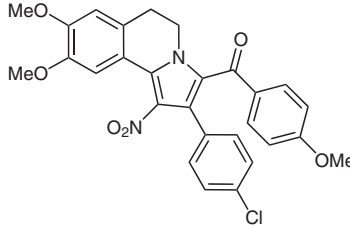
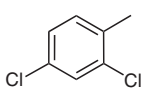
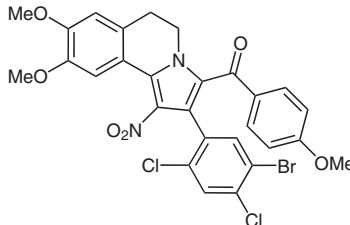
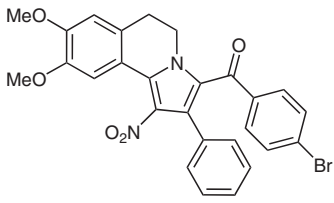
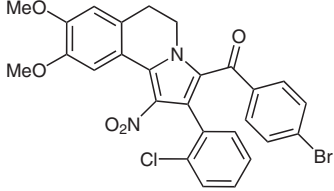
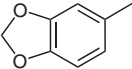
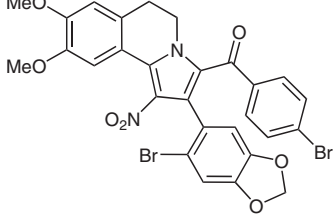
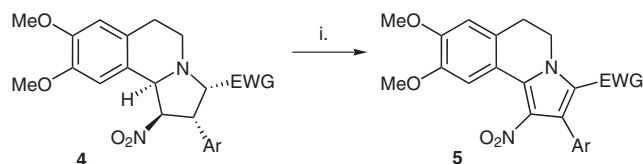
Entry	Cycloadduct ^a	EWG	Ar	Temp	Product ^b	Yield (%)
8	4h (69%)	CO ₂ Me		r.t.	5h 	78
9	4i ^{13g}	COPh		r.t.	5i 	85
10	4j (75%)	COPh		r.t.	5j 	63
11	4k (69%)	COPh		r.t.	5k 	58
12	4l (70%)	4-MeOC ₆ H ₄ CO		r.t.	5l 	77
13	4m (70%)	4-MeOC ₆ H ₄ CO		r.t.	5m 	68
14	4n (58%)	4-MeOC ₆ H ₄ CO		r.t.	5n 	54

Table 1 5,6-Dihydropyrrolo[2,1-*a*]isoquinolines **5** Obtained (continued)

Entry	Cycloadduct ^a	EWG	Ar	Temp	Product ^b	Yield (%)
15	4o (77%)	4-BrC ₆ H ₄ CO		r.t.	5o 	65
16	4p (73%)	4-BrC ₆ H ₄ CO		r.t.	5p 	59
17	4q (84%)	4-BrC ₆ H ₄ CO		0 °C to r.t.	5q 	53

^a Where the cycloadduct is new, the yield has been given and spectroscopic data are given in Table 2.^b Spectroscopic data are given in Table 3.^c NBS (3 equiv) was used.

To our delight, we found that on treatment with *N*-bromosuccinimide at room temperature the colorless solution of **4** in chloroform immediately became yellow and, after a simple workup procedure, the desired 5,6-dihydropyrrolo[2,1-*a*]isoquinolines **5** were obtained (Scheme 2).

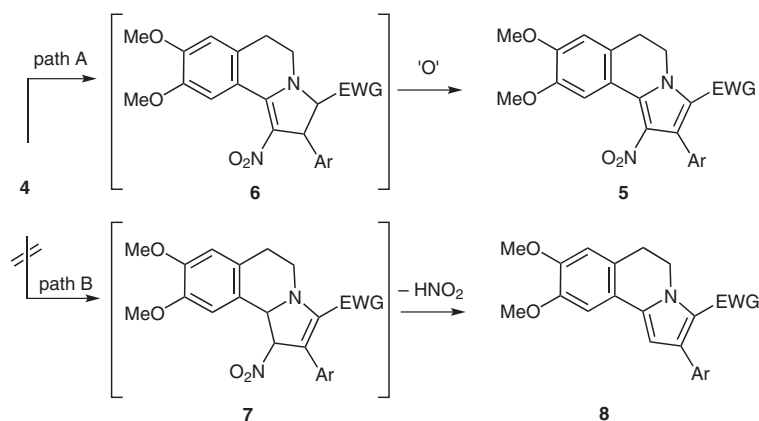
**Scheme 2** Reagents and conditions: (i) NBS, CHCl₃, r.t.

The reaction is exothermic and on a larger scale, external ice-water cooling is necessary. To demonstrate the generality of this methodology, a broad range of different cycloadducts were chosen to explore the scope of this approach. The results are summarized in Table 1. In general, modest to good overall yields were obtained for all substrates. A limitation of this method is that in cases when the aromatic ring has two or more electron-donating substituents (Table 1, entries 4, 5, 14, and 17) the concomitant bromination of the 2-aryl substituent was observed concurring with the dehydrogenation process, which can be avoided applying a lower reaction temperature.

The structures of compound **5** were elucidated by NMR spectroscopy using ¹H, ¹³C, ¹H–¹H COSY, ¹H–¹H NOE, and ¹H–¹³C HSQC techniques (Table 3).

The mechanism of oxidation of pyrrolidines **4** with *N*-bromosuccinimide has not been clearly established, although based on the earlier interpretations it is generally accepted that a positive halogen is the attacking species giving a brominated intermediate.¹⁴ The spontaneous elimination of hydrogen bromide occurs facilitated by the high conjugation of the newly formed double bond. We believe that the pyrrolidines **4** reacts with *N*-bromosuccinimide to form pyrroline **6** exclusively accordingly to path A. The formation of isomeric pyrroline **7** is unlikely because that would readily lose nitrous acid to form a different pyrrole **8** as the product.^{4c} The last step is a spontaneous dehydrogenation leading to the formation of the isolated pyrroles **5** (Scheme 3).¹²

In summary we have explored a convenient two-step reaction path which provides a useful route to 5,6-dihydropyrrolo[2,1-*a*]isoquinolines **5** via a 1,3-dipolar cycloaddition; *N*-bromosuccinimide-promoted oxidation sequence. The obtained new pyrrolo[2,1-*a*]isoquinoline derivatives **5** could be useful intermediates in the synthesis of lamellarine-type heterocycles through a standard NO₂ to Br functional group exchange followed by a Suzuki coupling with arylboronic acid derivatives, which is well established in this series.²⁴ These studies are in progress in our laboratories.



Scheme 3

Table 2 Spectral Data of Compounds 4 Prepared

Product	IR (KBr, cm^{-1})	^1H NMR ^a (CDCl_3 , TMS) δ	^{13}C NMR (CDCl_3 , TMS) δ
4h	2936, 2907, 2843, 2803, 1748, 1611, 1548, 1518, 1462, 1383, 1364, 1317, 1273, 1244, 1227, 1145, 1106, 1090, 1044, 1020	7.38 (m, 5 H, H_{BN}), 7.24 (d, $J = 8.7$ Hz, 2 H, H_2' , H_6'), 6.94 (d, $J = 8.7$ Hz, 2 H, H_3' , H_5'), 6.61 (s, 1 H, H_7), 6.52 (s, 1 H, H_{10}), 5.55 (dd, $J = 3.5$, 7.1 Hz, 1 H, H_1), 5.37 (d, $J = 7.1$ Hz, 1 H, H_{10b}), 5.04 (s, 2 H, OCH_2), 4.51 (d, $J = 7.8$ Hz, 1 H, H_3), 4.36 (dd, $J = 3.5$, 7.8 Hz, 1 H, H_2), 3.84 (s, 3 H, OMe), 3.81 (s, 3 H, OMe), 3.39 (s, 3 H, OMe), 3.30 (m, 1 H, H_5), 2.85 (m, 1 H, H_5), 2.65 (m, 2 H, H_6)	171.3 (C_q), 158.4 (C_q), 147.4 (C_q), 136.7 (C_q), 129.8 (C_q), 129.1 (2 CH), 128.6 (2 CH), 128.5 (CH), 128.0 (C_q), 127.4 (2 CH), 115.2 (2 CH), 114.8 (C_q), 111.4 (CH), 109.1 (CH), 95.6 (CH), 70.3 (CH), 70.0 (CH_2), 64.0 (CH), 55.9 (CH_3), 55.7 (CH_3), 51.6 (CH_3), 51.4 (CH), 46.1 (CH_2), 26.7 (CH_2)
4j	2918, 2849, 1671, 1611, 1545, 1521, 1495, 1369, 1275, 1263, 1232, 1137, 1121, 1096, 1014	7.86 (d, $J = 7.4$ Hz, 2 H, H_2'' , H_6''), 7.61 (d, $J = 7.4$ Hz, 2 H, H_3'' , H_5''), 7.48 (t, $J = 7.4$ Hz, 1 H, H_4''), 7.33 (d, $J = 8.2$ Hz, 2 H, H_2' , H_6'), 7.31 (d, $J = 8.2$ Hz, 2 H, H_3' , H_5'), 6.91 (s, 1 H, H_7), 6.74 (s, 1 H, H_{10}), 6.12 (t, $J = 6.5$ Hz, 1 H, H_1), 5.82 (d, $J = 6.5$ Hz, 1 H, H_3), 5.13 (d, $J = 6.5$ Hz, 1 H, H_{10b}), 4.74 (t, $J = 6.5$ Hz, 1 H, H_2), 3.75 (s, 3 H, OMe), 3.70 (s, 3 H, OMe), 3.39 (m, 1 H, H_5), 3.22 (m, 1 H, H_5), 2.81 (m, 1 H, H_6), 2.68 (m, 1 H, H_6)	196.6 (C_q), 147.9 (C_q), 146.9 (C_q), 136.3 (C_q), 136.0 (C_q), 133.5 (C_q), 131.8 (C_q), 129.9 (2 CH), 128.9 (2 CH), 128.5 (2 CH), 128.3 (2 CH), 127.9 (CH), 122.9 (C_q), 111.6 (CH), 110.7 (CH), 95.9 (CH), 71.6 (CH), 63.7 (CH), 55.7 (CH_3), 55.5 (CH_3), 50.7 (CH), 46.1 (CH_2), 27.5 (CH_2)
4k	2955, 2926, 2872, 2837, 1677, 1579, 1550, 1519, 1478, 1463, 1447, 1386, 1370, 1349, 1326, 1290, 1270, 1137, 1118, 1090, 1037, 1010	7.74 (d, $J = 7.4$ Hz, 2 H, H_2'' , H_6''), 7.65 (d, $J = 8.0$ Hz, 2 H, H_3'' , H_5''), 7.47 (t, $J = 7.4$ Hz, 1 H, H_4''), 7.35 (d, $J = 7.4$ Hz, 2 H, H_2' , H_6'), 7.22 (t, $J = 8.0$ Hz, 1 H, H_1), 7.18 (d, $J = 8.0$ Hz, 1 H, H_3'), 7.09 (t, $J = 8.0$ Hz, 1 H, H_4'), 6.62 (s, 1 H, H_7), 6.56 (s, 1 H, H_{10}), 5.88 (dd, $J = 5.3$, 7.5 Hz, 1 H, H_1), 5.66 (d, $J = 7.3$ Hz, 1 H, H_3), 5.28 (d, $J = 7.5$ Hz, 1 H, H_{10b}), 5.08 (dd, $J = 5.3$, 7.3 Hz, 1 H, H_2), 3.85 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 3.52 (m, 1 H, H_5), 3.28 (m, 1 H, H_5), 2.90 (m, 1 H, H_6), 2.80 (m, 1 H, H_6)	197.0 (C_q), 148.2 (C_q), 147.4 (C_q), 136.4 (C_q), 133.8 (C_q), 133.2 (CH), 132.8 (C_q), 129.6 (CH), 129.4 (CH), 128.9 (CH), 128.5 (2 CH), 128.1 (C_q), 127.9 (2 CH), 127.3 (CH), 122.3 (C_q), 111.3 (CH), 109.3 (CH), 95.1 (CH), 71.1 (CH), 63.7 (CH), 55.9 (CH_3), 55.7 (CH_3), 48.6 (CH), 46.8 (CH_2), 27.5 (CH_2)
4l	3006, 2942, 2839, 1666, 1602, 1576, 1549, 1522, 1467, 1443, 1423, 1368, 1317, 1266, 1232, 1182, 1134, 1115, 1057, 1025	7.87 (d, $J = 8.7$ Hz, 2 H, H_2'' , H_6''), 7.28 (d, $J = 7.7$ Hz, 2 H, H_2' , H_6'), 7.22 (d, $J = 7.7$ Hz, 2 H, H_3' , H_5'), 7.13 (t, $J = 7.7$ Hz, 1 H, H_4'), 6.96 (d, $J = 8.7$ Hz, 2 H, H_3'' , H_5''), 6.89 (s, 1 H, H_7), 6.72 (s, 1 H, H_{10}), 6.18 (t, $J = 7.0$ Hz, 1 H, H_1), 5.77 (d, $J = 7.0$ Hz, 1 H, H_3), 5.13 (d, $J = 7.0$ Hz, 1 H, H_{10b}), 4.69 (t, $J = 7.0$ Hz, 1 H, H_2), 3.81 (s, 3 H, OMe), 3.72 (s, 3 H, OMe), 3.68 (s, 3 H, OMe), 3.39 (m, 1 H, H_5), 3.21 (m, 1 H, H_5), 2.79 (m, 1 H, H_6), 2.70 (m, 1 H, H_6)	194.8 (C_q), 163.4 (C_q), 147.8 (C_q), 146.8 (C_q), 137.0 (C_q), 130.8 (2 CH), 129.3 (C_q), 128.5 (2 CH), 127.8 (2 CH), 127.6 (CH), 127.0 (C_q), 123.0 (C_q), 114.0 (2 CH), 111.5 (CH), 110.6 (CH), 96.3 (CH), 71.2 (CH), 63.9 (CH), 55.7 (CH_3), 55.6 (CH_3), 55.5 (CH_3), 51.5 (CH), 46.3 (CH_2), 27.9 (CH_2)

Table 2 Spectral Data of Compounds **4** Prepared (continued)

Product	IR (KBr, cm ⁻¹)	¹ H NMR ^a (CDCl ₃ , TMS) δ	¹³ C NMR (CDCl ₃ , TMS) δ
4m	3003, 2932, 2867, 2841, 1658, 1601, 1550, 1519, 1495, 1462, 1365, 1342, 1320, 1269, 1239, 1179, 1131, 1118, 1097, 1024, 1017	7.80 (d, J = 7.0 Hz, 2 H, H2'', H6''), 7.18 (d, J = 8.6 Hz, 2 H, H2', H6'), 7.11 (d, J = 8.6 Hz, 2 H, H3'', H5''), 6.87 (d, J = 7.0 Hz, 2 H, H3', H5'), 6.61 (s, 1 H, H7), 6.54 (s, 1 H, H10), 5.80 (dd, J = 4.8, 7.6 Hz, 1 H, H1), 5.50 (d, J = 7.1 Hz, 1 H, H3), 5.24 (d, J = 7.6 Hz, 1 H, H10b), 4.48 (dd, J = 4.8, 7.1 Hz, 1 H, H2), 3.85 (s, 3 H, OMe), 3.84 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 3.45 (m, 1 H, H5), 3.26 (m, 1 H, H5), 2.86 (m, 1 H, H6), 2.75 (m, 1 H, H6)	194.4 (C _q), 163.7 (C _q), 148.2 (C _q), 147.3 (C _q), 134.6 (C _q), 133.3 (C _q), 130.4 (2 CH), 129.4 (C _q), 129.2 (2 CH), 128.9 (2 CH), 128.1 (C _q), 122.4 (C _q), 113.9 (2 CH), 111.2 (CH), 109.3 (CH), 91.2 (CH), 71.4 (CH), 63.9 (CH), 55.9 (CH ₃), 55.7 (CH ₃), 55.5 (CH ₃), 51.7 (CH), 46.6 (CH ₂), 27.1 (CH ₂)
4n	2935, 2838, 1662, 1600, 1572, 1550, 1519, 1464, 1424, 1386, 1366, 1270, 1233, 1176, 1138, 1119, 1024	7.79 (d, J = 7.0 Hz, 2 H, H2'', H6''), 7.63 (d, J = 8.5 Hz, 1 H, H6'), 7.23 (d, J = 2.1 Hz, 1 H, H3'), 7.20 (dd, J = 2.1, 8.5 Hz, 1 H, H5'), 6.86 (d, J = 7.0 Hz, 2 H, H3'', H5''), 6.61 (s, 1 H, H7), 6.55 (s, 1 H, H10), 5.90 (dd, J = 5.6, 7.6 Hz, 1 H, H1), 5.59 (d, J = 7.1 Hz, 1 H, H3), 5.25 (d, J = 7.6 Hz, 1 H, H10b), 5.00 (dd, J = 5.6, 7.1 Hz, 1 H, H2), 3.84 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 3.82 (s, 3 H, OMe), 3.51 (m, 1 H, H5), 3.26 (m, 1 H, H5), 2.86 (m, 2 H, H6)	194.8 (C _q), 163.8 (C _q), 148.2 (C _q), 147.3 (C _q), 134.4 (C _q), 134.0 (C _q), 131.6 (C _q), 130.45 (2 CH), 130.4 (CH), 129.3 (CH), 129.0 (C _q), 127.9 (C _q), 127.5 (CH), 122.1 (C _q), 113.8 (2 CH), 111.2 (CH), 109.2 (CH), 95.1 (CH), 70.4 (CH), 63.6 (CH), 55.9 (CH ₃), 55.7 (CH ₃), 55.4 (CH ₃), 48.3 (CH), 46.8 (CH ₂), 27.5 (CH ₂)
4o	2934, 2836, 1676, 1612, 1584, 1547, 1520, 1465, 1405, 1366, 1339, 1318, 1273, 1231, 1135, 1120, 1073, 1010	7.71 (d, J = 8.5 Hz, 2 H, H2'', H6''), 7.60 (d, J = 8.5 Hz, 2 H, H3'', H5''), 7.22 (d, J = 7.5 Hz, 2 H, H2', H6'), 7.18 (d, J = 7.5 Hz, 2 H, H3', H5'), 7.10 (t, J = 7.5 Hz, 1 H, H4'), 6.87 (s, 1 H, H7), 6.69 (s, 1 H, H10), 6.05 (dd, J = 5.6, 7.2 Hz, 1 H, H1), 5.74 (d, J = 7.4 Hz, 1 H, H3), 5.09 (d, J = 7.2 Hz, 1 H, H10b), 4.66 (dd, J = 5.6, 7.4 Hz, 1 H, H2), 3.69 (s, 3 H, OMe), 3.64 (s, 3 H, OMe), 3.55 (m, 1 H, H5), 3.18 (m, 1 H, H5), 2.78 (m, 1 H, H6), 2.66 (m, 1 H, H6)	196.1 (C _q), 147.8 (C _q), 146.9 (C _q), 136.8 (C _q), 135.4 (C _q), 131.8 (2 CH), 130.3 (2 CH), 128.6 (2 CH), 128.0 (2 CH), 127.9 (CH), 127.5 (C _q), 127.2 (C _q), 123.0 (C _q), 111.6 (CH), 110.7 (CH), 96.0 (CH), 71.7 (CH), 63.8 (CH), 55.7 (CH ₃), 55.5 (CH ₃), 51.4 (CH), 46.1 (CH ₂), 27.6 (CH ₂)
4p	2908, 2833, 1671, 1582, 1553, 1524, 1480, 1468, 1399, 1376, 1289, 1259, 1232, 1216, 1180, 1154, 1119, 1071, 1054, 1040, 1015, 1009	7.62 (m, 3 H, H6', H2'', H6''), 7.49 (m, 3 H, H5', H3'', H5''), 7.21 (d, J = 7.7 Hz, 1 H, H3'), 7.11 (d, J = 7.7 Hz, 1 H, H4'), 6.62 (s, 1 H, H10), 6.56 (s, 1 H, H7), 5.85 (dd, J = 5.1, 7.5 Hz, 1 H, H1), 5.60 (d, J = 7.3 Hz, 1 H, H3), 5.27 (d, J = 7.5 Hz, 1 H, H10b), 5.06 (dd, J = 5.1, 7.3 Hz, 1 H, H2), 3.85 (s, 3 H, OMe), 3.82 (s, 3 H, OMe), 3.50 (m, 1 H, H5), 3.29 (m, 1 H, H5), 2.91 (m, 1 H, H6), 2.80 (m, 1 H, H6)	196.1 (C _q), 148.2 (C _q), 147.3 (C _q), 135.0 (C _q), 133.7 (C _q), 132.6 (CH), 131.8 (2 CH), 129.3 (CH), 129.1 (C _q), 128.4 (C _q), 128.1 (C _q), 127.3 (CH), 122.1 (C _q), 111.2 (CH), 109.3 (CH), 94.9 (CH), 71.0 (CH), 63.6 (CH), 55.9 (CH ₃), 55.7 (CH ₃), 48.5 (CH), 46.8 (CH ₂), 27.4 (CH ₂)
4q	3002, 2937, 2835, 1733, 1653, 1611, 1546, 1514, 1465, 1365, 1232, 1179, 1136, 1119, 1013	7.64 (d, J = 8.6 Hz, 2 H, H2'', H6''), 7.51 (d, J = 8.6 Hz, 2 H, H3'', H5''), 6.69 (s, 1 H, H7), 6.61 (d, J = 8.1 Hz, 1 H, H5'), 6.57 (d, J = 8.1 Hz, 1 H, H6'), 6.53 (s, 1 H, H2'), 6.06 (s, 1 H, H10), 5.89 (s, 2 H, OCH ₂ O), 5.63 (dd, J = 3.9, 7.3 Hz, 1 H, H1), 5.46 (d, J = 7.2 Hz, 1 H, H3), 5.28 (d, J = 7.3 Hz, 1 H, H10b), 4.36 (dd, J = 3.9, 7.2 Hz, 1 H, H2), 3.85 (s, 3 H, OMe), 3.82 (s, 3 H, OMe), 3.40 (m, 1 H, H5), 3.26 (m, 1 H, H5), 2.88 (m, 1 H, H6), 2.70 (m, 1 H, H6)	195.8 (C _q), 148.2 (C _q), 148.0 (C _q), 147.4 (C _q), 147.1 (C _q), 139.1 (C _q), 135.5 (C _q), 131.9 (2 CH), 129.4 (2 CH), 128.4 (C _q), 126.6 (C _q), 122.5 (C _q), 121.6 (CH), 111.3 (CH), 109.3 (CH), 108.42 (CH), 108.40 (CH), 101.2 (CH ₂), 96.3 (CH), 71.8 (CH), 63.8 (CH), 55.9 (CH ₃), 55.7 (CH ₃), 52.1 (CH), 46.5 (CH ₂), 26.7 (CH ₂)

^a Aryl groups at C2 are indicated using ' , while those at C3 are indicated by ''.

IR spectra were measured on a Bruker Vector 22 FT-IR instrument. NMR spectra were recorded on a Bruker Avance DRX-500 spectrometer relative to TMS. All solvents were purified according to standard procedures.

5,6-Dihydropyrrolo[2,1-*a*]isoquinoline-3-carboxylates **5a–l**; General Procedure

The cycloadduct **4** (1.0 mmol) was dissolved in CHCl₃ (10 mL) and NBS (0.17 g, 1.1 mmol) was added in 1 portion at the temperature

given in Table 1. The solution immediately turned yellow. The mixture was stirred for 30 min and then H₂O (10 mL) was added and the organic layer was washed with further portions of H₂O (2 × 10 mL) and brine (10 mL), dried (MgSO₄), and evaporated in vacuo. The residue was triturated with cold EtOH and filtered to yield the title products as yellow powders.

Table 3 Spectral Data of Compounds **5** Prepared

Product	IR (KBr, cm ⁻¹)	¹ H NMR ^a (CDCl ₃ , TMS) δ , <i>J</i> (Hz)	¹³ C NMR (CDCl ₃ , TMS) δ
5a	2956, 2833, 1700, 1609, 1591, 1561, 1547, 1506, 1452, 1439, 1355, 1284, 1262, 1236, 1217, 1195, 1181, 1136, 1100, 1072, 1016	7.39 (m, 4 H, H _{Ph} , H10), 7.29 (m, 2 H, H _{Ph}), 6.79 (s, 1 H, H7), 4.58 (t, <i>J</i> = 6.7 Hz, 2 H, H5), 3.94 (s, 3 H, OMe), 3.86 (s, 3 H, OMe), 3.53 (s, 3 H, OMe), 3.06 (t, <i>J</i> = 6.7 Hz, 2 H, H6)	161.3 (C _q), 150.2 (C _q), 147.9 (C _q), 136.4 (C _q), 132.3 (C _q), 130.9 (C _q), 129.6 (C _q), 129.5 (2 CH), 128.1 (C _q), 127.8 (CH), 127.6 (2 CH), 117.2 (C _q), 114.7 (C _q), 110.5 (CH), 109.9 (CH), 56.5 (CH ₃), 56.0 (CH ₃), 51.4 (CH ₃), 43.0 (CH ₂), 28.8 (CH ₂)
5b	3000, 2939, 2845, 1680, 1499, 1310, 1287, 1175, 1142, 1133, 1097, 1011	7.21 (s, 1 H, H10), 7.16 (d, <i>J</i> = 8.8 Hz, 2 H, H2', 6'H), 7.05 (s, 1 H, H7), 6.92 (d, <i>J</i> = 8.8, 2 H, H3', H5'), 4.45 (t, <i>J</i> = 5.6 Hz, 2 H, H5), 3.83 (s, 3 H, OMe), 3.79 (s, 3 H, OMe), 3.70 (s, 3 H, OMe), 3.51 (s, 3 H, OMe), 3.04 (t, <i>J</i> = 6.7 Hz, 2 H, H6)	160.9 (C _q), 159.1 (C _q), 155.2 (C _q), 150.6 (C _q), 147.6 (C _q), 130.8 (2 CH), 130.5 (C _q), 129.1 (C _q), 129.0 (C _q), 124.3 (C _q), 119.0 (C _q), 116.8 (C _q), 113.6 (2 CH), 111.8 (CH), 110.2 (CH), 56.6 (CH ₃), 56.1 (CH ₃), 55.5 (CH ₃), 52.0 (CH ₃), 43.3 (CH ₂), 28.2 (CH ₂)
5c	2932, 1697, 1560, 1531, 1502, 1463, 1422, 1373, 1320, 1232, 1175, 1122	7.22 (s, 1 H, H10), 6.91 (d, <i>J</i> = 8.3 Hz, 1 H, H5'), 6.85 (s, 1 H, H2'), 6.74 (d, <i>J</i> = 8.3 Hz, 1 H, H6'), 6.72 (s, 1 H, H7), 4.45 (t, <i>J</i> = 5.5 Hz, 2 H, H5), 3.96 (s, 3 H, OMe), 3.88 (s, 3 H, OMe), 3.82 (s, 3 H, OMe), 3.79 (s, 3 H, OMe), 3.56 (s, 3 H, OMe), 3.02 (t, <i>J</i> = 5.5 Hz, 2 H, H6)	161.8 (C _q), 159.2 (C _q), 149.0 (C _q), 148.5 (C _q), 146.7 (C _q), 137.3 (C _q), 133.1 (C _q), 131.6 (C _q), 129.5 (C _q), 129.1 (C _q), 128.5 (C _q), 124.9 (C _q), 120.1 (CH), 115.4 (CH), 114.2 (CH), 112.9 (CH), 112.4 (CH), 59.2 (CH ₃), 58.9 (CH ₃), 56.6 (CH ₃), 56.3 (CH ₃), 52.0 (CH ₃), 44.2 (CH ₂), 28.2 (CH ₂)
5d	2956, 1685, 1610, 1532, 1462, 1372, 1275, 1210, 1170, 1132, 1011	7.20 (s, 1 H, H10), 6.86 (s, 1 H, H6'), 6.72 (s, 1 H, H2'), 6.79 (s, 1 H, H7), 4.40 (t, <i>J</i> = 5.5 Hz, 2 H, H5), 3.89 (s, 3 H, OMe), 3.85 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 3.79 (s, 3 H, OMe), 3.54 (s, 3 H, OMe), 3.03 (t, <i>J</i> = 5.5 Hz, 2 H, H6)	166.1 (C _q), 150.3 (C _q), 148.1 (C _q), 146.3 (C _q), 136.2 (C _q), 134.8 (C _q), 133.7 (C _q), 131.5 (C _q), 130.1 (C _q), 129.1 (C _q), 127.9 (C _q), 123.6 (C _q), 117.9 (CH), 116.4 (CH), 115.7 (CH), 115.1 (C _q), 114.5 (CH), 59.1 (CH ₃), 59.3 (CH ₃), 56.7 (CH ₃), 56.5 (CH ₃), 56.1 (CH ₃), 43.4 (CH ₂), 28.1 (CH ₂)
5e	2993, 2940, 2840, 1709, 1669, 1563, 1505, 1475, 1443, 1427, 1387, 1343, 1301, 1287, 1260, 1214, 1195, 1138, 1107, 1049, 1013	7.49 (s, 1 H, H10), 6.79 (s, 1 H, H7), 6.63 (s, 1 H, H6'), 4.61 (m, 2 H, H5), 3.96 (s, 3 H, OMe), 3.95 (s, 3 H, OMe), 3.93 (s, 3 H, OMe), 3.89 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 3.34 (s, 3 H, OMe), 3.06 (m, 2 H, H6)	160.9 (C _q), 152.2 (C _q), 150.7 (C _q), 150.4 (C _q), 147.7 (C _q), 142.5 (C _q), 131.6 (C _q), 131.5 (C _q), 129.7 (C _q), 128.0 (C _q), 127.4 (C _q), 118.6 (C _q), 117.1 (C _q), 111.0 (C _q), 110.5 (CH), 110.4 (CH), 109.8 (CH), 61.2 (CH ₃), 61.0 (CH ₃), 56.13 (CH ₃), 56.12 (CH ₃), 56.0 (CH ₃), 51.7 (CH ₃), 43.0 (CH ₂), 28.8 (CH ₂)
5f	2956, 1708, 1581, 1521, 1502, 1472, 1456, 1442, 1395, 1350, 1262, 1216, 1197, 1143	8.26 (d, <i>J</i> = 7.7 Hz, 1 H, H6'), 8.17 (s, 1 H, H2'), 7.77 (d, <i>J</i> = 7.7 Hz, 1 H, H4'), 7.71 (t, <i>J</i> = 7.7 Hz, 1 H, H5'), 7.39 (s, 1 H, H10), 7.08 (s, 1 H, H7), 4.37 (t, <i>J</i> = 6.5 Hz, 2 H, H5), 3.86 (s, 3 H, OMe), 3.72 (s, 3 H, OMe), 3.32 (s, 3 H, OMe), 3.07 (t, <i>J</i> = 6.5 Hz, 2 H, H6)	160.1 (C _q), 150.6 (C _q), 147.4 (C _q), 147.2 (C _q), 136.6 (CH), 134.7 (C _q), 131.7 (CH), 130.8 (C _q), 129.3 (CH), 129.2 (CH), 125.3 (C _q), 124.6 (CH), 122.6 (C _q), 119.2 (C _q), 116.3 (C _q), 111.3 (CH), 110.8 (CH), 55.8 (2 CH ₃), 51.9 (CH ₃), 43.2 (CH ₂), 28.0 (CH ₂)
5g	3000, 2957, 2834, 1701, 1552, 1496, 1474, 1356, 1263, 1217, 1137, 1116, 1078, 1044, 1015	8.57 (dd, <i>J</i> = 1.7, 4.9 Hz, 1 H, H4'), 8.47 (dd, <i>J</i> = 0.7, 2.2 Hz, 1 H, H2'), 7.73 (ddd, <i>J</i> = 1.7, 2.2, 7.8 Hz, 1 H, H5'), 7.43 (ddd, <i>J</i> = 0.7, 4.9, 7.8 Hz, 1 H, H6'), 7.34 (s, 1 H, H10), 7.07 (s, 1 H, H7), 4.50 (t, <i>J</i> = 6.5 Hz, 2 H, H5), 3.72 (s, 3 H, OMe), 3.51 (s, 3 H, OMe), 3.34 (s, 3 H, OMe), 3.07 (t, <i>J</i> = 6.5 Hz, 2 H, H6)	160.3 (C _q), 150.5 (C _q), 149.8 (C _q), 148.6 (C _q), 147.2 (C _q), 137.3 (CH), 131.6 (CH), 129.1 (CH), 128.9 (C _q), 128.3 (C _q), 124.2 (C _q), 122.9 (C _q), 119.3 (C _q), 116.3 (CH), 111.4 (C _q), 110.6 (C _q), 55.9 (2 CH ₃), 51.8 (CH ₃), 43.2 (CH ₂), 28.0 (CH ₂)
5h	2952, 1710, 1612, 1506, 1441, 1354, 1261, 1245, 1215, 1198, 1174, 1135, 1070, 1008	7.47 (d, <i>J</i> = 7.5 Hz, 2 H, H2 _{Bn} , H6 _{Bn}), 7.40 (t, <i>J</i> = 7.5 Hz, 2 H, H3 _{Bn} , H5 _{Bn}), 7.36 (s, 1 H, H10), 7.34 (t, <i>J</i> = 7.5 Hz, 1 H, H4 _{Bn}), 7.22 (d, <i>J</i> = 8.8 Hz, 2 H, H2', H6'), 7.00 (d, <i>J</i> = 8.8 Hz, 2 H, H3', H5'), 6.78 (s, 1 H, H7), 5.10 (s, 2 H, OCH ₂), 4.56 (t, <i>J</i> = 6.7 Hz, 2 H, H5), 3.94 (s, 3 H, OMe), 3.87 (s, 3 H, OMe), 3.56 (s, 3 H, OMe), 3.04 (t, <i>J</i> = 6.7 Hz, 2 H, H6)	161.5 (C _q), 158.4 (C _q), 150.2 (C _q), 147.9 (C _q), 136.9 (C _q), 130.9 (2 CH), 130.7 (C _q), 128.6 (2 CH), 128.4 (C _q), 128.0 (CH), 127.7 (C _q), 127.6 (2 CH), 127.1 (C _q), 124.5 (C _q), 118.4 (C _q), 117.3 (C _q), 114.0 (2 CH), 110.5 (CH), 109.9 (CH), 70.0 (CH ₂), 56.2 (CH ₃), 56.0 (CH ₃), 51.4 (CH ₃), 43.0 (CH ₂), 28.8 (CH ₂)

Table 3 Spectral Data of Compounds **5** Prepared (continued)

Product	IR (KBr, cm ⁻¹)	¹ H NMR ^a (CDCl ₃ , TMS) δ , <i>J</i> (Hz)	¹³ C NMR (CDCl ₃ , TMS) δ
5i	2937, 1705, 1630, 1569, 1520, 1499, 1349, 1264, 1216, 1178, 1147, 1133, 1093, 1004	8.16 (s, 1 H, H2'), 7.92 (t, <i>J</i> = 7.3 Hz, 1 H, H5'), 7.79 (d, <i>J</i> = 7.3 Hz, 1 H, H4'), 7.62 (t, <i>J</i> = 8.5 Hz, 1 H, H4''), 7.59 (d, <i>J</i> = 8.5 Hz, 2 H, H2'', H6''), 7.52 (d, <i>J</i> = 8.5 Hz, 2 H, H3'', H5''), 7.45 (s, 1 H, H10), 7.41 (d, <i>J</i> = 7.3 Hz, 1 H, H6'), 7.10 (s, 1 H, H7), 4.27 (t, <i>J</i> = 6.1 Hz, 2 H, H5), 3.87 (s, 3 H, OMe), 3.65 (s, 3 H, OMe), 3.10 (t, <i>J</i> = 6.1 Hz, 2 H, H6)	187.2 (C _q), 150.6 (C _q), 147.2 (C _q), 146.9 (C _q), 137.6 (CH), 137.1 (C _q), 133.6 (C _q), 132.9 (CH), 129.6 (2 CH), 129.4 (CH), 129.3 (C _q), 128.8 (C _q), 128.7 (C _q), 128.1 (2 CH), 127.7 (C _q), 125.3 (CH), 124.4 (C _q), 122.4 (CH), 116.4 (C _q), 111.5 (CH), 110.8 (CH), 55.9 (CH ₃), 55.8 (CH ₃), 43.3 (CH ₂), 28.2 (CH ₂)
5j	2939, 1627, 1500, 1468, 1431, 1411, 1390, 1353, 1265, 1214, 1147, 1084, 1013	7.51 (d, <i>J</i> = 7.4 Hz, 2 H, H2'', H6''), 7.43 (s, 1 H, H10), 7.33 (t, <i>J</i> = 7.4 Hz, 1 H, H4''), 7.14 (t, <i>J</i> = 7.4 Hz, 2 H, H3'', H5''), 7.02 (s, 4 H, H _{Ar2}), 6.80 (s, 1 H, H7), 4.35 (t, <i>J</i> = 6.5 Hz, 2 H, H5), 3.95 (s, 3 H, OMe), 3.89 (s, 3 H, OMe), 3.08 (t, <i>J</i> = 6.5 Hz, 2 H, H6)	187.9 (C _q), 150.4 (C _q), 147.9 (C _q), 137.5 (C _q), 133.7 (C _q), 132.7 (q, CH), 131.7 (2 CH), 131.2 (C _q), 129.6 (C _q), 129.5 (2 CH), 128.0 (C _q), 127.9 (2 CH), 127.8 (2 CH), 126.9 (C _q), 126.3 (C _q), 117.0 (C _q), 110.6 (CH), 110.0 (CH), 56.2 (CH ₃), 56.0 (CH ₃), 43.2 (CH ₂), 28.9 (CH ₂)
5k	2938, 2836, 1677, 1645, 1550, 1500, 1468, 1450, 1356, 1267, 1236, 1216, 1147, 1092, 1055, 1036, 1016	7.57 (m, 3 H, H _{Ph} , H10), 7.26 (t, <i>J</i> = 7.4 Hz, 1 H, H5'), 7.14 (m, 3 H, H _{Ph}), 6.98 (m, 2 H, H3', H6'), 6.92 (t, <i>J</i> = 7.4 Hz, 1 H, H4'), 6.81 (s, 1 H, H7), 4.44 (m, 1 H, H5), 4.33 (m, 1 H, H5), 3.95 (s, 3 H, OMe), 3.90 (s, 3 H, OMe), 3.10 (t, <i>J</i> = 6.7 Hz, 2 H, H6)	187.7 (C _q), 150.4 (C _q), 147.7 (C _q), 137.8 (C _q), 134.3 (C _q), 132.5 (CH), 132.2 (CH), 131.8 (C _q), 131.1 (C _q), 129.2 (2 CH), 129.1 (CH), 128.9 (CH), 128.4 (C _q), 128.3 (C _q), 127.7 (2 CH), 127.1 (C _q), 126.1 (CH), 124.9 (C _q), 117.1 (C _q), 110.6 (CH), 110.5 (CH), 56.2 (CH ₃), 56.0 (CH ₃), 43.3 (CH ₂), 29.0 (CH ₂)
5l	3004, 2935, 2839, 1630, 1597, 1505, 1471, 1443, 1429, 1409, 1394, 1353, 1321, 1281, 1258, 1214, 1167, 1142, 1084, 1035, 1016	7.55 (d, <i>J</i> = 7.0 Hz, 2 H, H2'', H6''), 7.48 (s, 1 H, H10), 7.10 (m, 5 H, H _{Ph}), 6.78 (s, 1 H, H7), 6.60 (d, <i>J</i> = 7.0 Hz, 2 H, H3'', H5''), 4.26 (t, <i>J</i> = 6.8 Hz, 2 H, H5), 3.94 (s, 3 H, OMe), 3.90 (s, 3 H, OMe), 3.73 (s, 3 H, OMe), 3.06 (t, <i>J</i> = 6.8 Hz, 2 H, H6)	185.5 (C _q), 163.2 (C _q), 150.1 (C _q), 147.8 (C _q), 132.1 (2 CH), 131.2 (C _q), 130.8 (C _q), 130.4 (C _q), 130.3 (2 CH), 130.2 (C _q), 127.8 (CH), 127.7 (2 CH), 127.5 (C _q), 127.0 (C _q), 126.3 (C _q), 117.4 (C _q), 113.1 (2 CH), 110.6 (CH), 109.8 (CH), 56.1 (CH ₃), 55.9 (CH ₃), 55.3 (CH ₃), 43.0 (CH ₂), 29.0 (CH ₂)
5m	3022, 2964, 2840, 1628, 1601, 1574, 1504, 1473, 1423, 1351, 1256, 1214, 1170, 1143, 1113, 1091, 1080, 1027	7.53 (d, <i>J</i> = 8.9 Hz, 2 H, H2'', H6''), 7.47 (s, 1 H, H10), 7.07 (s, 4 H, H _{Ar2}), 6.79 (s, 1 H, H7), 6.64 (d, <i>J</i> = 8.9 Hz, 2 H, H3'', H5''), 4.26 (t, <i>J</i> = 6.5 Hz, 2 H, H5), 3.95 (s, 3 H, OMe), 3.90 (s, 3 H, OMe), 3.78 (s, 3 H, OMe), 3.06 (t, <i>J</i> = 6.5 Hz, 2 H, H6)	186.3 (C _q), 163.6 (C _q), 150.3 (C _q), 147.9 (C _q), 133.6 (C _q), 132.1 (2 CH), 131.6 (2 CH), 130.8 (C _q), 130.7 (C _q), 130.0 (C _q), 129.9 (C _q), 127.9 (2 CH), 127.8 (C _q), 127.2 (C _q), 125.0 (C _q), 117.2 (C _q), 113.4 (2 CH), 110.6 (CH), 110.0 (CH), 56.2 (CH ₃), 56.0 (CH ₃), 55.5 (CH ₃), 43.1 (CH ₂), 29.0 (CH ₂)
5n	2936, 2840, 1629, 1599, 1573, 1505, 1469, 1369, 1265, 1217, 1167, 1145, 1030, 1014	7.61 (s, 1 H, H10), 7.58 (d, <i>J</i> = 8.8 Hz, 2 H, H2'', H6''), 6.96 (s, 2 H, H3', H6'), 6.80 (s, 1 H, H7), 6.68 (d, <i>J</i> = 8.8 Hz, 2 H, H3'', H5''), 4.36 (m, 1 H, H5), 4.22 (m, 1 H, H5), 3.95 (s, 3 H, OMe), 3.90 (s, 3 H, OMe), 3.78 (s, 3 H, OMe), 3.07 (t, <i>J</i> = 6.8 Hz, 2 H, H6)	185.9 (C _q), 163.6 (C _q), 150.4 (C _q), 147.7 (C _q), 135.2 (C _q), 134.2 (C _q), 132.9 (CH), 131.7 (2 CH), 131.6 (C _q), 130.9 (C _q), 130.3 (C _q), 130.1 (C _q), 128.9 (CH), 128.2 (C _q), 127.6 (C _q), 126.5 (C _q), 122.5 (C _q), 117.1 (C _q), 113.3 (2 CH), 110.7 (CH), 110.5 (CH), 56.2 (CH ₃), 56.0 (CH ₃), 55.5 (CH ₃), 43.3 (CH ₂), 29.0 (CH ₂)
5o	3008, 2941, 2833, 1625, 1609, 1586, 1508, 1466, 1440, 1411, 1354, 1322, 1281, 1261, 1214, 1195, 1171, 1143, 1084, 1068, 1011	7.41 (s, 1 H, H10), 7.35 (d, <i>J</i> = 8.3 Hz, 2 H, H2'', H6''), 7.20 (d, <i>J</i> = 8.3 Hz, 2 H, H3'', H5''), 7.08 (m, 5 H, H _{Ph}), 6.81 (s, 1 H, H7), 4.36 (t, <i>J</i> = 6.0 Hz, 2 H, H5), 3.95 (s, 3 H, OMe), 3.89 (s, 3 H, OMe), 3.08 (t, <i>J</i> = 6.0 Hz, 2 H, H6)	186.8 (C _q), 150.4 (C _q), 147.9 (C _q), 136.4 (C _q), 131.2 (C _q), 130.95 (2 CH), 130.9 (3 CH), 130.8 (C _q), 130.4 (2 CH), 128.0 (C _q), 127.9 (C _q), 127.8 (C _q), 127.7 (2 CH), 127.4 (C _q), 126.3 (C _q), 117.0 (C _q), 110.6 (CH), 109.8 (CH), 56.1 (CH ₃), 56.0 (CH ₃), 43.1 (CH ₂), 28.9 (CH ₂)
5p	3010, 2943, 1633, 1586, 1502, 1471, 1442, 1405, 1355, 1261, 1218, 1148, 1095, 1068, 1056, 1014	7.54 (s, 1 H, H10), 7.41 (d, <i>J</i> = 8.4 Hz, 2 H, H2'', H6''), 7.25 (d, <i>J</i> = 8.4 Hz, 2 H, H3'', H5''), 7.19 (d, <i>J</i> = 7.9 Hz, 1 H, H6'), 7.07 (t, <i>J</i> = 7.9 Hz, 1 H, H5'), 6.97 (d, <i>J</i> = 7.9 Hz, 1 H, H3'), 6.95 (d, <i>J</i> = 7.9 Hz, 1 H, H4'), 6.81 (s, 1 H, H7), 4.45 (m, 1 H, H5), 4.34 (m, 1 H, H5), 3.96 (s, 3 H, OMe), 3.90 (s, 3 H, OMe), 3.10 (m, 2 H, H6)	186.6 (C _q), 150.6 (C _q), 147.8 (C _q), 136.7 (C _q), 134.3 (C _q), 133.1 (C _q), 132.3 (CH), 132.2 (C _q), 131.0 (C _q), 130.9 (2 CH), 130.5 (2 CH), 129.3 (CH), 129.1 (CH), 128.3 (C _q), 127.5 (C _q), 126.7 (C _q), 126.3 (CH), 125.3 (C _q), 117.0 (C _q), 110.6 (CH), 110.5 (CH), 56.2 (CH ₃), 56.0 (CH ₃), 43.3 (CH ₂), 29.0 (CH ₂)

Table 3 Spectral Data of Compounds **5** Prepared (continued)

Product	IR (KBr, cm ⁻¹)	¹ H NMR ^a (CDCl ₃ , TMS) δ , <i>J</i> (Hz)	¹³ C NMR (CDCl ₃ , TMS) δ
5q	2877, 1633, 1584, 1502, 1431, 1354, 1259, 1171, 1139, 1066, 1041, 1010	7.39 (s, 1 H, H10), 7.36 (d, <i>J</i> = 8.5 Hz, 2 H, H2'', H6''), 7.29 (d, <i>J</i> = 8.5 Hz, 2 H, H3'', H5''), 6.80 (s, 1 H, H7), 6.52 (s, 2 H, H2', H5'), 5.87 (s, 2 H, OCH ₂ O), 4.37 (t, <i>J</i> = 6.6 Hz, 2 H, H5), 3.95 (s, 3 H, OMe), 3.89 (s, 3 H, OMe), 3.08 (t, <i>J</i> = 6.6 Hz, 2 H, H6)	186.9 (C _q), 150.4 (C _q), 147.9 (C _q), 147.4 (C _q), 147.0 (C _q), 136.7 (C _q), 131.2 (C _q), 130.9 (2 CH), 130.8 (2 CH), 128.0 (C _q), 127.7 (C _q), 127.2 (C _q), 126.4 (C _q), 124.5 (C _q), 124.3 (C _q), 117.0 (C _q), 111.0 (CH), 110.6 (CH), 109.8 (CH), 107.8 (CH), 101.1 (CH ₂), 56.1 (CH ₃), 56.0 (CH ₃), 43.0 (CH ₂), 28.9 (CH ₂)

^a Aryl groups at C2 are indicated using ', while those at C3 are indicated by ''.

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References

- (1) Present address: Servier Research Institute of Medicinal Chemistry, Záhony utca 7, Graphisoft Park, 1031 Budapest, Hungary.
- (2) (a) Jones, R. A.; Bean, G. P. *The Chemistry of Pyrroles*; Academic Press: London, **1977**. (b) Sundberg, R. J. In *Comprehensive Heterocyclic Chemistry*, Vol. 4; Katritzky, A.; Rees, C. W., Eds.; Pergamon: Oxford, **1984**, 313.
- (3) (a) La Porta, P.; Capuzzi, L.; Bettarini, F. *Synthesis* **1994**, 287. (b) DeShong, P.; Kell, D. A.; Sidler, D. R. *J. Org. Chem.* **1985**, 50, 2309. (c) Padwa, A.; Norman, B. H. *J. Org. Chem.* **1990**, 55, 4801. (d) Cironi, P.; Cuevas, C.; Albericio, F.; Alvarez, M. *Tetrahedron* **2004**, 60, 8669. (e) Cironi, P.; Manzanera, I.; Albericio, F.; Alvarez, M. *Org. Lett.* **2003**, 5, 2959. (f) Ridley, C. P. M.; Reddy, V. R.; Rocha, G.; Bushman, F. D.; Faulkner, D. J. *Bioorg. Med. Chem.* **2002**, 10, 3285. (g) Banwell, M.; Flynn, B.; Hockless, D. *Chem. Commun.* **1997**, 2259. (h) Poissonnet, G.; Theret-Bettiol, M.-H.; Dodd, R. H. *J. Org. Chem.* **1996**, 61, 2273.
- (4) (a) Southwick, P. L.; Sapper, D. I.; Pursglove, L. A. *J. Am. Chem. Soc.* **1950**, 72, 4940. (b) Cossy, J.; Pete, J.-P. *Tetrahedron Lett.* **1978**, 19, 4941. (c) Cervinka, O. *Chem. Ind. (London)* **1959**, 1129. (d) Oussaid, B.; Garrigues, B.; Soufiaoui, M. *Can. J. Chem.* **1994**, 72, 2483. (e) Bonnaud, B.; Bigg, D. C. H. *Synthesis* **1994**, 465. (f) Gupta, P.; Bhaduri, A. P. *Synth. Commun.* **1998**, 28, 3151. (g) Fejes, I.; Nyerges, M.; Blaskó, G.; Töke, L.; Pak, C. S. *Tetrahedron* **2000**, 56, 8545.
- (5) This work has been published in preliminary form: Tóth, J.; Váradi, L.; Blaskó, G.; Dancsó, A.; Töke, L.; Nyerges, M. *Synlett* **2007**, 1259.
- (6) (a) Andersen, R. J.; Faulkner, D. J.; Cun-heng, H.; Van Duyne, G. D.; Clardy, J. *J. Am. Chem. Soc.* **1985**, 107, 5492. (b) Cironi, P.; Albericio, F.; Alvarez, M. *Progress in Heterocyclic Chemistry*, Vol. 16; Gribble, G. W.; Joule, J. A., Eds.; Pergamon: Oxford, **2004**, 1–26. (c) Fan, H.; Peng, J.; Hamann, M. T.; Hu, J.-F. *Chem. Rev.* **2008**, 108, 264.
- (7) (a) Yamaguchi, T.; Fukuda, T.; Ishibashi, F.; Iwao, M. *Tetrahedron Lett.* **2006**, 47, 3755. (b) Fujikawa, N.; Ohta, T.; Yamaguchi, T.; Fukuda, T.; Ishibashi, F.; Iwao, M. *Tetrahedron* **2006**, 62, 594. (c) Iwao, M.; Takeuchi, T.; Fujikawa, N.; Fukuda, T.; Ishibashi, F. *Tetrahedron Lett.* **2003**, 44, 4443.
- (8) (a) Díaz, M.; Guitián, E.; Castedo, L. *Synlett* **2001**, 1164. (b) Zhao, B.-X.; Yu, Y.; Eguchi, S. *Tetrahedron* **1996**, 52, 12049.
- (9) Olsen, C. A.; Parera, N.; Albericio, F.; Alvarez, M. *Tetrahedron Lett.* **2005**, 46, 2041.
- (10) (a) Ploypradith, P.; Kagan, R. K.; Ruchirawat, S. *J. Org. Chem.* **2005**, 70, 5119. (b) Ploypradith, P.; Mahidol, C.; Sahakitpichan, P.; Wongbudit, S.; Ruchirawat, S. *Angew. Chem. Int. Ed.* **2004**, 43, 866. (c) Kuo, R.-Y.; Wu, C.-C.; Chang, F.-R.; Yeh, J.-L.; Chen, I.-J.; Wu, Y.-C. *Bioorg. Med. Chem. Lett.* **2003**, 13, 821. (d) Ishibashi, F.; Tanabe, S.; Oda, T.; Iwao, M. *J. Nat. Prod.* **2002**, 65, 500. (e) Ruchirawat, S.; Mutarapat, T. *Tetrahedron Lett.* **2001**, 42, 1205.
- (11) Fujita, R.; Watanabe, N.; Tomisawa, H. *Chem. Pharm. Bull.* **2002**, 50, 225.
- (12) (a) Nyerges, M.; Töke, L. *Tetrahedron Lett.* **2005**, 46, 7531. (b) Tóth, J.; Nedves, A.; Blaskó, G.; Dancsó, A.; Töke, L.; Nyerges, M. *Synthesis* **2007**, 1003.
- (13) (a) Bende, Z.; Simon, K.; Tóth, G.; Töke, L.; Weber, L. *Liebigs Ann. Chem.* **1982**, 924. (b) Bende, Z.; Bitter, I.; Töke, L.; Weber, L.; Tóth, G.; Janke, F. *Liebigs Ann. Chem.* **1982**, 2146. (c) Bende, Z.; Töke, L.; Weber, L.; Tóth, G.; Janke, F.; Csonka, G. *Tetrahedron* **1984**, 40, 369. (d) Tischer, T.; Töke, L.; Tóth, G. *Acta Chim. Hung.* **1990**, 127, 171. (e) Fejes, I.; Nyerges, M.; Töke, L.; Pak, C. S. *Tetrahedron* **2000**, 56, 639. (f) Fejes, I.; Nyerges, M.; Szöllösy, ; Blaskó, G.; Töke, L. *Tetrahedron* **2001**, 57, 1129. (g) Nyerges, M.; Somfai, B.; Tóth, J.; Dancsó, A.; Blaskó, G.; Töke, L. *Synthesis* **2005**, 46, 2039.
- (14) Filler, R. *Chem. Rev.* **1963**, 63, 21.
- (15) (a) Ali, M. H.; Hartman, M.; Lamp, K.; Schmitz, C.; Wencewicz, T. *Synth. Commun.* **2006**, 36, 1769. (b) Harville, R.; Rees, S. F. Jr. *J. Org. Chem.* **1968**, 33, 3976. (c) More, K. M.; Wemple, J. *Synthesis* **1977**, 791. (d) Surendra, K.; Krishnaveni, N. S.; Kumar, V. P.; Sridhar, R.; Rao, K. R. *Tetrahedron Lett.* **2005**, 46, 4581.
- (16) (a) Jain, S. L.; Sain, B. *Synth. Commun.* **2006**, 36, 1459. (b) Lee, J. C.; Lee, J. Y.; Lee, J. M. *Synth. Commun.* **2005**, 35, 1911. (c) Sharma, V. B.; Jain, S. L.; Sain, B. *J. Mol. Catal. A: Chem.* **2005**, 227, 47. (d) Khurana, J. M.; Kandpal, B. M. *Tetrahedron Lett.* **2003**, 44, 4909.
- (17) Cheung, Y. F. *Tetrahedron Lett.* **1979**, 20, 3809.
- (18) Bandgar, B. P.; Makone, S. S. *Synth. Commun.* **2006**, 36, 1347.
- (19) Tatsugi, J.; Zhiwei, T.; Izawa, Y. *ARKIVOC* **2001**, (i), 67.
- (20) Suzuki, H.; Tsutsui, H.; Kano, A.; Katoh, S.; Morita, T.; Matsuda, K.; Iibuchi, N.; Ogawa, M. *Heterocycles* **1997**, 45, 1657.
- (21) Kovganko, V. N.; Kovganko, N. N. *Russ. J. Org. Chem.* **2006**, 42, 243.
- (22) (a) Pelletier, J. C.; Cava, M. P. *J. Org. Chem.* **1987**, 52, 616. (b) Pelletier, J. C.; Cava, M. P. *Synthesis* **1987**, 474.

- (23) Stanforth, S. P. *J. Heterocycl. Chem.* **1987**, *24*, 531.
- (24) (a) Handy, S. T.; Zhang, Y.; Bregman, H. *J. Org. Chem.* **2004**, *69*, 2362. (b) Marfil, M.; Albericio, F.; Alvarez, M. *Tetrahedron* **2004**, *60*, 8659. (c) Olsen, C. A.; Parera, N.; Albericio, F.; Alvarez, M. *Tetrahedron Lett.* **2005**, *46*, 2041. (d) Pla, D.; Marchal, A.; Olsen, C. A.; Albericio, F.; Alvarez, M. *J. Org. Chem.* **2005**, *70*, 8231. (e) Banwell, M. G.; Hamel, E.; Hockless, D. C. R.; Verdier-Pinard, P.; Willis, A. C.; Wong, D. J. *Bioorg. Med. Chem.* **2006**, *14*, 4627. (f) Handy, S. T.; Sabatini, J. J. *Org. Lett.* **2006**, *8*, 1537.