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Synthesis of 2,2'-Dipyrryl Ketones from Pyrrole-2-carboxylic Acids with Trifluoroacetic Anhydride

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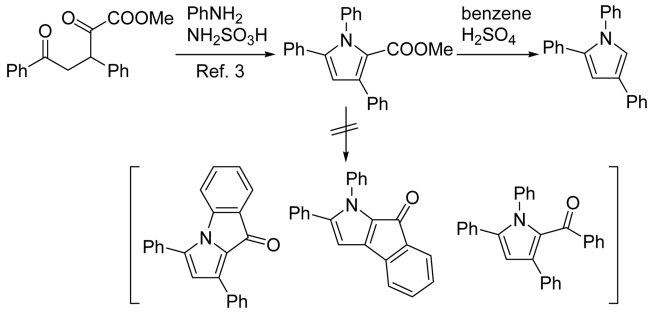
An efficient synthesis of 2,2'-dipyrryl ketones has been carried out from pyrrole-2-carboxylic acids using trifluoroacetic anhydride (TFAA). Simultaneous generation of both mixed anhydride and 2-unsubstituted pyrrole, *via* facile decarboxylation with *in-situ* generated TFA, made their cross reaction (intermolecular Friedel-Crafts acylation) possible and efficient.

Key Words : Dipyrryl ketones, Pyrrole-2-carboxylic acid, Trifluoroacetic anhydride, Mixed anhydride

Introduction

Dipyrryl ketone derivatives have been studied extensively due to their synthetic usefulness as precursors for the synthesis of porphyrin derivatives,[1a-d] Oxophlorin derivatives,[1e-g] and 10-oxo-Bilirubin.[1h] Dipyrryl ketones have been prepared usually by oxidation of the corresponding dipyrrylmethanes with cerium(IV) ammonium nitrate (CAN).[2a-c] Phosphoric acid-promoted acylation of pyrroles with mixed anhydride derived from pyrrole carboxylic acid has also been reported.[2d]

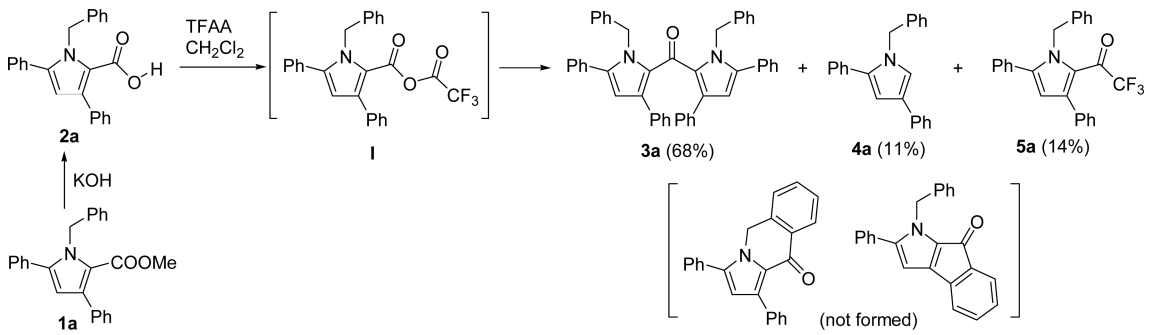


Scheme 1

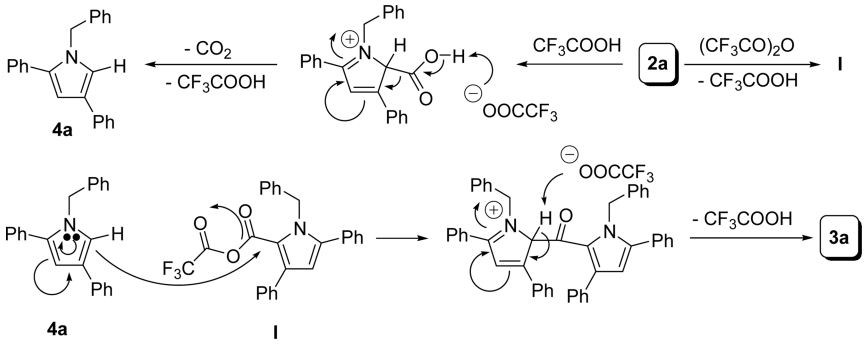
Results and Discussion

Recently, we reported an efficient synthesis of pyrrole-2-carboxylates starting from 2,5-diketoesters *via* a Paal-Knorr synthesis.[3] During the studies we found that the ester group at 2-position of the pyrrole could be removed easily by treatment with H_2SO_4 presumably *via* an acid-catalyzed hydrolysis and decarboxylation.[3-5] In the reaction we did not observe the formation of any intra- or intermolecular Friedel-Crafts reaction products, as shown in Scheme 1.

In order to check the feasibility for the synthesis of tricyclic pyrrole derivatives, we examined an intramolecular Friedel-Crafts acylation reaction of *in-situ* generated mixed anhydride **I** from **2a** and trifluoroacetic anhydride (TFAA), as shown in Scheme 2. Intramolecular Friedel-Crafts reactions using mixed anhydride derived from TFAA have been used frequently by us and others.[6] Thus, we prepared an acid derivative **2a** by a base-mediated hydrolysis of **1a**, as shown in Scheme 2. However, a treatment of **2a** with TFAA (2.0 equiv) in CH_2Cl_2 (rt, 24 h) produced 2,2'-dipyrryl ketone **3a** in moderate yield (68%) along with a low yield of **4a** (11%) and trifluoroacetyl derivative **5a** (14%),[7] instead of the Friedel-Crafts products shown in the parenthesis. When we carried out the reaction in the presence of an excess amount (3.0 equiv) of TFAA under refluxing condition (24 h), **5a** was isolated in an increased yield (51%) along with **3a** (31%) and **4a** (12%).[7] The yield of **3a** increased to 73% when we used 0.6 equiv of TFAA at room temperature (vide



Scheme 2

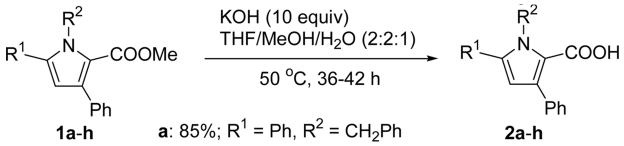


Scheme 3

infra, Table 1). In this reaction, **4a** was isolated in low yield (24%) and **5a** was not formed at all.

The reaction mechanism for the formation of 2,2'-dipyrryl ketone **3a** could be proposed as shown in Scheme 3. The reaction of **2a** and TFAA would produce a mixed anhydride **I**.[2d,6] In one part, a facile *in-situ* generated CF_3COOH (TFA)-catalyzed decarboxylation of **2a** produced an electron-rich pyrrole **4a**.[3-5,8] A following Friedel-Crafts acylation reaction between **4a** and **I** produced **3a**. The 2,3'-dipyrryl ketone was not formed at all.

Encouraged by the results we prepared starting materials **2a-h**, as shown in Scheme 4. Various pyrrole-2-carboxylates **1a-h** were prepared according to our previous paper,[3] and a subsequent base-mediated hydrolysis was carried out to prepare **2a-h**. The hydrolysis was quite sluggish, to our surprise, and actually the reaction was not completed even after 3 days under the influence of KOH (10 equiv) in refluxing aqueous dioxane.[9] After much trials we found that the



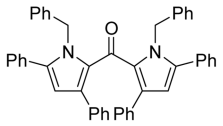
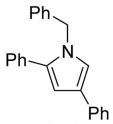
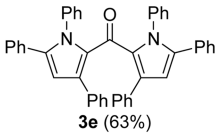
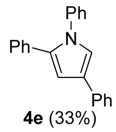
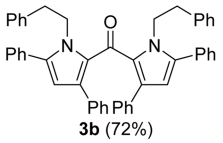
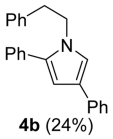
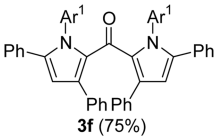
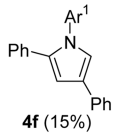
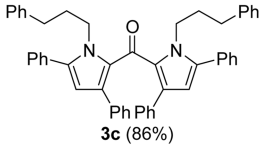
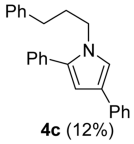
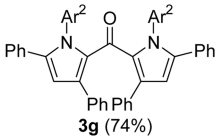
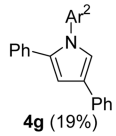
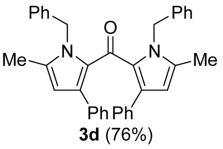
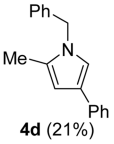
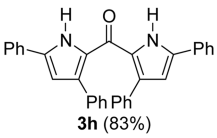
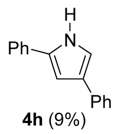
a: 85%; R^1 = Ph, R^2 = CH_2Ph
b: 85%; R^1 = Ph, R^2 = CH_2CH_2Ph
c: 80%; R^1 = Ph, R^2 = $CH_2CH_2CH_2Ph$
d: 73%; R^1 = Me, R^2 = CH_2Ph
e: 74%; R^1 = Ph, R^2 = Ph
f: 89%; R^1 = Ph, R^2 = 4-$MeOC_6H_4$
g: 66%; R^1 = Ph, R^2 = 2,4-$(MeO)_2C_6H_3$
h: 78%; R^1 = Ph, R^2 = H

Scheme 4

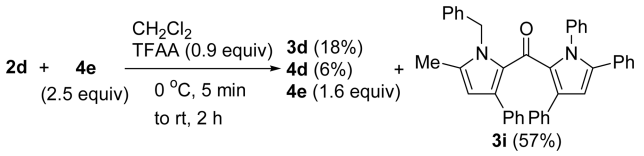
hydrolysis was conducted efficiently in a mixed solvent, THF/MeOH/H_2O (2:2:1), at 50 °C in the presence of an excess amount of KOH (10 equiv) within shorter time (36-42 h).

With pyrrole-2-carboxylic acids **2b-h**, syntheses of 2,2'-

Table 1. Synthesis of 2,2'-dipyrryl ketones **3a-h** from **2a-h**[a]

Substrate	Products (%)		Substrate	Products (%)	
2a	 **3a** (73%)	 **4a** (24%)	**2e**	 **3e** (63%)	 **4e** (33%)
2b	 **3b** (72%)	 **4b** (24%)	**2f**[b]	 **3f** (75%)	 **4f** (15%)
2c	 **3c** (86%)	 **4c** (12%)	**2g**[c,d]	 **3g** (74%)	 **4g** (19%)
2d	 **3d** (76%)	 **4d** (21%)	**2h**[d]	 **3h** (83%)	 **4h** (9%)

[a]Conditions: substrate **2** (0.5 mmol), CH_2Cl_2, TFAA (0.6 equiv), rt, 20 h. [b]Ar^1 = 4-$MeOC_6H_4$. [c]Ar^2 = 2,4-$(MeO)_2C_6H_3$. [d]Conditions: substrate **2** (0.5 mmol), CH_2Cl_2, TFAA (0.9 equiv), 0 °C (5 min) to rt (2 h).



Scheme 5

dipyrryl ketones **3b-h** were carried out in the presence of TFAA (0.6 equiv) in CH_2Cl_2 at room temperature for 20 h. The results are summarized in Table 1. *N*-Phenethyl derivative **3b**, *N*-(3-phenylpropyl) derivative **3c**, and 5-methyl derivative **3d** were obtained in good yields (72-86%). Three *N*-aryl derivatives **3e-g** and NH derivative **3h** were synthesized in similar yields (63-83%). The yields of **3g** and **3h** were moderate (50-55%) when we carried out the reactions under the typical reaction conditions using 0.6 equiv of TFAA. In these cases, addition of TFAA (0.9 equiv) at 0 °C improved the yields, as noted in Table 1. In these cases, the reactions were completed in short reaction time (2 h); however, the reason is not clear at this stage. In all cases, 2-unsubstituted pyrrole derivatives **4a-h** were isolated as minor products (9-33%).

As a last entry, we examined the synthesis of unsymmetrical 2,2'-dipyrryl ketone **3i**, as shown in Scheme 5. The reaction of pyrrole acid **2d** and pyrrole **4e** (2.5 equiv) produced a low yields of **3d** (18%) and **4d** (6%) along with a desired unsymmetrical ketone **3i** as a major product (57%) and recovered **4e** (1.6 equiv).

In summary, we disclosed an efficient synthesis of 2,2'-dipyrryl ketones from pyrrole-2-carboxylic acids using TFAA. Simultaneous generation of both mixed anhydride and 2-unsubstituted pyrrole (*via* facile decarboxylation with *in-situ* generated TFA) made their cross reaction (intermolecular Friedel-Crafts acylation) as possible and efficient.

Experimental Section

Preparation of Starting Materials 1a-h. Pyrrole-2-carboxylates **1a-h** were prepared from the corresponding 2,5-diketoesters and amines according to our previous paper.[3] The spectroscopic data of unknown compounds **1b-d**, **1f** and **1g** are as follows.

Compound 1b: white solid, mp 106-108 °C; IR (KBr) 1697, 1457, 1224 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.91 (t, *J* = 7.5 Hz, 2H), 3.66 (s, 3H), 4.54 (t, *J* = 7.5 Hz, 2H), 6.17 (s, 1H), 6.93-6.96 (m, 2H), 7.16-7.44 (m, 13H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 38.11, 47.71, 50.79, 112.03, 118.45, 126.37, 126.56, 127.54, 128.21, 128.35, 128.37, 128.76, 129.34, 129.62, 132.18, 134.02, 136.80, 138.22, 140.38, 162.40; ESIMS *m/z* 382 $[M+H]^+$.

Compound 1c: white solid, mp 76-78 °C; IR (KBr) 1697, 1456, 1217 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.84-1.95 (m, 2H), 2.39 (t, *J* = 7.5 Hz, 2H), 3.55 (s, 3H), 4.29 (t, *J* = 7.5 Hz, 2H), 6.13 (s, 1H), 6.92-6.96 (m, 2H), 7.01-7.40 (m, 13H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.77, 33.10, 45.91, 50.77, 112.02, 118.70, 125.80, 126.54, 127.55, 128.14, 128.17, 128.27, 128.51, 129.30, 129.52, 132.29, 133.97, 136.76, 140.22, 141.11, 162.38; ESIMS *m/z* 396 $[M+H]^+$.

Compound 1d: white solid, mp 58-60 °C; IR (KBr) 1695, 1437, 1284 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.13 (s, 3H), 3.46 (s, 3H), 5.27 (s, 2H), 5.99 (s, 1H), 6.89-6.92 (m, 2H), 7.11-7.34 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.47, 48.55, 50.54, 111.04, 117.90, 125.75, 126.46, 126.91, 127.48, 128.60, 129.35, 133.75, 135.93, 136.88, 138.35, 162.13; ESIMS *m/z* 306 $[M+H]^+$.

Compound 1f: yellow solid, mp 136-138 °C; IR (KBr) 1708, 1512, 1249 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.42 (s, 3H), 3.73 (s, 3H), 6.39 (s, 1H), 6.77 (d, *J* = 8.7 Hz, 2H), 7.04-7.45 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.88, 55.29, 111.94, 113.55, 121.37, 126.79, 127.33, 127.72, 128.04, 128.88, 129.26, 129.51, 131.84, 132.11, 133.24, 136.11, 139.85, 158.91, 161.80; ESIMS *m/z* 384 $[M+H]^+$.

Compound 1g: yellow solid, mp 133-135 °C; IR (KBr) 1707, 1514, 1210 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.49 (s, 3H), 3.67 (s, 3H), 3.79 (s, 3H), 6.39 (dd, *J* = 8.7 and 2.4 Hz, 1H), 6.46 (s, 1H), 6.48 (d, *J* = 2.4 Hz, 1H), 6.99 (d, *J* = 8.7 Hz, 1H), 7.18-7.40 (m, 8H), 7.51-7.54 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.70, 55.30, 55.60, 99.05, 103.72, 111.66, 121.05, 121.80, 126.62, 127.27, 127.59, 127.89, 128.48, 129.36, 129.92, 132.11, 133.13, 136.33, 139.91, 156.45, 160.39, 161.62; ESIMS *m/z* 414 $[M+H]^+$.

Typical Procedure for the Synthesis of 2a. A solution of **1a** (367 mg, 1.0 mmol) and KOH (560 mg, 10 mmol) in a mixed solvent of THF/MeOH/H_2O (3 mL, 2:2:1) was heated to 50 °C for 36 h. After the usual aqueous workup and column chromatographic purification process (CH_2Cl_2/MeOH, 50:1) compound **2a** was obtained as a white solid, 301 mg (85%). Other compounds **2b-h** were prepared similarly, and the spectroscopic data of **2a, 2c** and **2e** are as follows.

Compound 2a: 85%; white solid, mp 162-164 °C; IR (KBr) 3418, 1655, 1460, 1272 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.58 (s, 2H), 6.32 (s, 1H), 6.83-6.87 (m, 2H), 7.14-7.51 (m, 13H), 10.10 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 49.75, 112.96, 118.06, 125.86, 126.87, 126.96, 127.71, 128.39, 128.49, 128.53, 129.51, 129.59, 131.78, 136.09, 136.15, 139.09, 142.09, 165.34; ESIMS *m/z* 354 $[M+H]^+$.

Compound 2c: 80%; white solid, mp 130-132 °C; IR (KBr) 3415, 1653, 1464, 1277 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.94-2.04 (m, 2H), 2.44 (t, *J* = 7.5 Hz, 2H), 4.35 (t, *J* = 7.5 Hz, 2H), 6.21 (s, 1H), 6.98-7.52 (m, 15H), 11.34 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.80, 33.07, 46.22, 112.84, 117.45, 125.81, 126.89, 127.69, 128.13, 128.28, 128.37, 128.56, 129.54, 129.62, 132.13, 136.14, 136.45, 141.02, 141.57, 166.07; ESIMS *m/z* 382 $[M+H]^+$.

Compound 2e: 74%; white solid, mp 153-155 °C; IR (KBr) 3464, 1686, 1454, 1215 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6) δ 6.38 (s, 1H), 7.01-7.33 (m, 13H), 7.49-7.53 (m, 2H), 11.10 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) δ 111.44, 121.86, 126.14, 126.75, 127.16, 127,21, 127.48, 127.80, 128.07, 128.34, 128.91, 131.46, 131.91, 135.54, 138.40, 139.01, 162.15; ESIMS *m/z* 340 $[M+H]^+$.

Typical Procedure for the Synthesis of Dipyrryl Ketone 3a: To a stirred solution of **2a** (177 mg, 0.5 mmol) in CH_2Cl_2

(2 mL) was added TFAA (63 mg, 0.3 mmol) at room temperature, and the reaction mixture was stirred for 20 h. After the usual aqueous workup and column chromatographic purification process (hexanes/ether/CH_2Cl_2, 25:1:1) compound **3a** was obtained as a yellow solid, 118 mg (73%) along with **4a** (37 mg, 24%) as a white solid. Other compounds **3b-h** and **4b-h** were prepared similarly. Compounds **4a**,[10a] **4b**,[10a] **4d**,[10b] **4e**,[3] **4f**,[10c] and **4h**[10d] are known compounds, and the spectroscopic data of unknown compounds **3a-i**, **4c**, **4g**, and **5a** are as follows.

Compound 3a: 73%; yellow solid, mp 74-76 °C; IR (KBr) 1596, 1455, 1180 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.10 (d, J = 15.6 Hz, 2H), 5.34 (d, J = 15.6 Hz, 2H), 5.94 (s, 2H), 6.74-6.78 (m, 4H), 6.92-7.25 (m, 26H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 49.23, 111.72, 125.93, 126.88 (2C), 127.43, 127.99, 128.11, 128.22, 128.85, 129.61, 130.26, 133.28, 133.69, 135.49, 138.73, 139.90, 178.12; ESIMS *m/z* 645 $[M+H]^+$. Anal. Calcd for $C_{47}H_{36}N_2O$: C, 87.55; H, 5.63; N, 4.34. Found: C, 87.81; H, 5.77; N, 4.19.

Compound 3b: 72%; yellow solid, mp 66-68 °C; IR (KBr) 1595, 1456, 1348 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.87-2.97 (m, 2H), 3.27-3.37 (m, 2H), 4.24-4.35 (m, 4H), 5.78 (s, 2H), 6.90-6.94 (m, 4H), 7.02-7.22 (m, 20H), 7.30-7.39 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 38.57, 47.80, 110.69, 125.77, 126.43, 127.19, 128.17, 128.36, 128.48, 128.81, 128.89, 129.61, 129.98, 132.52, 133.20, 135.58, 138.69, 139.01, 179.58; ESIMS *m/z* 673 $[M+H]^+$. Anal. Calcd for $C_{49}H_{40}N_2O$: C, 87.47; H, 5.99; N, 4.16. Found: C, 87.32; H, 6.10; N, 4.03.

Compound 3c: 86%; yellow solid, mp 50-52 °C; IR (KBr) 1594, 1455, 1349 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.86-2.01 (m, 2H), 2.09-2.24 (m, 2H), 2.83-2.54 (m, 4H), 4.10-4.16 (m, 4H), 5.78 (s, 2H), 6.91-7.17 (m, 24H), 7.25-7.30 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.92, 32.95, 45.59, 110.96, 125.76, 127.19, 127.96, 128.16, 128.29, 128.36, 128.78, 129.39, 129.97, 132.50, 133.34, 135.60, 139.10, 141.09, 179.19 (one carbon was overlapped); ESIMS *m/z* 701 $[M+H]^+$. Anal. Calcd for $C_{51}H_{44}N_2O$: C, 87.39; H, 6.33; N, 4.00. Found: C, 87.51; H, 6.56; N, 3.87.

Compound 3d: 76%; yellow solid, mp 62-64 °C; IR (KBr) 1590, 1509, 1467, 1345 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.91 (s, 6H), 5.11 (d, J = 15.9 Hz, 2H), 5.44 (d, J = 15.9 Hz, 2H), 5.58 (s, 2H), 6.74-6.80 (m, 4H), 6.97-7.17 (m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.27, 48.31, 109.97, 125.46, 126.72, 126.97, 127.05, 128.42, 128.76, 129.48, 133.16, 134.95, 135.80, 138.16, 177.82; ESIMS *m/z* 521 $[M+H]^+$. Anal. Calcd for $C_{37}H_{32}N_2O$: C, 85.35; H, 6.19; N, 5.38. Found: C, 85.47; H, 6.17; N, 5.21.

Compound 3e: 63%; yellow solid, mp 100-102 °C; IR (KBr) 1601, 1495, 1453, 1265 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.12 (s, 2H), 6.87-6.92 (m, 4H), 7.15-7.38 (m, 26H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 111.48, 126.33, 127.09, 127.43, 127.56, 127.84, 128.03, 128.75, 129.13, 129.36, 132.04, 132.07, 133.32, 135.07, 138.77, 139.04, 177.26; ESIMS *m/z* 617 $[M+H]^+$. Anal. Calcd for $C_{45}H_{32}N_2O$: C, 87.63; H, 5.23; N, 4.54. Found: C, 87.74; H, 5.56; N, 4.59.

Compound 3f: 75%; yellow solid, mp 128-130 °C; IR (KBr) 1602, 1511, 1455, 1249 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.72 (s, 6H), 5.97 (s, 2H), 6.69 (d, J = 8.4 Hz, 4H), 6.82-6.87 (m, 4H), 7.02-7.24 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.31, 111.11, 113.14, 126.17, 127.01, 127.35, 127.89, 128.70, 129.29, 130.22, 131.65, 132.18, 132.43, 133.07, 135.25, 139.24, 158.61, 177.39; ESIMS *m/z* 677 $[M+H]^+$. Anal. Calcd for $C_{47}H_{36}N_2O_3$: C, 83.41; H, 5.36; N, 4.14. Found: C, 83.79; H, 5.61; N, 4.02.

Compound 3g: 74% (atropisomeric mixture, 3:2); yellow solid, mp 104-106 °C; IR (KBr) 1603, 1513, 1455, 1210 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.26 (s, 3H*0.6), 3.45 (s, 3H*0.4), 3.46 (s, 3H*0.6), 3.47 (s, 3H*0.4), 3.72 (s, 3H*0.6), 3.76 (s, 6H*0.4), 3.79 (s, 3H*0.6), 6.03-7.47 (m, 28H); ESIMS *m/z* 737 $[M+H]^+$. Anal. Calcd for $C_{49}H_{40}N_2O_5$: C, 79.87; H, 5.47; N, 3.80. Found: C, 80.03; H, 5.41; N, 3.94.

Compound 3h: 83%; yellow solid, mp > 140 °C (dec.); IR (KBr) 3424, 1574, 1467, 1270 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.41 (s, 2H), 7.05-7.40 (m, 20H), 9.74 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.54, 124.86, 126.69, 127.49, 127.81, 127.85, 128.85, 128.91, 130.89, 133.61, 134.79, 136.49, 175.68; ESIMS *m/z* 465 $[M+H]^+$. Anal. Calcd for $C_{33}H_{24}N_2O$: C, 85.32; H, 5.21; N, 6.03. Found: C, 85.20; H, 5.45; N, 5.87.

Compound 3i: 57%; yellow solid, mp 76-78 °C; IR (KBr) 1597, 1496, 1455 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.99 (s, 3H), 5.36 (d, J = 15.9 Hz, 1H), 5.58 (d, J = 15.9 Hz, 1H), 5.63 (s, 1H), 6.04 (s, 1H), 6.87-6.92 (m, 4H), 7.03-7.34 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.43, 48.48, 110.67, 110.94, 125.75, 125.95, 126.89, 126.99, 127.03, 127.29, 127.40, 127.84, 128.07, 128.49, 128.76, 128.99, 129.23, 129.29, 131.60, 131.62, 132.35, 134.59, 135.08, 135.75, 136.32, 137.79, 138.09, 138.68, 177.91 (two carbons were overlapped); ESIMS *m/z* 569 $[M+H]^+$. Anal. Calcd for $C_{41}H_{32}N_2O$: C, 86.59; H, 5.67; N, 4.93. Found: C, 86.37; H, 5.71; N, 4.69.

Compound 4c: 12%; colorless oil; IR (film) 1603, 1453, 1196 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.82-1.98 (m, 2H), 2.44 (t, J = 7.5 Hz, 2H), 3.88 (t, J = 7.5 Hz, 2H), 6.42 (d, J = 2.1 Hz, 1H), 6.96-7.34 (m, 14H), 7.44-7.48 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.66, 32.70, 46.73, 106.85, 118.73, 124.27, 124.87, 125.37, 126.00, 127.07, 128.27, 128.40, 128.45, 128.60, 128.81, 133.26, 135.35, 135.62, 140.86; ESIMS *m/z* 338 $[M+H]^+$. Anal. Calcd for $C_{25}H_{23}N$: C, 88.98; H, 6.87; N, 4.15. Found: C, 88.85; H, 6.81; N, 4.06.

Compound 4g: 19%; white solid, mp 48-50 °C; IR (KBr) 1605, 1517, 1209 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.53 (s, 3H), 3.82 (s, 3H), 6.45 (dd, J = 7.2 and 2.7 Hz, 1H), 6.47 (s, 1H), 6.73 (s, 1H), 7.08-7.36 (m, 10H), 7.56-7.61 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.50 (2C), 99.69, 104.20, 106.65, 121.57, 122.82, 124.76, 125.03, 125.46, 126.16, 127.32, 127.88, 128.54, 128.99, 133.38, 135.48, 135.95, 155.30, 160.12; ESIMS *m/z* 356 $[M+H]^+$. Anal. Calcd for $C_{24}H_{21}NO_2$: C, 81.10; H, 5.96; N, 3.94. Found: C, 81.29; H, 5.74; N, 3.95.

Compound 5a: 14%; yellow solid, mp 84-86 °C; IR (KBr) 1660, 1456, 1204, 1150 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.44 (s, 2H), 6.31 (s, 1H), 6.77-6.81 (m, 2H), 7.09-7.38 (m,

13H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.14, 114.11, 115.83 (q, J_{CF} = 287.9 Hz), 123.81, 125.74, 127.30, 127.80, 127.86, 128.58, 128.81, 129.19, 129.30, 129.41, 130.84, 135.13, 138.10, 138.83, 145.14, 174.28 (q, J_{CF} = 36.6 Hz); ESIMS *m/z* 406 $[M+H]^+$. Anal. Calcd for $C_{25}H_{18}F_3NO$: C, 74.06; H, 4.48; N, 3.45. Found: C, 74.37; H, 4.71; N, 3.23.

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7. The reaction of **2a** in the presence of an excess amount of TFAA could be rationalized as follows. Compound **2a** could be converted rapidly to a mixed anhydride **I** (see, Scheme 3) with liberation of TFA. The reaction between TFA and **I** could generate pyrrole **4a** in conjunction with the release of TFAA and CO_2. A subsequent reaction between **4a** and **I** could form the dipyrryl ketone **3a**. Compound **5a** must be formed from **4a** and TFAA.
8. Actually, the reaction of **2a** and TFA (2.0 equiv) in CH_2Cl_2 at room temperature for 2 h afforded **4a** in quantitative yield (97%).
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