4a (56%): mp 309–311 °C (from toluene); ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3 H, Me), 7.2 (s, 4 H, OArH), 7.4–8.0 (m, 2 H, H-2,3), 8.4 (d, J = 8 Hz, 1 H, H-4), 8.8 (s, 1 H, H-9), 9.7 (d, J = 8 Hz, 1 H, H-1), 12.3 (br s, 1 H, OH).

B. From EMMN. 5a (94%): mp 220–221 °C (from MeOH); ^{1}H NMR [$(CD_3)_2SO$] δ 7.0 (s, 1 H, H-5), 7.2–7.6 (m, 2 H, H-8,9), 7.75 (s, 1 H, H-3), 7.8–8.2 (m, 2 H, H-7,10). Anal. Calcd for $C_{17}H_{13}N_3O_3$: C, 66.5; H, 4.2; N, 13.6. Found: C, 66.2; H,4.4; N,13.8.

5b (96%): mp 256–258 °C (from dioxane); ^{1}H NMR (CF_3CO_2H) δ 3.74, 3.79 (s + s, 6 H, MeO), 6.7, 7.0 (d + d, J = 8 Hz, 2 H, H-8,9), 6.9 (s, 1 H, H-5), 7.6 (br s, 2 H, NH_2), 8.2 (s, 1 H, H-3).

6 (73%): mp 225–227 °C (from a large volume of EtOH); ^{1}H NMR [$(CD_3)_2SO/CF_3CO_2H$] δ 2.4 (s, 3 H, Me), 7.1–7.4 (d + d, J = 8 Hz, 4 H, Ar H), 7.6–8.05 (m, 2 H, H-9,10), 8.1, 8.45 (s + s, 2 H, H-2,13), 8.5 (d, J = 8 Hz, 1 H, H-8), 9.4 (br s, 2 H, NH_2), 9.6 (d, J = 8 Hz, 1 H, H-11).

These compounds were isomerized by adding to stirring paraffin oil at 280–290 °C and heating for 0.5 h. Light petroleum (bp 60–90 °C) was added to the cooled mixture, and the product was filtered off, dried, and recrystallized from toluene.

3d (79% from **5a**): mp 263–265 °C; ^{1}H NMR (CF_3CO_2H) δ 6.9–7.6 (m, 3 H, H-5,6,7), 7.75 (d, J = 8 Hz, 1 H, H-8), 8.0 (s, 1 H, H-3). Anal. Calcd for $C_{17}H_{13}N_3O_3$: C, 66.5; H, 4.2; N, 13.6. Found: C, 66.4; H, 4.5; N, 13.5.

3e (79% from **5b**): mp 270–272 °C; ^{1}H NMR (CF_3CO_2H) δ 3.8, 3.92 (s + s, 6 H, MeO), 6.8, 7.2 (d + d, J = 9 Hz, 2 H, H-6,7), 8.5 (s, 1 H, H-3).

4b (67% from **6**): mp 273–275 °C; ^{1}H NMR (200 MHz/CF_3CO_2H) δ 2.6 (s, 3 H, Me), 7.4, 7.6 (d + d, J = 8 Hz, 4 H, Ar H), 8.0, 8.35 (t + t, J = 8 Hz, 2 H, H-2,3), 8.5 (s, 1 H, H-9), 8.87 (d, J = 8 Hz, 1 H, H-4), 10.0 (d, J = 8 Hz, 1 H, H-1).

C. From EMCA. 5c (90%): mp 201–203 °C (from toluene); ^{1}H NMR [$(CD_3)_2SO/CF_3CO_2H$] δ 7.3–7.5 (m, 2 H), 7.4 (s, 1 H, H-5), 7.9–8.3 (m, 2 H), 8.3 (s, 1 H, H-3).

3f (64%) was then obtained by thermal isomerization as for the EMMN reactions above and had mp 200–201 °C (from toluene): ^{1}H NMR (CF_3CO_2H) δ 7.0–7.6 (m, 3 H, H-5,6,7), 7.75 (d, J = 8 Hz, 1 H, H-8), 8.5 (s, 1 H, H-3). A sample for analysis was further purified by eluting through a short alumina column with $CHCl_3$ (R_f 0.95). Anal. Calcd for $C_{19}H_{18}N_2O_5$: C, 64.4; H, 5.1; N, 7.9. Found: C, 64.4; H, 5.0; N, 7.9.

D. From DEAD. 7a (50%): mp 140–141 °C (from acetone); ^{1}H NMR ($CDCl_3$) δ 3.84 (s, 2 H, CH_2), 7.0 (s, 1 H, H-4), 7.3, 7.6 (t + t, J = 8 Hz, 2 H, H-7,8), 8.1 (d, J = 8 Hz, 1 H, H-6), 8.64 (d, J = 8 Hz, 1 H, H-9); ^{13}C NMR ($CDCl_3$) δ 14.0, 30.5, 61.6, 62.3, 113.2, 117.0, 123.2, 125.5, 126.7, 134.6, 136.9, 139.4, 144.1, 160.7, 166.2, 167.9, 180.0. Anal. Calcd for $C_{19}H_{17}NO_6$: C, 64.2; H, 4.8; N, 3.9. Found: C, 64.3; H, 5.0; N, 4.1.

A sample of this compound, when hydrogenated in EtOH over 10% Pd/carbon, rapidly took up 1 mol of hydrogen. Removal of catalyst and solvent gave **8a** as a yellow glass: ^{1}H NMR ($CDCl_3$) δ 2.9–3.1 (m, 2 H, CH_2CO_2Et), 3.5–3.8 (m, 1 H, $CHCH_2CO_2Et$), 4.1 (with ester CH_2, 1 H, $CHCO_2Et$), 6.4 (d, J = 1.5 Hz, 1 H, H-4), 7.25–7.7 (m, 2 H, H-7,8), 8.15 (dd, J = 8,2 Hz, 1 H, H-6), 8.95 (d, J = 8 Hz, 1 H, H-9); ^{13}C NMR ($CDCl_3$) δ 14.0, 33.4, 40.0, 46.4, 61.3, 62.7, 109.0, 117.8, 124.9, 126.1, 126.5, 133.2, 136.3, 150.1, 168.3, 170.4, 174.5, 178.8.

7b (55%): mp 139–140 °C (from acetone); ^{1}H NMR (200 MHz/$CDCl_3$) δ 3.84 (s, 2 H, CH_2), 3.9 (s, 3 H, MeO), 7.0 (s, 1 H, H-4), 7.2 (dd, J = 9, 3 Hz, 1 H, H-8), 7.5 (d, J = 3 Hz, 1 H, H-6), 8.6 (d, J = 9 Hz, 1 H, H-9).

9 (59%): mp 210–212 °C (from acetone); ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3 H, Me), 3.8 (s, 2 H, CH_2), 7.1 (s, 1 H, H-12), 7.3 (d + d, J = 8 Hz, 4 H, Ar H), 7.5–8.0 (m, 2 H, H-8,9), 8.45 (d, J = 8 Hz, 1 H, H-7), 9.8 (d, J = 8 Hz, 1 H, H-10).

Registry No. **1a**, 109152-04-7; **1b**, 109152-05-8; **1c**, 109152-06-9; **1d**, 109152-07-0; **2**, 109152-08-1; **3a**, 109152-09-2; **3b**, 109152-10-5; **3c**, 109152-11-6; **3d**, 109152-12-7; **3e**, 109152-13-8; **3f**, 109152-14-9; **4a**, 109152-15-0; **4b**, 109152-16-1; **5a**, 109152-17-2; **5b**, 109152-18-3; **5c**, 109152-19-4; **6**, 109152-20-7; **7a**, 109152-21-8; **7b**, 109152-22-9; **8a**, 109152-23-0; **9**, 109152-24-1; EMME, 87-13-8; EMMN, 123-06-8; EMCA, 94-05-3; DEAD, 762-21-0; aniline, 62-53-3; 1-(*p*-methylphenoxy)isoquinoline-3-amine, 106051-96-1; diethyl 3-oxoglutarate, 105-50-0; 4-methoxyaniline, 104-94-9; 5-aminobenzodioxole, 14268-66-7; 2,5-dimethoxyaniline, 102-56-7.

Synthesis and Stereochemistry of Novel Triarylmesitylenes. Bases for Rigid Tridentate Ligands

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Syn–anti stereochemistry is rarely encountered in substituted benzenoid aromatic compounds, even though it is a fundamental consideration for saturated carbocycles. It has been previously noted[1] that relative orientation of substituents on benzene rings gives rise to only a small subset of the limited number of geometrically isomeric aromatics. In the past year, however, three papers have appeared[1,2] in which the relative conformations of substituents on hexasubstituted benzenes have been at issue. In all of those cases, the six substituents about the central benzene ring have been identical. Also, it was not apparent that any of the compounds were intended for further derivitization.

Recent advances in the construction of strong binders for cations,[3] anions[4], and transition metals[5] have been aided by the availability of rigid, bidentate subunits, including orthodisubstituted benzenes, *peri*-naphthalenes, and 1,8-disubstituted biphenylenes. On the other hand, there are no higher order (tridentate, etc.) binding units that are rigidly oriented, convergent, and amenable to functional group transformation, although the interesting special case of *all-cis*-1,3,5-trimethylcyclohexane-1,3,5-tricarboxylic acid has been cleverly exploited[6] in the synthesis of more elaborate binders.

If substituents at the 1, 3, and 5 positions of a benzene ring could be held at 60–90° angles and all-syn with respect to the plane of the benzene ring, the result would be a useful well-oriented tridentate binding unit. In the hope that 2-, 4-, and 6-methyl groups would enforce the necessary stereochemistry, we investigated compounds of general structure A. Before incorporating the actual ligating groups, two preliminary questions needed to be addressed: the synthesis of the structural unit and the ability of the methyl groups to hold the other substituents in place. These two issues are the subject of the present investigation.

Experimental Section

Solvents and reagents were commercially available except as noted and were used without further purification. Boronic acids were prepared when necessary from the corresponding lithium reagents and trialkylborates by using standard methodology. Tribromomesitylene was prepared[7] from mesitylene and Br_2/Fe. Separations were performed on a Beckman HPLC apparatus with variable wavelength UV detection; the preparative column was 1.5 × 50 cm packed with silica gel, and the analytical column was 1 × 25 cm C_{18}-silicate. Proton and carbon NMR spectra (vs. Me_4Si) were obtained on a Bruker 360-MHz spectrometer; ^{13}C spectra were fully decoupled. Analytical data were obtained by

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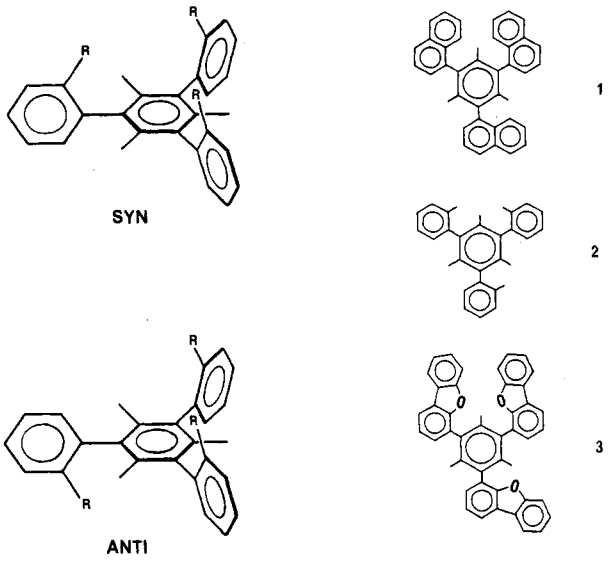

Galbraith Laboratories, Knoxville, TN.

1,3,5-Trimethyl-2,4,6-tri-1-naphthylbenzene (1). A solution of 2,4,6-tribromomesitylene (0.7 g, 2 mmol), 1-naphthylboronic acid (KNK, 2.2 g, 12.8 mmol), and $(PPh_3)_4Pd$ (275 mg) in toluene (75 mL) was stirred at reflux under Ar with solid K_2CO_3 (2.6 g, 19 mmol) and 18-crown-6 (0.15 g initially present, 1.3 g added in the first 24 h). After 4 days the solution was allowed to cool, washed with 2 × 100 mL of H_2O, dried, filtered, concentrated, and chromatographed (CH_2Cl_2–petroleum ether) to obtain a "center cut" of 0.22 g (23%) of product. An analytical sample was obtained by recrystallization from $CHCl_3$: ^1H NMR ($CDCl_3$) δ 1.519, 1.529 (2 s, 9, Me), 7.4–7.9 (m, 21, Ar H); ^{13}C NMR ($CDCl_3$) δ 18.54, 18.56 (Me), 125.5, 125.7 (t), 126.1 (d), 127.1 (t), 128.3 (d), 132.2, 133.8 (d), 134.98, 137.47, 137.7, 139.8 (d); MS, *m/e* 498 (M^+, bp).

Anal. Calcd for $C_{39}H_{40}$: C, 93.94; H, 6.06. Found: C, 93.76; H, 6.16.

1,3,5-Trimethyl-2,4,6-tris(2-methylphenyl)benzene (2). A solution of tribromomesitylene (0.40 g, 1.1 mmol), *o*-tolylboronic acid (1.0 g, 7 mmol), Cs_2CO_3 (3.5 g, 11 mmol), $(PPh_3)_4Pd$ (160 mg), and 20 mL of $MeCONMe_2$ (DMA) was stirred for 2 days at 100 °C under Ar. After cooling, the solution was poured into 100 mL of Et_2O and the organic mixture was washed with 3 × 100 mL of H_2O, dried, filtered, concentrated, and chromatographed twice by hexane elution of a column that had been previously exposed to CH_2Cl_2: yield 50 mg (11%); ^1H NMR ($CDCl_3$) δ 1.556, 1.560 (2 s, 9, central Me), 2.020, 2.079 (2 s, 9, peripheral Me), 7.0–7.3 (m, 12, Ar H); ^{13}C NMR ($CDCl_3$) δ 17.98, 18.04, 19.47, 19.73 (Me), 126.0 (d), 126.7, 129.3 (d), 129.9, 132.1 (d), 135.9 (d), 138.9 (d), 141.8; MS, *m/e* 390 (M^+, bp).

Anal. Calcd for $C_{30}H_{30}$: C, 92.26; H, 7.74. Found: C, 91.87; H, 7.82.

1,3,5-Trimethyl-2,4,6-tris(4-dibenzofuranyl)benzene (3). The reagents and conditions were the same as in the previous preparation, except for the use of 1.5 g (7 mmol) of 1-dibenzofuranboronic acid instead of *o*-tolylboronic acid. Purification was by chromatography, eluting twice with CH_2Cl_2–hexane: yield 250 mg (36%); ^1H NMR ($CDCl_3$) δ 1.83 (s, 9, Me), 7.3–8.0 (m, 21, Ar H); ^{13}C NMR ($CDCl_3$) δ 19.00, 19.04 (Me), 112.1 (t), 119.5, 120.6 (d), 122.6 (d), 123.0 (t), 124.5, 125.8, 127,1 (d), 129.0 (d), 134.3, 135.9 (d), 153.9, 156.3; MS, *m/e* 618 (M^+, bp). The analytical sample was recrystallized from CH_2Cl_2–hexane.

Anal. Calcd for $C_{45}H_{30}O_3 \cdot H_2O$: C, 84.88, H, 5.07. Found: C, 84.78; H, 5.38.[8]

Kinetics of Interconversion of Isomers of 3. Samples of the minor (all-syn) isomer of **3** were isolated by analytical HPLC. The samples were dissolved in 1,2,3-trichloropropane and heated with a thermostated oil both in closed pear-shaped flasks. Aliquots were withdrawn periodically and checked by analytical HPLC at 300 nm, giving the ratio (x) of the major (anti) to minor (syn) isomer concentrations. Final values of x (K) were 4 ± 0.5 at all temperatures. Plots of ln [$(K - x)/(x + 1)$] vs. t gave straight lines[9] ($r \geq 0.998$) whose slopes were equal to the negatives of the sums of the forward and reverse rate constants ($-(k_1 + k_{-1})$, $-k_{-1}(K + 1)$) and enabled the direct calculation of k_{-1}.

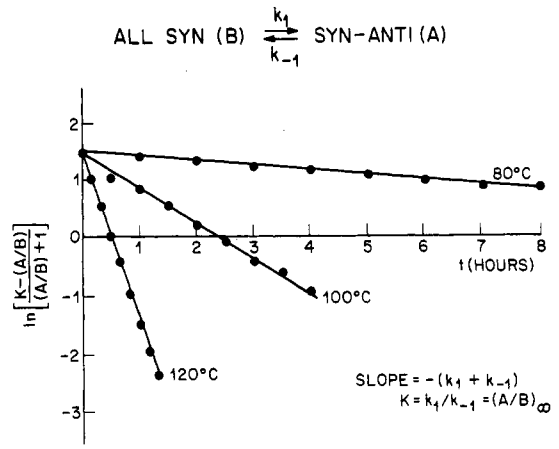

Figure 1. Plots of ln [$(K - x)/(x + 1)$] vs. t for the equilibration of *syn*-**3** to a mixture of isomers at 80, 100, and 120 °C.

Results and Discussion

The syntheses of new compounds **1–3**, the first reported triarylmesitylenes except for triphenylmesitylene, were performed by using the Pd-catalyzed arylboronic acid coupling methodology of Suzuki[10] rather than the Ni-catalyzed Grignard condensations of Kumada[11] because the Kumada method is troublesome when the halide to be displaced is sterically hindered. Even the less sterically demanding Suzuki reaction was barely able to accomplish the coupling of all three aryls to one mesitylene. The large amounts of diarylmesitylene byproducts (detected by TLC, NMR, and MS) indicated that the third displacement was especially hindered due to the buttressing of the 1,2,3,4,5-substituents. Side reactions that diverted some of the aryl bromide included reduction–protonation and oxidative homocoupling of boronic acids. The boronic acids were further subject to protonolysis.

The conditions described here are modifications of those originally reported (H_2O–EtOH–toluene) and seemed to suppress the side reactions, particularly those that are proton-dependent. Higher yields were obtained in DMA, although the amount of the harder-to-separate hydridodiarylmesitylenes was less using toluene-18-crown-6. Other methods of hexaarylbenzene synthesis such as metal-catalyzed[2b,12] and other[13] cycloadditions are not suited to the preparation of derivatives of C_3 symmetry.

The methyl groups on **1–3** do in fact provide a sufficient barrier to aryl–aryl bond rotation to prevent rapid isomer interconversion at room temperature. Many of the NMR signals of these compounds are split because of the presence of two isomers, one having C_{3v} symmetry while the other has C_s symmetry. (The detection of a C_s isomer even in the absence of a C_3 isomer would establish such a barrier as well). Although the isomers of **2** were not resolvable by HPLC, those of **1**, **3**, and dinaphthylmesitylene were resolvable. The isomers of **3** were base-line-separated, so that

(8) Though apparently pure by ^{13}C NMR and MS, samples of **3** tenaciously retained H_2O and/or other solvent-derived impurities, even after repeated recrystallization or HPLC.

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relative peak heights could be used to monitor their interconversion.

Figure 1 shows plots of ln $[(K - x)/(x + 1)]$ vs. t for **3** at three different temperatures (x = [anti]/[syn]) starting from *syn*-**3**. (A similar plot was obtained for 100 °C by using 1-nonanol as solvent, suggesting that H bonds do not contribute to the barriers.) The slopes of these lines, equal to the negatives of the sums of the forward and reverse rate constants, indicate the rapidity with which equilibrium ($x = K$) is approached at the various temperatures. If $\Delta H - T\Delta S = 0$ for the conversion of one isomer to the other, we would expect $K = 3$ based on statistics. In fact, we measure $K = 4 \pm 0.5$, indicating $\Delta H - T\Delta S < 0.5$ kcal/mol. (We also cannot rule out slight differences in ϵ_{300} contributing to the deviation from $K = 3$.) From the slopes of the lines in Figure 1, we can calculate k_1 and k_{-1} directly, knowing K. A linear plot of log (k_{-1}/T) vs. $1000/T$ for the three equilibrations was used to calculate $\Delta G^{\ddagger} = 30$ kcal/mol at 373 K, $\Delta H^{\ddagger} = 23$ kcal/mol, $\Delta S^{\ddagger} = -17$ cal/deg·mol, and k_{-1} (298 K) $\sim$ 1/year. Molecular models of **1** and **2** indicate that their rotational barriers should be at least as high. The most nearly analogous values of $\Delta G^{\ddagger}$ reported in the literature, those of unsymmetrically substituted hexaphenylbenzenes[13] and bromophenyl-substiuted porphyrins,[14] are also approximately 30 kcal/mol. A related study of atropisomerism has also been performed on tetraarylporphyrins, whose geometries have been exploited in the construction of hemoprotein models.[15]

The generalizability of the Suzuki coupling will enable us to prepare derivatives of **1–3** by employing functionalized boronic acids in the coupling reactions. Alternatively, we can carry out direct reactions on **2** or **3**. Furthermore, these derivatives will be rigid not only with respect to conformational interconversion but also with respect to significant deviations from 90° aryl–aryl dihedral angles. Ultimately, our goal of synthesizing rigid tridentate binding units should be realized through analogues of the compounds just discussed.

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Indole *N*-Carbonyl Compounds: Preparation and Coupling of Indole-1-carboxylic Acid Anhydride

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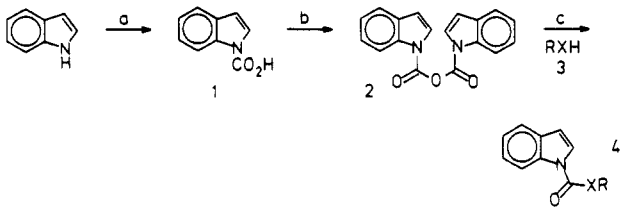
The preparation of indole *N*-carbonyl compounds requires the selective N-acylation of indole with accessible, available acylating agents,[2] and the well-recognized, competitive N-1 vs. C-3 acylation of indole has required the empirical determination of experimental conditions which favor predominant or exclusive N-acylation.[2,3] In addition, for systems for which no activated acylation reagent is available, the indole *N*-carbonyl compounds are currently inaccessible.

Scheme I[a]



[a] (a) 1.0 equiv of *n*-BuLi, ether, 0 °C, 0.5 h; CO_2, 88–94%; (b) 0.6 equiv of EDCI·HCl, CH_2Cl_2, 25 °C, 15 min, 86%; (c) Table I.

Herein, we detail the preparation and characterization of indole-1-carboxylic acid anhydride (**2**) and describe its use in selective, controlled coupling reactions with representative nucleophilic *and* nonnucleophilic alcohols, phenols, amines, anilines, thiols, indoles, and pyrroles (Scheme I). The use of indole-1-carboxylic acid anhydride (**2**) in selective, intermolecular coupling reactions provides the control for exclusive indole N-acylation *and* permits the preparation of indole *N*-carbonyl compounds for which no accessible, activated acylation reagent is available.

Indole-1-carboxylic acid (**1**),[4,5] free of indole-3-carboxylic acid, was prepared by treatment of *N*-lithioindole with carbon dioxide (indole, 1.0 equiv of *n*-BuLi, ether; CO_2, 2 h) and was found to proceed with exclusive N-carboxylation.[4] Treatment of indole-1-carboxylic acid (**1**) with 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide (EDCI·HCl, 0.6 equiv; methylene chloride, 25 °C, 15 min) provided indole-1-carboxylic acid anhydride (**2**, 86%), which was isolated as a stable, crystalline solid.

The results of a study of the intermolecular coupling of indole-1-carboxylic acid anhydride (**2**) with representative nucleophiles are detailed in Table I. Nucleophilic substrates including amines (Table I, entries 7, 10) and anilines (Table I, entry 6) were found to react rapidly with **2** to provide the mixed urea and urethanes cleanly. In the instances of the use of nonnucleophilic coupling substrates including alcohols (Table I, entry 8), phenols (Table I, entries 3–5), thiols (Table I, entry 9), or electron-deficient indoles and pyrroles (Table I, entries 1, 2, 11), the indole *N*-carbonyl compound formation was observed only with the use of the preformed sodium salts of the coupling substrates.

Although the stoichiometric use of the preformed, isolated reagent **2** proved to be the most dependable procedure for the formation of indole *N*-carbonyl compounds,

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