Regioselective Synthesis of 3-Alkylindoles Mediated by Zinc Triflate

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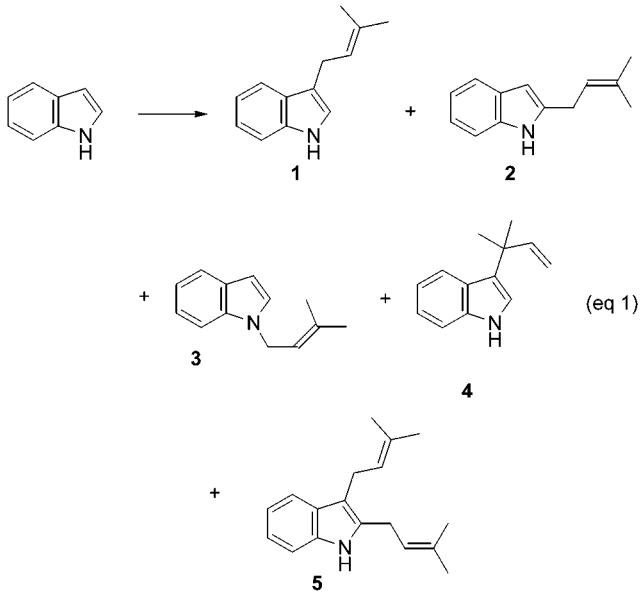
Abstract: Zinc triflate was found to be an effective reagent for the C3-alkylation of indoles by alkyl halides in the presence of Hünig's base and tetrabutylammonium iodide. This new method for indole alkylation proceeds by a S_N1-like pathway, and is general for allylic, benzylic, and tertiary halides.

The alkylation of indole by a prenyl electrophile (eq 1) has been reported[1] on a number of occasions. However, it suffers from several fundamental problems. First, there is the question of regioselectivity with respect to the indole: alkylation at C-3 versus C-2 and N-1 to give **1**−**3** respectively. Second, there is a regiochemical issue with the alkylating agent, as varying amounts of the 'reverse-prenyl' isomer **4** arising from S_N2' attack are also produced. Finally, the desired product **1** remains reactive to further alkylation, resulting in diprenylated compounds such as **5**. In their seminal studies,[2] Wenkert et al. investigated several approaches for a high yielding synthesis of **1**. Treatment of indole with a Grignard reagent to form the indolylmagnesium salt, a common method[3] of activating indole prior to alkylation, afforded only 34% of **1** and **4** in a 17:1 ratio, together with small quantities of **3** and **5**. The preferred route involved protecting the nitrogen of 3-bromoindole as a sulfonamide followed by low-temperature generation of the 3-lithio species with *tert*-butyllithium, transmetalation to the cuprate, reaction with prenyl bromide, and sulfonamide deprotection. The ratio of **1**:**4** was undisclosed, but was reported to be 4:1 in the related alkylation[4] of a *N*-silyl-protected 3-cuproindole.

In the course of synthetic studies directed toward alkaloid natural products, we needed access to indoles containing an isoprenoid unit at C-3. As the multistep sequence via metalation appeared impractical for scale-up, we reinvestigated the direct alkylation of indole with prenyl bromide. An early attempt involved transition metal catalyzed cross-coupling reactions. However, the coupling of indoles with either prenyl bromide or acetate



under several Pd(0)-catalyzed conditions was unsuccessful, and we are unaware of any precedents for similar reactions.

Studies of *N*- versus *C*-protonation and alkylation with ambident metal indolyl salts indicate[5] that reaction at C-3 is favored by more covalently coordinated metals, soft leaving groups, and nonpolar solvents. With this as our starting point, we screened a set of 10 metal triflates (excluding alkali or alkaline earth metals) for their ability to effect the prenylation of indole. Metal triflates were chosen because of numerous examples of their ability to promote C−C bond-forming reactions under mild conditions, as well as their commercial availability at relatively low cost. Furthermore, the elegant work by Carreira[6] has shown that metal acetylides are generated by reaction of an acetylene with a metal triflate and a tertiary amine. Since indole is significantly more acidic ($pK_a \sim 16$) than acetylenes, it was anticipated that the indolylmetal salt would be generated in situ, thus avoiding the need for strong bases such as a Grignard reagent.

The results (Table 1) indicate that all the triflates studied are capable of effecting prenylation, although the yield and regioselectivity is highly dependent on the nature of the metal. Zinc triflate gave by far the highest yield, and it was selected for further optimization of reaction conditions. Switching the solvent from toluene to THF, CH_2Cl_2, or DMF was less satisfactory by HPLC analysis of the reaction mixture. This result is consistent with a lower degree of dissociation of the nitrogen−metal bond in a nonpolar medium, promoting *C*-alkylation. Several tertiary amine bases were examined, and *N*,*N*-diisopropylethylamine found to give the best result (yields and ratio of **1**:**4** given in parentheses): *N*,*N*-diisopropylethylamine (59%, 20:1), pempidine (36%, 23:1), pyridine (35%, 12:1), DBU (45%, 18:1). Compared to zinc triflate,

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Table 1. Screening of Metal Triflates for the Promotion of Indole Prenylation

metal triflate	yield of **1** + **4** (%)[a]	ratio of **1**:**4**[b]
Cu(I)	18	2:1
Cu(II)	5	1:1
Ag(I)	29	32:1
Zn(II)	55	10:1
Hg(II)	36	>80:1
In(III)	30	13:1
Sn(II)	2[c]	nd[c]
Sc(III)	2[c]	nd[c]
La(III)	4[c]	nd[c]
Yb(III)	13	37:1

[a] Reaction conditions: 0.43 mmol of prenyl bromide, 2 equiv of indole, 1.2 equiv of metal triflate, and 2.2 equiv of Et_3N in 2.5 mL anhydrous toluene, stirred overnight at room temperature. The yield refers to isolated pure material after preparative TLC and is based on prenyl bromide. [b] The ratio was determined by NMR peak integration. [c] Yields estimated by HPLC, ratio of **1**:**4** not determined.

both zinc bromide (44%, 37:1) and zinc acetate (33%, 45:1) gave enhanced regioselectivity disfavoring the formation of reverse-prenyl isomer **4**, but at the expense of poorer yields.

By HPLC analysis, the zinc triflate mediated prenylation was complete within 1.5 h at room temperature, or 4 h at 0 °C. The reaction was also carried out with substoichiometric (0.25, 0.5) molar equivalents of zinc triflate. However, as yields were decreased and longer reaction times were required, we prefer to use a full equivalent of zinc triflate. Changing the electrophile from prenyl bromide to the iodide (either preformed from the bromide by Finkelstein exchange or more simply by in situ generation with tetrabutylammonium iodide) dramatically improved the regioselectivity, the ratio of **1**:**4** now being >70:1. The major isolable byproduct (~10%) is the isomeric 2-prenylindole **2**, with traces of **3** and **5** also observed.

The optimized reaction conditions were then tested with substituted indoles as well as other alkyl halides (Chart 1). Two molar equivalents of indole were employed throughout to minimize the formation of dialkylation products, and yields were calculated based on the limiting (and usually significantly more expensive) alkyl bromide. Since 58% of the total indole used was recovered during the formation of **4**, this does not limit the method with more valuable indole substrates. All the successful alkylations occurred with tertiary, allylic, or benzylic halides, which can presumably react by a S_N1-like pathway. Meanwhile, no product was observed in the reaction with isoamyl bromide, a saturated primary alkyl halide. Mechanistically, this suggests that the zinc species is mainly serving as a Lewis acid in activating the halide, and this is supported by ^1H NMR experiments. Upon addition of zinc triflate (1 equiv), the proton spectrum of prenyl bromide immediately shows additional sets of signals. In the case of the less acidic zinc acetate, such changes only began to appear after 2 h. On the other hand, no changes in NMR spectrum were observed with zinc triflate and an unactivated halide such as isoamyl bromide. These facts are counter to our initial premise that the primary role of the metal triflate would be the formation of an indolylmetal species. Nevertheless, this hypothesis does not appear to be completely unfounded, as evidenced by the poorer yield of **12** with *N*-methylindole, which cannot form an indolylmetal salt. Furthermore, several metals that form stronger Lewis acidic triflates than zinc were poorer reagents (Table 1). It is possible that zinc represents the optimal balance in its ability to both activate the halide and coordinate to the indole nitrogen.

Zinc triflate has previously been employed[7] in the ring opening of *N*-acylaziridines by indole, although the reaction is likely to be S_N2 in character, and yields were higher[8] with scandium triflate, unlike our alkylation. The closest precedent to our reaction is a Russian report[9] of Friedel–Crafts indole alkylation with benzylic and tertiary halides using zinc chloride–pyridine in nitromethane as solvent. However, an attempt to follow their procedure for prenylation gave only a 28% yield of **1**:**4** in a 4.5:1 ratio.

The synthesis of **13** and **14** highlights the application of our methodology in the conjugation of indoles to the natural products (−)-carveol and cholest-4-en-3-ol. Compared to the results with prenyl bromide, with the more complex geranyl and farnesyl-derived isoprenoid halides, we did not observe any 'reverse-prenyl' isomers accompanying **16**–**21**. The synthesis of 3-geranylindole **18** exemplifies the effectiveness of our methodology: previously, this compound was prepared[10] in only 35% yield using 8 equiv of the indolylmagnesium salt. The mildness of the reaction conditions can also be discerned by the tolerance of epoxides during the synthesis of **19**–**21**.

In summary, we have developed a simple one-pot procedure for the direct formation of 3-alkylindoles in good yield from indole and alkyl halides that can react by a S_N1 pathway. The indole nitrogen does not require prior protection and the avoidance of strong bases for deprotonation permits compatibility with a wide range of functional groups. Our method nicely complements the classical alkylation of indolylmagnesium salts, which proceeds by a S_N2-like pathway. Further applications of this alkylation protocol to alkaloid total synthesis and biomimetic polyene cyclizations will be reported in due course.

Experimental Section

General. All chemicals obtained commercially were used without further purification. TLC was carried out with precoated silica plates: analytical (60 F-254) and preparative-scale (1 mm thick). Column chromatography was performed on silica (70–230 mesh). ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. Low resolution mass spectra were obtained by electron impact (EI) or electrospray (ESI) ionization, with relative abundances of ions indicated in parentheses.

General Procedure for Indole Alkylation. To a mixture of the indole (2 equiv), zinc triflate (1.2 equiv), and tetrabutylammonium iodide (1 equiv) in anhydrous toluene (ca. 3 mL per mmol indole) was added *N*,*N*-diisopropylethylamine (2.2 equiv) at room temperature under argon. The reaction mixture was stirred for 15 min at room temperature, followed by addition of the alkyl bromide (1 equiv). Upon completion as judged by TLC, the reaction mixture was quenched with saturated aq NH_4Cl, diluted with water, and extracted with ether. The combined organics were washed with water, dried over Na_2SO_4, concentrated, and purified by column chromatography.

3-(3-Methylbut-2-enyl)indole (1), 3-benzyl-1*H*-indole (10), and 3-*tert*-Butylindole (11). The spectroscopic properties of

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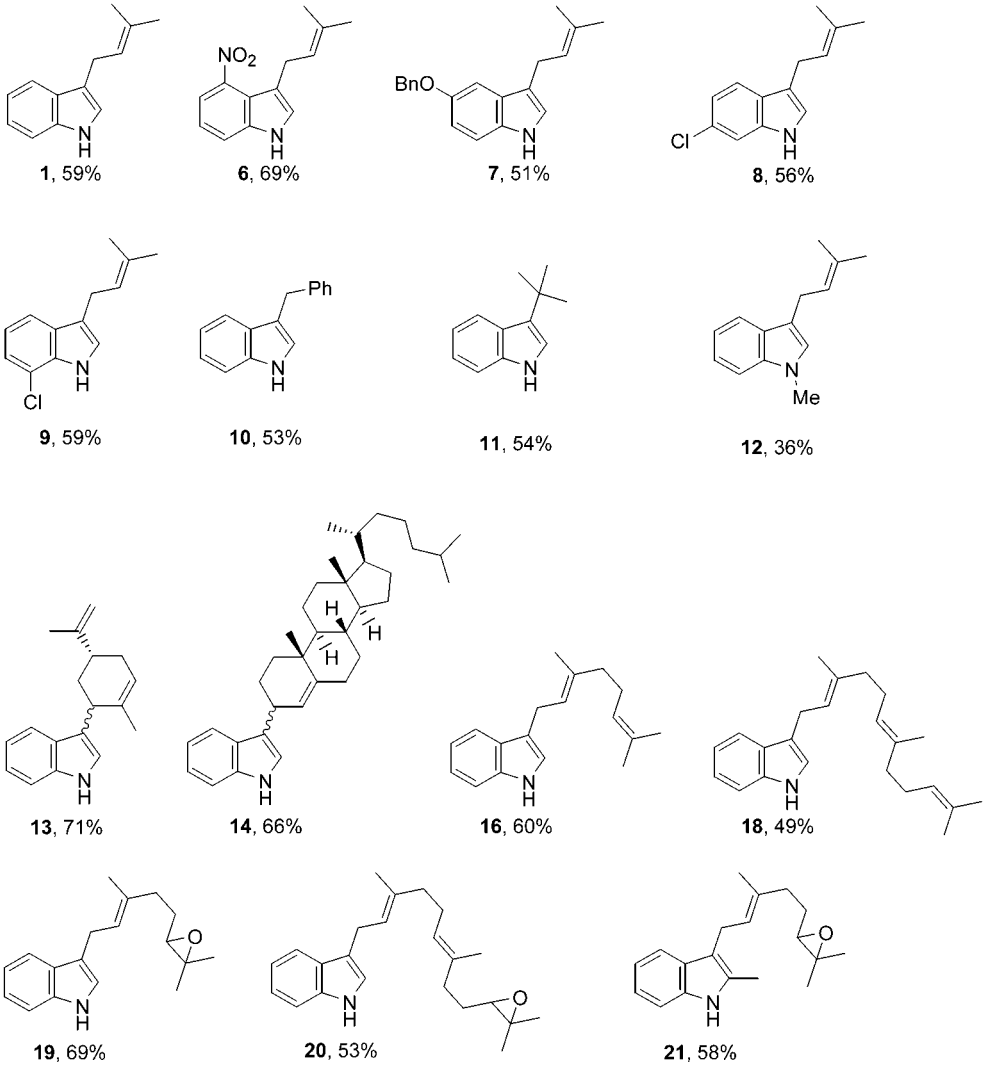
Chart 1. Indoles Prepared by the Zinc Triflate Alkylation Method, with % Yields



these known compounds were identical to that reported in the literature.

4-Nitro-3-(3-methyl-but-2-enyl)-1*H*-indole (6). From the alkylation of 4-nitroindole with prenyl bromide, which was carried out in 1:3 CH_2Cl_2:toluene due to the poor solubility of the indole in toluene alone. Chromatography eluent 50% ether in hexanes. Orange-red solid, mp 107−108 °C; IR ν 3369, 1536 cm^{-1}; ^1H NMR δ 1.69 (s, 3H), 1.73 (s, 3H), 3.52 (d, J = 7.0 Hz, 2H), 5.30 (br t, J = 7.0 Hz, 1H), 7.17−7.22 (m, 2H), 7.59 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 8.43 (br s, 1H); ^{13}C NMR δ 17.8, 25.7, 26.1, 116.0, 116.8, 117.2, 119.2, 120.6, 122.8, 126.3, 132.9, 139.2, 143.5; ESI MS m/z 229 (M^+-1, 5), 146 (100).

5-Benzyloxy-3-(3-methyl-but-2-enyl)-1*H*-indole (7). From the alkylation of 5-benzyloxyindole with prenyl bromide. Chromatography eluent 20% ether in hexanes. Pale yellow solid, mp 60−62 °C; IR ν 3400, 1619 cm^{-1}; ^1H NMR δ 1.74 (s, 6H), 3.38 (d, J = 6.6 Hz, 2H), 5.10 (s, 2H), 5.40 (br t, J = 6.6 Hz, 1H), 6.85 (d, J = 2.2 Hz, 1H), 6.91 (dd, J = 2.2, 8.8 Hz, 1H), 7.10 (d, J = 2.2 Hz, 1H), 7.16 (d, J = 8.8 Hz, 1H), 7.25−7.50 (m, 5H), 7.72 (br s, 1H); ^{13}C NMR δ 17.8, 24.1, 25.7, 71.0, 102.6, 111.7, 112.7, 115.7, 122.1, 123.0, 127.6, 127.7, 128.5, 131.78, 131.87, 137.7, 152.9; ESI MS m/z 290 (M^+-1, 100), 143 (92).

6-Chloro-3-(3-methyl-but-2-enyl)-1*H*-indole (8). From the alkylation of 6-chloroindole with prenyl bromide. Chromatography eluent 20% ether in petroleum ether. Pale yellow solid, mp 84−85 °C; IR ν 3400, 1610 cm^{-1}; ^1H NMR δ 1.75 (s, 6H), 3.41 (d, J = 7.3 Hz, 2H), 5.40 (br t, J = 7.3 Hz, 1H), 6.90 (d, J = 1.5 Hz, 1H), 7.06 (dd, J = 1.5, 8.1 Hz, 1H), 7.28 (d, J = 2.2 Hz, 1H), 7.46 (d, J = 8.1 Hz, 1H), 7.82 (br s, 1H); ^{13}C NMR δ 17.8, 23.9, 25.7, 110.9, 116.3, 119.84, 119.88, 121.8, 122.6, 126.1, 127.8, 132.3, 136.7; ESI MS m/z 218 (M^+-1, 22), 143 (100).

7-Chloro-3-(3-methyl-but-2-enyl)-1*H*-indole (9). From the alkylation of 7-chloroindole with prenyl bromide. Chromatography eluent 20% ether in petroleum ether. Pale yellow oil; IR ν 3421, 1620 cm^{-1}; ^1H NMR δ 1.76 (s, 6H), 3.43 (d, J = 6.6 Hz, 2H), 5.40 (br t, J = 6.6 Hz, 1H), 7.03 (m, 2H), 7.18 (d, J = 7.4 Hz, 1H), 7.48 (d, J = 7.4 Hz, 1H), 8.09 (br s, 1H); ^{13}C NMR δ 17.8, 24.2, 25.7, 116.5, 117.3, 117.7, 119.9, 121.3, 121.8, 122.6, 128.9, 132.3, 133.7; ESI MS m/z 218 (M^+ − 1, 12), 143 (24).

1-Methyl-3-(3-methyl-but-2-enyl)-1*H*-indole (12). From the alkylation of *N*-methylindole with prenyl bromide. Chromatography eluent 15% ethyl acetate in hexanes. Colorless oil; IR ν 1613 cm^{-1}; ^1H NMR δ 1.75 (s, 3H), 1.76 (s, 3H), 3.43 (d, J = 6.6 Hz, 2H), 3.70 (s, 3H), 5.42 (m, 1H), 6.78 (s, 1H), 7.05−7.28 (m, 3H), 7.58 (d, J = 8.1 Hz, 1H); ^{13}C NMR δ 17.8, 24.0, 25.7, 32.5, 109.1, 114.5, 118.5, 119.1, 121.4, 123.3, 126.0, 127.7, 131.7, 137.1; EI MS m/z 199 (M^+, 100), 184 (98), 168 (77), 144 (86).

3-(5-Isopropenyl-2-methylcyclohex-2-enyl)-1*H*-indole (13). From the alkylation of indole with (−)-carveyl bromide (prepared from (−)-carveol by MsCl, Et_3N; LiBr). Chromatography eluent 15% ethyl acetate in hexanes. Obtained as a 3.2:1 mixture of the equatorial (colorless oil) and axial (colorless plates upon recrystallization) diastereomers. The identity of the axial isomer was established by X-ray crystallography.

Equatorial *cis*-isomer: IR ν 3412, 1738, 1642 cm^{-1}; ^1H NMR δ 1.48 (s, 3H), 1.74 (s, 3H), 1.82−2.45 (m, 5H), 3.63 (m, 1H), 4.70 (m, 2H), 5.65 (m, 1H), 7.00 (d, J = 2.2 Hz, 1H), 7.05−7.22 (m, 2H), 7.34 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 8.1 Hz, 1H), 7.87 (br s, 1H); ^{13}C NMR δ 20.8, 21.8, 31.4, 37.6, 39.4, 42.1, 108.5, 111.1, 119.1, 119.56, 119.64, 121.74, 121.80, 122.5, 126.6, 136.2, 136.5, 150.0; ESI MS m/z 251 (M^+, 100), 236 (45), 182 (91), 167 (89).

Axial *trans*-isomer: mp 67−69 °C; IR ν 3400, 1738, 1643 cm^{-1}; ^{1}H NMR δ 1.61 (s, 3H), 1.70 (s, 3H), 1.70−2.00 (m, 3H), 2.15−2.30 (m, 2H), 3.68 (m, 1H), 4.61 (m, 2H), 5.65 (m, 1H), 6.85 (d, J = 2.2 Hz, 1H), 7.10−7.25 (m, 2H), 7.34 (d, J = 7.4 Hz, 1H), 7.66 (d, J = 8.1 Hz, 1H), 7.89 (br s, 1H); ^{13}C NMR δ 21.0, 22.6, 31.1, 34.2, 35.8, 36.7, 108.4, 111.1, 118.8, 119.1, 119.3, 121.8, 122.5, 122.8, 127.2, 134.8, 136.5, 150.0; ESI MS *m*/*z* 251 (M$^+$, 95), 236 (37), 182 (95), 167 (86).

3-(4-Cholestenyl)-1*H*-indole (14). From the alkylation of indole with cholest-4-en-3-yl bromide (prepared from cholest-4-en-3-ol by MsCl, Et_3N; LiBr). Chromatography eluent 15% ethyl acetate in hexanes. Obtained as a white foam, 1:1 mixture of diastereomers.

Diastereomer 1: IR ν 3400, 1738, 1643 cm^{-1}; ^{1}H NMR δ 0.69 (s, 3H), 0.85 (d, J = 1.5 Hz, 3H), 0.87 (d, J = 1.5 Hz, 3H), 0.90 (d, J = 6.6 Hz, 3H), 1.07 (s, 3H), 0.70−2.15 (m, 27H), 2.22−2.38 (m, 1H), 3.69 (m, 1H), 5.49 (d, J = 5.2 Hz, 1H), 6.85 (d, J = 2.2 Hz, 1H), 7.08−7.34 (m, 2H), 7.32 (d, J = 8.1 Hz, 1H), 7.64 (d, J = 7.2 Hz, 1H), 7.85 (br s, 1H); ^{13}C NMR δ 12.0, 18.7, 19.3, 21.6, 22.6, 22.8, 23.8, 24.3, 25.3, 28.0, 28.3, 31.8, 32.7, 33.2, 33.9, 35.8, 36.1, 36.2, 37.3, 39.5, 40.0, 42.6, 54.9, 56.28, 56.33, 111.2, 118.98, 119.08, 120.5, 120.9, 121.8, 122.7, 126.7, 136.7, 146.1.

Diastereomer 2: IR ν 3413 cm^{-1}; ^{1}H NMR δ 0.72 (s, 3H), 0.86 (d, J = 1.5 Hz, 3H), 0.88 (d, J = 1.5 Hz, 3H), 0.91 (d, J = 6.6 Hz, 3H), 1.12 (s, 3H), 0.85−2.10 (m, 27H), 2.20−2.35 (m, 1H), 3.56−3.60 (m, 1H), 5.47 (s, 1H), 6.95 (d, J = 2.2 Hz, 1H), 7.06−7.20 (m, 2H), 7.33 (d, J = 7.4 Hz, 1H), 7.65 (d, J = 7.4 Hz, 1H), 7.86 (br s, 1H); ^{13}C NMR δ 12.0, 18.7, 19.5, 21.4, 22.6, 22.9, 23.9, 24.3, 27.6, 28.0, 28.3, 32.6, 33.4, 34.4, 35.8, 36.1, 36.2, 37.2, 37.9, 39.5, 40.0, 42.5, 54.6, 56.2, 56.3, 111.1, 119.0, 119.5, 120.3, 121.7, 121.8, 123.2, 126.7, 136.6, 145.0; ESI MS *m*/*z* 485 (M$^+$, 14), 468 (100), 438 (57).

1-(4-Cholestenyl)-1*H*-indole (15). Byproduct (22%) in the preparation of **14**. IR ν 1737 cm^{-1}; ^{1}H NMR δ 0. 70 (s, 3H), 0.86 (d, J = 1.5 Hz, 3H), 0.88 (d, J = 1.5 Hz, 3H), 0.91 (d, J = 6.6 Hz, 3H), 1.08 (s, 3H), 0.70−2.40 (m, 28H), 4.92 (m, 1H), 5.48 (d, J = 4.4 Hz, 1H), 6.44 (d, J = 2.9 Hz, 1H), 7.00−7.30 (m, 3H), 7.39 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 7.4 Hz, 1H); ^{13}C NMR δ 12.0, 18.63, 18.66, 21.5, 22.6, 22.8, 23.8, 24.3, 25.7, 28.0, 28.2, 32.61, 32.69, 33.3, 35.8, 35.9, 36.1, 37.5, 39.5, 39.8, 42.5, 50.0, 54.4, 56.05, 56.18, 99.6, 109.5, 116.5, 119.3, 120.9, 121.0, 127.0, 129.2, 135.3, 152.2; EI MS *m*/*z* 368 (M$^+$-117, 29), 147 (64), 105 (70).

3-(3,7-Dimethylocta-2,6-dienyl)-1*H*-indole (3-Geranylindole) (16). From the alkylation of indole with geranyl bromide. Chromatography eluent 15% ether in petroleum ether. Pale yellow oil; IR ν 3410 cm^{-1}; ^{1}H NMR δ 1.60 (s, 3H), 1.68 (s, 3H), 1.75 (s, 3H), 2.05−2.15 (m, 4H), 3.45 (d, J = 6.7 Hz, 2H), 5.15 (m, 1H), 5.45 (dt, J = 1.5, 6.6 Hz, 1H), 6.87 (d, J = 1.5 Hz, 1H), 7.05−7.18 (m, 2H), 7.28 (d, J = 8.0 Hz, 1H), 7.59 (d, J = 7.4 Hz, 1H), 7.73 (br s, 1H); ^{13}C NMR δ 16.0, 17.7, 24.0, 25.7, 26.6, 39.7, 111.0, 116.0, 119.0, 119.1, 121.2, 121.9, 122.9, 124.4, 127.4, 131.4, 135.6, 136.4; EI MS *m*/*z* 253 (M$^+$, 74), 184(100), 168 (65).

2-(3,7-Dimethylocta-2,6-dienyl)-1*H*-indole (2-Geranylindole) (17). Byproduct (9%) in the preparation of **16**. ^{1}H NMR δ 1.63 (s, 3H), 1.71 (s, 3H), 1.72 (s, 3H), 2.05−2.16 (m, 4H), 3.50 (d, J = 7.3 Hz, 2H), 5.12 (br t, J = 6.6 Hz, 1H), 5.40 (dt, J = 1.5, 7.3 Hz, 1H), 6.23 (s, 1H), 7.00−7.15 (m, 2H), 7.28 (d, J = 8.1 Hz, 1H), 7.52 (d, J = 7.4 Hz, 1H), 7.86 (br s, 1H); ^{13}C NMR δ 16.1, 17.8, 25.8, 26.5, 27.0, 39.6, 99.5, 110.3, 119.6, 119.8, 120.1, 120.9, 124.1, 129.0, 131.8, 135.9, 138.2, 138.6; EI MS *m*/*z* 253 (M$^+$, 85), 185 (100), 168 (68).

3-(3,7,11-Trimethyldodeca-2,6,10-trienyl)-1*H*-indole (3-Farnesylindole) (18). From the alkylation of indole with farnesyl bromide. Chromatography eluent 15% ether in hexanes. Pale yellow oil; IR ν 3412 cm^{-1}; ^{1}H NMR δ 1.60 (s, 6H), 1.67 (s, 3H), 1.76 (s, 3H), 1.90−2.20 (m, 8H), 3.46 (d, J = 6.7 Hz, 2H), 5.10 (m, 2H), 5.45 (br t, J = 7.3 Hz, 1H), 6.90 (d, J = 1.5 Hz, 1H), 7.00−7.25 (m, 2H), 7.31 (d, J = 7.4 Hz, 1H), 7.58 (d, J = 7.4 Hz, 1H), 7.83 (br s, 1H); ^{13}C NMR δ 16.0, 16.1, 17.7, 24.0, 25.7, 26.6, 26.7, 39.70, 39.74, 111.0, 116.1, 119.03, 119.09, 121.2, 121.9, 122.9, 124.2, 124.4, 127.4, 131.3, 135.0, 135.6, 136.4; EI MS *m*/*z* 321 (M$^+$, 10), 184 (84), 168 (41).

3-[5-(3,3-Dimethyloxiranyl)-3-methylpent-2*E*-enyl]-1*H*-indole (19). From the alkylation of indole with ω-epoxygeranyl bromide. Chromatography eluent 15% ethyl acetate in petroleum ether. Pale yellow oil; IR ν 3410, 3333 cm^{-1}; ^{1}H NMR δ 1.25 (s, 3H), 1.26 (s, 3H), 1.63−1.72 (m, 2H), 1.78 (s, 3H), 2.09−2.27 (m, 2H), 2.73 (t, J = 6.3 Hz, 1H), 3.46 (d, J = 7.3 Hz, 2H), 5.49 (dt, J = 1.5, 7.1 Hz, 1H), 6.90 (d, J = 2.2 Hz, 1H), 7.06−7.22 (m, 2H), 7.31 (d, J = 8.1 Hz, 1H), 7.57 (d, J = 8.1 Hz, 1H), 7.96 (br s, 1H); ^{13}C NMR δ 16.1, 18.7, 24.0, 24.8, 27.4, 36.3, 58.4, 64.2, 111.0, 115.7, 118.9, 119.0, 121.2, 121.8, 123.6, 127.3, 134.5, 136.4; EI MS *m*/*z* 269 (M$^+$, 19), 170 (67), 130 (100).

3-[9-(3,3-Dimethyloxiranyl)-3,7-dimethylnona-2*E*,6*E*-dienyl]-1*H*-indole (20). From the alkylation of indole with ω-epoxyfarnesyl bromide. Chromatography eluent 20% ether in hexanes. Pale yellow oil; IR ν 3413 cm^{-1}; ^{1}H NMR δ 1.24 (s, 3H), 1.30 (s, 3H), 1.61 (s, 3H), 1.55−1.65 (m, 2H), 1.75 (s, 3H), 1.90−2.20 (m, 6H), 2.71 (t, J = 5.8 Hz, 1H), 3.45 (d, J = 6.6 Hz, 2H), 5.18 (t, J = 6.6 Hz, 1H), 5.45 (br t, J = 7.1 Hz, 1H), 6.90 (d, J = 1.5 Hz, 1H), 7.00−7.20 (m, 2H), 7.32 (d, J = 8.1 Hz, 1H), 7.58 (d, J = 7.4 Hz, 1H), 8.09 (br s, 1H); ^{13}C NMR δ 15.9, 16.0, 18.7, 23.9, 24.9, 26.4, 27.4, 36.3, 39.5, 58.5, 64.3, 111.0, 115.9, 118.9, 119.0, 121.3, 121.8, 123.2, 124.8, 127.4, 134.0, 135.3, 136.5; ESI MS *m*/*z* 337 (M$^+$, 7), 249 (96), 192 (100), 130 (75).

3-[5-(3,3-Dimethyloxiranyl)-3-methylpent-2*E*-enyl]-2-methyl-1*H*-indole (21). From the alkylation of 2-methylindole with ω-epoxygeranyl bromide. Chromatography eluent 15% ethyl acetate in hexanes. Yellow oil; IR ν 3321, 1694, 1582 cm^{-1}; ^{1}H NMR δ 1.22 (s, 6H), 1.55−1.70 (m, 2H), 1.83 (s, 3H), 2.03−2.18 (m, 2H), 2.34 (s, 3H), 2.68 (t, J = 6.3 Hz, 1H), 3.39 (d, J = 6.6 Hz, 2H), 5.33 (dt, J = 1.5, 6.6 Hz, 1H), 7.00−7.15 (m, 2H), 7.17 (d, J = 6.6 Hz, 1H), 7.44 (d, J = 8.1 Hz, 1H), 7.76 (br s, 1H); ^{13}C NMR δ 11.7, 16.2, 18.7, 23.1, 24.8, 27.3, 36.2, 58.4, 64.2, 110.1, 111.0, 118.2, 119.0, 120.8, 124.5, 128.6, 130.5, 133.3, 135.2; EI MS *m*/*z* 283 (M$^+$, 19), 144 (100).

Supporting Information Available: Spectral characterization data (^{1}H NMR) for all new compounds and crystallographic information files for *trans*-**13**. This material is available free of charge via the Internet at http://www.pubs.acs.org.

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