Article

Household Infrared Technology as an Energy-Efficient Approach to Achieve C−Cπ Bond Construction Reactions

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We examined the ability of short-wave infrared (IR) light in the $\lambda_{1.5\text{-}3.0\ \mu m}$ region of the infrared emission spectrum to accomplish C−Cπ bond construction reaction between π-excessive azaheteroaromatic and different carbonyl substrates supported on a bentonitic clay catalyst in solventless condition via a three-component condensation reaction. Preliminary studies show that the implementation of a domestic Flavor-Wave® oven fitted with a halogen heater lamp as a chemical reactor was as effective as the use of near IR light ($\lambda_{1.1\ \mu m}$) in fostering batch-wise organic reactions. Overall, this approach reveals its potential exploitation as an energy-efficient source to assemble biologically engaging (hetero)arenebisindolylmethanes framework, in the same way, that assure its sustainable development as for efficient generation of small libraries of molecules comparable to high-tech instrumentations performances.

Keywords: electromagnetic radiation, (hetero)arenebisindolylmethane, bentonite tonsil-actisil FF (TAFF), Brønsted-Lowry acid

Introduction

Although less dedicated light sources such as visible light have driven C−C and C−Het bond construction reactions since the genesis of prebiotic synthesis,[1-7] its feeble penetration through most reaction media undermines its effectiveness in most synthetic transformations carried out in the laboratory. However, an engaging solution is to harness infrared light that ensures deeper penetration.[8] From this perspective, Pool and Teuben[9] envisaged the implementation of Philips IR (infrared) heat lamps as a non-conventional and innovative source with potential application in research areas (Figure 1). Notwithstanding, its acceptance has followed a sluggish growth even though light-powered chemicals technologies have gained further ground as a benign method congruent with green chemistry principles.[10]

Infrared light as electromagnetic radiation has a spectral emission in the range of 0.3 to 430 THz (that is, wavelengths ranging from 0.7 μm up to 1 mm).[11] All IR heater lamps and domestic oven (*viz.* 250 W/250 V Theraterm Osram Red IR bulb and 1300 W/120 V Flavor-Wave® oven) devised for chemical transformation (Figure 1) operates at a frequency of *v* (number of wave cycles passing through a fixed point in each unit of time) = ca. 364 THz and ca. 112-230 THz (corresponding to $\lambda = 1.1$ μm ($\lambda_{1.1\mu m}$) and $\lambda = 1.5\text{-}3.0$ μm ($\lambda_{1.5-3.0\ \mu m}$), respectively). However, the photons of infrared radiation have energies from ca. 171 to 0.119 KJ mol^{-1} (Planck's law, $E = hc/\lambda$; where E is energy of the photons, h is Planck's constant, c is the speed of light in vacuum and λ is the wavelength of the photon) low enough to break chemical bonds (300-799 KJ mol^{-1}). Notwithstanding, this

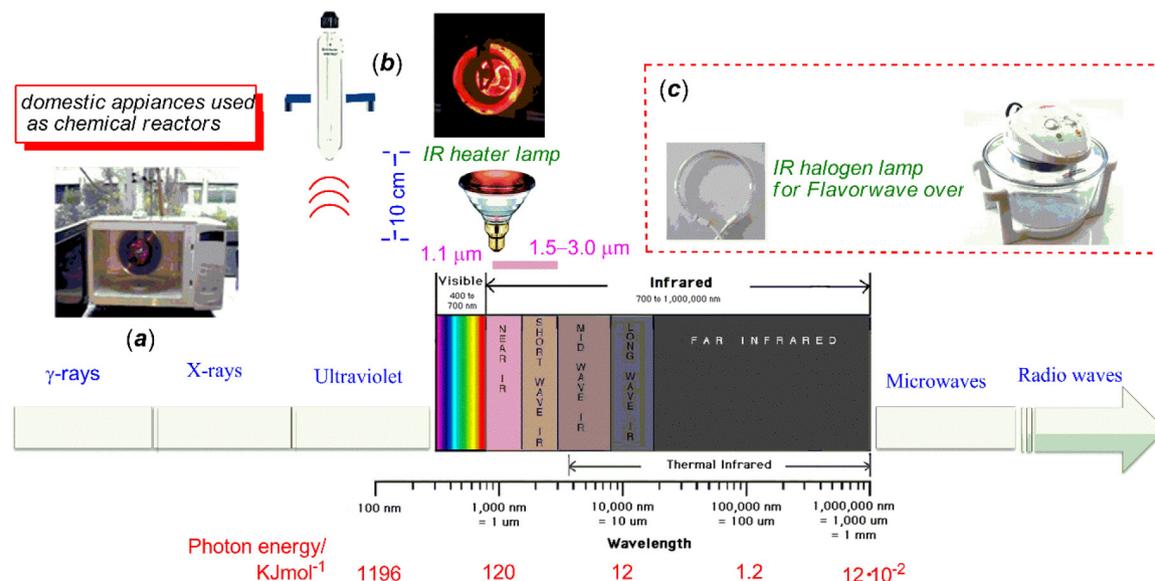*e-mail: hulmerg@yahoo.com; paulricardo1@yahoo.com.mx

Figure 1. Applicable infrared instrumentations: infrared (IR) oven modified from a domestic microwave (MW) oven (a), homemade reactor equipped with Osram IR heater lamp (b) as devised by Pool and Teuben,[9] and commercial Flavor-Wave® oven with its IR halogen heater lamps (c). The achievable energies in the IR region and the IR heating zone (divided into five subgroups) are also shown.

kind of thermal wave, wherein chemical transformations have been interpreted in terms of excitation of vibrational modes dependent on the kind of incident radiative energy, can furnish the quanta of energy required to attain the electronically excited species that are crucial for promoting the primary photo process (i.e., chemical reactions) predicted by photochemistry law.[12-15]

Over the years, the IR-powered reactions have slowly been incorporated into the chemical toolbox as an efficient synthetic approach for accessing structurally diverse molecules of scholarly, industrial, and pharmaceutical interest. In this fashion, the assembly of 3,4-dihydropyrimidin-2(1*H*)one,[16] 1,4-dihydropyridine,[17] α-ketothioamide,[18] ε-caprolactam,[19] (*Z*)-(aminomethyl)

(aryl)phenylhydrazone,[20] 3,5-diphenyltetrahydrobenzo [*d*]oxazol-2-one,[21] biaryls[22] and benzylidnomalonates[23] trough C–C and C–N bond construction reaction by exposure to the wavelength of 1.1 µm under Biginelli reaction, Hantzsch reaction, Willgerodt-Kindler reaction, Beckmann rearrangement reaction, palladium-catalyzed Heck reaction, Diels-Alder cycloaddition reaction, Suzuki-Miyaura cross-coupling reaction, and Knoevegenagel reaction, represents one of the major contributions achieved until now by the implementation of such cost-effective alternative energy appliances (Figure 2a).

Accordingly, we intend to exploit herein the IR zone of $\lambda_{1.5-3.0\ \mu m}$ of the infrared emission spectrum to achieve C–Cπ bond construction reactions between indole
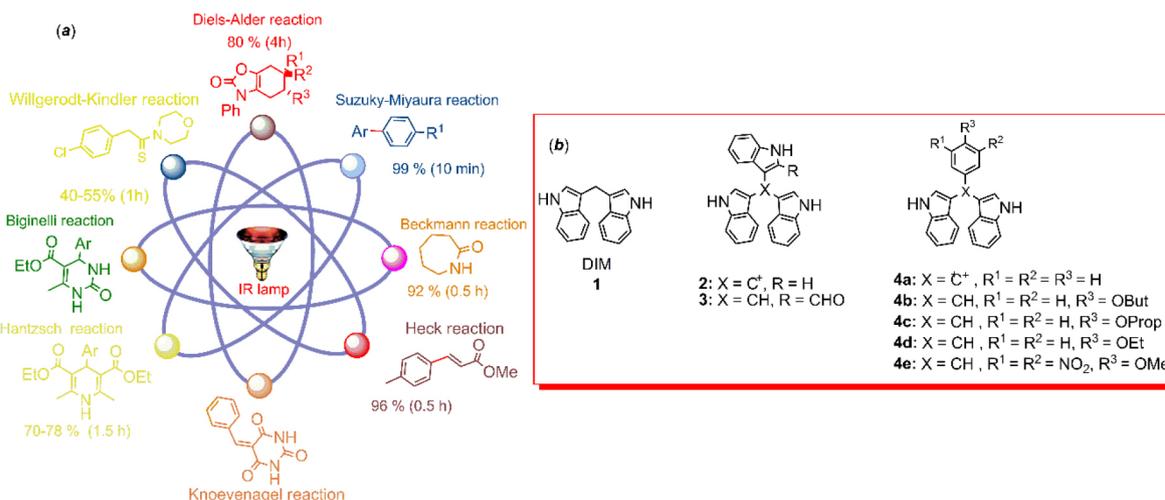

Figure 2. (a) Named reactions activated by an IR halogen heater lamp through exposure in the near-infrared region and (b) naturally occurring alkaloids **1-4a-4e** of biological relevance.

derivatives and different (hetero)arenecarboxaldehydes supported on bentonitic-tonsil-actisil FF (TAFF) clay under solventless condition for obtaining diversely decorated (hetero)arenebisindolylmethanes via a three-component condensation reaction.

Our interest in this kind of biologically relevant structure stems from the fact that they share the diindolylmethane (DIM) pharmacophoric scaffold **1** found in natural alkaloids skeleton as turbomycin A **2**, trisindolal **3**, turbomycin B **4a**, and turbomycin C–F (**4b-4e**, Figure 2b) and its derivatives, which exhibit promising antibiotic activity against Gram (+) and Gram (−) microorganism as well as cytotoxicity towards human tumor cell lines.[24-26]

In this regard, our findings show that the domestic Flavor-Wave® oven intended as an infrared-unconventional chemical reactor proved to be not only feasible for driving C–Cπ bond construction reaction, considering its high rate of reaction (20 min) and quantitative yield (60-95%) achieved as a result of its efficient heat and mass transfer, it also represents an excellent energy-efficient and cost-effective alternative with low environmental-charge able to runs up to eighteen reactions in parallels.

Experimental

All reactants used as substrates are commercially available (Sigma-Aldrich Chemical Co., Mexico city, México) and were employed without further purification. The reactions were monitored by thin layer chromatography (TLC) using percolated (0.25 mm) Merck silica-gel 60-F254 aluminum sheets. Product visualization was carried out using a 254 and 365 nm UV lamp and I_2. All melting points were measured on a Fisher-Johns SEV PF-300 apparatus and remain uncorrected. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a 300 MHz spectrometer in dimethyl sulfoxide (DMSO-d_6) or CDCl$_3$. Chemical shifts (δ) are expressed in ppm relative to the tetramethylsilane (TMS) peak used as internal standard. The *J* values are in hertz, and the splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; and bs, broad singlet. IR spectra on a Fourier transform infrared (FTIR) Bruker spectrophotometer using attenuated total reflection (ATR) method were recorded. Mass spectra (MS) and high-resolution mass spectra (HRMS) were obtained using a JEOL Accu TOF JMST100LC spectrometer, by direct analysis in real-time (DART) method.

Experimental IR equipment

Commercial infrared oven

The device used herein is a commercial Flavor-Wave® turbo oven 120 V/1300 W halogen heater lamp with a wavelength in the range of 1.5-3.0 μm.

Infrared device

An electric home-made metallic cylindrical can (29.5 cm in length with a diameter of 15.3 cm of width) designed to fix and adjust the position of an IR emission bulb was assembled with a THERATHERM OSRAM 125 V/250 W red infrared bulb with a peak wavelength of 1.1 μm (9.09 cm^{-1}). The device is adapted with a varicap diode to regulating the power output. All reactions were promoted by placing the IR bulb at ca. 10 cm away from the reaction flask and the reaction temperature was monitored with an InfraPro® infrared thermometer.

General procedure for the synthesis of indole derivatives (**13-31** and **43-63**)

Near-infrared reactions (method a): all reactions were promoted by exposure to $\lambda_{1.1\mu m}$ using a 120 V/250 W THERA-TERM OSRAM red infrared heater bulb for 15 min at 180 ± 2 °C by reproduction of the experimental procedure described.[27]

Middle infrared reactions (method b): into a 10 mL flask containing 4.0 g of bentonitic clay was placed 8.54 mmol of the corresponding indole derivative and 4.27 mmol of the (hetero)arene carboxaldehyde. After thoroughly mixing the reagents with the clay, the reaction mixture was exposed to react under $\lambda_{1.5-3.0\ \mu m}$ using a commercial Flavor-Wave® oven for 20 min at 150 °C. Once extracted the crude of reaction with hot ethanol (5 × 20 mL), the filtrate was poured onto crushed ice and left until no further precipitation occurs (in many cases, though, the filtrate needed to be stored in the refrigerator around 30 min at a temperature of 0-5 °C to obtain the precipitate). The obtained solid was filtered off and dried to obtain the spectroscopic pure product.

General procedure for the synthesis of compounds **13**, **15**, and **18** at room temperature

In a flask loaded with a stirrer, 60 mL of EtOH, 8.54 mmol of the corresponding indole, 4.27 mmol of the respective benzaldehyde, and *p*-toluenesulfonic acid in catalytic amount was added. This mixture was left stirring for 10 days at room temperature. Then, crushed ice was added until precipitate was formed (if necessary, the mixture can be stored in the refrigerator for about 30 min at a temperature of 0-5 °C to obtain the precipitate). After filtration, the solid obtained was purified by preparative chromatography using hexane:ethyl acetate in a ratio of

6:4. The scraped silica was extracted with acetone, filtered, and dried to obtain the pure product.

3,3'-(Phenylmethylene)bis(1*H*-indole) (**13**)

White solid, yield 70%, mp 142-144 ℃; IR (ATR) ν / cm⁻¹ 3053, 3048 (CH's ar), 2927 (C-H met), 1598, 1412 (C=C), 1200, 1010, 739; ¹H NMR (300 MHz, DMSO-*d₆*) δ 10.78 (bs, 2H, NH), 7.32-7.36 (m, 4H), 7.24-7.28 (m, 4H), 7.14-7.18 (m, 1H), 7.00-7.04 (m, 2H), 6.85-6.87 (t, *J* 6.8 Hz, 2H), 6.81 (d, *J* 2.0 Hz, 2H), 5.82 (s, 1H, Ar-CH); ¹³C NMR (75 MHz, DMSO-*d₆*) δ 144.8, 136.5, 128.2, 127.9, 126.5, 125.6, 123.4, 120.7, 119.0, 118.08, 118.00, 111.3, 39.6; HRMS (DART) *m/z*, calcd. for $C_{23}H_{18}N_2$ [M + H]⁺: 322.14700, found: 322.14543.

3,3'-(*p*-Tolylmethylene)bis(1*H*-indole) (**14**)

Red solid, yield 85%, mp 196-198 ℃; IR (ATR) ν / cm⁻¹ 3407 (NHas), 3054 (CH's), 2923 (C-H met), 1605, 1455 (C=C), 1091, 739; ¹H NMR (300 MHz, CDCl₃) δ 7.70 (s, 2H), 7.37 (d, *J* 8.0 Hz, 2H), 7.27 (d, *J* 8.5 Hz, 2H), 7.20 (d, *J* 8.0 Hz, 2H), 7.14 (t, *J* 7.5 Hz, 2H), 7.06 (d, *J* 8.0 Hz, 2H), 6.98 (t, *J* 7.5 Hz, 2H), 6.55 (d, *J* 2.0 Hz, 2H), 5.82 (s, 1H), 2.30 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 141.1, 136.8, 135.7, 129.1, 128.7, 127.2, 123.7, 122.0, 120.1, 120.0, 119.3, 111.2, 39.9, 21.2; HRMS (ESI) *m/z*, calcd. for $C_{24}H_{20}N_2$ [M + 1]⁺: 335.1543, found: 335.1530.

3,3'-((4-Methoxyphenyl)methylene)bis(1*H*-indole) (**15**)

Orange solid, yield 90%, mp 211-213 ℃; IR (ATR) ν / cm⁻¹ 3391 (NH), 3055 (CH's), 2931 (C-H met), 2381, 1611, 1508 (CN), 1021 (C-O), 739; ¹H NMR (300 MHz, DMSO-*d₆*) δ 10.78 (bs, 2H), 7.33 (d, *J* 8.4 Hz, 2H), 7.27-7.24 (m, 4H), 7.02 (t, *J* 8.0 Hz, 2H), 6.87-6.81 (m, 6H), 5.76 (s, 1H), 3.70 (s, 3H); ¹³C NMR (75 MHz, DMSO-*d₆*) δ 157.2, 136.9, 136.5, 129.1, 126.5, 123.3, 120.7, 119.1, 118.3, 118.0, 113.6, 113.3, 111.3, 54.8; HRMS (ESI) *m/z*, calcd. for $C_{24}H_{20}N_2O$ [M + H]⁺: 351.1492, found: 351.1481.

4-(Di(1*H*-indol-3-yl)methyl)-*N*,*N*-dimethylaniline (**16**)

Yellow solid, yield 90%, mp 165-167 °C; IR (ATR) ν / cm⁻¹ 3548 (NHas), 3392, 3233 (NHsim), 3047 (CH's ar), 2960, 2911 (C-H met), 1601, 1093, 740; ¹H NMR (300 MHz, DMSO-*d₆*) δ 10.68 (s, 2H), 7.24-7.17 (m, 2H), 7.00 (d, *J* 8.4 Hz, 2H), 6.93-6.84 (m, 4H), 6.68 (dd, *J* 8.2, 6.8 Hz, 2H), 6.65-6.57 (m, 2H), 5.81 (s, 1H), 2.83 (s, 6H), 2.07 (s, 6H); ¹³C NMR (75 MHz, DMSO-*d₆*) δ 148.6, 135.0, 131.8, 131.7, 129.1, 128.4, 119.4, 118.6, 117.8, 112.9, 112.2, 110.2, 40.3, 37.6, 11.9; HRMS (ESI) *m/z*, calcd. for $C_{25}H_{24}N_3$ [M + H]⁺: 366.19702, found: 366.19570.

4-(Di(1*H*-indol-3-yl)methyl)benzaldehyde (**17**)

Orange solid, yield 90%, mp 253-256 °C; IR (ATR) ν / cm⁻¹ 3404 (NHas), 3051 (CH's), 2935 (C-H met), 2835, 1691 (C=O), 1602, 1574 (CN), 1415 (C=C), 1337, 783, 737; ¹H NMR (300 MHz, CDCl₃/TMS) δ 9.97 (s, 1H), 8.01 (s, 2H), 7.97 (s, 2H, NH₂, D₂O), 7.78-7.81 (d, *J* 8.0 Hz, 2H), 7.50-7.52 (d, *J* 7.0 Hz, 2H), 7.36 (t, *J* 6.0 Hz, 2H), 7.25 (t, *J* 6.0 Hz, 2H), 6.97-7.04 (t, *J* 6.0 Hz, 2H), 6.66 (s, 2H), 5.96 (s, 1H); ¹³C NMR (75 MHz, CDCl₃/TMS) δ 192.2, 151.9, 137.5, 134.8, 129.9, 129.4, 127.2, 123.6, 121.7, 119.8, 118.9, 117.1, 109.3, 40.4; HRMS (ESI) *m/z*, calcd. for $C_{24}H_{19}N_2O$ [M + H]⁺: 351.14943, found: 351.14995.

3,3'-((4-Nitrophenyl)methylene)bis(1*H*-indole) (**18**)

Yellow needles, yield 70%, mp 211-213 °C; IR (ATR) ν / cm⁻¹ 3444 (NH), 3054 (CH's), 2918 (C-H met), 1594, 1339 (NO₂), 1501 (CN), 1065, 732; ¹H NMR (300 MHz, DMSO-*d₆*) δ 10.95 (s, 2H), 8.15 (d, *J* 8.0 Hz, 2H), 7.61 (d, *J* 8.0 Hz, 2H), 7.37 (d, *J* 7.5 Hz, 2H), 7.29 (d, *J* 7.5 Hz, 2H), 7.06 (t, *J* 7.0 Hz, 2H), 6.90 (s, 2H), 6.89 (t, *J* 7.0 Hz, 2H), 6.03 (s, 1H); ¹³C NMR (75 MHz, DMSO-*d₆*) δ 153.1, 145.7, 136.6, 129.4, 126.3, 123.9, 123.4, 121.1, 118.9, 118.4, 116.7, 111.6, 54.6; HRMS (ESI) *m/z*, calcd. for $C_{23}H_{18}N_3O_2$ [M + H]⁺: 367.13208, found: 367.13187.

3,3'-((3-Nitrophenyl)methylene)bis(1*H*-indole) (**19**)

Yellow solid, yield 95%; mp 161-163 °C; IR (ATR) ν / cm⁻¹ 3444 (NHas), 3054 (CH's), 2920 (C-H met), 1594 (NO₂), 1339, 1501 (CN), 732; ¹H NMR (300 MHz, CDCl₃) δ 8.21 (t, *J* 2.0 Hz, 1H), 8.06-8.08 (m, 1H), 7.98 (bs, 2H, NH), 7.68 (d, *J* 7.2 Hz, 2H), 7.43 (d, *J* 7.6 Hz, 2H), 7.34-7.39 (m, 4H), 7.17-7.21 (m, 2H), 7.00-7.04 (m, 2H), 6.67 (d, *J* 2.0 Hz, 2H), 5.99 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 148.3, 146.3, 136.6, 134.8, 129.0, 126.5, 123.6, 123.4, 122.1, 121.3, 119.4, 118.1, 111.2, 39.9; HRMS (ESI) *m/z*, calcd. for $C_{23}H_{17}N_3O_2$ [M + H]⁺: 367.13208, found: 367.13187.

3,3'-((4-Bromophenyl)methylene)bis(1*H*-indole) (**20**)

Dark pink solid, yield 77%, mp 110-113 °C; IR (ATR) ν / cm⁻¹ 3404 (NHas), 3051 (CH's), 2921 (C-H met), 1484 (CN), 1455 (C=C), 1009, 739; ¹H NMR (300 MHz, CDCl₃) δ 7.81-7.71 (m, 2H), 7.45 (d, *J* 2.2 Hz, 2H), 7.43 (d, *J* 2.2 Hz, 2H), 7.35 (d, *J* 8.2 Hz, 2H), 7.30-7.27 (m, 1H), 7.28-7.21 (m, 3H), 7.09-7.12 (m, 2H), 6.57 (d, *J* 2.3 Hz, 2H), 5.89 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 143.1, 136.7, 131.4, 130.6, 126.9, 123.8, 122.2, 120.0, 119.9, 119.4, 119.0, 111.3, 111.2, 39.7; HRMS (ESI) *m/z*, calcd. for $C_{23}H_{18}BrN_2$ [M + H]⁺: 400.05751, found: 400.05763.

2-(Bis(1*H*-indol-3-yl)methyl)benzaldehyde (**21**)

Colorless crystals, yield 94%, mp 117-119 °C; IR (ATR) ν / cm^{-1} 3400 (NHas), 3051, 2957 (CH's), 2919 (C-H met), 1702 (C=O), 1541 (CN), 1452 (C=C), 1317, 739; ^{1}H NMR (300 MHz, CDCl$_3$/TMS) δ 9.99 (s, 1H), 7.76 (s, 2H), 7.08-7.37 (m, 10H), 6.96 (t, *J* 15.0 Hz, 2H), 6.56 (s, 2H), 5.83 (s 1H); ^{13}C NMR (75 MHz, CDCl$_3$/TMS) δ 193.4, 143.8, 137.7, 130.4, 128.5, 128.0, 126.8, 125.9, 123.4, 121.7, 119.7, 119.5, 116.6, 110.8, 109.9, 39.9; HRMS (ESI) *m/z*, calcd. for C$_{24}$H$_{19}$N$_2$O [M + H]$^+$: 351.14191, found: 351.14211.

4-(Di(1*H*-indol-3-yl)methyl)phenol (**22**)

Dark orange solid, yield 78%, mp 122-124 °C; IR (ATR) ν / cm^{-1} 3400 (NHas), 3051 (CH's), 2928 (C-H met), 1511 (CN), 1455 (C=C), 1170, 1009, 739; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.76 (d, *J* 1.5 Hz, 2H), 9.15 (s, 1H), 7.33 (d, *J* 8.0 Hz, 2H), 7.25 (d, *J* 8.0 Hz, 2H), 7.13 (d, *J* 8.5 Hz, 2H), 7.02 (t, *J* 7.5 Hz, 2H), 6.84 (t, *J* 7.5 Hz, 2H), 6.77 (d, *J* 2.0 Hz, 2H), 6.65 (d, *J* 8.5 Hz, 2H), 5.70 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 155.2, 136.5, 135.2, 129.1, 126.6, 123.3, 120.7, 119.1, 118.6, 118.0, 114.7, 111.3, 54.6; HRMS (ESI) *m/z*, calcd. for C$_{23}$H$_{19}$N$_2$O [M + H]$^+$: 338.14191, found: 338.14093.

3,3'-((3,4-Dichlorophenyl)methylene)bis(1*H*-indole) (**23**)

Dark orange solid, yield 65%, mp 153-155 °C; IR (ATR) ν / cm^{-1} 3405, 3054 (CH's), 2920 (C-H met), 1468 (CN), 1455 (C=C), 1092, 739; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.90 (s, 2H), 7.40 (d, *J* 8.0 Hz, 2H), 7.35 (d, *J* 8.0 Hz, 2H), 7.16 (t, *J* 7.5 Hz, 2H), 7.00 (t, *J* 7.5 Hz, 2H), 6.92 (d, *J* 1.5 Hz, 1H), 6.83 (dd, *J* 8.0, 1.5 Hz, 1H), 6.76 (d, *J* 8.0 Hz, 1H), 6.65 (d, *J* 1.0 Hz, 2H), 5.83 (s, 1H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 148.8, 147.4, 136.8, 127.2, 123.7, 122.0, 120.7, 120.13, 120.10, 119.3, 112.3, 111.1, 111.0, 54.1; HRMS (ESI) *m/z*, calcd. for C$_{23}$H$_{17}$Cl$_2$N$_2$ [M + H]$^+$: 390.06905, found: 390.06792.

3-(Di(1*H*-indol-3-yl)methyl)benzonitrile (**24**)

Yellow solid, yield 90%, mp 102-104 °C; IR (ATR) ν / cm^{-1} 3044 (CH's-ar), 2916 (C-H met), 2229, 1485 (CN), 1456 (C=C), 1094, 740; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.96 (s, 2H), 7.37-7.39 (m, 5H), 7.22-7.27 (m, 5H), 7.21 (d, *J* 6.0 Hz, 2H), 7.04 (t, *J* 7.2 Hz, 2H), 6.77 (s, 2H), 5.88 (s, 1H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 146.2, 136.6, 134.0, 129.4, 128.7, 126.9, 126.8, 126.4, 123.6, 122.0, 119.7, 119.3, 118.9, 111.0, 39.9; HRMS (ESI) *m/z*, calcd. for C$_{24}$H$_{17}$N$_3$ [M + H]$^+$: 347.14225, found: 347.14123.

3-(Di(1*H*-indol-3-yl)methyl)benzaldehyde (**25**)

Colorless crystals, yield 90%, mp 176-178 °C; IR

(ATR) ν / cm^{-1} 3399 (NHas), 3051 (CH's ar), 2908 (C-H met), 1686 (C=O), 1602, 1451 (C=C), 1310, 843, 737; ^{1}H NMR (300 MHz, CDCl$_3$/TMS) δ 9.99 (s, 1H), 8.17 (s, 2H, NH, D$_2$O), 8.06-8.08 (d, *J* 6.0 Hz, 2H), 7.83 (d, *J* 6.0 Hz, 2H), 7.58 (t, *J* 6.0 Hz, 2H), 7.36 (d, *J* 3.0 Hz, 2H), 7.29 (d, *J* 3.0 Hz, 2H), 7.06 (t, *J* 6.0 Hz, 2H), 6.89 (t, *J* 7.0 Hz, 2H), 6.07 (s, 1H); ^{13}C NMR (75 MHz, CDCl$_3$/TMS) δ 192.2, 137.4, 136.5, 132.2, 130.9, 127.6, 126.5, 124.2, 123.0, 122.6, 119.5, 119.3, 117.4, 111.0, 108.5, 34.7; HRMS (ESI) *m/z*, calcd. for C$_{24}$H$_{19}$N$_2$O [M + H]$^+$: 351.14974, found: 351.14890.

3,3'-(Pyridin-4-ylmethylene)bis(1*H*-indole) (**26**)

Dark brown solid, yield 70%, mp 160-162 °C; IR (ATR) ν / cm^{-1} 3397 (NH), 3155, 2969 (CH's), 2918 (C-H met), 1598 (C=N), 1412 (C-N), 738 (CH's-Ar); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.5 (s, 2H, NH), 7.31-7.34 (d, *J* 7.3 Hz, 6H), 7.14-7.19 (t, *J* 7.2 Hz, 5H), 7.00 (t, *J* 7.5 Hz, 2H), 6.60 (s, 2H), 5.84 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.4, 149.2, 136.9, 136.9, 127.2, 122.9, 121.4, 119.4, 119.2, 118.7, 111.9, 111.8, 43.1, 40.5, 40.2, 39.9, 39.7, 39.4; HRMS (DART) *m/z*, calcd. for C$_{13}$H$_{12}$N$_3$ [M + H]$^+$: 324.15007, found: 324.15045.

3,3'-(Thiophen-2-ylmethylene)bis(1*H*-indole) (**27**)

Pink solid, yield 85%, mp 186-188 °C; IR (ATR) ν / cm^{-1} 3404 (NHas), 3383 (NHsim), 3062 (CH's ar), 2916 (C-H met), 1455 (C=C), 1274, 1007, 739; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.82 (s, 2H), 7.45 (d, *J* 8.0 Hz, 2H), 7.31 (d, *J* 8.5 Hz, 2H), 7.16 (t, *J* 7.5 Hz, 2H), 7.14 (d, *J* 5.0 Hz, 1H), 7.02 (t, *J* 7.5 Hz, 2H), 6.91-6.89 (m, 2H), 6.78 (s, 2H), 6.14 (s, 1H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 148.7, 136.7, 126.8, 126.5, 125.3, 123.7, 123.3, 122.1, 119.9, 119.8, 119.5, 111.2, 45.5, 35.4; HRMS (DART) *m/z*, calcd. for C$_{21}$H$_{16}$N$_2$S [M + H]$^+$: 328.1032, found: 328.10315.

3,3'-((5-Methylthiophen-2-yl)methylene)bis(1*H*-indole) (**28**)

Red solid, yield 78%, mp 150-152 °C; IR (ATR) ν / cm^{-1} 3405 (NHas), 3052 (CH's), 2920 (C-H met), 1454 (C=C), 1042, 743; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.90 (s, 2H), 7.58 (d, *J* 7.9 Hz, 2H), 7.36 (d, *J* 7.9 Hz, 4H), 7.04 (dd, *J* 6.9, 8.9 Hz, 3H), 6.95 (s, 2H), 5.87 (d, *J* 17.3 Hz, 1H), 4.69 (s, 1H), 1.83 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 157.0, 153.8, 141.1, 131.7, 127.2, 123.8, 116.8, 112.0, 111.7, 110.1, 109.9, 106.6, 101.7, 77.2, 76.9, 76.7, 43.1, 34.2, 14.8; HRMS (ESI) *m/z*, calcd. for C$_{22}$H$_{18}$N$_2$S [M + H]$^+$: 343.11907, found: 343.12242.

3,3'-(Pyridin-3-ylmethylene)bis(1*H*-indole) (**29**)

Dark pink, yield 65%, mp 139-141 °C; IR (ATR) ν / cm^{-1} 3399, 3277 (NH), 3040 (CH's ar), 2924 (C-H met), 733

(CH's), 1521 (C=C), 1427 (C=N), 1094 (C-N); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.94 (s, 2H, 2NH$_2$), 8.65 (s, 1H), 8.43 (s, 1H), 7.75 (d, *J* 7.5 Hz, 1H), 7.38 (d, *J* 8.1 Hz, 2H), 7.32 (t, *J* 7.5 Hz, 3H), 7.06 (t, *J* 7.5 Hz, 2H), 6.89 (t, *J* 6.0 Hz, 4H), 5.95 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 149.6, 147.1, 141.0, 137.0, 136.6, 126.8, 124.2, 121.5, 119.4, 118.8, 117.5, 112.0, 56.3; HRMS (DART) *m/z*, calcd. for C$_{13}$H$_{12}$N$_3$ [M + H]$^+$: 324.15007, found: 324.15016.

3,3'-(Pyridin-2-ylmethylene)bis(1*H*-indole) (30)

Brown solid, yield 60%, mp 184-185 °C; IR (ATR) ν / cm^{-1} 3444 (NH), 3133, 3099 (CH's), 2927 (C-H met), 1585 (C=N), 1434 (C-N), 733 (CH's Ar); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.88 (s, 2H, NH), 7.66 (t, *J* 7.5 Hz, 1H), 7.34-7.41 (m, 6H), 7.00-7.09 (m, 3H), 6.97 (s, 2H), 6.89 (t, *J* 7.5 Hz, 2H), 5.97 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 149.6, 147.1, 141.0, 137.0, 136.6, 126.8, 124.2, 124.5, 119.4, 118.8, 117.5, 112.0, 56.5; HRMS (DART) *m/z*, calcd. for C$_{13}$H$_{12}$N$_3$ [M + H]$^+$: 324.15007, found: 324.14993.

3,3'-(Naphthalen-2-ylmethylene)bis(1*H*-indole) (31)

Light pink solid, yield 80%, mp 110-112 °C; IR (ATR) ν / cm^{-1} 3420 (NHas), 3399 (NHsim), 3051 (CH's), 2924 (C-H met), 1455 (C=C), 1293, 838, 739; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.63 (d, *J* 1.5 Hz, 2H), 8.15 (d, *J* 8.5 Hz, 1H), 7.82 (d, *J* 8.0 Hz, 1H), 7.67 (d, *J* 8.0 Hz, 1H), 7.35 (t, *J* 7.5 Hz, 1H), 7.34 (d, *J* 8.0 Hz, 2H), 7.29 (t, *J* 8.0 Hz, 1H), 7.23 (t, *J* 7.5 Hz, 1H), 7.19 (d, *J* 8.5 Hz, 3H), 6.99 (t, *J* 7.5 Hz, 2H), 6.76 (t, *J* 8.0 Hz, 2H), 6.67 (d, *J* 1.5 Hz, 2H), 6.56 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 141.0, 137.4, 134.4, 132.1, 129.5, 127.6, 127.4, 126.8, 126.33, 126.28, 126.1, 125.0, 124.5, 122.1, 119.7, 119.4, 118.7, 112.5, 36.1; HRMS (DART) *m/z*, for C$_{27}$H$_{20}$N$_2$ [M + H]$^+$: 372.15430, found 372.15765.

4-(Bis(2-methyl-1*H*-indol-3-yl)methyl)benzaldehyde (43)

Violet solid, yield 60%, mp 127-128 °C; IR (ATR) ν / cm^{-1} 3400 (NHas), 3302 (NHsim), 3052 (CH's ar), 2920 (C-H met), 2853, 1684 (C=O), 1573 (CN), 1458 (C=C), 1302, 829, 811, 740; ^{1}H NMR (300 MHz, CDCl$_3$/TMS) δ 9.98 (s, 1H), 7.80 (s, 2H, NH, D$_2$O), 7.76 (d, *J* 8.1 Hz, 2H), 7.43 (d, *J* 8.1 Hz, 2H), 7.26 (d, *J* 7.5 Hz, 2H), 7.05 (t, *J* 8.1 Hz, 2H), 6.83-6.95 (m, 4H), 6.05 (s, 1H), 2.08 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$/TMS) δ 192.2, 151.9, 135.2, 134.5, 132.3, 129.8, 129.7, 128.7, 120.6, 119.0, 112.0, 110.2, 39.9, 12.4; HRMS (ESI) *m/z*, calcd. for C$_{26}$H$_{23}$N$_2$O [M + H]$^+$: 379.18104, found: 379.18073.

3-(Bis(2-methyl-1*H*-indol-3-yl)methyl)benzaldehyde (44)

Colorless crystals, yield 94%, mp 140-142 °C; IR (ATR)

ν / cm^{-1} 3404 (NH), 3050 (CH's), 2920 (C-H met), 2838, 1686 (C=O), 1515 (CN), 1454 (C=C), 1336, 792, 739; ^{1}H NMR (300 MHz, CDCl$_3$/TMS) δ 9.93 (s, 1H), 7.70 (d, *J* 6.0 Hz, 2H), 7.40 (d, *J* 9.0 Hz, 2H), 7.23 (d, *J* 9.0 Hz, 2H), 6.98 (t, *J* 9.0 Hz, 3H), 6.90 (d, *J* 6.0 Hz, 2H), 6.80 (t, *J* 9.0 Hz, 3H), 6.00 (s, 1H), 2.12 (s, 6H, 2CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$/TMS) δ 192.2, 137.6, 136.8, 135.2, 134.5, 132.3, 129.2, 128.5, 128.2, 127.2, 120.6, 119.9, 119.3, 112.1, 110.2, 40.2, 12.4; HRMS (ESI) *m/z*, calcd. for C$_{26}$H$_{23}$N$_2$O [M + H]$^+$: 379.18104, found: 379.18038.

2-(Bis(2-methyl-1*H*-indol-3-yl)methyl)benzaldehyde (45)

Colorless crystals, yield 91%, mp 218-220 °C; IR (ATR) ν / cm^{-1} 3279 (NH), 3050 (CH's ar), 2931 (C-H met), 2870, 2827, 1609 (C=O), 1583 (CN), 1468 (C=C), 1327, 794, 767, 737; ^{1}H NMR (300 MHz, CDCl$_3$/TMS) δ 9.94 (s, 1H), 7.89 (s, 2H, NH), 7.85 (t, *J* 7.5 Hz, 1H), 7.71 (t, *J* 7.5 Hz, 3H), 7.53 (d, *J* 8.0 Hz, 2H), 7.37 (dd, *J* 10.0, 8.0 Hz, 2H), 7.13 (t, *J* 12.0 Hz, 2H), 6.93 (t, *J* 12.0 Hz, 1H), 6.87 (s, 1H), 6.00 (s, 1H), 1.96 (s, 6H, 2CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$/TMS) δ 191.5, 141.9, 139.1, 138.2, 136.4, 134.9, 132.2, 129.3, 127.9, 126.5, 122.8, 121.3, 118.7, 112.8, 110.6, 40.6, 31.3, 12.4; HRMS (ESI) *m/z*, calcd. for C$_{26}$H$_{23}$N$_2$O [M + H]$^+$: 379.17321, found: 379.17222.

3,3'-(Pyridin-4-ylmethylene)bis(2-methyl-1*H*-indole) (46)

Violet solid, yield 74%, mp 160-162 °C; IR (ATR) ν / cm^{-1} 3390 (NH), 3141, 3049 (CH's), 3021 (CH's), 2924 (C-H met), 1597 (C=N), 1417 (C-N), 739 (CH's-Ar); ^{1}H NMR (300 MHz, CDCl$_3$) δ 10.81 (s, 2H, 2NH), 10.52 (s, 2H), 8.54 (d, *J* 3.9 Hz, 1H), 7.28 (d, *J* 7.4 Hz, 2H), 7.20-7.24 (m, 3H), 6.94 (t, *J* 7.2 Hz, 2H), 6.84 (d, *J* 7.4 Hz, 2H), 6.73 (t, *J* 7.5 Hz, 2H), 6.03 (s, 1H), 2.15 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 153.7, 149.3, 136.7, 126.7, 124.3, 123.8, 122.2, 119.5, 119.4, 117.5, 111.3, 102.5, 39.7; HRMS (DART) *m/z*, calcd. for C$_{13}$H$_{12}$N$_3$ [M + H]$^+$: 352.18137, found: 352.18218.

3,3'-(Pyridin-3-ylmethylene)bis(2-methyl-1*H*-indole) (47)

Light pink solid, yield 70%, mp 156-158 °C; IR (ATR) ν / cm^{-1} 3392 (NH), 3141, 3060 (CH's), 2964, 2915 (C-H met), 2876, 733 (CH's), 1587 (C=C), 1459 (C=N), 1128 (C-N); ^{1}H NMR (300 MHz, CDCl$_3$) δ 10.81 (s, 2H, 2NH), 8.54 (d, *J* 3.9 Hz, 1H), 7.67 (t, *J* 6.0 Hz, 1H), 7.28 (d, *J* 8.1 Hz, 2H), 7.23 (t, *J* 3.0 Hz, 1H), 7.20 (s, 1H), 6.94 (t, *J* 4.5 Hz, 2H), 6.83 (d, *J* 7.8 Hz, 2H), 6.73 (t, *J* 7.5 Hz, 2H), 6.03 (s, 1H), 2.10 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 164.4, 149.2, 136.9, 136.9, 127.2, 122.9, 121.4, 119.4, 119.2, 118.7, 111.9, 111.8, 43.1, 12.4; HRMS (DART) *m/z*, calcd. for C$_{13}$H$_{12}$N$_3$ [M + H]$^+$: 352.18137, found: 352.18240.

3,3'-(Pyridin-2-ylmethylene)bis(2-methyl-1H-indole) (48)

Light pink solid, yield 70%, mp 92-94 °C; IR (ATR) ν / cm⁻¹ 3392 (NH), 3141, 3060 (CH's), 2920 (C-H met), 1587 (C=N), 1432 (C-N), 733 (CH's-Ar); ¹H NMR (300 MHz, CDCl₃) δ 10.81 (s, 2H, NH), 8.54 (s, 1H), 7.68 (t, *J* 7.8 Hz, 1H), 7.27 (d, *J* 8.1 Hz, 2H), 7.20-7.24 (m, 2H), 6.94 (t, *J* 7.2 Hz, 2H), 6.83 (d, *J* 7.8 Hz, 2H), 6.73 (t, *J* 7.5 Hz, 2H), 5.03 (s, 1H), 2.10 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 163.7, 149.0, 136.7, 135.5, 132.6, 128.8, 121.4, 120.0, 118.7, 118.5, 112.1, 110.8, 42.4, 40.5, 40.2, 39.9, 39.6, 39.4, 12.3; HRMS (DART) *m/z*, calcd. for C₁₃H₁₂N₃ [M + H]⁺: 352.18137, found: 352.18223.

3,3'-((5-Methylthiophen-2-yl)methylene)bis(2-methyl-1H-indole) (49)

Red solid, yield 65%, mp 148-152 °C; IR (ATR) ν / cm⁻¹ 3396 (NH), 3047 (CH's), 2915 (C-H met), 1562 (CN), 1460 (C=C), 1217, 1009, 746; ¹H NMR (300 MHz, CDCl₃) δ 7.56-7.63 (m, 1H), 7.38-7.40 (m, 2H), 7.29-7.35 (m, 1H), 7.18-7.27 (m, 7H), 7.06-7.12 (m, 2H), 6.60 (s, 1H), 5.89 (s, 1H), 2.20 (s, 3H, CH₃), 1.92 (s, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 157.0, 153.8, 141.1, 131.7, 127.2, 123.8, 116.8, 112.0, 111.7, 110.1, 109.9, 106.6, 101.7, 34.2, 11.4, 9.9; HRMS (ESI) *m/z*, calcd. for C₂₄H₂₂N₂S [M + H]⁺: 370.15037, found: 370.14964.

4-(Bis(2-phenyl-1H-indol-3-yl)methyl)benzaldehyde (50)

Colorless crystals, yield 96%, mp 260-262 °C; IR (ATR) ν / cm⁻¹ 3399 (NH), 3056, 3027 (CH's), 2934 (C-H met), 1694 (C=O), 1575 (CN), 1449 (C=C), 1336, 773, 733, 696; ¹H NMR (300 MHz, CDCl₃/TMS) δ 9.95 (s, 1H), 7.86 (s, 2H), 7.73-7.76 (d, *J* 9.0 Hz, 2H), 7.62-7.65 (d, *J* 9.0 Hz, 2H), 7.44 (t, *J* 9.0 Hz, 2H), 7.15-7.37 (m, 14H), 6.99 (t, *J* 15.0 Hz, 2H), 6.98 (d, *J* 12.0 Hz, 2H), 5.97 (s, 1H); ¹³C NMR (75 MHz, CDCl₃/TMS) δ 192.7, 145.8, 137.5, 136.5, 134.9, 130.2, 128.9, 128.3, 127.5, 127.2, 121.6, 119.8, 118.8, 117.4, 109.2, 109.0, 39.9; HRMS (FAB⁺, fast atom bombardment) *m/z*, calcd. for C₃₆H₂₇N₂O [M + H]⁺: 502.20450, found: 502.20490.

3-(Bis(2-phenyl-1H-indol-3-yl)methyl)benzaldehyde (51)

Colorless crystals, yield 93%, mp 202-204 °C; IR (ATR) ν / cm⁻¹ 3424 (NHas), 3395 (NHsim), 3053, 2931 (C-H met), 1686, 1598 (CN), 1485 (C=C), 1339, 1310, 740, 698; ¹H NMR (300 MHz, CDCl₃/TMS) δ 9.98 (s, 1H), 7.15-7.39 (m, 18H), 7.00 (t, *J* 7.5 Hz, 2H), 6.90 (d, *J* 8.0 Hz, 2H), 6.67 (t, *J* 6.0 Hz, 2H), 5.99 (s, 1H); ¹³C NMR (75 MHz, CDCl₃/TMS) δ 192.7, 137.4, 137.4, 136.5, 134.9, 130.2, 129.6, 129.4, 128.9, 128.3, 128.2, 127.5, 127.2, 121.6, 121.2, 120.1, 119.8, 109.2, 109.0, 40.2; HRMS (ESI) *m/z*, calcd. for C₃₆H₂₇N₂O [M + H]⁺: 503.21234, found: 503.20105.

2-(Bis(2-phenyl-1H-indol-3-yl)methyl)benzaldehyde (52)

Colorless crystals, yield 94%, mp 100-102 °C; IR (ATR) ν / cm⁻¹ 3413 (NHas), 3387, 3335 (NHsim), 3057, 3028 (CH's), 2934 (C-H met), 1684, 1575 (CN), 1425 (C=C), 1342, 765, 744; ¹H NMR (300 MHz, CDCl₃/TMS) δ 9.90 (s, 1H), 7.98 (s, 2H), 7.54 (d, *J* 9.0 Hz, 2H), 7.19-7.42 (m, 16H), 7.07 (t, *J* 9.0 Hz, 2H), 6.85 (t, *J* 9.0 Hz, 2H), 5.52 (s, 1H); ¹³C NMR (75 MHz, CDCl₃/TMS) δ 191.7, 138.8, 137.5, 135.2, 134.2, 133.3, 131.2, 129.8, 129.3, 128.2, 127.5, 127.5, 126.3, 123.3, 121.6, 119.9, 118.9, 111.1, 108.9, 42.9; HRMS (ESI) *m/z*, calcd. for C₃₆H₂₇N₂O [M + H]⁺: 503.21234, found: 503.21120.

3,3'-(Pyridin-4-ylmethylene)bis(2-phenyl-1H-indole) (53)

Grey solid, yield 82%, mp 170-173 °C; IR (ATR) ν / cm⁻¹ 3385 (NH), 3162, 3051 (CH's), 2922 (C-H met), 1598 (C=N), 1450 (C-N), 737 (CH's-Ar); ¹H NMR (300 MHz, DMSO-d₆) δ 11.51 (s, 2H, 2NH), 8.48 (s, 2H), 7.44 (t, *J* 6.5 Hz, 4H), 7.24-7.30 (m, 11H), 7.05 (t, *J* 7.5 Hz, 4H), 6.90-6.96 (m, 3H), 6.02 (s, 1H); ¹³C NMR (75 MHz, DMSO-d₆) δ 190.1, 186.3, 180.7, 178.8, 171.0, 166.7, 165.9, 165.4, 164.1, 157.6, 154.5, 153.6, 151.7, 149.3, 146.9, 136.1, 42.8; HRMS (DART) *m/z*, calcd. for C₁₃H₁₂N₃ [M + H]⁺: 476.21267, found: 476.21212.

3,3'-(Pyridin-3-ylmethylene)bis(2-phenyl-1H-indole) (54)

White solid, yield 85%, mp 161-163 °C; IR (ATR) ν / cm⁻¹ 3403 (NH), 3049, 733 (CH's), 2924 (C-H met), 1449 (C=C), 1305 (C=N), 1012 (C-N); ¹H NMR (300 MHz, DMSO-d₆) δ 11.39 (s, 2H, 2NH), 8.46 (d, *J* 4.2 Hz, 1H), 7.74 (t, *J* 7.8 Hz, 1H), 7.40 (d, *J* 8.1 Hz, 3H), 7.24-7.30 (m, 10H), 7.04 (t, 3H), 6.87 (d, *J* 7.8 Hz, 2H), 6.71 (t, *J* 7.2 Hz, 2H), 6.03 (s, 1H); ¹³C NMR (75 MHz, DMSO-d₆) δ 151.5, 148.7, 138.1, 136.3, 132.6, 129.8, 128.7, 127.8, 127.5, 123.4, 122.2, 117.2, 114.9, 113.9, 111.8, 46.3; HRMS (DART) *m/z*, calcd. for C₁₃H₁₂N₃ [M + H]⁺: 476.21267, found: 476.21064.

3,3'-(Pyridin-2-ylmethylene)bis(2-phenyl-1H-indole) (55)

Light pink solid, yield 90%, mp 96-98 °C; IR (ATR) ν / cm⁻¹ 3403 (NH), 3049 (CH's), 2920 (C-H met), 1589 (C=N), 1429 (C-N), 733 (CH's-Ar); ¹H NMR (300 MHz, DMSO-d₆) δ 11.39 (s, 2H, NH), 7.71 (t, *J* 7.2 Hz, 1H), 7.40 (d, *J* 7.8 Hz, 2H), 7.24-7.30 (m, 12H), 7.03 (t, *J* 7.2 Hz, 2H), 6.87 (d, *J* 7.8 Hz, 2H), 6.70 (t, *J* 7.5 Hz, 2H), 6.04 (s, 1H); ¹³C NMR (75 MHz, DMSO-d₆) δ 165.0, 149.5, 136.8, 136.7, 135.9, 133.2, 128.7, 128.5, 123.6, 121.4, 121.4, 120.8, 119.1, 114.2, 111.8, 43.5; HRMS (DART) *m/z*, calcd. for C₁₃H₁₂N₃ [M + H]⁺: 476.21267, found: 476.21173.

4-(Bis(1-methyl-1*H*-indol-3-yl)methyl)benzaldehyde (**56**)

Pink solid, yield 90%, mp 148-150 °C; IR (ATR) ν / cm^{-1} 3047 (CH's), 2910 (C-H met), 2878, 1698, 1546 (CN), 1468 (C=C), 788, 737; ^{1}H NMR (300 MHz, CDCl$_3$/TMS) δ 9.98 (s, H), 7.80 (d, *J* 9.0 Hz, 2H), 7.53 (d, *J* 9.0 Hz, 2H), 7.29-7.37 (m, 4H), 7.24 (t, *J* 7.0 Hz, 2H), 7.00 (t, *J* 7.0 Hz, 2H), 6.54 (s, 2H), 5.95 (s, 1H), 3.69 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$/TMS) δ 192.2, 151.9, 137.5, 134.8, 129.9, 129.4, 128.3, 127.2, 121.7, 118.9, 117.1, 109.3, 40.4, 32.8; HRMS (ESI) *m/z*, calcd. for [M + H]$^+$: 379.18104, found 379.18068.

3-(Bis(1-methyl-1*H*-indol-3-yl)methyl)benzaldehyde (**57**)

Colorless crystals, yield 90%, mp 139-142 °C; IR (ATR) ν / cm^{-1} 3050, 2931 (CH's), 2910 (C-H met), 2838, 2821, 1687, 1610, 1546 (CN), 1469 (C=C), 1327, 794, 737; ^{1}H NMR (300 MHz, CDCl$_3$/TMS) δ 9.95 (s, 1H), 7.86 (s, 1H), 7.74 (d, *J* 6.0 Hz, 1H), 7.64 (d, *J* 6.0 Hz, 1H), 7.37 (t, *J* 6.0 Hz, 1H), 7.24-7.30 (m, 6H), 7.00 (t, *J* 6.0 Hz, 2H), 6.53 (s, 2H), 5.97 (s, 1H), 3.70 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$/TMS) δ 192.0, 146.0, 144.5, 137.4, 134.7, 129.8, 128.4, 127.7, 121.3, 119.7, 118.9, 117.1, 109.4, 109.2, 40.3, 32.4; HRMS (ESI) *m/z*, calcd. for C$_{26}$H$_{23}$N$_2$O [M + H]$^+$: 379.18104, found: 379.18068.

2-(Bis(1-methyl-1*H*-indol-3-yl)methyl)benzaldehyde (**58**)

Colorless crystals, yield 90%, mp 179-181 °C; IR (ATR) ν / cm^{-1} 3050, 3019 (CH's), 2928 (C-H met), 2879, 2841, 1539 (CN), 1473 (C=C), 1344, 1317, 866, 828, 740; ^{1}H NMR (300 MHz, CDCl$_3$/TMS) δ 9.98 (s, 1H), 7.78 (d, *J* 9.0 Hz, 2H), 7.52 (d, *J* 9.0 Hz, 2H), 7.25-7.33 (m, 6H), 7.00 (t, *J* 6.0 Hz, 2H), 6.53 (s, 2H), 5.95 (s, 1H), 3.69 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$/TMS) δ 191.8, 138.9, 137.1, 135.2, 134.5, 130.2, 129.1, 128.3, 127.6, 126.9, 120.6, 119.0, 117.6, 112.2, 110.2, 52.5, 39.6, 30.9; HRMS (FAB$^+$) *m/z*, calcd. for C$_{26}$H$_{22}$N$_2$O [M + H]$^+$: 378.17320, found: 378.17290.

3,3'-(Pyridin-4-ylmethylene)bis(1-methyl-1*H*-indole) (**59**)

Light pink solid, yield 82%, mp 192-195 °C; IR (ATR) ν / cm^{-1} 3128 (NH), 3050, 3020 (CH's), 2933 (C-H met), 1590 (C=N), 1423 (C-N), 739 (CH's-Ar); ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.46 (s, 2H), 7.32-7.41 (m, 7H), 7.13 (t, *J* 7.2 Hz, 2H), 6.91-6.96 (m, 4H), 5.89 (s, 1H), 3.71 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 153.9, 149.9, 137.4, 128.5, 127.1, 124.1, 121.7, 119.5, 119.0, 116.1, 110.2, 55.2, 32.7; HRMS (DART) *m/z*, calcd. for C$_{13}$H$_{12}$N$_3$ [M + H]$^+$: 352.18137, found: 352.18098.

3,3'-(Pyridin-3-ylmethylene)bis(1-methyl-1*H*-indole) (**60**)

Light pink solid, yield 80%, mp 172-175 °C; IR (ATR) ν / cm^{-1} 3049, 2995 (CH's), 2928 (C-H met), 2822 (CH's), 1564 (C=C), 1428 (C=N), 1129 (C-N); ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.52 (d, *J* 4.5 Hz), 7.69 (t, *J* 7.5 Hz, 1H), 7.37-7.43 (m, 5H), 7.21 (t, *J* 6.6 Hz), 7.13 (t, *J* 7.8 Hz, 2H), 6.92-6.98 (m, 4H), 5.97 (s, 1H), 3.70 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 163.9, 149.2, 137.2, 137.1, 128.3, 127.4, 122.9, 121.8, 121.6, 119.5, 118.9, 116.5, 110.1, 42.6, 32.7; HRMS (DART) *m/z*, calcd. for C$_{13}$H$_{12}$N$_3$ [M + H]$^+$: 352.18137, found: 352.18242.

3,3'-(Pyridin-2-ylmethylene)bis(1-methyl-1*H*-indole) (**61**)

Light brown solid, yield 85%, mp 136-138 °C; IR (ATR) ν / cm^{-1} 3049 (CH's), 2995 (CH's), 2925 (C-H met), 1586 (C=N), 1464 (C-N), 726 (CH's-Ar); ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.51 (s, 1H), 7.67 (t, *J* 7.2 Hz, 1H), 7.36-7.42 (m, 5H), 7.19 (t, *J* 6.6 Hz, 1H), 7.12 (t, *J* 7.5 Hz, 2H), 6.91-6.97 (m, 4H), 6.00 (s, 1H), 3.70 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 164.1, 149.2, 137.2, 137.0, 128.4, 127.4, 122.9, 121.8, 121.5, 119.5, 118.9, 116.5, 110.0, 53.7, 32.7; HRMS (DART) *m/z*, calcd. for C$_{13}$H$_{12}$N$_3$ [M + H]$^+$: 352.18137, found: 352.18252.

3,3'-(Thiophen-2-ylmethylene)bis(1-methyl-1*H*-indole) (**62**)

Light pink solid, yield 85%, mp 140-143 °C; IR (ATR) ν / cm^{-1} 3041 (CH's), 2932 (C-H met), 1546 (CN), 1473 (C=C), 1328, 1131, 736, 690; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.56 (d, *J* 6.0 Hz, 2H), 7.38 (d, *J* 3.0 Hz, 2H), 7.30 (t, *J* 3.0 Hz, 2H), 7.23 (s, 1H), 7.12 (t, *J* 6.0 Hz, 2H), 7.0 (s, 2H), 6.81 (s, 2H), 6.25 (s, 1H), 3.77 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 149.4, 137.5, 127.9, 127.4, 126.5, 125.1, 123.6, 121.7, 120.0, 119.0, 118.5, 109.3, 35.4, 32.8; HRMS (DART) *m/z*, calcd. for C$_{23}$H$_{20}$N$_2$S [M + H]$^+$: 356.13472, found: 356.13367.

3,3'-((5-Methylthiophen-2-yl)methylene)bis(1-methyl-1*H*-indole) (**63**)

Light red solid, yield 78%, mp 132-136 °C; IR (ATR) ν / cm^{-1} 3056, (CH's), 2915 (C-H met), 1550 (CN), 1472 (C=C), 1347, 1329, 1204, 740; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.46 (d, *J* 7.8 Hz, 2H), 7.25 (d, *J* 8.4 Hz, 2H), 7.17 (t, *J* 8.1 Hz, 2H), 7.00 (t, *J* 6.9 Hz, 2H), 6.69 (s, 2H), 5.84 (s, 2H), 3.69 (s, 6H, 2CH$_3$), 2.25 (s. 3H, CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$) δ 155.5, 150.4, 137.3, 127.5, 127.3, 121.4, 119.9, 118.7, 116.0, 109.0, 107.1, 106.0, 32.9, 32.6, 13.7; HRMS (ESI) *m/z*, calcd. for C$_{24}$H$_{22}$N$_2$S [M + H]$^+$: 370.15037, found: 370.14964.

Results and Discussion

The three-component condensation of 2 mmol of indole **5** with 1 mmol of arenecarbaldehydes **6-12** supported on 4 g of

bentonitic clay exposed to near IR light (*viz.* Osram IR heater lamp powered at emission peak of $\lambda = 1.1$ µm) has been reported as an efficient unconventional approach to achieving the synthesis arenebisindolylmethanes **13-19**.[27] However, due to the controversial data found in the literature related to its physical characterization, in addition to the lack of in-depth studies and the scarcity of instrumentation specifically designed for infrared reactions, the preliminary assembly of said set of biologically attractive arenebisindolylmethanes was reexamined. In addition, additional data was collected for the comparative analysis of the reaction efficiency under short-wave IR light at an emission power of 1.5-3.0 µm using a Flavor-Wave® domestic oven as a chemical reactor and the results are shown in Table 1.

Although all the compounds were obtained by reproducing the experimental procedure described,[27] the experimental melting points were determined to exhibit wide discrepancies with the reported data (entries 1-3 and 5-7), except for compound **16** (entry 4). Our results were found to correlate well with the publication by Velasco-Bejarano *et al.*[28] To avoid unnecessary assessment, its structural attributes were corroborated based on IR, ^{1}H, and ^{13}C NMR spectroscopy, HRMS method, and by comparison with previously reported data.[24] Briefly, the analysis of ^{1}H NMR spectral data collected for the compounds **13-19** enables us to ascribe the key methine singlet unambiguously. The singlets for all compounds appear deshielding between δ 5.76-6.03 ppm due to the

magnetic anisotropy of the neighboring aromatic rings, whereas their respective ^{13}C NMR signals were found in the range of δ 39.6 to 54.8 ppm. Further, these assignations were complemented with the sp[3] C–H spectral fingerprint observed around 2911-2935 cm^{-1} by IR spectroscopy as well as their corresponding molecular mass (*m/z*) determined by the DART-HRMS method.

The comparative analysis of the results obtained in this regard shows that, even though the thermal wave emitted from the tungsten filament lamp has lower energy than the near infrared (NIR) region (12-40 kcal mol^{-1}), both kinds of sources furnish comparable quantitative yields in excellent reaction time (15 min *vs.* 20 min) regardless of the nature of the emission peak and temperature of reaction implemented (*viz.*, $^{150}\lambda_{1.5-3.0 \, µm}$ *vs.* $^{180}\lambda_{1.1 \, µm}$). Furthermore, it was found that stereoelectronic effects normally associate with the position and nature (electron-withdrawing, EW or electron-donating, ED) of the groups attached to the aromatic ring of the aldehyde do not exert a paramount effect on the rate of the condensation reaction or the overall yield of the products (see Table 1, entries 3 *vs.* 6). It is also worth highlighting that in the case of the bifunctionalized substrate **10**, the reaction proceeds under regioselective control to furnish compound **17** as the major product. Only traces of 1,4-bis(di(1*H*-indol-3-yl)methyl)benzene **17a** was identified as by-product. These outcomes suggest that the overall process depends on a restricted transition state and the stoichiometric ratio implemented.[23] This preliminary conclusion was drawn

Table 1. Comparative results of the assembly of the phenylbisindolylmethanes **13-19** fostering by Osram IR heater lamp and Flavor-Wave® oven

| entry | Product | Yield / % | | | mp exp. (lit.)[c] / °C |
		$^{150}\lambda_{1.5-3µm}$[a]	$^{180}\lambda_{1.1µm}$[b]	$^{180}\lambda_{1.1µm(Lit)}$[c]	
1	**13**	72	76	75	142-144 (125-127)
2	**14**	83	85	70	196-198 (83-85)
3	**15**	88	80	70	211-213 (191-193)
4	**16**	89	82	55	165-167 (166-168)
5	**17**	88	88	85	253-256 (203-204)
6	**18**	80	86	96	211-213 (221-223)
7	**19**	93	79	93	161-163 (265-266)

[a]Reaction condition implemented with Flavor-Wave® oven (method b): indole (8.54 mmol), benzaldehyde (4.27 mmol) and 4 g of TAFF were reacted for 20 min at 150 ± 2 °C. [b]Reaction condition implemented with IR heater lamp (method a): ran as above, except for a shorter time (15 min) and a higher reaction temperature (180 °C).[27] [c]Literature yield/mp, see references 27 and 28. λ: wavelength; mp: melting point; exp.: experimental; lit.: literature.

considering that 1,4-phenylenebis((1*H*-indol-3-yl)methanol) **I** was not detected as a side-product during the course of the reaction. However, its validation needs further experimental or theoretical support.

After a precise analysis of the existing literature on the subject, it was found that Brønsted-Lowry (BLAS) intrinsic acid sites and the Lewis base sites (LBS) have been invoked as the driving force of chemical transformation (Scheme 1).[29] The rationale behind this approach suggests that the effectiveness of TAFF bentonitic clay as an acid catalyst is highly dependent on the BLAS[30] and, to a lesser extent, on the LBS. Thus, they can activate the C=O function through their interaction with BLAS as outlined in Scheme 1-**II**. In such a way that the establishment of the hydrogen bond (HB) leads to a decrease in its lowest unoccupied molecular orbital (LUMO) energy to enable the nucleophilic addition of the π-excessive partner (indole) in the electrophilic position of the C−O sp^2 bond, while protonates the carbonyl oxygen atom (Scheme 1-**III**). Most prominently, this premise leads to the assumption that the incipient cationic intermediate **III** goes through a highly stabilized transition state as a result of the further formation of HB's and the development of ion-dipole interactions between the negatively charged tetrahedral sheet of the montmorillonite[31] (Scheme 1a) and the positive transient charge that is a lodge in the nitrogen atom. The conclusion drawn from these assumptions is that the

thermodynamically stable alcohol **IV**, di(1*H*-indol-3-yl) (phenyl)methanol, evolves from the rearomatization of the species **III** through the removal of the proton H3 of the indolyl moiety by interplay with the LBS, undergoes a restricted conformation due to its propensity to form an additional 5-membered ring intramolecular C−H/π interaction (edge-to-face staking geometry, 0.5-2.5 KJ mol^{-1}).[32-34] However, its subsequent activation by interaction with BLAS leads it to undergo further nucleophilic reaction with another indole partner which accounts for the obtention of the three-component product along with H$_2$O as a byproduct and ultimate isolation of the reusable natural catalyst after simple work-up.

In this regard, in contrast with the overall promotion reaction, when comparing the two domestic approaches performance, this survey reveals that the Flavor-Wave® oven surpasses the IR heater lamp performance, thanks to its capacity to undertake batchwise reactions, up to 16 reactions in parallel (**20**-**31**, Figure 3) without detriment to the efficiency of the reaction (60-94%). Noteworthy is the fact that, for the preparation of the diversely decorated heteroarenebisindolylmethanes skeleton (**26**-**30**), the utilization of π-excessive and π-deficient heteroarenecarbaldehyde substrate did not substantially undermine the overall yield of the reaction (60-85%).

In this connection, to assess a possible synergistic effect derived from the combinatorial effect of IR irradiation
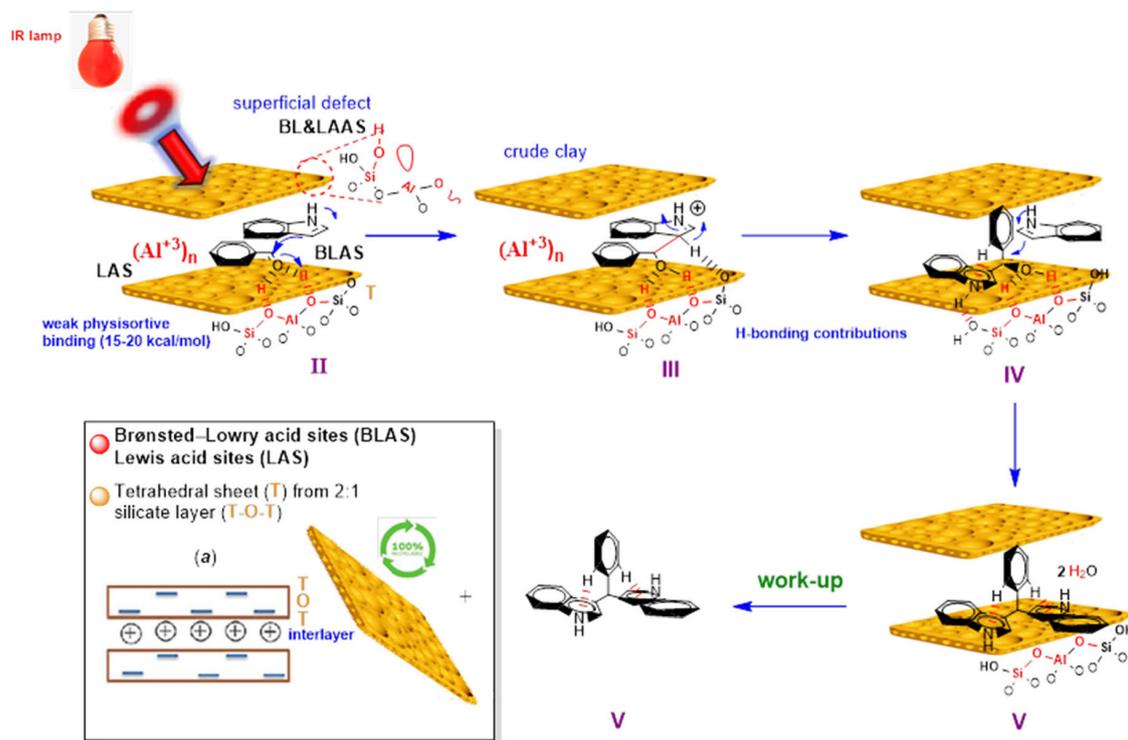
Scheme 1. Outline of the proposed mechanism for the formation of arenebisindolylmethanes using TAFF bentonitic clay as Brønsted-Lowry acid catalyst and a thumbnail sketch of the structure of montmorillonite (a) highlighting the negatively charged tetrahedral sheet.
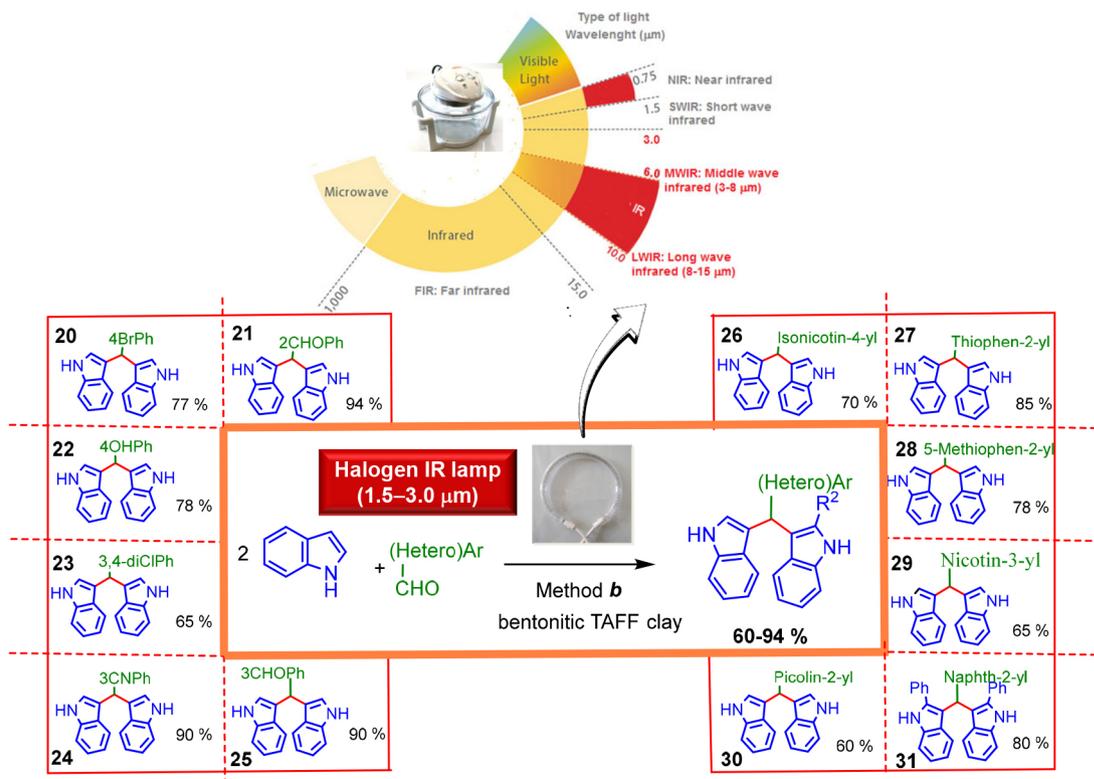
Figure 3. The one-pot reaction in the inset shows the general reaction foster by the tungsten filament lamp (shown) using Flavor-Wave® oven as an infrared reactor and its general assessment to carry out the batch-wise organic reaction.

sources and solar radiation that leaks into the reaction flask, as well as plausible effects induced by cations (K^+ and Na^+) other than the BLAS and LAS that could impair TAFF-catalyzed reactions with aromatic substrates, three model reactions (Scheme 2a, inset box, entries 1a, 3a, and 6a) was examined under darkness conditions (covered setting) and under normal laboratory lights conditions (on the laboratory bench, uncovered setting) with or without using a catalyst, and a combination thereof. The findings and their rationalization are outlined in Scheme 2.

Notably, the suppression of scattered natural sunlight ($\lambda = 0.38\text{-}2.5$ µm) incident on the reaction flask causes a marked detriment to the reaction efficiency by up to 50%, regardless of the type of IR energy source used, while the reactivity trend that appears to be modulated by electron donating group (EDG-) and EDG-induced electronic effects remains unchanged. Furthermore, as expected, worse results (up to 69% reduction) were obtained in the dark in the absence of TAFF clay (Scheme 2a, inset box). These outcomes were very similar to the yields
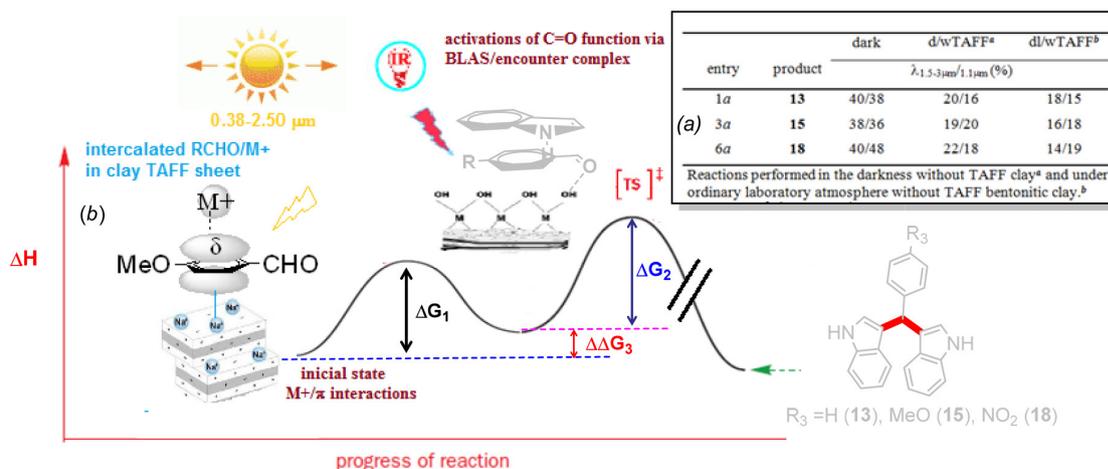
Scheme 2. (a) The results of experiments conducted under diverse controlled conditions are shown in box. (b) Schematic representation of the energy profile of the DIM reaction showing stabilization of the M+/π-interaction of the reagents and encounter offset staked complex of the reagents.

of the reactions promoted in absence of TAFF clay on the laboratory bench, whereas these reactions that were carried out in the darkness and on the laboratory bench without IR energy supply give no product. However, only traces of products were observed by TLC after their reaction for ten days at room temperature.

The discrepancy of the observed results between the covered and uncovered reactions was rationalized by postulating the formation of stabilized cation (M+)/π-interactions[35] in the initial state of the (aza)aromatic reagents with alkali cations (Scheme 2b) that are part from the natural composition of TAFF clay,[30,36] whose magnitude can be even as strong as non-covalent interactions as indicated by the experimental binding energy determined for the alkali metals/benzene complex: 38.3 (Li^+) > 28.0 (Na^+) > 19.2 kcal mol^{-1} (K^+).[37-40] This binding strength suggests that electrostatic control plays a pivotal role in the formation of the complex. Consequently, the more stable the M^+/π-complex formed, the higher is the activation energy required to the forward reaction (Gibbs free energy, $\Delta\Delta G_2 + \Delta G_3$, Scheme 2b).[41] This condition seems to be fulfilled in dark conditions, it is also clear that its stability is enhanced by R+ electronic contributions of the substituents, as indicated by the highest yield drops (50%) observed with phenyl substrates bearing EDG MeO- which contrasts with electron withdrawing groups (EWG)–NO_2 (40%). On the contrary, the uncovered reacting mixture benefits from the blending of heating waves IR (51%), Vis (47%), and UV (2%) that reach the reactor[42] with enough energy to destabilize the M^+/π-interaction in the initial state of the reagents. The absorption of energy fosters the formation of an encounter offset staked complex while triggering the

physisorption interactions with the BLAS that, ultimately, favor the activation of the forward reaction. Thereby, the ability of daylight to perturb the initial M^+/π-complex reduces the activation energy by an amount of $\Delta\Delta G_2$ and accelerates the forward condensation reaction to give higher reaction efficiency. Overall, chemical or physical factors that impair the stabilization of the encounter complex between the aromatic reagents lead to a decrease in the reaction rate; in contrast, if they perturb the electrostatic stabilization of the M^+/π-interaction of the initial state of the reagents, they accelerate the chemical reaction.

In an attempt to support the M^+/π-interactions formation hypothesis, as control experiments, we assessed the uncovered model reactions by replacing the TAFF clay catalyst with *p*-toluenesulfonic acid and EtOH to favor the formation of the encounter complex, based on its inability to form the M^+/π-interactions of the reagents in the initial state in protic polar medium without alkali cations. The yields of products **13**, **15**, and **18** obtained after ten days of reaction at room temperature were excellent (75%), contrasted results with the use of TAFF clay as catalyst (0%). Based on this observation, it is rational to propose that cation/π-interactions play an important role in the efficiency of the reactions that involve the use of aromatic reagents.

Given the results achieved, it was of particular concern for us to examine the scope and limitations of the infrared reaction about the more sterically hindered indole substrates supported on TAFF clay (Figure 4). Noteworthy, the sterically demanding building blocks **32**-**34** bearing Me− and Ph− groups either on N1 or C2 positions afford excellent yields as compared to the unsubstituted substrate. Despite this, the outcomes gathered in Figure 4 show that
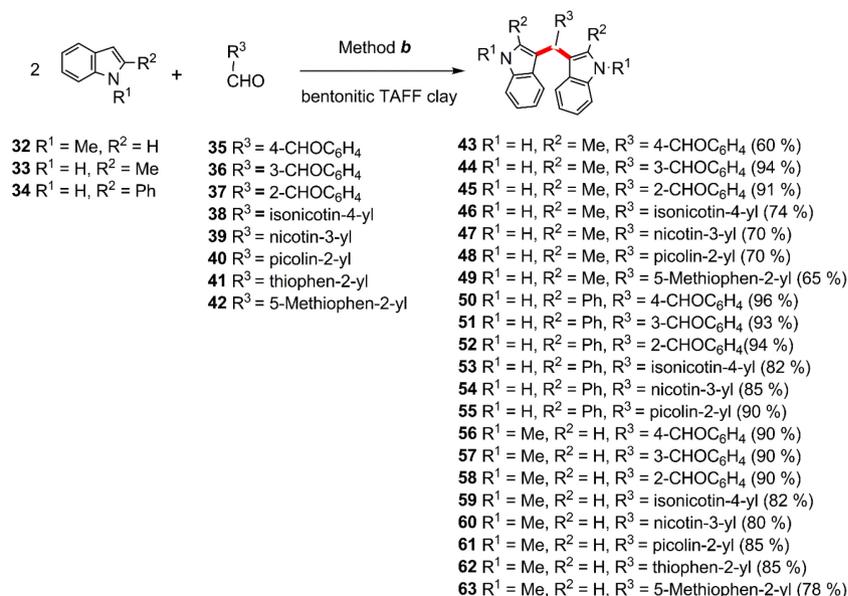

32 R^1 = Me, R^2 = H
33 R^1 = H, R^2 = Me
34 R^1 = H, R^2 = Ph

35 R^3 = 4-$CHOC_6H_4$
36 R^3 = 3-$CHOC_6H_4$
37 R^3 = 2-$CHOC_6H_4$
38 R^3 = isonicotin-4-yl
39 R^3 = nicotin-3-yl
40 R^3 = picolin-2-yl
41 R^3 = thiophen-2-yl
42 R^3 = 5-Methiophen-2-yl

43 R^1 = H, R^2 = Me, R^3 = 4-$CHOC_6H_4$ (60 %)
44 R^1 = H, R^2 = Me, R^3 = 3-$CHOC_6H_4$ (94 %)
45 R^1 = H, R^2 = Me, R^3 = 2-$CHOC_6H_4$ (91 %)
46 R^1 = H, R^2 = Me, R^3 = isonicotin-4-yl (74 %)
47 R^1 = H, R^2 = Me, R^3 = nicotin-3-yl (70 %)
48 R^1 = H, R^2 = Me, R^3 = picolin-2-yl (70 %)
49 R^1 = H, R^2 = Me, R^3 = 5-Methiophen-2-yl (65 %)
50 R^1 = H, R^2 = Ph, R^3 = 4-$CHOC_6H_4$ (96 %)
51 R^1 = H, R^2 = Ph, R^3 = 3-$CHOC_6H_4$ (93 %)
52 R^1 = H, R^2 = Ph, R^3 = 2-$CHOC_6H_4$ (94 %)
53 R^1 = H, R^2 = Ph, R^3 = isonicotin-4-yl (82 %)
54 R^1 = H, R^2 = Ph, R^3 = nicotin-3-yl (85 %)
55 R^1 = H, R^2 = Ph, R^3 = picolin-2-yl (90 %)
56 R^1 = Me, R^2 = H, R^3 = 4-$CHOC_6H_4$ (90 %)
57 R^1 = Me, R^2 = H, R^3 = 3-$CHOC_6H_4$ (90 %)
58 R^1 = Me, R^2 = H, R^3 = 2-$CHOC_6H_4$ (90 %)
59 R^1 = Me, R^2 = H, R^3 = isonicotin-4-yl (82 %)
60 R^1 = Me, R^2 = H, R^3 = nicotin-3-yl (80 %)
61 R^1 = Me, R^2 = H, R^3 = picolin-2-yl (85 %)
62 R^1 = Me, R^2 = H, R^3 = thiophen-2-yl (85 %)
63 R^1 = Me, R^2 = H, R^3 = 5-Methiophen-2-yl (78 %)

Figure 4. Synthesis of (hetero)arenebisindolylmethanes bearing sterically demanding group either on N1 or C2 of the indolyl motif.

the efficiency of the reaction depends to a minor extent on the nature of the aldehyde substrate used as well as the position of the bulky substituent.

Overall, promoting of C–Cπ bond construction reaction within the short wave IR region comprised of $\lambda_{1.5–3\,\mu m}$ proves to be as efficient as the near IR light with an emission peak of $\lambda_{1.1\,\mu m}$. Therefore, this less energetic wavelength light emerges as an efficient synthetic tool with potential application in the field of organic chemistry. Exactly how this thermal wave speeds up the overall rate of reaction remains to be disclosed and is beyond the scope of the present evaluation. However, its use should be encouraged in the future, to gain an in-depth understanding of the phenomenon, as well as to improve the design, manufacture, and efficiency of chemical devices intended to be applied in future synthetic transformations.

Conclusions

Structurally simple and sterically demanding (hetero) arenebisindolylmethanes were successfully assembled under short-wave IR light using Flavor-Wave® oven as a novel integrated technology in presence of bentonitic TAFF clay as Brønsted-Lowry acid catalyst. The excellent yields and short time of reaction obtained under solventless conditions via the one-pot reaction, in addition to the outstanding regioselectivity observed with bifunctionalized substrates as well as its capacity to perform multiple reactions in parallels, highlight its potential application not only in the straightforward C–Cπ bond formation but also in the construction of more elaborated molecules.

Supplementary Information

Supplementary information (IR, HRMS, and NMR ^{1}H and ^{13}C spectra) is available free of charge at http://jbcs.sbq.org.br as a PDF file.

Acknowledgments

Author Contributions

Hulme Ríos-Guerra was responsible for writing-original draft; Guillermo Penieres-Carrillo for formal analysis, funding acquisition; Francisco Barrera-Téllez for data curation; Alejandro Martínez-Záldivar for validation; Javier Pérez-Flores for formal analysis; Adrian Ricardo Hipólito-Nájera for methodology; Ricardo Alfredo Luna-Mora for investigation and supervision.

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