Structure and Reactivity of Indolylmethylium Ions: Scope and Limitations in Synthetic Applications

*Elsa Follet, Guillaume Berionni, Peter Mayer, and Herbert Mayr**

Department Chemie,

Ludwig-Maximilians-Universität München,

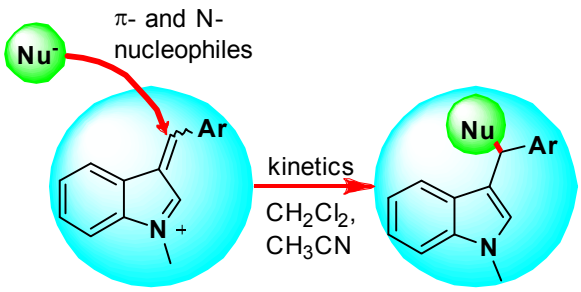
Butenandtstrasse 5–13, Haus F, 81377 München (Germany).

Fax: (+49) 089 2180 77717

Phone: (+49) 089 2180 77719

E-mail: herbert.mayr@cup.uni-muenchen.de

ABSTRACT



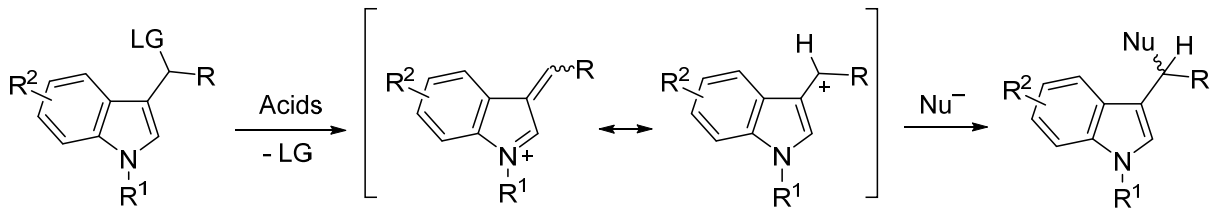
Eight substituted aryl(indol-3-yl)methylium tetrafluoroborates **3(a-h)-BF$_4$** and three bis(indol-3-yl)methylium tetrafluoroborates **3(i-k)-BF$_4$** have been synthesized and characterized by NMR spectroscopy and X-ray crystallography. Their reactions with π-nucleophiles **8(a-j)** (silylated enol ethers, and ketene acetals) were studied kinetically using photometric monitoring at 20 °C. The resulting second-order rate constants were found to follow the correlation log *k* (20 °C) = $s_N(N + E)$, in which nucleophiles are characterized by the two solvent-dependent parameters *N* and s_N, and electrophiles are characterized by one parameter, *E*. From

the previously reported *N* and s_N parameters of the employed nucleophiles, and the measured rate constants, the electrophilicities of the indol-3-ylmethylium ions **3(a-k)** were derived and used to predict potential nucleophilic reaction partners. A discrepancy between published rate constants for the reactions of morpholine and piperidine with the (2-methylindol-3-yl)phenylmethylium ion **3h** and that calculated from *E*, *N* and s_N was analyzed and demonstrated to be due to a mistake of the value reported in the literature.

INTRODUCTION

Indolyl-substituted carbenium ions have recently been employed as prochiral intermediates in asymmetric Diels-Alder reactions,[1] Friedel-Crafts reactions,[2,3a] additions to aliphatic π-systems,[3] α-alkylations of aldehydes and other CH acidic compounds,[4] hydrogenation reactions,[5] and other asymmetric syntheses.[6] They are commonly generated by treatment of readily available precursors with Brønsted or Lewis acids (Scheme 1), and subsequently trapped by hydride donors, organometallic reagents, and other nucleophiles to give a wide variety of functionalized indole derivatives.[1-6]

Scheme 1. *In situ* Generation and Trapping of Aryl(indol-3-yl)methylium Ions with Nucleophiles



Leaving Group = SO_2Ar, Cl, OH, NR_2

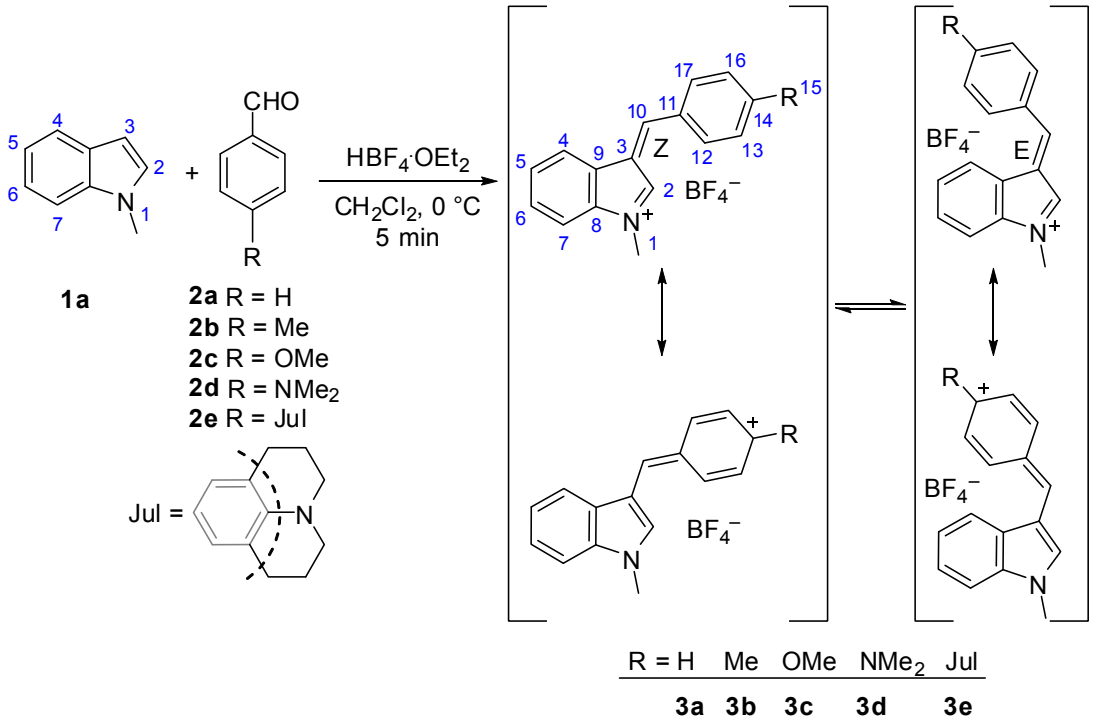
While some electron-donor substituted aryl(indol-3-yl)methylium ions (Scheme 1, R = Ar) have previously been characterized in solution and in the solid-state[7] and have been used as dyes,[7c-g] quantitative information about their electrophilic reactivity is rare. Apart from investigations of their Lewis acidities (pK_{R^+}),[8a-c] we are aware of only one kinetic investigation of their reactions with amines and hydride nucleophiles.[8d]

In order to evaluate the scope and limitations of their reactions with nucleophiles we have now quantified the electrophilicities of aryl(indol-3-yl)methylium ions using a method analogous to that which we have used previously for quantifying the electrophilicity of a large number of iminium and carbenium ions. These results have then been integrated into a comprehensive electrophilicity scale.[9a-f,10]

RESULTS AND DISCUSSION

Synthesis of Aryl(indol-3-yl)methylium Ions. Substituted aryl(indol-3-yl)methylium tetrafluoroborates **3(a-e)-BF$_4$** were obtained in good yields in a one-pot procedure by adding 1.5 equivalent of $HBF_4 \cdot OEt_2$ to 1:1-mixtures of *N*-methylindole **1a** and one of the benzaldehydes **2a-e** in CH_2Cl_2 solution (Table 1). An optimization of these reaction conditions has recently been reported and used to synthetise a large variety of diarylmethylium tetrafluoroborates, including several indolyl-substituted systems.[7b] The mechanism of the formation of **3** has been reported previously.[6c] Whereas the less stabilized aryl(indol-3-yl)methylium tetrafluoroborates **3(a-c)-BF$_4$** decomposed within few hours at ambient temperature, **3(d-e)-BF$_4$** did not change when stored in ordinary atmosphere for a year.

Table 1. Syntheses, Structures, Yields, Visible-Absorption Maxima λ_{max}, and Molar Absorbances ε of the Aryl(*N*-methylindol-3-yl)methylium Tetrafluoroborates 3(a-e)-BF_4

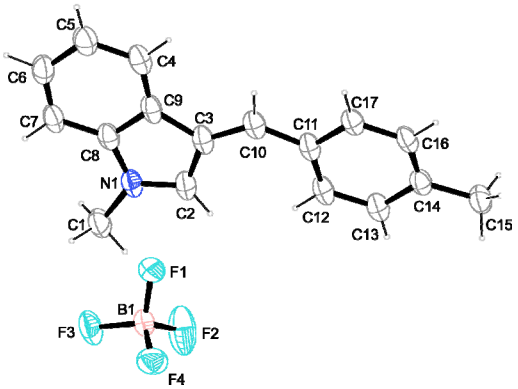


R	Aldehyde	Indolylmethylium ions	Isolated yields (%)	λ_{max} (nm) in CH_2Cl_2	ε (L mol^{-1} cm^{-1}) in CH_2Cl_2	*Z*:*E* ratio in CD_2Cl_2	
						exp.[a]	calcd.[b]
H	**2a**	**3a**	36	425	2.34×10^4	75:25[c]	73:27
Me	**2b**	**3b**	79	431	2.81×10^4	77:23[c]	82:18
OMe	**2c**	**3c**	60	492	2.84×10^4	78:22[c]	88:12
NMe_2	**2d**	**3d**	57	580	8.88×10^4	> 99:1	97:3
Jul	**2e**	**3e**	68	589	9.22×10^4	> 99:1	99.8:0.2

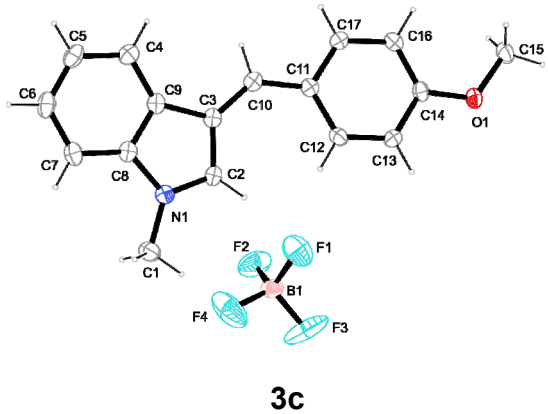
[a] Determined by ^{1}H NMR at 27 °C. [b] Calculated at the B3LYP/6-31G(d) DFT level in CH_2Cl_2 for the tetrafluoroborate salts see details in the Supporting Information. [c] The *Z*/*E* ratio in CD_3CN was for **3a**: 83/17, for **3b**: 85/15, and for **3c**: 87/13.

Most known aryl(indol-3-yl)methylium ions are substituted at C2; because of the steric repulsion between the C2 substituent and the aryl ring, they generally adopted the (*E*)-configuration as revealed by NMR spectroscopy and X-ray crystallography.[7a-b,d-e] In contrast, the carbenium ions **3a-c**, which are unsubstituted at C2, give a ≈ 3:1 (*Z*:*E*) diastereomeric mixture in CD_2Cl_2 and a ≈ 5:1 mixture in CD_3CN at 27 °C. The predominant (*Z*)-configuration of **3c** was derived from a NOE effect observed between 2-H and 12-H and 17-H (Table 1). The (*Z*):(*E*) ratio of **3c** is almost independent of temperature. Between +27 °C and -80 °C in CD_2Cl_2, the (*Z*):(*E*) ratio changes from 78:22 to 86:14 and between +27 °C to +60 °C in CD_3CN, the (*Z*):(*E*) ratio changes from 87:13 to 83:17 (see SI S39-41).

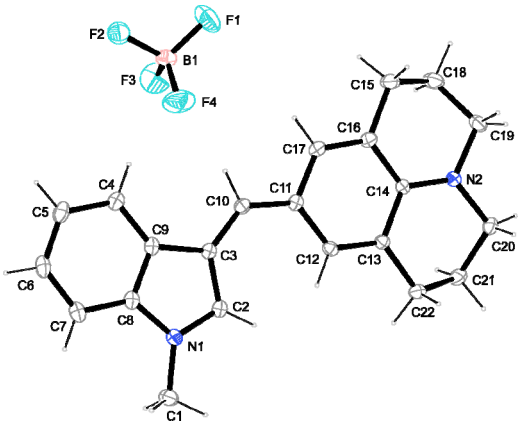
DFT calculations of the tetrafluoroborate salts showed that the (*Z*)-isomers have smaller dipole moments than the (*E*)-isomers, and are more stable by several kJ mol^{-1} (see SI S33). As the (*Z*):(*E*) ratio increases with increasing electron-donating substituents in the phenyl ring (Table 1), only the (*Z*)-isomers of **3d-e** were observed by ^1H NMR in CD_2Cl_2. The (*Z*)-isomers crystallized preferentially as shown by the X-ray structures of the aryl(indol-3-yl)methylium ions **3b**, **3c**, and **3e** (Figure 1).[11]



3b



3c



3e

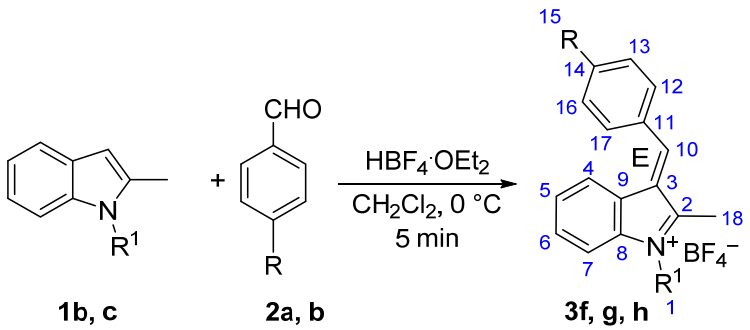
Figure 1. ORTEP drawings (50% probability ellipsoids) of the (*Z*)-aryl(indol-3-yl)methylium tetrafluoroborates **3b-BF$_4$**, **3c-BF$_4$**, **3e-BF$_4$**. Selected interatomic distances (Å) and angles (°) for **3b**: N1–C2 = 1.311(3), C2–C3 = 1.432(3), C3-C10 = 1.365(3), C10–C11 = 1.439(3) and N1–C2–C3 = 110.0(2), C2–C3–C10 = 130.7(2), C3–C10–C11 = 133.2(2), C2–C3–C10–C11 = 2.9(4), C3–C10–C11–C12 = 5.7(3). For **3c**: N1-C2 = 1.319(3), C2-C3 = 1.430(3), C3-C10 = 1.373(3), C10-C11 = 1.430(3), N1-C2-C3 = 110.19(18), C2-C3-C10 = 130.64(19), C3-C10-C11 = 132.8(2), C2–C3–C10–C11 = -3.1(4), C3–C10–C11–C12 = -6.2(4). For **3e**: N1-C2 = 1.339(3), C2-C3 = 1.408(3), C3-C10 = 1.395(3), C10-C11 = 1.404(3), N1-C2-C3 = 110.53(17), C2-C3-C10 = 130.58(18), C3-C10-C11 = 132.77(19), C2–C3–C10–C11 = 1.0(4), C3–C10–C11–C17 = -179.7(2).[11]

According to the X-ray structures shown in Figure 1, the molecules are almost planar, with dihedral angles between the aryl ring and the indole ring of less than 10 degrees. The considerably shorter bond length C3-C10 (1.37 Å) compared to C10-C11 (1.43 - 1.44 Å) shows that the positive charge is more stabilized by the indole ring than the aryl ring in the case of **3b** and **3c**, as represented by the upper resonance structures in Table

1. However, in the case of the -Jul substituted indolylmethylium ion **3e**, the increasing stabilizing effect of the anilino ring is indicated by the similar C3-C10 and C10-C11 bond lengths (1.400 ± 0.005 Å) (Figure 1c). As a consequence of the increased double-bond character between C10 and C11, the rotation around this bond is restricted, as revealed by a distinct resonances for the 12-H and 17-H signals in the 400 MHz ^{1}H NMR spectra below -20 °C (**3d**) and +25 °C (**3e**) (see Supporting Information pp S40 and S43). Analogous dynamic effects were not observed in the ^{1}H NMR spectra of **3a-c** and there was no evidence for the interconversion of the (*Z*)- and (*E*)-isomers on the NMR time scale.

In agreement with a recently published X-ray structure by Barbero et al.,[7a-b] and subsequent NMR investigations of related compounds,[7b] the aryl(indol-3-yl)methylium ions **3f**-**h** with a methyl group at C2 of the indole ring were formed exclusively as the (*E*)-isomers (Table 2) from the 2-methyl substituted indoles **1b**-**c**. DFT calculations showed that even in case of the julolidyl substituted analogue (2-methyl derivative of **3e**) the (*E*)-isomer is more stable than the (*Z*)-isomer by 18.7 kJ mol^{-1}, i.e. the steric repulsion by the 2-methyl group is so large that now the isomer with the larger dipole moment is preferred.

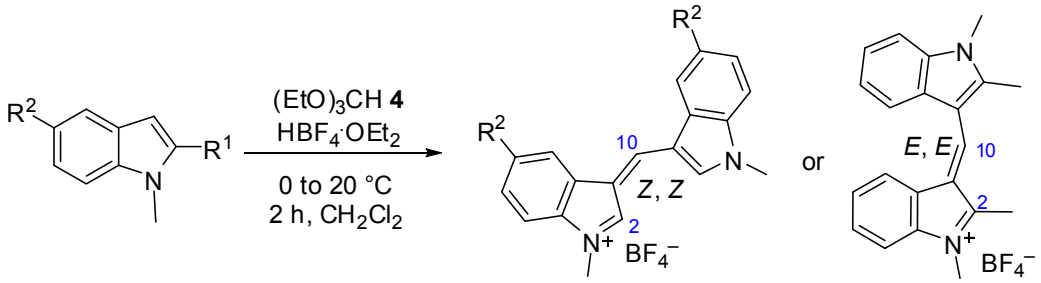
Table 2. Syntheses, Structures, Yields, Visible-Absorption Maxima λ_{max} and Molar Absorbances ε of the Aryl(indol-3-yl)methylium Tetrafluoroborates 3(f-h)-BF_4



R^1	Indole	R	Aldehyde	Indolylmethylium ions	Isolated yields (%)	λ_{max} (nm) in CH_2Cl_2	ε (L mol^{-1} cm^{-1}) in CH_2Cl_2
H	**1b**	Me	**2b**	**3f**	71	417	2.15×10^4
Me	**1c**	Me	**2b**	**3g**	88	425	2.28×10^4
Me	**1c**	H	**2a**	**3h**	84	405	-

The bis(indol-3-yl)methylium tetrafluoroborates **3(i-k)-BF_4** were synthesized from the indoles **1** and triethyl orthoformate **4** following the procedure of Pindur et al.[12] as shown in Table 3.

Table 3. Syntheses, Structures, Yields, Visible-Absorption Maxima λ_{max} and Molar Absorbances ε of the Symmetrical Bis(indol-3-yl)methylium Tetrafluoroborates 3(i-k)-BF_4

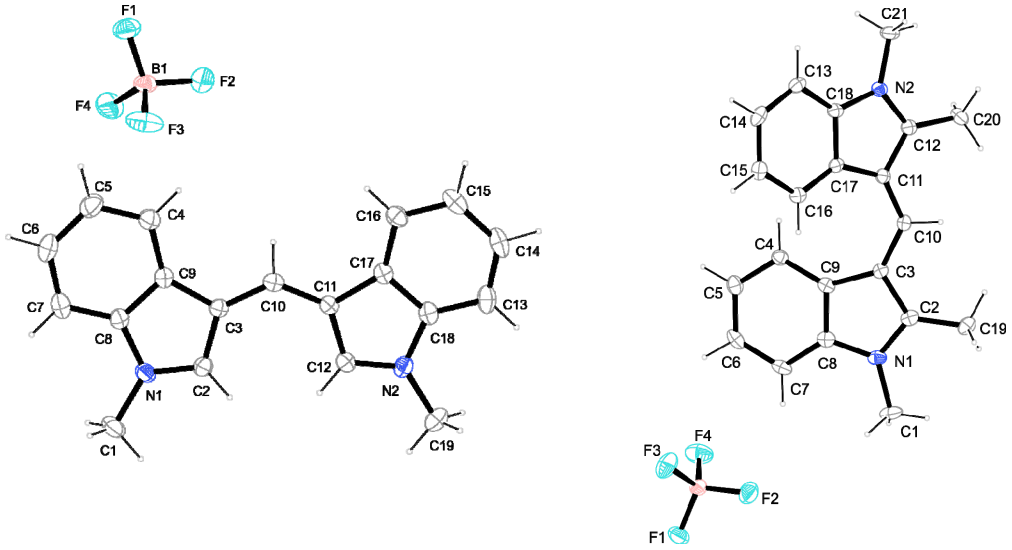


1a, c, d **3 i, j** **3k**

R^1	R^2	Indole	Indolylmethylium ions	Isolated yields (%)	λ_{max} (nm) in CH_2Cl_2	ε (L mol^{-1} cm^{-1}) in CH_2Cl_2
H	H	**1a**	**3i**	86	540[a]	4.87×10^{4}[a]
H	OMe	**1d**	**3j**	69	540[a]	2.39×10^{4}[a]
Me	H	**1c**	**3k**	74	497	5.33×10^{4}

[a] 5% (v/v) of CH_3CN was added for full solubilization of **3i** and **3j**.

The X-ray structures of the bis(indol-3-yl)methylium ions **3i** and **3k** depicted in Figure 2 illustrate that a methyl group at C2 of the indole rings induces a change of configuration. Whereas the 2-unsubstituted indole-derivative **3i** is almost planar with a twist angle of 7.21° between the two indole planes and adopts the (*Z*,*Z*)-configuration, the bis-methylated derivative **3k** adopts the *(E*,*E*)-configuration and has an indole-indole twist angle of 42.57°.



3i **3k**

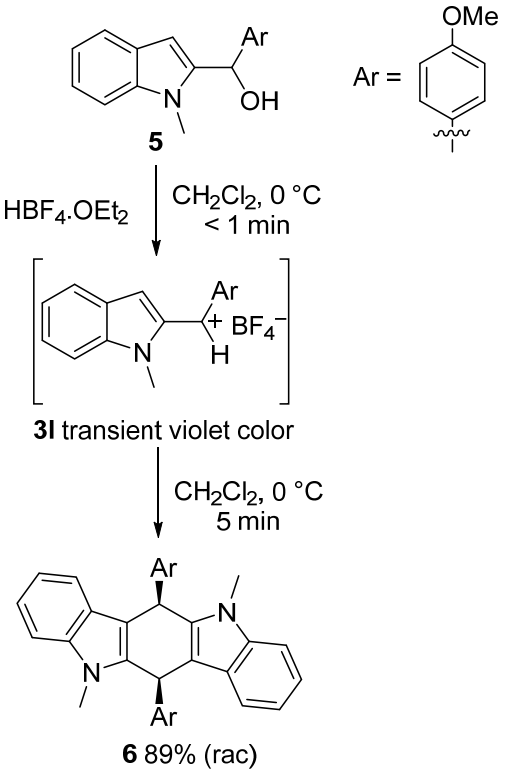
Figure 2. ORTEP drawing (50% probability ellipsoids) of the bis(indol-3-yl)methylium tetrafluoroborates **3i-BF$_4$** and **3k-BF$_4$**.[11] Selected interatomic distances (Å) and angles (°) for **3i**: N1-C2 = 1.329(2), C2-C3 = 1.410(2), C3-C10 = 1.391(2), C10-C11 = 1.392(2), N1-C2-C3 = 110.39(13), C2-C3-C10 = 130.09(14), C3-C10-C11 = 131.49(14), C2–C3–C10–C11 = 2.6(3), C3–C10–C11–C12 = 2.1(3). For **3k**: N1-C2 = 1.343(2), C2-C3 = 1.425(2), C3-C10 = 1.397(2), C10-C11 = 1.394(2), N1-C2-C3 = 109.02(14), C2-C3-C10 = 121.82(15), C3-C10-C11 = 130.37(14), C2–C3–C10–C11 = -162.78(16), C3–C10–C11–C12 = -160.44(16).

We also attempted to synthesize the indol-2-yl(*p*-methoxyphenyl)methylium ion **3l** from the alcohol **5**, as shown in Scheme 2. Dropwise addition of $HBF_4 \cdot OEt_2$ to a solution of the *p*-anisyl(indol-2-yl)methanol **5** in CH_2Cl_2 at 0 °C produced a deep violet solution, attributed to **3l**, which faded spontaneously. After 5 min the pentacyclic compound **6** precipitated as a colorless solid. The inverse addition of a CH_2Cl_2 solution of **5** to an

equimolar amount of $HBF_4 \cdot OEt_2$ dissolved in CH_2Cl_2 also produced a transient violet species which yielded **6**, and we did not succeed to isolate **3l**.

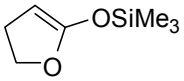
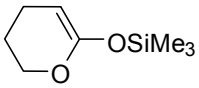
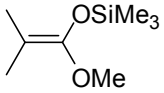
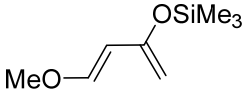
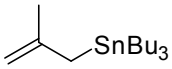
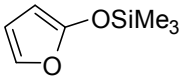
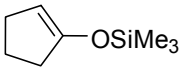
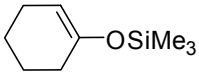
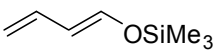
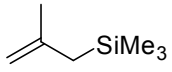
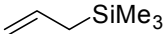
Only one diastereoisomer of **6** was formed and we were not able to assign its configuration. The acid-catalyzed cyclization of aryl(indol-2-yl)methanols has been previously reported by Santoso et al.[13] to give pentacyclic dihydro-indolo[3,2-b]carbazoles analogous to **6** with cis configuration (X-ray analysis). We, therefore, assume that the phenyl groups in product **6** also are in cis configuration.

Scheme 2. Attempted Synthesis of the *p*-Anisyl(indol-2-yl)methylium Tetrafluoroborate 3l-BF_4 and Formation of the Dihydro-indolo[3,2-b]carbazole 6



Product Studies. For the quantification of the electrophilic reactivities of indolylmethylium ions **3a-k** we have studied their reactions with representative π-nucleophiles of known nucleophilicity (Table 4).

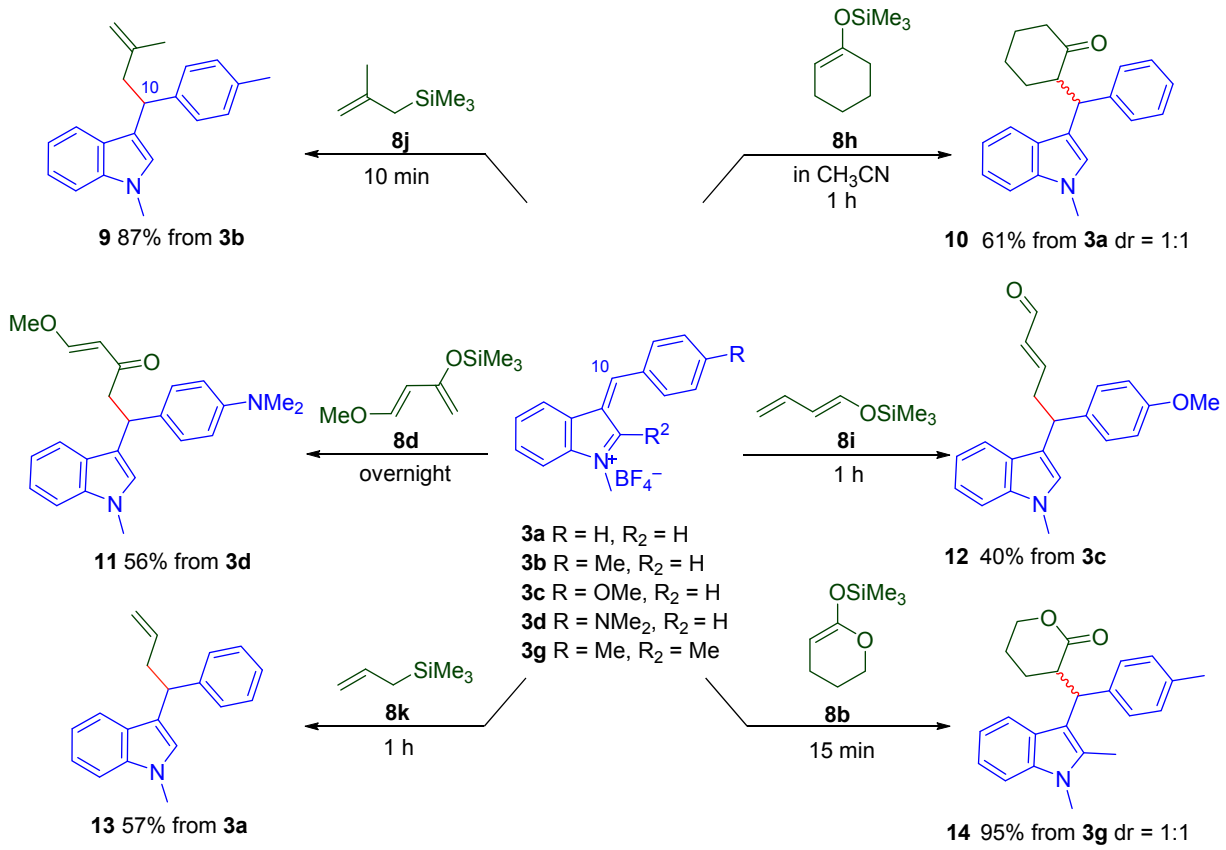
Table 4. π-Nucleophiles 8 Employed as Reference Compounds for the Determination of the Electrophilicity of the indolylmethylium Ions 3a-k

Nu	Structure	*N* (s_N)[a] in CH_2Cl_2
8a		12.56 (0.70)
8b		10.61 (0.86) 10.52 (0.78)[b]
8c		9.00 (0.98) 9.11 (0.88)[b]
8d		8.57 (0.84)
8e		7.48 (0.89)
8f		7.22 (1.00)
8g		6.57 (0.93)
8h		5.21 (1.00)
8i		4.60 (0.90)
8j		4.41 (0.96)
8k		1.68 (1.00)

[a] Nucleophilicity parameters *N* and nucleophile-specific sensitivity parameters s_N for **8a**-**k** from ref. 9f. [b] In CH_3CN.

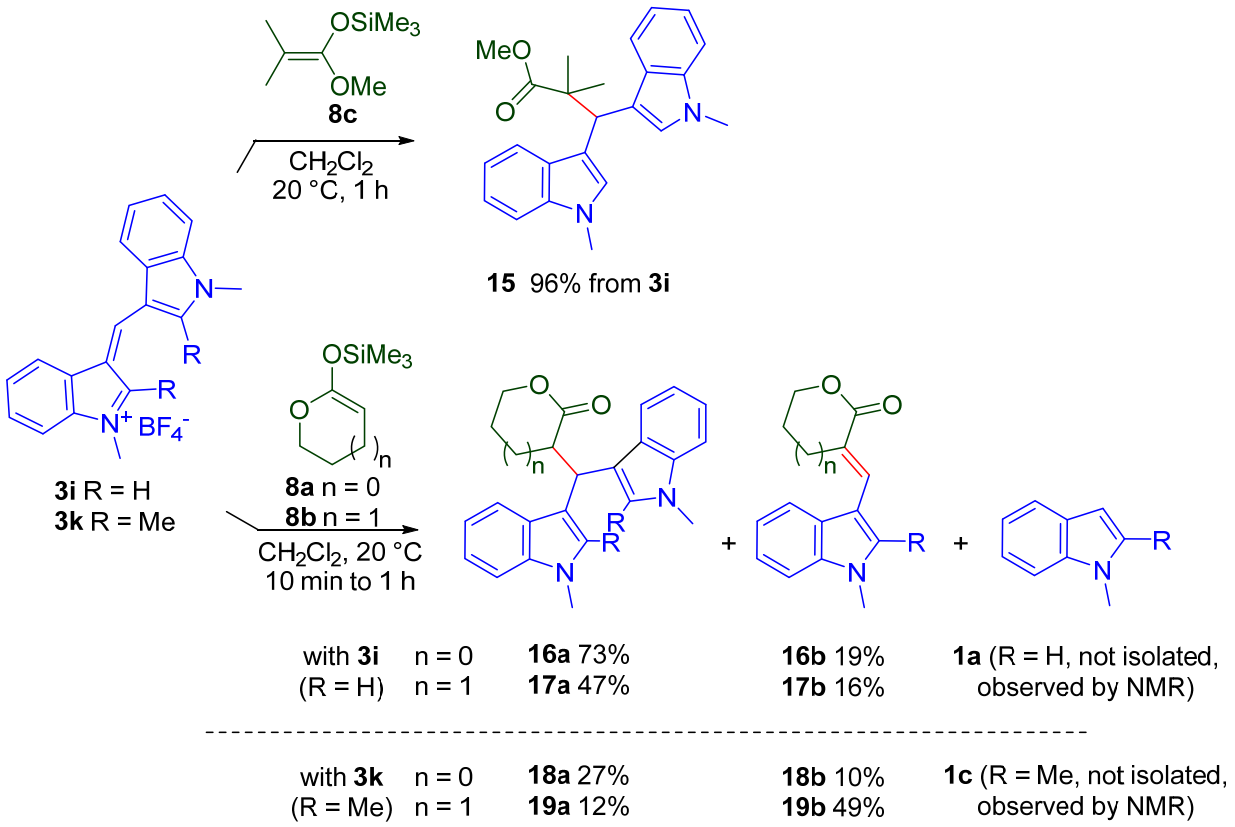
As depicted in Scheme 3 for a series of representative combinations of aryl(indol-3-yl)methylium ions **3** with π-nucleophiles **8**, all reactions occurred regioselectively at the 10 position of **3,** but were not diastereoselective when prochiral π-nucleophiles **8b**,**h** were used.[14] Reactions of aryl(indol-3-yl)methylium ions **3** with electron-rich dienes, such as Danishefsky´s diene **8d** and 1-(trimethylsiloxy)buta-1,3-diene **8i,** yielded the α,β-unsaturated compounds **11** and **12**, respectively.

Scheme 3. Reactions of Representative π-Nucleophiles 8 with Aryl(indol-3-yl)-methylium Tetrafluoroborates 3-BF_4 (in CH_2Cl_2 at 20 °C)



The reactions of π-nucleophiles with the bis(indol-3-yl)methylium ions **3i**,**k** sometimes followed a different pattern, as shown for the silyl enol ethers **8a**-**c** (Scheme 4).[12]

Scheme 4. Reactions of Bis(indol-3-yl)methylium Ions 3i,k with Silyl Enol Ethers 8a-c



Whereas the reaction of the bis(indol-3-yl)methylium ion **3i** with the ketene acetal **8c** gave the expected product **15** in high yield, the reactions of **3i**,**k** with the cyclic ketene acetals **8a-b** gave a mixture of the analogously formed products (**16-19**)**a**, accompanied by the alkylidene lactones (**16-19**)**b** and the indoles **1a,c**. Single crystals of **19b** were obtained, and the X-ray diffraction analysis confirmed its *(E)*-configuration in the solid-state with a dihedral angle C3–C10–C11–C12 of 178.8° (Figure 3).[11]

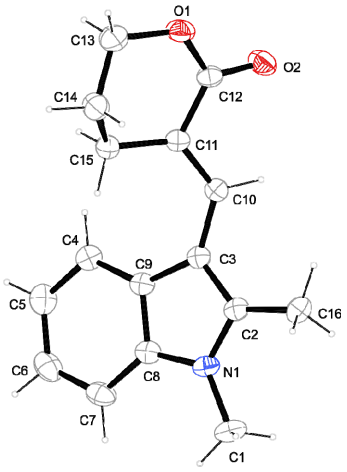
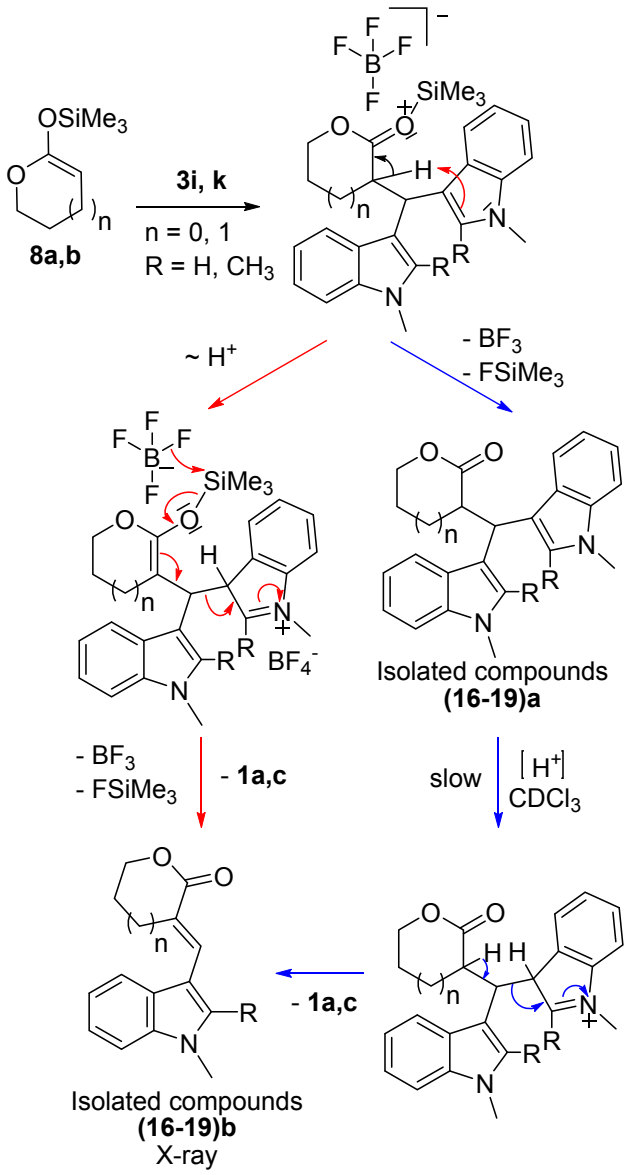


Figure 3. ORTEP drawing (50% probability ellipsoids) of the alkylidene lactone **19b**.[11] Selected interatomic distances (Å) and angles (°): N1-C2 = 1.375(2), C2-C3 = 1.383(2), C3-C10 = 1.452(2), C10-C11 = 1.347(2), C11-C12 = 1.488(2), C12-O2 = 1.209(2), N1-C2-C3 = 109.64(13), C2-C3-C10 = 123.78(14), C3-C10-C11 = 128.00(14), C10-C11-C12 = 116.08(14), C11-C12-O2 = 124.11(14), C2–C3–C10–C11 = -139.90(17), C3–C10–C11–C12 = 178.80(14).

The formation of the latter product may occur via two different pathways. As shown in Scheme 5 for the reaction of **3i**,**k** with **8a-b**, the cleavage of one indole ring may in principle occur before or after desilylation. As fragmentation of the isolated compound **17a** observed by ^{1}H NMR takes days in $CDCl_3$ solution, we can conclude that the elimination of an indole ring occurs before desilylation (left pathway in Scheme 5) or via BF_3 induced cleavage of the initial adducts (**16-19**)**a**. This type of β-elimination of indole was previously observed in other cases.[15] Compound **15**, obtained by the reaction with **8c** cannot undergo this cleavage because there are no hydrogens in β-position which are needed for the 1,2-elimination of indole.

Scheme 5. Possible Mechanisms for the Formation of (16-19)b



Kinetic Investigations. The kinetics of these reactions were determined in CH_2Cl_2 by following the disappearance of the absorbances of **3a**-**k** at their maximum wavelengths λ_{max} (Tables 1-3). In the presence of an excess (10−200 equivalents) of the nucleophiles **8a**-**j** (Table 4), pseudo first-order conditions were achieved, as indicated by the mono-exponential decays of the absorbances of **3a**-**k**, which is illustrated in Figure 4 for the reaction of the ketene acetal **8j** with the indolylmethylium ion **3b**. Plots of k_{obs} (s^{-1})

against the concentrations of the nucleophiles were linear with negligible intercepts as illustrated in Figure 4. The second-order rate constants k_2 for the reactions of **3a**-**k** with the nucleophiles **8a**-**j** were derived from the slopes of these linear plots (see Supprting Information pp S2-S14) and are reported in Table 5.

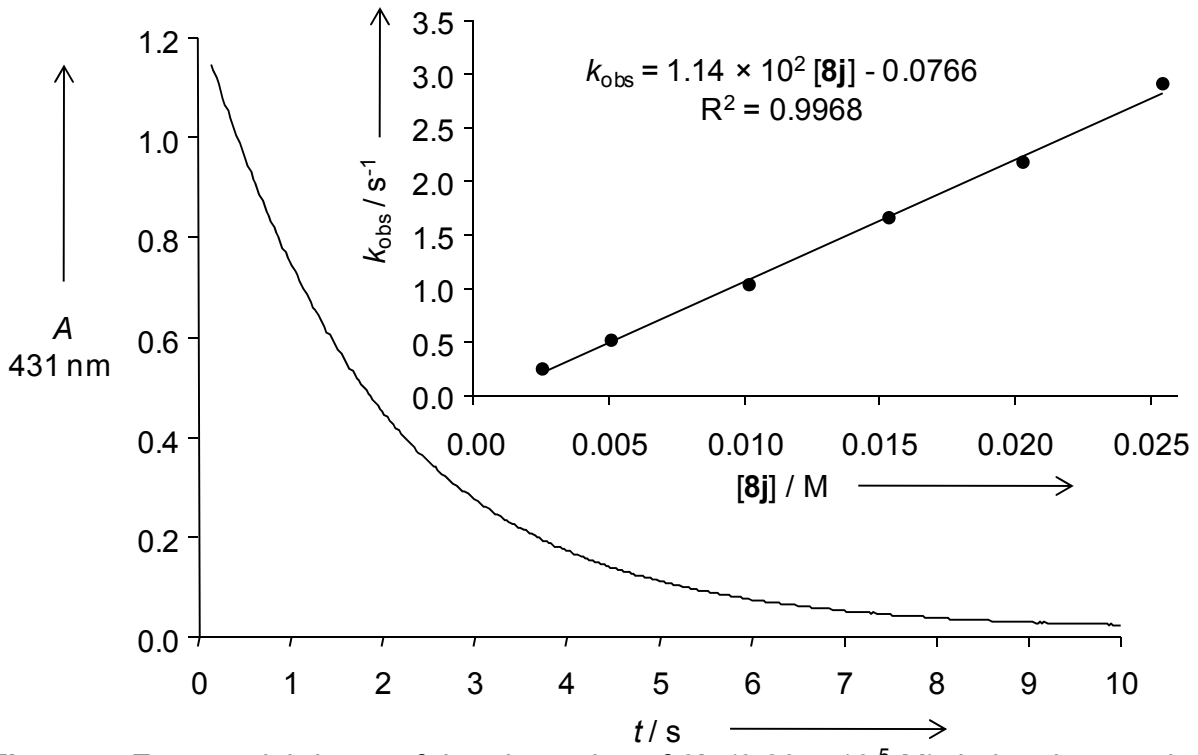


Figure 4. Exponential decay of the absorption of **3b** (9.28×10^{-5} M) during the reaction with **8j** (5.09×10^{-3} M) ($k_{obs} = 5.23 \times 10^{-1}$ s^{-1}) in CH_2Cl_2. Inset: plot of the first-order rate constants k_{obs} versus the nucleophile concentrations [**8j**] $k_2 = 1.14 \times 10^2$ M^{-1} s^{-1}.

Table 5. Second-Order Rate Constants k_2 for the Reactions of the Nucleophiles 8a-j with the Indolylmethylium Tetrafluoroborates 3(a-k)-BF_4 in CH_2Cl_2 at 20 °C

Electrophile	Nucleophile	k_2 / M^{-1} s^{-1}	k_{calc}[a] / M^{-1} s^{-1}	E[b]
3a	**8g**	3.07×10^4	2.73×10^4	-1.80
(R = H)	**8h**	2.22×10^3	2.57×10^3	
	8j	3.42×10^2	3.20×10^2	
3b	**8g**	1.35×10^4	1.18×10^4	-2.19
(R = Me)	**8h**	1.08×10^3	1.05×10^3	
	8j	1.14×10^2	1.35×10^2	
3c	**8g**	1.91×10^3	2.00×10^3	-3.02
(R = OMe)	**8h**	1.48×10^2	1.55×10^2	
	8j	2.34×10^1	2.16×10^1	
3d	**8d**	1.36×10^2	8.72×10^1	-6.26
(R = NMe_2)	**8e**	9.19	1.22×10^1	
	8g	1.71	1.94	
3e	**8b**	3.62×10^2	2.66×10^2	-7.79
(R = Jul)		3.65×10^2[c]	2.66×10^2	
		1.78×10^2[d]	1.35×10^2	
	8c	9.35	1.53×10^1	
		9.02[c]	1.53×10^1	
		6.70[d]	1.45×10^1	
	8e	8.78×10^{-1}	5.30×10^{-1}	
	8g	5.56×10^{-2}	7.33×10^{-2}	

Table 5. (continued)

Electrophile	Nucleophile	k_2 / M^{-1} s^{-1}	k_{calc}[a] / M^{-1} s^{-1}	E[b]
3f	**8d**	6.32×10^2	7.46×10^2	-5.15
	8e	1.67×10^2	1.18×10^2	
	8g	1.72×10^1	2.09×10^1	
	8h	1.13	1.15	
3g	**8b**	3.50×10^4	6.05×10^4	-5.05
	8d	1.43×10^3	9.05×10^2	
	8g	2.62×10^1	2.59×10^1	
	8h	1.54	1.45	
3h	**8g**	3.30×10^1	3.14×10^1	-4.96
	8h	1.70	1.78	
3i	**8b**	1.32×10^4	9.40×10^3	-5.99
	8c	5.21×10^2	8.91×10^2	
	8f	2.39×10^1	1.70×10^1	
	8g	3.07	3.46	
3j	**8b**	2.23×10^3	1.55×10^3	-6.90
	8c	5.92×10^1	1.14×10^2	
	8g	7.15×10^{-1}	4.93×10^{-1}	
3k	**8a**	2.96×10^1	4.28×10^1	-10.23
	8b	1.57	2.12	
	8d	7.49×10^{-2}	4.03×10^{-2}	

[a] Calculated by using Equation (1), N and s_N from Table 4 and E from this table. [b] For the determination of E, see Figure 5 and accompanying text. [c] Counterion PF_6^-; [d] In CH_3CN.

As shown in Table 5, the second-order rate-constants k_2 for the reactions of the ketene acetals **8b** and **8c** with the aryl(indol-3-yl)methylium ion **3e** differ by less than a factor of 2 in CH_3CN and in CH_2Cl_2, illustrating that the solvent has little effect on the reaction kinetics, as previously reported for analogous reactions of benzhydrylium and iminium ions with neutral π-nucleophiles.[9] Variation of the counterion (BF_4^- vs. PF_6^-) of aryl(indol-3-yl)methylium ion **3e** affected the second-order rate constants in CH_2Cl_2 by less than 5% indicating that the counterion effects on the kinetics of these reactions are negligible.[16]

Determination of the electrophilicity of 3a-k. Since the pioneering work of Swain and Scott[10a] numerous attempts have been made to quantify nucleophilicity and electrophilicity,[10b-j] among which Ritchie's constant selectivity relationship[10h,i] and its extensions by Kane-Maguire and Sweigart[10j] are the most prominent ones. In 1994 we have introduced Equation (1) which characterizes electrophiles by one parameter, *E,* and nucleophiles by the solvent-dependent nucleophilicity parameter *N* and the sensitivity parameter s_N.[9d]

$$\log k_2\ (20\ ^\circ\mathrm{C}) = s_N(N + E) \qquad (1)$$

Figure 5 shows that plots of $(\log k_2)/s_N$ *vs*. the nucleophilicity *N* of **8a**-**j** are linear with slopes close to 1, which indicates the applicability of Equation (1). By enforcing a slope of 1.0 for the least-squares minimization it was possible to evaluate the electrophilicities *E* of **3a**-**k** which are listed in Table 5. Only the correlation lines for cations **3e, 3i** and **3j**, which include reactions with the sterically most demanding π-nucleophile **8c**, showed

some scatter presumably because the steric crowding at the disubstituted nucleophilic site of **8c** affected the transition states of the reactions with **3e,i,j** more than those of the reactions with benzhydrylium ions, which were used for the calibration of the nucleophile-specific parameters *N* and s_N for **8a-k**.

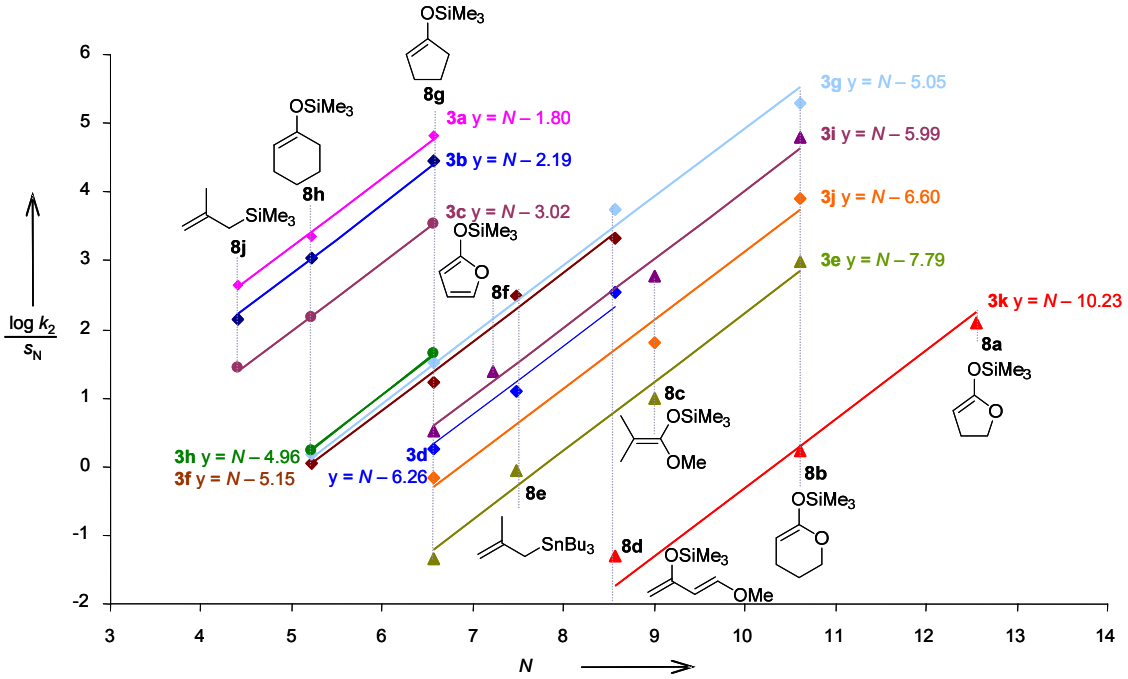


Figure 5. Plots of (log k_2)/s_N vs. *N* for the reactions of indolylmethylium ions **3a**-**k** with the nucleophiles **8a**-**j** in CH_2Cl_2 at 20 °C. k_2 values from Table 5 and *N* and s_N values for **8a**-**j** from Table 4.

Figure 6 shows a linear correlation of the electrophilicity *E* of the four para-substituted aryl(indol-3-yl)methylium ions **3a**-**d** with Hammett's σ_p constants of the substituents of the phenyl ring, which is of higher quality than the corresponding correlation with σ_{p+}. The slope of this correlation (5.59) corresponds to the Hammett reaction constant ρ for reactions with nucleophiles of s_N = 1. It is considerably larger than the corresponding slopes of *E* vs σ_p correlations for substituted benzylidene malonates (3.45), quinone

methides (1.79) and *trans*-*β*-nitrostyrenes (2.08), comparable to that of aryl-*para*-methoxyphenylmethylium ions (7.38), which can be explained by the more efficient ground-state effects of the substituents in the more electron-deficient aryl-indolyl and benzhydryl cations.

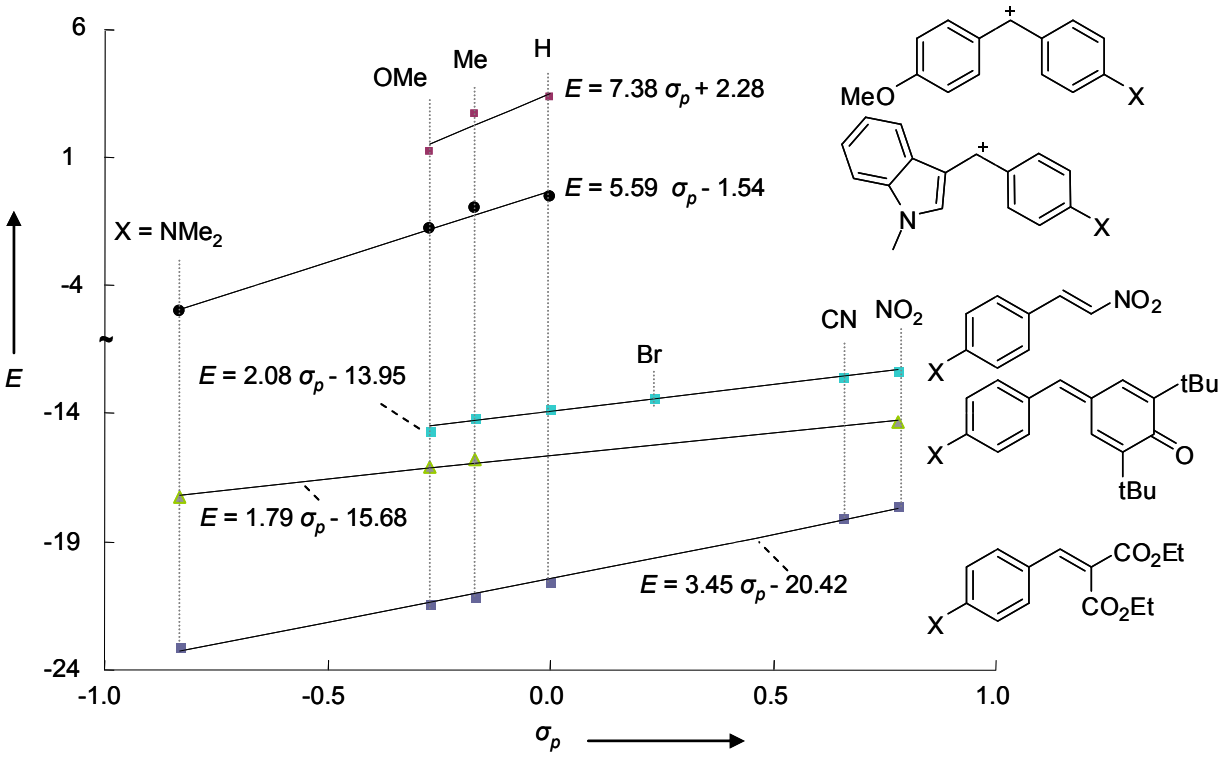


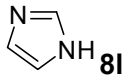
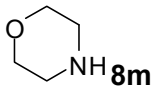
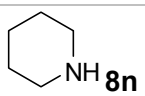
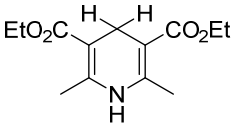
Figure 6. Correlation of the *E* values of aryl(indol-3-yl)methylium ions **3a**-**d**, benzhydrylium ions, benzylidene malonates, quinone methides and *trans*-*β*-nitrostyrenes with Hammett's σ_p constants (σ_p = 0.78 (NO_2), 0.66 (CN), 0.23 (Br), -0.17 (Me), -0.27 (OMe), -0.83 (NMe_2)).[17]

From the electrophilicity parameter of **3h** given in Table 5 (*E* = -4.96) and the previously reported reactivity parameters for the Hantzsch ester **8o** (*N* = 9.00, s_N = 0.90 in CH_2Cl_2)[9g] one can calculate the rate constant for hydride transfer of 4.33 × 10^3 $M^{-1}s^{-1}$ (CH_2Cl_2, 20 °C) by Equation (1). This value agrees within the confidence limit of

Equation (1) (factor 10-100) with the experimental rate constant of 1.32×10^4 $M^{-1}s^{-1}$ (CH_3CN, 30 °C) for this reaction reported by Huffman et al.[8d] (Table 6, entry 4). While calculated (Equation 1) and reported experimental rate constants also agree nicely for the reaction of **3h** with imidazole (**8l**, Table 6, entry 1), the calculated values for the reactions of the indolylmethylium ion **3h** with morpholine (**8m**) and piperidine (**8n**) were approximately 3 orders of magnitude larger than those reported by Huffman et al.[8d] (Table 6, entries 2 and 3). Apart from the discrepancy with the rate constants predicted by eq. (1), Huffman´s report that morpholine (**8m**) and piperidine (**8n**) reacted more slowly than imidazole (**8l**) appeared surprising to us, since in all reactions of carbocations and Michael acceptors studied so far, the reactivity order was always the other way around. In order to clarify the origin of this discrepancy, we have repeated the reactions of the N-nucleophiles **8l-n** with the aryl(indol-3-yl)methylium ion **3h** using different counterions.

The kinetic investigations, which were performed under pseudo-first-order conditions as described above, gave a rate constant of 2.65×10^5 $M^{-1}s^{-1}$ for the reaction of imidazole (**8l**) with **3h**, close to Huffman's value[8d] and to the rate constant calculated by Equation (1). As expected from the calculations based on Equation (1), the reactions of **3h** with morpholine (**8m**) and piperidine (**8n**) were much faster than reported by Huffman, and were too fast to be followed with our stopped-flow equipment.

Table 6. Experimental and Calculated Second-Order Rate-Constants k_2 for the Reactions of the Nucleophiles 8l-o with the indolylmethylium ions 3h,k

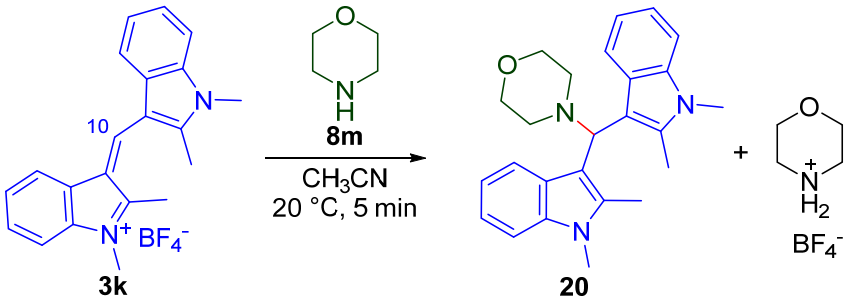
Entry	N-Nucleophiles	N, s_N (CH_3CN)[a] pK_{aH} (H_2O)[b]	Indolylmethylium ions / (E)	k_2^{exp} / M^{-1} s^{-1} CH_3CN, 30°C HSO_4^-, Huffman [c]	k_2^{exp}/ M^{-1} s^{-1} CH_3CN, 20°C BF_4^-, this work	k_2^{calcd} / M^{-1} s^{-1} CH_3CN, 20°C from Eq(1)
1	 **8l**	11.47, 0.79 pK_{aH} = 6.9	**3h** / -4.96	4.26×10^5 [d]	2.65×10^5	1.39×10^5
2	 **8m**	15.65, 0.74 pK_{aH} = 8.4	**3h** / -4.96	1.15×10^5	>> 10^6	8.14×10^7
			3k / -10.23	Not studied	2.90×10^4	1.03×10^4
3	 **8n**	17.35, 0.68 pK_{aH} = 11.2	**3h** / -4.96	2.30×10^5	>> 10^6	2.66×10^8
4	 **8o**	9.00, 0.90 (CH_2Cl_2)	**3h** / -4.96	1.32×10^4	Not studied	4.33×10^3 (in CH_2Cl_2)

[a]From Ref. 9; [b]From Ref. 18a; [c]From Ref. 8d; [d]Average of two kinetic measurements at 30 °C[8d].

For that reason, we measured the rate constant for the reaction of morpholine **8m** with the less electrophilic bis(indol-3-yl)methylium ion **3k**, which proceeded selectively at C10 according to NMR of the crude material (Scheme 6, the poor yield of isolated adduct **20** is due to losses during recrystallization). Since the measured rate constant is in accord with that calculated by equation (1), we can conclude that equation (1) is also applicable to reactions of the carbenium ions **3** with amines and that the rate constants for the reactions of **3h** with **8m** and **8n** reported by Huffman cannot refer to the attack of the amines at the carbenium ions. Unfortunately, the experimental part of Huffman's article

does not give detailed information about the concentrations used for the different kinetic experiments. Possibly the amines **8m** and **8n** were not used in high excess over the indolylmethylium hydrogen sulfate, that protonation of the amines by the HSO_4^- counterion accounts for the incorrect rate constants reported for these reactions.

Scheme 6. Reaction of Bis(indol-3-yl)methylium Tetrafluoroborate 3k-BF_4 with Morpholine (8m)



Structure-reactivities relationships. The right column of Figure 7 compares the reactivities of the aryl(indol-3-yl)methylium ions **3a-k** with those of structurally related benzhydrylium ions. One can see that replacement of the NH group of the aryl(*N*-methylindol-3-yl)methylium ion **3f** (*E* = -5.15) by NMe to give **3g** (*E* = -5.05) has a negligible effect on electrophilicity, analogous to the small *N*-methyl effect on the relative nucleophilicities of indole and *N*-methylindole.[19] The indol-3-ylmethylium ion **3d** (*E* = -6.26) has a similar electrophilicity as the bis(*p*-dimethylamino)benzhydrylium ion (*E* = -7.02) and the bis(*N*-methylindol-3-yl)methylium ion **3i** (*E* = -5.99), indicating that the *N*,*N*-dimethylaminophenyl group and the *N*-methyl-indole ring stabilize carbenium ions to

a similar extent, in agreement with the similar magnitudes of the Hammett σ^+ constants for the *N*,*N*-dimethylamino group (σ^+_p = -1.70)[20a] and *N*-methylindole (σ^+_{arene} = -1.93).[20b]

In order to demonstrate the practical use of the electrophilicity parameters of the indolylmethylium ions determined in this work, we have complemented the electrophilicity scale on the right of Figure 7 with a nucleophilicity scale on the left side. By arranging the reactivities of electrophiles and nucleophiles in opposite order, electrophiles and nucleophiles which are placed on the same level react with a rate constant of 1 M^{-1} s^{-1}. Using the rule of thumb[9b] that electrophile-nucleophile combinations may take place at room temperature if $E + N > -5$, one can derive that the indolylmethylium ions will react with those nucleophiles which are positioned below them or not more than 5 units above them in Figure 7.

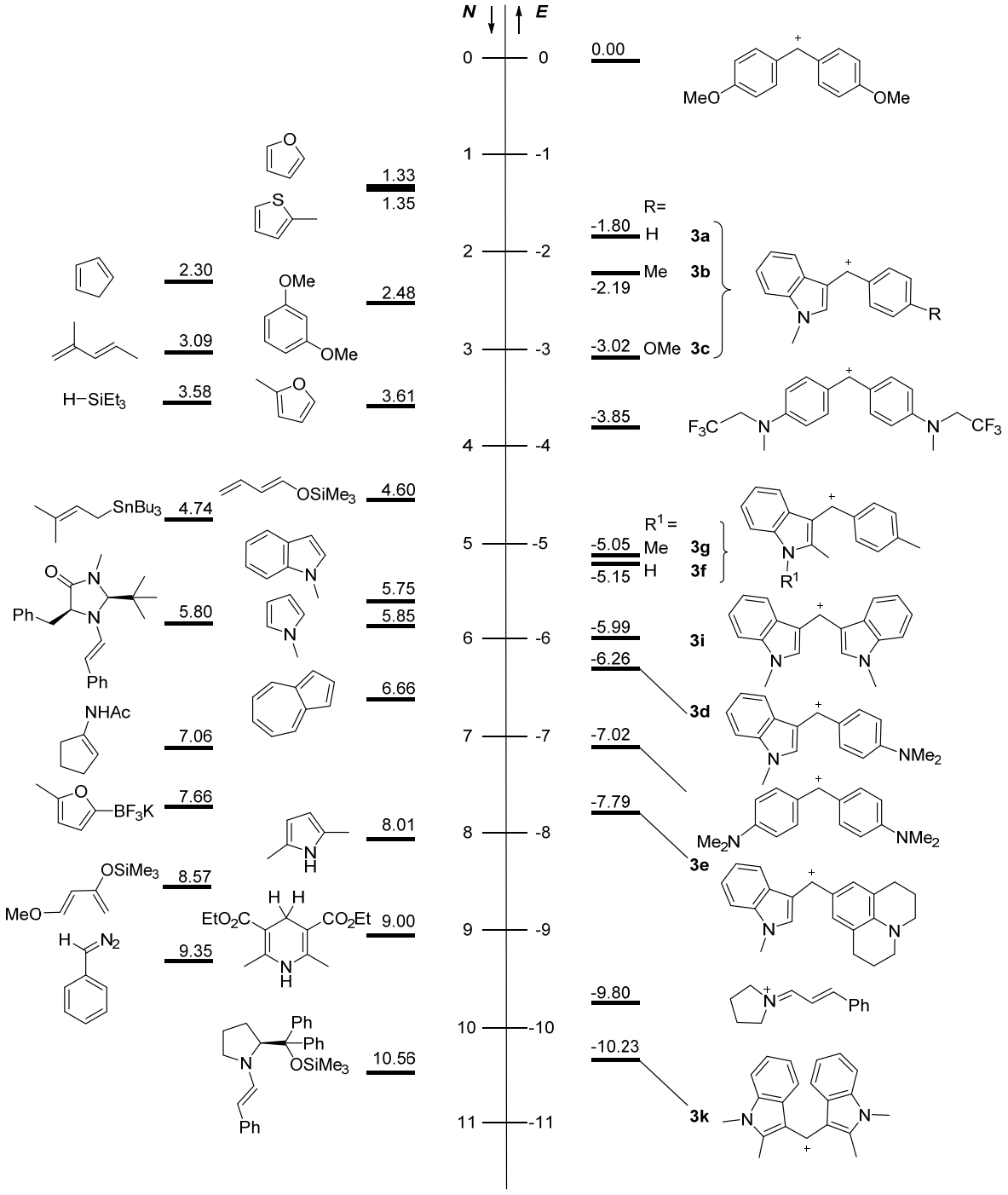


Figure 7. Ranking of the indolylmethylium ions **3a-g**,**i**,**k** in the electrophilicity scale and scope of their reaction with nucleophiles.

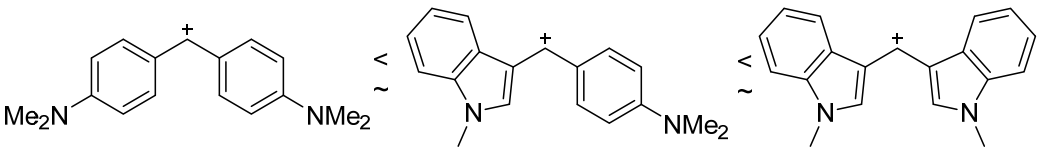
One can, thus, expect that indoles, furans, thiophenes, and pyrroles which have *N*

parameters from 1 to 8, undergo Friedel-Crafts reactions with most aryl(indol-3-yl)methylium ions to give tris(heteroaryl)methanes. Organocatalytic reactions of indolylmethylium ions with enamines and enamides, which are good nucleophiles ($5 < N < 19$)[9f] have been reported to proceed smoothly even at low temperature.[4a-c, 6a] Trialkylsilanes $HSiR_3$ are not sufficiently nucleophilic to react with the least reactive indolylmethylium ions **3e,k** ($E + N < -5$), but stronger hydride donors such as the Hantzsch ester (**8o**, $N = 9.00$) can be used to reduce all **3a-k** with formation of bis-indolyl-methanes or aryl(indolyl)methanes. Allylsilane, stannane and organoboron nucleophiles, which have been calibrated in our scale,[9f] are also suitable reaction partners for indolylmethylium ions.[2c, 3a] The data reported in this work can thus be employed for designing syntheses of bis(indol-3-yl)methane derivatives, which have been identified as building blocks of several alkaloids.[21]

CONCLUSION

The second-order rate constants for the reactions of the indolylmethylium ions **3**(**a-k**) with π-nucleophiles follow Equation (1), which allowed us to derive the electrophilicitiy parameters $-10.2 < E < -1.8$ for these substituted indolylmethylium ions and to predict potential mucleophilic reaction partners. In line with the similar values of σ^+_p (NMe_2) and σ^+_{arene} (1-methylindol-3-yl), the bis(4-dimethylamino)-substituted benzhydrylium ion and the substituted indol-3-ylmethylium ion **3d** and **3i** were found to have similar electrophilic reactivities (Scheme 7).

Scheme 7. Comparison of the Electrophilic Reactivities of Benzhydrylium Ions and Indol-3-ylmethylium Ions



E = -7.02 *E* = -6.24 *E* = -5.98

Earlier attempts in our group to generate benzhydrylium ions in the reactivity range -6 < *E* < -2 by combining strong (NMe_2) and weak (Me, OMe) electron donating substituents at the two phenyl rings failed, because electrophilic attack at the NMe_2 group (protonation?) could not be avoided. Since 1-methylindole is a considerably weaker Bronsted base (pK_{aH} = -2.32 in H_2O)[18b] than N,N-dimethylaniline (pK_{aH} = 5.15 in H_2O) [18c], the strong electron-donating indolyl group can be combined with weaker electron donating groups as phenyl, tolyl, and anisyl to give the stable diarylcarbenium ions **3**(**a-c**) which may be used as readily accessible reference electrophiles in future mechanistic investigations.

EXPERIMENTAL SECTION

Materials. Dichloromethane was freshly distilled over CaH_2 prior to use, and Et_2O was distilled over sodium/benzophenone. Commercially available acetonitrile (99.9%, extra dry) and dimethyl sulfoxide (99.7%, extra dry) were used as received. Indoles (**1**), 4-(dimethylamino)benzaldehyde (**2d**), $HBF_4{\cdot}OEt_2$, HPF_6 (65 wt % in H_2O), triethyl orthoformate (**4**), nucleophiles (**8c-e**, **g-i**, **k-l, n**) were purchased and used without further purification. Aldehydes (**2a-c**) and nucleophile **8m** were purchased and distilled prior to use. 1,2,3,5,6,7-Hexahydropyrido[3,2,1-ij]quinoline-9-carbaldehyde (**2e**),[9a] nucleophiles (**8a**[22], **8b**[22], **8f**[23], **8j**[24]) were synthesized as described in the literature.

Analytics. The ^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR chemical shifts are in ppm and recorded in $CDCl_3$ (δ_H = 7.26, δ_C = 77.16), CD_3CN (δ_H = 1.94, δ_C = 118.69), $(CD_3)_2SO$ (δ_H = 2.50, δ_C = 39.52), and in CD_2Cl_2 (δ_H = 5.32, δ_C = 53.84). The following abbreviations were used for signal multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, sept = septet. NMR signal assignments were based on additional 2D-NMR experiments (COSY, HSQC, HMBC and NOESY). HRMS in EI and ESI mode were performed on a LTQ mass spectrometer. Melting points were determined in capillary tubes with a standard melting point device and were not corrected. An IR spectrometer with an ATR unit (attenuated total reflection) was used to record the IR spectra of neat compounds. The composition of the compounds was determined with a conventional C-, H-, N- , S- elemental analyzer. All yields refer to non-optimized procedures.

Synthesis of aryl(indol-3-yl)methylium tetrafluoroborates 3(a-g)-BF_4.

General procedure: Benzaldehyde **2** was dissolved in a mixture of CH_2Cl_2 (5 mL) and Et_2O (5 mL) in a flame-dried Schlenk-flask; flushed with nitrogen. Then an indole **1** (1.00 g, 1.00 equiv.) was added to the mixture and the solution was stirred until complete homogenization (2 min). The solution was cooled to 0 °C, and $HBF_4 \cdot Et_2O$ (1.50 equiv.) was added dropwise at this temperature. After 10 min, the solution was allowed to warm at room temperature whilst a strongly colored solid precipitated (see Tables 1 and 2). After 10 min the solid was filtered and washed thoroughly with Et_2O (4 x 25 mL) and was crystallized in CH_3CN/Et_2O (1/1) to give the aryl(indol-3-yl)methylium tetrafluoroborates **3-BF_4** as colored crystals of high purity.

(1-Methyl-1H-indol-3-yl)(phenyl)methylium tetrafluoroborate (**3a-BF_4**). From **1a** (1.00 g, 7.62 mmol), **2a** (809 mg, 7.62 mmol) and $HBF_4 \cdot OEt_2$ complex (1.85 g, 11.4 mmol): 850 mg (2.77 mmol, 36%), bright yellow-orange solid, mp 137-139 °C (dec.). Major isomer ((*Z*)-isomer): ^{1}H NMR (CD_3CN, 400 MHz) δ 9.20 (s, 1H, H-2), 9.06 (s, 1H, H-10), 8.18 – 8.11 (m, 1H, H-4), 8.00 (d, 2H, *J* = 8.0 Hz, H-12 and H-17), 7.83 – 7.76 (m, 2H, H-7 and H-14), 7.75 – 7.66 (m, 4H, H-5, H-6, H-13 and H-16), 4.15 (s, 3H, H-1); ^{13}C NMR (CD_3CN, 101 MHz) δ 159.3 (C-10), 158.0 (C-2), 142.7 (C-8), 136.7 (C-14), 135.3 (C-11), 134.9 (C-12 and C-17), 131.5 (C-13 and C-16), 131.1 (C-6), 130.9 (C-5), 130.1 (C-3), 129.1 (C-9), 122.9 (C-4), 116.1 (C-7), 38.4 (C-1); ^{19}F NMR (CD_3CN, 376 MHz) δ -151.7. HRMS (ESI) *m*/*z*: $[M\text{-}BF_4^-]^+$ Calcd for $C_{16}H_{14}N^+$ 220.1121; Found 220.1119. IR (ATR) ν (cm^{-1}) = 1621, 1608, 1588, 1570, 1548, 1457, 1414, 1348, 1293, 1253, 1214, 1129, 1105, 1049, 1037, 759, 678, 620.

(1-Methyl-1H-indol-3-yl)(p-tolyl)methylium tetrafluoroborate (**3b-BF_4**). From **1a** (1.00 g, 7.62 mmol), **2b** (917 mg, 7.63 mmol) and $HBF_4 \cdot OEt_2$ complex (1.85 g, 11.4 mmol): 1.93 g (6.01 mmol, 79%), bright orange solid, mp 162-169 °C (dec.). Major isomer ((*Z*)-isomer): ^{1}H NMR (CD_3CN, 400 MHz) δ 9.19 (s, 1H, H-2), 8.99 (s, 1H, H-10), 8.16 – 8.09 (m, 1H, H-4), 7.94 (d, 2H, *J* = 8.3 Hz, H-12 and H-17), 7.80 – 7.74 (m, 1H, H-7), 7.73 – 7.66 (m, 2H, H-5 and H-6), 7.53 (d, 2H, *J* = 8.2 Hz, H-13 and H-16), 4.15 (s, 3H, H-1), 2.51 (s, 3H, H-15); ^{13}C NMR (CD_3CN, 101 MHz) δ 159.6 (C-10), 156.9 (C-2), 149.8 (C-14), 142.3 (C-8), 135.5 (C-12 and C-17), 132.8 (C-11), 132.4 (C-13 and C-16), 130.7 (C-6), 130.6 (C-5), 129.4 (C-9), 128.7 (C-3), 122.6 (C-4), 115.9 (C-7), 38.2 (C-1), 22.6 (C-15); ^{19}F NMR (CD_3CN, 376 MHz) δ -151.7. HRMS (ESI) *m*/*z*: $[M\text{-}BF_4^-]^+$ Calcd for $C_{17}H_{16}N^+$ 234.1277; Found 234.1281. Anal. Calcd for $C_{17}H_{16}BF_4N$: C, 63.58; H, 5.02; N,

4.36. Found: C, 63.53; H, 5.10; N, 4.38. IR (ATR) ν(cm^{-1}) = 1619, 1584, 1540, 1457, 1409, 1344, 1259, 1188, 1130, 1103, 1047, 1032, 1009, 984, 951, 901, 821, 770, 751, 625.

(4-Methoxyphenyl)(1-methyl-1H-indol-3-yl)methylium tetrafluoroborate (**3c-BF$_4$**). From **1a** (500 mg, 3.81 mmol), **2c** (520 mg, 3.82 mmol) and $HBF_4{\cdot}OEt_2$ complex (928 mg, 5.73 mmol): 770 mg (2.28 mmol, 60%), bright red solid, mp 198-208 °C (dec.). Major isomer ((*Z)*-isomer): ^{1}H NMR (CD_3CN, 400 MHz) δ 9.13 (d, 1H, *J* = 0.9 Hz, H-2), 8.91 (s, 1H, H-10), 8.12 – 8.05 (m, 3H, H-4, H-12 and H-17), 7.78 – 7.71 (m, 1H, H-7), 7.70 – 7.61 (m, 2H, H-5 and H-6), 7.22 (d, 2H, *J* = 8.9 Hz, H-13 and H-16), 4.12 (d, 3H, *J* = 0.9 Hz, H-1), 3.99 (s, 3H, H-15). ^{13}C NMR (CD_3CN, 101 MHz) δ 168.9 (C-14), 159.3 (C-10), 154.8 (C-2), 141.7 (C-8), 139.1 (C-12 and C-17), 130.0 (C-6), 129.9 (C-5), 129.8 (C-9), 128.5 (C-11), 125.9 (C-3), 122.1 (C-4), 117.7 (C-13 and C-16), 115.5 (C-7), 57.7 (C-15), 37.9 (C-1); ^{19}F NMR (CD_3CN, 376 MHz) δ -151.7. HRMS (ESI) *m*/*z*: [M-BF_4^-]$^+$ Calcd for $C_{17}H_{16}NO^+$ 250.1226; Found 250.1228. Anal. Calcd for $C_{17}H_{16}BF_4NO$: C, 60.57; H, 4.78; N, 4.15. Found: C, 60.46; H, 4.69; N, 4.14. IR (ATR) ν(cm^{-1}) = 1577, 1555, 1528, 1455, 1438, 1411, 1351, 1328, 1275, 1259, 1218, 1179, 1165, 1134, 1093, 1047, 1037, 1014, 1001, 883, 859, 838, 804, 765, 757.

(4-(Dimethylamino)phenyl)(1-methyl-1H-indol-3-yl)methylium tetrafluoroborate (**3d-BF$_4$**). From **1a** (1.12 g, 8.54 mmol), **2d** (1.28 g, 8.58 mmol) and $HBF_4{\cdot}OEt_2$ complex (1.67 g, 10.3 mmol): 1.70 g (4.85 mmol, 57%), dark blue solid, mp 204-206 °C (dec.). ^{1}H NMR (CD_3CN, 400 MHz) δ 8.60 (s, 1H, H-2), 8.42 (s, 1H, H-10), 8.11 – 7.86 (m, 3H, H-4, H-12 and H-17), 7.64 – 7.60 (m, 1H, H-7), 7.53 – 7.46 (m, 2H, H-5, H-6), 6.99 (d, 2H, *J* = 9.1 Hz, H-13 and H-16), 4.01 (s, 3H, H-1), 3.33 (s, 6H, H-15). ^{13}C NMR (CD_3CN, 101

MHz) δ 159.5 (C-14), 154.6 (C-10), 145.4 (C-2), 139.9 (C-8), 129.9 (C-9), 127.1 (C-6), 126.6 (C-5), 125.4 (C-11), 120.8 (C-4), 118.0 (C-3), 116.2 (C-13 and C-16), 113.7 (C-7), 42.1 (C-1), 36.1 (C-15), C12 and C17 not detected, probably overlapped with CD_3CN peak at 118.7 ppm. ^{19}F NMR (CD_3CN, 376 MHz) δ -151.8. HRMS (ESI) *m*/*z*: $[M\text{-}BF_4^-]^+$ Calcd for $C_{18}H_{19}N_2^+$ 263.1543; Found 263.1544. Anal. Calcd for $C_{18}H_{19}BF_4N_2$: C, 61.74; H, 5.47; N, 8.00. Found: C, 61.54; H, 5.41; N, 8.00. IR (ATR) ν (cm^{-1}) = 1607, 1577, 1531, 1509, 1469, 1388, 1365, 1340, 1314, 1268, 1202, 1182, 1161, 1130, 1093, 1048, 982, 938, 825, 764, 757, 753, 723, 679.

(Julolidin-9-yl)(1-methyl-1H-indol-3-yl)methylium tetrafluoroborate (**3e-BF_4**). From **1a** (316 mg, 2.41 mmol), **2e** (485 mg, 2.41 mmol) and $HBF_4 \cdot OEt_2$ complex (468 mg, 2.89 mmol): 662 mg (1.65 mmol, 68%), dark violet solid, mp 159-161 °C (dec.). ^1H NMR (CD_3CN, 400 MHz) δ 8.42 (s, 1H, H-2), 8.05 (br s, 1H, H-10), 7.93 – 7.89 (m, 1H, H-4), 7.85 (br s, 1H, H-12 or H-17), 7.59 – 7.53 (m, 1H, H-7), 7.47 – 7.39 (m, 2H, H-5 and H-6), 7.27 (br s, 1H, H-12 or H-17), 3.96 (s, 3H, H-1), 3.60 (t, 4H, *J* = 5.7 Hz, H-15 and H-22), 2.80 (2 x br s, 4H, H-19 and H-20), 2.03 – 1.96 (m, 4H, H-18 and H-21). ^{13}C NMR (CD_3CN, 101 MHz) δ 156.1 (C-14), 149.9 (C-10), 141.7 (C-2 and C-12 or C-17), 139.3 (C-8), 133.6 (C-12 or C-17), 129.9 (C-9), 128.7 (C-13 or C-16), 126.3 (C-6), 126.1 (C-11), 125.4 (C-5 and C-13 or C-16), 120.4 (C-4), 116.2 (C-3), 113.1 (C-7), 53.3 (C-15 and C-22), 35.5 (C-1), 28.1 (C-19 or C-20), 27.6 (C-19 or C-20), 21.5 (C-18 and C-21). ^{19}F NMR (CD_3CN, 376 MHz) δ -151.7. HRMS (ESI) *m*/*z*: $[M\text{-}BF_4^-]^+$ Calcd for $C_{22}H_{23}N_2^+$ 315.1856; Found 315.1859. IR (ATR) ν (cm^{-1}) = 1627, 1585, 1575, 1530, 1505, 1455, 1400, 1370, 1354, 1313, 1263, 1212, 1187, 1133, 1110, 1047, 1032, 975, 953, 912, 766, 749, 681.

(Julolidin-9-yl)(1-methyl-1H-indol-3-yl)methylium hexafluorophosphate(V) (**3e-PF_6**). From **1a** (170 mg, 1.30 mmol), **2e** (262 mg, 1.30 mmol) and HPF_6 (190 mg, 1.30 mmol): 52 mg (0.11 mmol, 8%), dark violet solid, mp 135-142 °C (dec.). ^{1}H NMR (CD_3CN, 400 MHz) δ 8.42 (s, 1H, H-2), 8.08 (s, 1H, H-10), 7.92 (dd, 1H, *J* = 1.6, 6.7 Hz, H-4), 7.87 (s, 1H, H-12 or H-17), 7.58 (dd, 1H, *J* = 1.3, 6.8 Hz, H-7), 7.49 – 7.37 (m, 2H, H-5 and H-6), 7.29 (s, 1H, H-12 or H-17), 3.98 (s, 3H, H-1), 3.61 (t, 4H, *J* = 5.7 Hz, H-15 and H-22), 2.81 (2 x br s, 4H, H-19 and H-20), 2.07 – 1.96 (m, 4H, H-18 and H-21). ^{19}F NMR (CD_3CN, 376 MHz) δ -72.9 (d, $J_{F,P}$ = 706 Hz). ^{31}P NMR (CD_3CN, 162 MHz) δ -144.64 (sept, $J_{P,F}$ = 706 Hz). HRMS (ESI) *m*/*z*: $[M\text{-}BF_4^-]^+$ Calcd for $C_{22}H_{23}N_2^+$ 315.1856; Found 315.1856. IR (ATR) ν (cm^{-1}) = 1608, 1533, 1507, 1464, 1369, 1357, 1314, 1264, 1229, 1216, 1113, 1074, 1011, 828, 762, 744, 736, 688.

(2-Methyl-1H-indol-3-yl)(p-tolyl)methylium tetrafluoroborate (**3f-BF_4**). From **1b** (1.08 g, 8.23 mmol), **2b** (989 mg, 8.23 mmol) and $HBF_4{\cdot}OEt_2$ complex (2.00 g, 12.3 mmol): 1.88 g (5.85 mmol, 71%), bright orange solid, mp 180-183 °C (dec.). ^{1}H NMR (CD_3CN, 400 MHz) δ 12.38 (br s, 1H, H-1), 8.68 (s, 1H, H-10), 8.17 (d, 1H, *J* = 7.9 Hz, H-4), 7.95 (d, 2H, *J* = 8.2 Hz, H-12 and H-17), 7.63 (d, 1H, *J* = 7.5 Hz, H-7), 7.60 – 7.55 (m, 1H, H-6), 7.51 (d, 2H, *J* = 8.1 Hz, H-13 and H-16), 7.48 – 7.43 (m, 1H, H-5), 2.92 (s, 3H, H-18), 2.51 (s, 3H, H-15). ^{13}C NMR (CD_3CN, 101 MHz) δ 175.2 (C-2), 160.5 (C-10), 148.3 (C-14), 141.9 (C-8), 134.1 (C-12 and C-17), 131.9 (C-11), 131.7 (C-13 and C-16), 131.6 (C-6), 131.5 (C-3), 129.6 (C-5), 125.7 (C-9), 124.7 (C-4), 116.6 (C-7), 22.6 (C-15), 15.2 (C-18). ^{19}F NMR (CD_3CN, 376 MHz) δ -151.0. HRMS (ESI) *m*/*z*: $[M\text{-}BF_4^-]^+$ Calcd for $C_{17}H_{16}N^+$ 234.1277; Found 234.1279. Anal. Calcd for $C_{17}H_{16}BF_4N$: C, 63.59; H, 5.02; N,

4.36. Found: C, 63.51; H, 4.93; N, 4.30. IR (ATR) ν(cm^{-1}) = 1579, 1551, 1456, 1406, 1383, 1334, 1321, 1295, 1211, 1181, 1125, 1077, 1024, 993, 913, 865, 812, 765.

(1,2-Dimethyl-1H-indol-3-yl)(p-tolyl)methylium tetrafluoroborate (**3g-BF$_4$**). From **1c** (1.01 g, 6.96 mmol), **2b** (840 mg, 6.99 mmol) and $HBF_4 \cdot OEt_2$ complex (1.70 g, 10.5 mmol): 2.04 g (6.09 mmol, 88%), bright yellow solid, mp 190-195 °C (dec.). ^{1}H NMR (CD_3CN, 400 MHz) δ 8.68 (s, 1H, H-10), 8.16 (d, 1H, *J* = 7.9 Hz, H-4), 7.91 (d, 2H, *J* = 8.2 Hz, H-12 and H-17), 7.70 (d, 1H, *J* = 8.0 Hz, H-7), 7.64 (td, 1H, *J* = 0.9, 7.8 Hz, H-6), 7.54-7.46 (m, 3H, H-5, H-13 and H-16), 3.94 (s, 3H, H-1), 2.89 (s, 3H, H-18), 2.51 (s, 3H, H-15). ^{13}C NMR (CD_3CN, 101 MHz) δ 174.0 (C-2), 158.7 (C-10), 147.6 (C-14), 144.6 (C-8), 133.8 (C-12 and C-17), 131.9 (C-11), 131.6 (C-13 and C-16), 131.5 (C-6), 131.4 (C-3), 130.0 (C-5), 125.5 (C-9), 124.6 (C-4), 115.4 (C-7), 34.9 (C-1), 22.5 (C-15), 13.9 (C-18). ^{19}F NMR (CD_3CN, 376 MHz) δ -151.8. HRMS (ESI) *m*/*z*: $[M\text{-}BF_4^-]^+$ Calcd for $C_{18}H_{18}N^+$ 248.1434; Found 248.1436. Anal. Calcd for $C_{18}H_{18}BF_4N$: C, 64.51; H, 5.41; N, 4.18. Found: C, 64.39; H, 5.42; N, 4.11. IR (ATR) ν(cm^{-1}) = 1613, 1591, 1566, 1554, 1458, 1360, 1222, 1210, 1185, 1031, 907, 827, 792, 754, 748.

(1,2-Dimethyl-1H-indol-3-yl)(phenyl)methylium tetrafluoroborate (**3h-BF$_4$**). From **1c** (1.12 g, 7.71 mmol), **2a** (820 mg, 7.73 mmol) and $HBF_4 \cdot OEt_2$ complex (1.50 g, 9.26 mmol): 2.09 g (6.51 mmol, 84%), bright yellow solid, mp 176-181 °C (dec.). ^{1}H NMR (CD_3CN, 400 MHz) δ 8.72 (s, 1H, H-10), 8.08 (d, 1H, *J* = 7.9 Hz, H-4), 7.99 – 7.91 (m, 2H, H-12 and H-17), 7.76 – 7.61 (m, 5H, H-6, H-7, H-13, H-14 and H-16), 7.48 (td, 1H, *J* = 1.1, 7.7 Hz, H-5), 3.96 (s, 3H, H-1), 2.91 (s, 3H, H-18).^{13}C NMR (CD_3CN, 101 MHz) δ 174.6 (C-2), 158.2 (C-10), 144.8 (C-8), 135.2 (C-14), 134.6 (C-11), 133.0 (C-12 and C-17), 132.5 (C-3), 131.8 (C-6), 130.8 (C-13 and C-16), 130.1 (C-5), 125.4 (C-9), 124.7 (C-4), 115.5

(C-7), 35.0 (C-1), 14.0 (C-18). ^{19}F NMR (CD_3CN, 376 MHz) δ -151.7. HRMS (ESI) *m*/*z*: $[M\text{-}BF_4^-]^+$ Calcd for $C_{17}H_{16}N^+$ 234.1277; Found 234.12745. IR (ATR) ν (cm^{-1}) = 1606, 1589, 1556, 1453, 1366, 1307, 1221, 1183, 1093, 1047, 1034, 916, 780, 757, 693.

General procedure for the synthesis of bis(indol-3-yl)methylium tetrafluoroborates **3(i-k)-BF$_4$**.

Analogous to ref 12, an indole **1a, c, d** (1.00 g, 2.00 equiv.) was dissolved in 20 mL of CH_2Cl_2 and the solution was stirred until the complete homogenization and cooled down at 0 °C. Then triethyl orthoformate **4** (1.00 equiv.) was added following by the dropwise addition of the $HBF_4{\cdot}OEt_2$ complex (1.00 equiv.). After addition, the solution was allowed to warm at room temperature and stirred for 2 hours. The colored crystals which precipitated were filtered and washed with a mixture of Et_2O and then recrystallized in CH_3CN/Et_2O.

Bis(1-methyl-1H-indol-3-yl)methylium tetrafluoroborate (**3i-BF$_4$**). From **1a** (1.03 g, 7.85 mmol), **4** (579 mg, 3.91 mmol) and $HBF_4{\cdot}OEt_2$ complex (633 mg, 3.91 mmol): 1.22 g (3.39 mmol, 86%), dark green solid, mp 235-240 °C (dec.). ^{1}H NMR ($(CD_3)_2SO$, 400 MHz) δ 9.28 (br s, 3H, H-2, H-10, H-12), 8.30 (d, 2H, *J* = 8.2 Hz, H-4, H-16), 7.81 – 7.75 (m, 2H, H-7, H-13), 7.58 – 7.50 (m, 4H, H-5, H-15, H-6, H-14), 4.09 (s, 6H, H-1, H-19). ^{1}H NMR spectra agreed with literature data (Ref. 12b). ^{13}C NMR ($(CD_3)_2SO$, 101 MHz) δ 147.5 (C-10), 146.2 (C-2 and C-12), 138.8 (C-8 and C-18), 128.1 (C-9 and C-17), 126.0 (C-6 and C-14), 125.7 (C-5 and C-15), 120.1 (C-4 and C-16), 117.1 (C-3 and C-11), 113.1 (C-7 and C-13), 35.3 (C-1 and C-19). ^{19}F NMR ($(CD_3)_2SO$, 376 MHz) δ -148.2. HRMS (ESI) *m*/*z*: $[M\text{-}BF_4^-]^+$ Calcd for $C_{19}H_{17}N_2^+$ 273.1386; Found 273.1388. IR (ATR) ν

(cm^{-1}) = 1613, 1590, 1567, 1504, 1473, 1445, 1421, 1398, 1311, 1283, 1253, 1211, 1096, 1062, 1029, 959, 806, 748, 681, 657.

Bis(5-methoxy-1-methyl-1H-indol-3-yl)methylium tetrafluoroborate (**3j-BF_4**). From **1d** (548 mg, 3.40 mmol), **4** (252 mg, 1.70 mmol) and $HBF_4{\cdot}OEt_2$ complex (275 mg, 1.70 mmol): 493 mg (1.17 mmol, 69%), dark brown solid, mp 256-258 °C (dec.). ^{1}H NMR ($(CD_3)_2SO$, 400 MHz) δ 9.23 (s, 1H, H-10), 9.18 (br s, 2H, H-2 and H-13), 7.87 (s, 2H, H-4 and H-17), 7.69 (d, 2H, *J* = 8.9 Hz, H-7 and H-14), 7.11 (dd, 2H, *J* = 2.4, 8.9 Hz, H-6 and H-15), 4.06 (s, 6H, H-1 and H-20), 3.92 (s, 6H, H-11 and H-21). ^{13}C NMR ($(CD_3)_2SO$, 101 MHz) δ 158.4 (C-5 and C-16), 146.2 (C-10), 144.9 (C-2 and C-13), 133.1 (C-8 and C-19), 129.7 (C-9 and C-18), 116.6 (C-3 and C-12), 114.0 (C-6, C-7, C-14 and C-15), 103.4 (C-4 and C-17), 55.9 (C-11 and C-21), 35.4 (C-1 and C-20).^{19}F NMR (CD_3CN, 376 MHz) δ -151.9. HRMS (ESI) *m*/*z*: $[M\text{-}BF_4^-]^+$ Calcd for $C_{21}H_{21}O_2N_2^+$ 333.1598; Found 333.1596. IR (ATR) ν (cm^{-1}) = 1617, 1579, 1550, 1511, 1473, 1439, 1400, 1306, 1243, 1219, 1184, 1135, 1049, 1036, 946, 917, 846, 799, 790, 769, 715.

Bis(1,2-dimethyl-1H-indol-3-yl)methylium tetrafluoroborate (**3k-BF_4**). From **1c** (1.37 g, 9.43 mmol), **4** (699 mg, 4.72 mmol) and $HBF_4{\cdot}OEt_2$ complex (765 mg, 4.72 mmol): 1.36 g (3.50 mmol, 74%), bright red orange solid, mp 252 °C (dec.). ^{1}H NMR (CD_3CN, 400 MHz) δ 8.85 (s, 1H, H-10), 7.68 (dt, 2H, *J* = 0.8, 8.2 Hz, H-4 and H-16), 7.54 – 7.47 (m, 2H, H-5 and H-15), 7.34 – 7.27 (m, 2H, H-6 and H-14), 7.05 (dt, 2H, *J* = 0.8, 7.1 Hz, H-7 and H-13), 3.93 (s, 6H, H-1 and H-21), 2.83 (s, 6H, H-19 and H20). ^{1}H NMR spectra agreed with literature data (Ref. 12b, in $(CD_3)_2SO/CDCl_3$: 1/1). ^{13}C NMR (CD_3CN, 101 MHz) δ 161.8 (C-2 and C-12), 148.1 (C-10), 141.8 (C-8 and C-18), 127.1 (C-5 and C-15), 126.1 (C-9 and C-17), 126.0 (C-6 and C-14), 124.9 (C-7 and C-13), 119.2 (C-3 and

C-11), 113.5 (C-4 and C-16), 33.1 (C-1 and C-21), 13.3 (C-19 and C-20). ^{19}F NMR (CD_3CN, 376 MHz) δ -151.8. HRMS (ESI) *m*/*z*: $[M\text{-}BF_4^-]^+$ Calcd for $C_{21}H_{21}N_2^+$ 301.1699; Found 301.1703. IR (ATR) ν(cm^{-1}) = 1563, 1496, 1480, 1387, 1356, 1322, 1290, 1229, 1177, 1094, 1049, 1035, 981, 896, 880, 813, 767, 759, 648, 613, 579.

Product Studies

(4-Methoxyphenyl)(1-methyl-1H-indol-2-yl)methanol (**5**). To a solution of **1a** (1.00 g, 7.63 mmol) in tetrahydrofuran (25 mL) at -78 °C was added dropwise *n*-BuLi (2.50 M, 3.05 mL, 7.63 mmol). After 3 hours at this temperature, **2c** (1.14 g, 8.38 mmol, 1.10 equiv.) was added to the pale-yellow solution which was then allowed to warm at room temperature and stirred overnight. The reaction was quenched by addition of 30 mL of water and extracted with Et_2O (2 x 20 mL). Solvent and volatile compounds were evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, *n*-pentane/EtOAc = 80/20): 1.36 g (5.11 mmol, 67%), yellow oil, Rf (*n*-pentane/EtOAc = 80/20) = 0.15. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.55 (dt, 1H, *J* = 0.9, 7.9 Hz), 7.34 – 7.25 (m, 3H), 7.20 (distorted ddd, 1H, *J* = 1.2, 7.0, 8.2 Hz), 7.08 (distorted ddd, 1H, *J* = 1.1, 7.0, 8.0 Hz), 6.91 – 6.86 (m, 2H), 6.30 (br s, 1H), 5.99 (d, 1H, *J* = 4.4 Hz), 3.80 (s, 3H), 3.63 (s, 3H), 2.27 (d, 1H, *J* = 4.7 Hz, OH). The decomposition of **5** in $CDCl_3$ is too fast to measure the ^{13}C NMR. HRMS (ESI) *m*/*z*: $[M+H^+]$ Calcd for $C_{17}H_{18}NO_2$ 268.1338; Found 268.1330.

6,12-Bis(4-methoxyphenyl)-5,11-dimethyl-5,6,11,12-tetrahydroindolo[3,2-b]carbazole (**6**). To a CH_2Cl_2 (5 mL) solution of **5** (1.20 g, 4.49 mmol, 1 equiv.) cooled at 0 °C was added dropwise $HBF_4{\cdot}Et_2O$ (728 mg, 4.49 mmol). Subsequently, the solution was allowed to warm at room temperature and Et_2O was added to give a brown precipitate.

After filtration and washing of the solid with cold Et_2O, **6** (1.00 g, 2.01 mmol, 89%) was obtained as a brown solid, mp. 335-346 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.46 (app d, 2H, *J* = 7.9 Hz), 7.24 – 7.21 (m, 4H), 7.16 (app d, 2H, *J* = 8.1 Hz), 7.09 (distorted ddd, 2H, *J* = 1.2, 7.0, 8.1 Hz), 6.96 (distorted ddd, 2H, *J* = 1.0, 7.0, 8.0 Hz), 6.77 – 6.73 (m, 4H), 5.70 (s, 2H), 3.71 (s, 6H), 3.42 (s, 6H). ^{13}C NMR ($CDCl_3$, 151 MHz) δ 158.3 (C), 138.3 (C), 136.6 (C), 136.1 (C), 130.0 (CH), 125.8 (C), 121.2 (CH), 119.3 (CH), 119.0 (CH), 114.1 (CH), 112.1 (C), 108.9 (CH), 55.4 (CH_3), 39.6 (CH), 30.6 (CH_3). HRMS (EI) *m*/*z*: [M] Calcd for $C_{34}H_{30}N_2O_2$ 498.2307; Found 498.2300. IR (ATR) ν (cm^{-1}) = 1608, 1507, 1474, 1401, 1376, 1302, 1253, 1224, 1174, 1112, 1032, 828, 806, 759, 737, 613.

1-Methyl-3-(3-methyl-1-(p-tolyl)but-3-en-1-yl)-1H-indole (**9**). To a CH_2Cl_2 (5 mL) solution of **3b-BF$_4$** (301 mg, 0.937 mmol, 1.00 equiv.) was added **8j** (143 mg, 1.12 mmol, 1.20 equiv.) and the solution was stirred for 10 min at 20 °C. Solvent and volatile compounds were evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, *n*-pentane/EtOAc = 95/5) to give **9** as a white oil (248 mg, 0.818 mmol, 87%), Rf (*n*-pentane/EtOAc = 95/5) = 0.62. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53 (app d, 1H, *J* = 8.0 Hz), 7.32 – 7.19 (m, 4H, contains $CHCl_3$ peak), 7.12 (app d, 2H, *J* = 7.9 Hz), 7.07 (distorted ddd, 1H, *J* = 1.1, 7.0, 8.0 Hz), 6.89 (s, 1H), 4.76 (br s, 1H), 4.71 (br s, 1H), 4.47 (app t, 1H, *J* = 7.8 Hz), 3.77 (s, 3H), 2.96 (dd, 1H, *J* = 6.9, 14.4 Hz), 2.78 (dd, 1H, *J* = 8.7, 14.5 Hz), 2.34 (s, 3H), 1.78 (s, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ 144.2 (C), 142.2 (C), 137.4 (C), 135.5 (C), 129.1 (2 x CH), 128.0 (2 x CH), 127.6 (C), 126.2 (CH), 121.6 (CH), 119.7 (CH), 118.9 (C), 118.8 (CH), 112.3 (CH_2), 109.3 (CH), 44.9 (CH_2), 40.8 (CH), 32.9 (CH_3), 22.8 (CH_3), 21.2 (CH_3). HRMS (EI) *m*/*z*: [M] Calcd for $C_{21}H_{23}N$ 289.1830; Found 289.1828.

2-((1-Methyl-1H-indol-3-yl)(phenyl)methyl)cyclohexanone (**10**). To a CH_3CN solution (5 mL) of **3a-BF$_4$** (175 mg, 0.570 mmol, 1.00 equiv.) was added neat **8h** (100 mg, 0.588 mmol, 1.05 equiv.) and the solution was stirred for 1 h at 20 °C. Solvent and volatile compounds were evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, *n*-pentane/EtOAc = 90/10) to give **10** as a yellow oil (108 mg, 0.34 mmol, 61%) as a 1:1 mixture of diastereoisomers. ^{1}H NMR spectra agreed with literature data in Ref. 25. HRMS (EI) *m*/*z*: [M] Calcd for $C_{22}H_{23}ON$ 317.1780; Found 317.1780.

(E)-5-(4-(Dimethylamino)phenyl)-1-methoxy-5-(1-methyl-1H-indol-3-yl)pent-1-en-3-one (**11**). To a CH_2Cl_2 solution (5 mL) of **3d-BF$_4$** (266 mg, 0.759 mmol, 1.00 equiv.) was added **8d** (157 mg, 0.912 mmol, 1.20 equiv.) and the solution was stirred overnight at 20 °C. Solvent and volatile compounds were evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, gradient eluent: *n*-pentane/EtOAc = 90/10 to 80/20) to give **11** as a yellow oil (154 mg, 0.425 mmol, 56%). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.50 (d, 1H, *J* = 12.6 Hz), 7.43 (app d, 1H, *J* = 7.9 Hz), 7.22 (app d, 1H, *J* = 8.2 Hz), 7.18 (br d, 2H, *J* = 7.2 Hz), 7.14 (app t, 1H, *J* = 7.6 Hz), 6.98 (app t, 1H, *J* = 7.5 Hz), 6.80 (s, 1H), 6.68 (br s, 2H), 5.54 (d, 1H, *J* = 12.6 Hz), 4.78 (t, 1H, *J* = 7.5 Hz), 3.70 (s, 3H), 3.59 (s, 3H), 3.23 (dd, 1H, *J* = 7.1, 15.4 Hz), 3.13 (dd, 1H, *J* = 7.9, 15.4 Hz), 2.88 (s, 6H). ^{13}C NMR ($CDCl_3$, 151 MHz) δ 198.4 (C), 162.8 (CH), 137.5 (C), 128.6 (2 x CH), 127.3 (C), 126.4 (3 x CH), 121.7 (CH), 120.0 (CH), 118.9 (CH), 118.5 (2 x C), 113.1 (C), 109.3 (CH), 105.9 (CH), 57.7 (CH_3), 48.6 (CH_2), 41.0 (2 x CH_3), 37.9 (CH), 32.9 (CH_3). HRMS (EI) *m*/*z*: [M] Calcd for $C_{23}H_{26}O_2N_2$ 362.1994; Found

362.1998. IR (ATR) ν (cm^{-1}) = 2962, 1673, 1612, 1589, 1517, 1471, 1444, 1414, 1326, 1258, 1083, 1012, 944, 864, 792, 738, 702, 661.

(E)-5-(4-Methoxyphenyl)-5-(1-methyl-1H-indol-3-yl)pent-2-enal (**12**). To a CH_2Cl_2 (10 mL) solution of **3c-BF$_4$** (337 mg, 1.00 mmol, 1.00 equiv.) was added **8i** (142 mg, 1.00 mmol, 1.00 equiv.) and the mixture was stirred for 1 hour at 20 °C. Solvent and volatile compounds were evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, eluent: *n*-pentane/EtOAc = 90/10) to give **12** as a yellow oil (128 mg, 0.401 mmol, 40%), Rf (*n*-pentane/EtOAc = 90/10) = 0.22. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 9.39 (d, 1H, *J* = 7.9 Hz), 7.40 (app d, 1H, *J* = 8.0 Hz), 7.27 (app d, 1H, *J* = 8.2 Hz), 7.22 – 7.16 (m, 3H), 7.02 (distorted ddd, 1H, *J* = 0.9, 7.1, 8.0 Hz), 6.82 – 6.76 (m, 4H), 6.13 (app ddt, 1H, *J* = 1.3, 7.9, 15.6 Hz), 4.35 (t, 1H, *J* = 7.7 Hz), 3.76 (s, 3H), 3.74 (s, 3H), 3.17 (m, 1H), 3.01 (m, 1H). ^{13}C NMR ($CDCl_3$, 151 MHz) δ 194.2 (CH), 158.4 (C), 157.3 (CH), 137.5 (C), 136.0 (C), 134.2 (CH), 128.9 (CH), 127.2 (C), 126.3 (CH), 122.1 (CH), 119.6 (CH), 119.2 (CH), 117.7 (C), 114.1 (CH), 109.5 (CH), 55.4 (CH_3), 41.5 (CH), 39.7 (CH_2), 33.0 (CH_3). HRMS (EI) *m*/*z*: [M] Calcd for $C_{21}H_{21}O_2N$ 319.1572; Found 319.1572. IR (ATR) ν (cm^{-1}) = 2922, 2852, 1683, 1609, 1509, 1465, 1422, 1372, 1327, 1301, 1244, 1174, 1110, 1029, 974, 829, 740.

1-Methyl-3-(1-phenylbut-3-enyl)-1H-indole (**13**). To a CH_2Cl_2 solution (10 mL) of **3a-BF$_4$** (200 mg, 0.651 mmol, 1.00 equiv.) was added **8k** (84.5 mg, 0.741 mmol, 1.14 equiv.) and the solution was stirred for 1 h at 20 °C. Then the reaction is treated with 10 mL of water and the organic phase was washed with brine and dried over $MgSO_4$. After evaporation of the solvent under reduced pressure, the crude product was purified by column chromatography (silica gel, *n*-pentane/EtOAc = 90/10) to give **13** as a colorless

oil (98 mg, 0.37 mmol, 57%), Rf (*n*-pentane/EtOAc = 90/10) = 0.60. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.62 – 7.55 (m, 1H), 7.52 – 7.24 (m, 7H), 7.21 – 7.09 (m, 1H), 6.98 (app s, 1H), 6.08 – 5.84 (m, 1H), 5.27 – 5.15 (m, 1H), 5.14 – 5.05 (m, 1H), 4.41 (app t, 1H, *J* = 7.6 Hz), 3.80 (s, 3H), 3.17 – 3.03 (m, 1H), 3.00 – 2.86 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.1 (C), 137.6 (CH), 137.4 (C), 128.4 (2 x CH), 128.2 (2 x CH), 127.6 (C), 126.3 (CH), 126.2 (CH), 121.7 (CH), 119.7 (CH), 118.9 (CH), 118.4 (C), 116.1 (CH_2), 109.3 (CH), 43.2 (CH), 40.8 (CH_2), 32.8 (CH_3). HRMS (EI) *m*/*z*: [M] Calcd for $C_{19}H_{19}N^+$ 261.1517; Found 261.1511.

3-((1,2-Dimethyl-1H-indol-3-yl)(p-tolyl)methyl)tetrahydro-2H-pyran-2-one (**14**). To a bright orange CH_2Cl_2 solution (10 mL) of **3g-BF$_4$** (261 mg, 0.779 mmol, 1.00 equiv.) was added **8b** (230 mg, 1.33 mmol, 1.71 equiv.) and the mixture was stirred for 15 min at 20 °C. Solvent and volatile compounds were evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, gradient eluent: *n*-pentane/EtOAc = 95/5 to 70/30) to give **14** (1:1 mixture of diastereoisomers) as a white solid (258 mg, 0.743 mmol, 95%), mp 68-80 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.39 (app d, 1H, *J* = 7.9 Hz), 7.35 (app d, 1H, *J* = 7.9 Hz), 7.24 – 7.14 (m, 6H), 7.14 – 7.06 (m, 2H), 7.06 – 6.90 (m, 5H), 5.01 (d, 1H, *J* = 7.0 Hz), 4.77 (d, 1H, *J* = 8.6 Hz), 4.41 – 4.28 (m, 3H), 4.25 – 4.14 (m, 1H), 3.80 – 3.68 (m, 1H), 3.63 (s, 6H), 3.49 – 3.32 (m, 1H), 2.43 (s, 3H), 2.37 (s, 3H), 2.27 (s, 3H), 2.24 (s, 3H), 2.08 – 1.71 (m, 6H), 1.65 – 1.46 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.6 (C), 174.0 (C), 140.5 (C), 138.5 (C), 137.1 (C), 137.0 (C), 135.6 (C), 135.4 (C), 134.6 (C), 134.3 (C), 129.2 (CH), 129.1 (CH), 128.5 (CH), 127.5 (CH), 126.9 (2 x CH), 120.6 (CH), 120.3 (CH), 119.7 (CH), 119.5 (CH), 119.0 (CH), 118.9 (CH), 112.9 (C), 111.6 (C), 109.1 (CH), 108.9 (CH), 68.3 (CH_2), 67.9

(CH_2), 44.2 (CH), 42.7 (CH), 42.6 (CH), 42.5 (CH), 29.8 (2 x CH_3), 23.6 (CH_2), 23.4 (CH_2), 22.7 (CH_2), 22.2 (CH_2), 21.1 (2 x CH_3), 11.1 (CH_3), 11.0 (CH_3). HRMS (EI) *m*/*z*: [M] Calcd for $C_{23}H_{25}O_2N$ 347.1885; Found 347.1880.

Methyl 2,2-dimethyl-3,3-bis(1-methyl-1H-indol-3-yl)propanoate (**15**). To a CH_2Cl_2 solution (10 mL) of **3i-BF$_4$** (312 mg, 0.866 mmol, 1.00 equiv.) was added **8c** (227 mg, 1.30 mmol, 1.50 equiv.) and stirred for 1 h at 20 °C. Solvent and volatile compounds were evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, gradient eluent: *n*-pentane/EtOAc = 90/10 to 80/20) to give **15** as a colorless solid (310 mg, 0.828 mmol, 96%), mp 130-133 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54 (app d, 2H, *J* = 8.0 Hz), 7.21 (app d, 2H, *J* = 8.2 Hz), 7.16 – 7.11 (distorted ddd, 2H, *J* = 1.0, 7.0, 8.1 Hz), 7.03 – 6.97 (m, 4H), 5.11 (s, 1H), 3.71 (s, 6H), 3.46 (s, 3H), 1.37 (s, 6H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ 179.0 (C), 136.5 (C), 129.0 (C), 127.6 (CH), 121.4 (CH), 119.9 (CH), 118.8 (CH), 115.9 (C), 109.0 (CH), 52.0 (CH_3), 47.4 (C), 40.4 (CH), 33.0 (2 x CH_3), 24.4 (2 x CH_3). HRMS (EI) *m*/*z*: [M] Calcd for $C_{24}H_{26}O_2N_2$ 374.1994; Found 374.1979. IR (ATR) ν (cm^{-1}) = 3050, 2946, 1728, 1613, 1537, 1465, 1430, 1373, 1330, 1251, 1205, 1183, 1152, 1123, 1112, 1060, 1014, 984, 938, 870, 818, 792, 739, 726, 709, 659, 569.

3-(Bis(1-methyl-1H-indol-3-yl)methyl)dihydrofuran-2(3H)-one (**16a**). To a CH_2Cl_2 solution (10 mL) of **3i-BF$_4$** (306 mg, 0.850 mmol, 1.00 equiv.) was added **8a** (180 mg, 1.14 mmol, 1.34 equiv.) and the solution was stirred for 10 min at 20 °C. Solvent and volatile compounds were evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, gradient eluent: *n*-pentane/EtOAc = 80/20 to 50/50) to give **16b** as a yellow oil (37 mg, 0.16 mmol, 19%), and **16a** as a white solid

(222 mg, 0.619 mmol, 73%), mp 90-100 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) of **16a** δ 7.41 (app t, 2H, *J* = 7.2 Hz), 7.27 (app d, 1H, *J* = 8.2 Hz), 7.25 – 7.22 (m, 1H), 7.18 (app t, 1H, *J* = 7.6 Hz), 7.14 (app t, 1H, *J* = 7.6 Hz), 7.05 (br s, 1H), 7.00 – 6.93 (m, 3H), 5.20 (d, 1H, *J* = 3.3 Hz), 4.14 – 4.06 (m, 1H), 3.84 (app td, 1H, *J* = 4.3, 8.7 Hz), 3.75 (s, 3H), 3.71 (s, 3H), 3.51 (app td, 1H, *J* = 3.4, 9.2 Hz), 2.49 – 2.42 (m, 1H), 2.42 – 2.35 (m, 1H). ^{13}C NMR ($CDCl_3$, 151 MHz) δ 178.9 (C), 137.2 (2 x C), 128.5 (CH), 127.9 (C), 127.8 (C), 126.8 (CH), 121.9 (CH), 121.6 (CH), 120.1 (CH), 119.6 (CH), 119.1 (2 x CH), 116.0 (C), 114.3 (C), 109.3 (2 x CH), 66.8 (CH_2), 45.0 (CH), 34.4 (CH), 33.0 (2 x CH_3), 26.6 (CH_2). HRMS (EI) *m*/*z*: [M] Calcd for $C_{23}H_{22}O_2N_2$ 358.1681; Found 358.1668. IR (ATR) ν(cm^{-1}) = 1761, 1612, 1542, 1469, 1423, 1371, 1328, 1213, 1153, 1024, 953, 738, 680.

(E)-3-((1-Methyl-1H-indol-3-yl)methylene)dihydrofuran-2(3H)-one (**16b**). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.88 (t, 1H, *J* = 2.7 Hz), 7.81 (app dt, 1H, *J* = 1.1, 7.7 Hz), 7.36 – 7.19 (m, 4H), 4.40 (app t, 2H, *J* = 7.4 Hz), 3.83 (s, 3H), 2.97 (app td, 2H, *J* = 2.8, 7.4 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.2 (C), 136.9 (C), 130.4 (CH), 128.1 (C), 127.8 (CH), 123.4 (CH), 121.3 (CH), 119.0 (C), 116.9 (CH), 112.1 (C), 109.9 (CH), 65.2 (CH_2), 33.6 (CH_3), 28.4 (CH_2). HRMS (EI) *m*/*z*: [M] Calcd for $C_{14}H_{13}O_2N$ 227.0946; Found 227.0950.

3-(Bis(1-methyl-1H-indol-3-yl)methyl)tetrahydro-2H-pyran-2-one (**17a**). To a CH_2Cl_2 solution (10 mL) of **3i-BF$_4$** (270 mg, 0.750 mmol, 1.00 equiv.) was added **8b** (157 mg, 0.911 mmol, 1.21 equiv.) and the solution was stirred for 10 min at 20 °C. Solvent and volatile compounds were evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, gradient eluent: *n*-pentane/EtOAc = 80/20 to 50/50) to give **17b** as a yellow oil (30 mg, 0.12 mmol, 16%), R_f (*n*-pentane/EtOAc =

70/30) = 0.2, and **17a** as a white solid (131 mg, 0.352 mmol, 47%), mp 64-76 °C, R_f (*n*-pentane/EtOAc = 70/30) = 0.09. ^{1}H NMR ($CDCl_3$, 300 MHz) of **17a** δ 7.55 – 7.46 (m, 2H), 7.29 – 7.11 (m, 4H), 7.06 – 6.93 (m, 4H), 5.35 (d, 1H, *J* = 4.4 Hz), 4.42 – 4.19 (m, 1H), 4.17 – 4.01 (m, 1H), 3.72 (s, 6H), 3.50 – 3.40 (m, 1H), 2.14 – 1.70 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.3 (C), 137.2 (2 x C), 128.2 (CH), 128.1 (C), 127.9 (C), 127.5 (CH), 121.7 (CH), 121.5 (CH), 120.4 (CH), 119.6 (CH), 119.0 (2 x CH), 116.0 (C), 115.1 (C), 109.3 (CH), 109.2 (CH), 69.0 (CH_2), 45.8 (CH), 35.3 (CH), 33.0 (2 x CH_3), 23.6 (CH_2), 23.0 (CH_2). HRMS (EI) *m*/*z*: [M] Calcd for $C_{24}H_{24}O_2N_2$ 372.1838; Found 372.1828. IR (ATR) ν (cm^{-1}) = 1720, 1612, 1423, 1371, 1327, 1260, 1152, 1084, 1012, 960, 910, 770, 737, 646.

(E)-3-((1-Methyl-1H-indol-3-yl)methylene)tetrahydro-2H-pyran-2-one (**17b**). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.29 (t, 1H, *J* = 2.2 Hz), 7.87 (app d, 1H, *J* = 7.8 Hz), 7.38 – 7.20 (m, 4H), 4.35 (app t, 2H, *J* = 5.2 Hz), 3.85 (s, 3H), 2.72 (app td, 2H, *J* = 2.2, 6.7 Hz), 2.09 – 1.99 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.1 (C), 136.6 (C), 133.1 (CH), 130.9 (CH), 128.7 (C), 123.3 (CH), 121.2 (CH), 119.3 (CH), 119.0 (C), 112.0 (C), 109.7 (CH), 68.3 (CH_2), 33.6 (CH_3), 27.1 (CH_2), 22.9 (CH_2). HRMS (EI) *m*/*z*: [M] Calcd for $C_{15}H_{15}O_2N$ 241.1103; Found 241.1081.

3-(Bis(1,2-dimethyl-1H-indol-3-yl)methyl)dihydrofuran-2(3H)-one (**18a**). To a CH_2Cl_2 solution (10 mL) of **3k-BF$_4$** (327 mg, 0.842 mmol, 1.00 equiv.) was added **8a** (230 mg, 1.45 mmol, 1.73 equiv.) and the solution was stirred for 1 hour at 20 °C. Solvent and volatile compounds were evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, gradient eluent: *n*-pentane/EtOAc = 80/20 to 50/50) to give **18b** as a colorless solid (20 mg, 0.08 mmol, 10%): mp 157-164 °C, Rf

(*n*-pentane/EtOAc = 80/20) = 0.08 and **18a** as a yellow solid (86 mg, 0.22 mmol, 27%): mp 206-213 °C, Rf (*n*-pentane/EtOAc = 80/20) = 0.37. ^{1}H NMR ($CDCl_3$, 200 MHz) of **18a** δ 7.65 (app d, 1H, *J* = 7.3 Hz), 7.39 – 6.96 (m, 6H), 6.95 – 6.78 (m, 1H), 5.11 (d, 1H, *J* = 5.3 Hz), 4.24 – 4.03 (m, 1H), 3.93 – 3.74 (m, 2H), 3.62 (s, 3H), 3.58 (s, 3H), 2.76 – 2.51 (m, 1H), 2.50 – 2.30 (m, 1H), 2.41 (s, 3H), 2.19 (s, 3H). The product is not sufficiently stable in $CDCl_3$ to measure the carbon NMR, it decomposed within one hour into compound **18b** and the corresponding indole. HRMS (EI) *m*/*z*: [M] Calcd for $C_{25}H_{26}O_2N_2$ 386.1994; Found 386.1987. IR (ATR) ν (cm^{-1}) = 3048, 2911, 1750, 1608, 1541, 1468, 1411, 1365, 1332, 1247, 1214, 1165, 1134, 1070, 1020, 965, 945, 925, 902, 821, 738, 695, 663, 608.

(E)-3-((1,2-Dimethyl-1H-indol-3-yl)methylene)dihydrofuran-2(3H)-one (**18b**). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.81 (app t, 1H, *J* = 2.5 Hz), 7.63 – 7.57 (m, 1H), 7.34 – 7.11 (m, 3H), 4.36 (app t, 2H, *J* = 7.3 Hz), 3.70 (s, 3H), 3.13 (app td, 2H, *J* = 2.5, 7.3 Hz), 2.46 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.6 (C), 140.3 (C), 137.5 (C), 131.2 (CH), 126.0 (C), 122.1 (C), 120.7 (CH), 120.1 (CH), 119.0 (CH), 109.6 (CH), 109.0 (C), 65.7 (CH_2), 30.1 (CH_3), 29.2 (CH_2), 11.5 (CH_3). HRMS (EI) *m*/*z*: [M] Calcd for $C_{15}H_{15}O_2N$ 241.1103; Found 241.1106.

3-(Bis(1,2-dimethyl-1H-indol-3-yl)methyl)tetrahydro-2H-pyran-2-one (**19a**). To a CH_2Cl_2 solution (5 mL) of **3k-BF$_4$** (310 mg, 1.03 mmol, 1.00 equiv.) was added **8b** (354 mg, 2.06 mmol, 2.00 equiv.) and the solution was stirred for 30 min at 20 °C. Solvent and volatile compounds were evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, gradient eluent: *n*-pentane/EtOAc = 90/10 to 60/40) and recrystallized from (*n*-pentane/EtOAc) to give **19b** as white solid (129 mg,

0.506 mmol, 49%): mp 144-153 °C and **19a** as a white solid (48 mg, 0.12 mmol, 12%): mp 188-197 °C. ^{1}H NMR ($CDCl_3$, 200 MHz) of **19a** δ 7.69 (app d, 1H, *J* = 7.2 Hz), 7.58 (app d, 1H, *J* = 8.0 Hz), 7.29 (app d, 2H, *J* = 5.1 Hz), 7.19 – 6.90 (m, 4H), 5.04 (d, 1H, *J* = 9.4 Hz), 4.55 – 4.30 (m, 2H), 4.26 – 4.05 (m, 1H), 3.67 (s, 3H), 3.61 (s, 3H), 2.46 (s, 3H), 2.34 (s, 3H), 2.01 – 1.81 (m, 2H), 1.76 – 1.50 (m, 2H). The product is not sufficiently stable in $CDCl_3$ to measure the carbon NMR, it decomposed within one hour into compound **19b** and the corresponding indole. HRMS (EI) *m*/*z*: [M] Calcd for $C_{26}H_{28}O_2N_2$ 400.2151; Found 400.2144.

(E)-3-((1,2-Dimethyl-1H-indol-3-yl)methylene)tetrahydro-2H-pyran-2-one (**19b**). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.12 (app t, 1H, *J* = 1.7 Hz), 7.44 (app d, 1H, *J* = 7.6 Hz), 7.29 (app d, 1H, *J* = 7.5 Hz), 7.24 – 7.11 (m, 2H), 4.41 (app t, 2H, *J* = 5.5 Hz), 3.70 (s, 3H), 2.69 – 2.58 (m, 2H), 2.39 (s, 3H), 1.93 – 1.81 (m, 2H). ^{13}C NMR ($CDCl_3$, 151 MHz) δ 167.4 (C), 138.6 (C), 137.1 (C), 136.3 (CH), 126.3 (C), 122.8 (C), 121.7 (CH), 120.3 (CH), 120.1 (CH), 109.3 (CH), 108.8 (C), 69.5 (CH_2), 30.0 (CH_3), 27.1 (CH_2), 23.7 (CH_2), 11.8 (CH_3). HRMS (EI) *m*/*z*: [M] Calcd for $C_{16}H_{17}O_2N$ 255.1259; Found 255.1249.

4-(Bis(1,2-dimethyl-1H-indol-3-yl)methyl)morpholine (**20**). To a CH_3CN solution (10 mL) of **3k-BF$_4$** (220 mg, 0.567 mmol, 1.00 equiv.) was added **8m** (172 mg, 1.98 mmol, 3.49 equiv.) and stirred for 5 min at 20 °C. Solvent and volatile compounds were evaporated under reduced pressure. The crude product was recrystallized from Et_2O, EtOAc, and acetonitrile to give **20** as a colorless solid (83 mg, 0.21 mmol, 38%). ^{1}H NMR (CD_3CN, 400 MHz) δ 7.98 (br d, 2H, *J* = 8.0 Hz, H-4), 7.22 (app dt, 2H, *J* = 0.9, 8.2 Hz, H-7), 7.03 (distorted ddd, 1H, *J* = 1.2, 7.1, 8.2 Hz, H-6), 6.93 (distorted ddd, 1H, *J* = 1.1, 7.0, 8.1 Hz, H-5), 4.97 (s, 1H, H-10), 3.66 (app t, 4H, *J* = 4.7 Hz, H-13), 3.58 (s, 6H, H-1), 2.49

(s, 6H, H-2), 2.43 (br s, 4H, H-12). ^{13}C NMR (CD_3CN, 101 MHz) δ 138.0 (C8), 135.4 (C2), 128.2 (C9), 121.5 (C4), 121.4 (C6), 119.8 (C5), 113.0 (C3), 110.0 (C7), 68.4 (C12), 63.1 (C10), 54.6 (C11), 30.3 (C1), 11.9 (C13). HRMS (EI) *m*/*z*: [M] Calcd for $C_{25}H_{29}ON_3$ 387.2311; Found 387.2312.

ASSOCIATED CONTENT

Supporting Information

Details of the kinetic experiments, quantum chemical calculations for compounds **3a-e**, copies of the NMR (for compounds: **3a-k**, **5-6**, **9-20**) and IR spectra (for compounds: **3a-k**, **6**, **11**, **12**, **15**, **16a**, **17a**, **18a**), X-ray crystallographic data files (CIF) for compounds **3b-c**,**e**,**l**,**k** and **19b**. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: herbert.mayr@cup.uni-muenchen.de.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGEMENTS

We thank the Alexander von Humboldt Foundation (grant for GB) and the Deutsche Forschungsgemeinschaft (SFB 749, project B1). We thank Dr. A. R. Ofial for help in the preparation of the manuscript (Munich, Germany), Dr. D. Stephenson (Munich, Germany), Dr. S. Lakhdar (Caen, France), Dr. P. Byrne (Munich, Germany), Prof. D. Lupton (Victoria, Australia) and Prof. F. Terrier (Versailles, France) for helpful discussions. Dedicated to Professor Stefan Spange on the occasion of his 65th birthday.

REFERENCES

(1) Xiao, Y.-C.; Zhou, Q.-Q.; Dong, L.; Liu, T.-Y.; Chen, Y.-C. *Org. Lett.* **2012**, *14*, 5940–5943.

(2) (a) Zhuo, M.-H.; Jiang, Y.-J.; Fan, Y.-S.; Gao, Y.; Liu, S.; Zhang, S. *Org. Lett*. **2014**, *16*, 1096–1099. (b) Enders, D.; Narine, A. A.; Toulgoat, F.; Bisschops, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 5661–5665. (c) Iwao, T.; Shimizu, M. *Heterocycles* **2009**, *77*, 767–772.

(3) (a) Marsili, L.; Palmieri, A.; Petrini, M. *Org. Biomol. Chem.* **2010**, *8*, 706–712. (b) Fu, T.-h.; Bonaparte, A.; Martin, S. F. *Tetrahedron Lett.* **2009**, *50*, 3253–3257. (c) Harrison, C.-A.; Leineweber, R.; Moody, C. J.; Williams, J. M. J. *Tetrahedron Lett.* **1993**, *34*, 8527–8530. (d) Comins, D. L.; Stroud, E. D. *Tetrahedron Lett.* **1986**, *27*, 1869–1872.

(4) (a) Cozzi, P. G.; Benfatti, F.; Zoli, L. *Angew. Chem., Int. Ed.* **2009**, *48*, 1313–1316. (b) Shaikh, R. R.; Mazzanti, A.; Petrini, M.; Bartoli, G.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2008**, *47*, 8707–8710. (c) Armenise, N.; Dughera, S.; Gualandi, A.; Mengozzi, L.; Barbero, M.; Cozzi, P. G. *Asian J. Org. Chem.* **2015**, *4*, 337–345. (d) Guo, C.; Song, J.; Luo, S.-W.; Gong, L.-Z. *Angew. Chem., Int. Ed.* **2010**, *49*, 5558–5562. (e) Xu, B.; Shi, L.-L.; Zhang, Y.-Z.; Wu, Z.-J.; Fu, L.-N.; Luo, C.-Q.; Zhang, L.-X.; Peng, Y.-G.; Guo, Q.-X. *Chem. Sci.* **2014**, *5*, 1988–1991. (f) Guo, Z.-L.; Xue, J.-H.; Fu, L.-N.; Zhang, S.-E.; Guo, Q.-X. *Org. Lett.* **2014**, *16*, 6472–6475.

(5) Wang, D.-S.; Tang, J.; Zhou, Y.-G.; Chen, M.-W.; Yu, C.-B.; Duan, Y.; Jiang, G.-F. *Chem. Sci.* **2011**, *2*, 803–806.

(6) For reviews see: (a) Wang, L.; Chen, Y.; Xiao, J. *Asian J. Org. Chem.* **2014**, *3*, 1036–1052. (b) Bartoli, G.; Bencivenni, G.; Dalpozzo, R. *Chem. Soc. Rev.* **2010**, *39*, 4449–

4465. (c) Palmieri, A.; Petrini, M.; Shaikh, R. R. *Org. Biomol. Chem.* **2010**, *8*, 1259–1270. (d) Shiri, M.; Zolfigol, M. A.; Kruger, H. G.; Tanbakouchian, Z. *Chem. Rev.* **2010**, *110*, 2250–2293. (e) Loh, C. C. J.; Enders, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 46–48.

(7) (a) Barbero, M.; Cadamuro, S.; Cauda, F.; Dughera, S.; Gervasio, G.; Venturello, P. *J. Org. Chem.* **2012**, *77*, 4278–4287. (b) Barbero, M.; Buscaino, R.; Cadamuro, S.; Dughera, S.; Gualandi, A.; Marabello, D.; Cozzi, P. G. *J. Org. Chem.* **2015**, *80*, 4791–4796. (c) Lv, X.; Liu, J.; Liu, Y.; Zhao, Y.; Sun, Y.-Q.; Wang, P.; Guo, W. *Chem. Commun.* **2011**, 47, 12843–12845. (d) Erdelmeier, I.; Gérard-Monnier, D.; Yadan, J.-C.; Chaudière, J. *Chem. Res. Toxicol*. **1998**, *11*, 1184–1194. (e) Johannes, H.-H.; Grahn, W.; Dix, I.; Jones, P. G. *Acta Crystallogr., Sect. C* **1997**, *53*, 1432–1434. (f) Brooker, L. G. S.; Sprague, R. H. *J. Am. Chem. Soc.* **1941**, *63*, 3203–3213. (g) Brooker, L. G. S.; Sprague, R. H.; Smyth, C. P.; Lewis, G. L. *J. Am. Chem. Soc.* **1940**, *62*, 1116–1125.

(8) (a) Kikuchi, S.; Iki, M.; Ikeda, C.; Imafuku, K. *Heterocycles* **2005**, *66*, 275–283. (b) Kogan, N. A. *Chem. Heterocycl. Compd.* **1980**, *16*, 373–376. (c) Battiste, M. A.; Hill, J. H. M. *Tetrahedron Lett.* **1968**, *9*, 5541-5544. (d) Huffman, R. W.; Bruice, T. C. *J. Am. Chem. Soc.* **1967**, *89*, 6243–6251.

(9) (a) Mayr, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A. R.; Remennikov, G.; Schimmel, H. *J. Am. Chem. Soc*. **2001**, *123*, 9500–9512. (b) Mayr, H.; Kempf, B.; Ofial, A. R. *Acc. Chem. Res.* **2003**, *36*, 66–77. (c) Mayr, H.; Ofial, A. R. *Pure Appl. Chem.* **2005**, *77*, 1807–1821. (d) Mayr, H.; Patz, M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 938–957. (e) Mayr, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 3612–3618. (f) Database for *N*, s_N and *E* parameters and references to

original literature: www.cup.lmu.de/oc/mayr/DBintro.html. (g) Richter, D.; Mayr, H. *Angew. Chem. Int. Ed.* **2009**, *48*, 1958–1961.

(10) For earlier attempts to organize electrophilic and nucleophilic reactivities see: (a) Swain, C. G.; Scott, C. B. *J. Am. Chem. Soc.* **1953**, *75*, 141–147. (b) Edwards, J. O. *J. Am. Chem. Soc*. **1954**, *76*, 1540-1547. (c) Edwards, J. O. *J. Am. Chem. Soc*. **1956**, *78*, 1819–1820. (d) Parker, A. J. *Chem. Rev*. **1969**, *69*, 1–32. (e) Bunnett, J. F. *Annu. Rev. Phys. Chem.* **1963**, *14*, 271–290. (f) *Nucleophilicity*; Harris, J. M., McManus, S. P., eds.; Advances in Chemistry Series, American Chemical Society: Washington, DC, **1987**, Vol. 215. (g) Pearson, R. G.; Sobel, H. R.; Songstad, J. *J. Am. Chem. Soc*. **1968**, *90*, 319–326. (h) Ritchie, C. D. *Acc. Chem. Res*. **1972**, *5*, 348–354. (i) Ritchie, C. D. *Can. J. Chem.* **1986**, *64*, 2239–2250. (j) Kane-Maguire, L. A. P.; Honig, E. D.; Sweigart, D. A. *Chem. Rev*. **1984**, *84*, 525–543.

(11) The CCDC numbers are: for **3b**: 996884; for **3c**: 996885; for **3e**: 1011256; for **3i**: 996886; for **3k**: 996887; for **19b**: 996888. For related X-ray structures of indolylmethylium ions, see Ref 7a and 7d. For X-ray structure of Michael acceptors similar to **19b**, see: (a) Grošelj, U.; Bevk, D.; Jakše, R.; Meden, A.; Rečnik, S.; Stanovnik, B.; Svete, J. *Synthesis* **2005**, 1087–1094. (b) Lóránd, T.; Forgó, P.; Földesi, A.; Ôsz, E.; Prókai, L. *Eur. J. Org. Chem*. **2002**, 2996–3003.

(12) (a) Pindur, U.; Müller, J. *J. Heterocycl. Chem.* **1987**, *24*, 159–163. (b) Pindur, U.; Flo, C.; Akgün, E.; Tunali, M. *Liebigs Ann. Chem.* **1986**, 1621–1627. (c) Müller, J.; Pfeuffer, L.; Pindur, U. *Monatsh. Chem.* **1985**, *116*, 365–370. (d) Müller, J.; Pindur, U. *Arch. Pharm. (Weinheim, Ger.)* **1984**, *317*, 555–561. (e) Akgün, E.; Pindur, U.; Müller, J.

J. Heterocycl. Chem. **1983**, *20*, 1303–1305. (f) Berti, C.; Greci, L., Marchetti, L. *J. Heterocycl. Chem*. **1978**, *15*, 433–437.

(13) Santoso, M.; Kumar, N.; Black, D. S. C. *Collect. Czech. Chem. Commun*. **2009**, *74*, 1137–1150.

(14) In contrast, the additions of π-nucleophiles to aryl(ferrocenyl)methylium ions, which are structural analogues of aryl(indol-3-yl)methylium ions **3,** were reported to occur with good diastereoselectivities, see: Richards, C. J.; Hibbs, D.; Hursthouse, M. B. *Tetrahedron Lett*. **1994**, *35*, 4215–4218.

(15) Fridkin, G.; Boutard, N.; Lubell, W. D. *J. Org. Chem.* **2009**, *74*, 5603–5606.

(16) In the case of indolylmethylium ions which are not substituted at nitrogen, Barbero et al. (ref. 7a) reported, however, that some counteranions can form hydrogen bonds with the NH of indole and can change the reactivities of the indolylmethylium ions.

(17) (a) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165-195. (b) Zenz, I.; Mayr, H. *J. Org. Chem.* **2011**, *76*, 9370–9378.

(18) (a) Christensen, J. J.; Izatt, R. M.; Wrathall, D. P.; Hansen, L. D. *J. Chem. Soc. A* **1969**, 1212–1223. (b) Hinman, R. L.; Lang, J. *J. Am. Chem. Soc.* **1964**, *86*, 3796-3806. (c) Marshall, H. P.; Grunwald, E. *J. Am. Chem. Soc.* **1954**, *76*, 2000-2004.

(19) Lakhdar, S.; Westermaier, M.; Terrier, F.; Goumont, R.; Boubaker, T.; Ofial, A. R.; Mayr, H. *J. Org. Chem.* **2006**, *71*, 9088–9095.

(20) (a) Exner, O. *Correlation Analysis of Chemical Data*, Plenum Press, New York, 1988. (b) Hill, E. A.; Gross, M. L.; Stasiewicz, M.; Manion, M. *J. Am. Chem. Soc.* **1969**, *91*, 7381–7392.

(21) Praveen, P. J.; Parameswaran, P. S.; Majik, M. S. *Synthesis* **2015**, *47*, 1827–1837.

(22) Oisaki, K.; Suto, Y.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 5644–5645.

(23) Boeckman, R. K.; Pero, Jr. J. E.; Boehmler, D. J. *J. Am. Chem. Soc.* **2006**, *128*, 11032–11033.

(24) Ishihara, K.; Mouri, M.; Gao, Q.; Maruyama, T.; Furuta, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 11490–11495.

(25) Weng, Z.-T.; Li, Y.; Tian, S.-K. *J. Org. Chem.* **2011**, *76*, 8095–8099.