Convenient One-pot Syntheses of Pyrazoles from Imines, a Vilsmeier Type Reagent and Hydrazine

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A simple one-pot procedure for the regioselective synthesis of pyrazoles from readily available starting materials is described. Vilsmeier type reagent **1** reacts with imines **10** (*via* the corresponding tautomeric secondary enamines) in tetrahydrofuran to give enaminoimine hydrochlorides **11**. Nonsymmetrical imines generally react preferentially with **1** at the sterically less hindered α-position. The enaminoimine hydrochlorides **11** are transformed *in situ* to the corresponding pyrazoles **12** in moderate to high yields by the addition of hydrazine.

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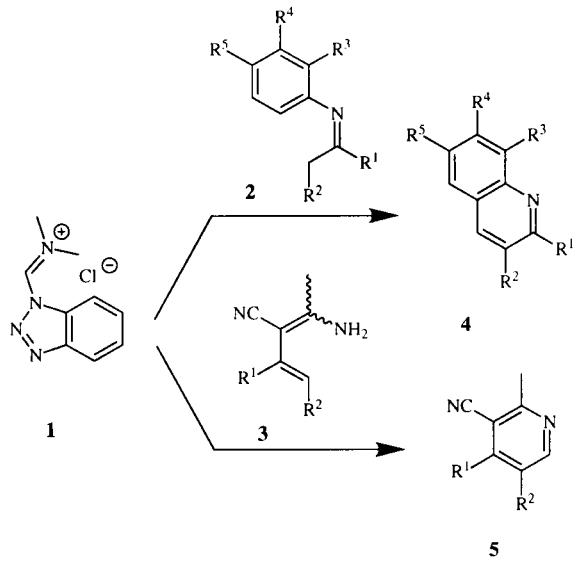
Introduction.

Recently, we disclosed a mild, straightforward, and highly regioselective synthesis of quinolines [1] using the benzotriazole iminium salt **1** [2], which is a stable synthetic chloroformiminium salt $[ClCH{=}NMe_2]^+X^-$ equivalent: *i.e.*, the benzotriazole moiety of **1** is easily substituted by nucleophiles. Salt **1** can be handled without the special precautions needed for chloroformiminium [3] and the use of **1** allows mild reaction conditions and a clean workup.

In our previous study of salt **1**, we discovered two examples of directing the regioselectivity, which is a central objective of modern chemistry. We demonstrated that the Vilsmeier type reagent **1** generally attacks the sterically less hindered α-position of nonsymmetrical imines, *e.g.*, *N*-arylimines **2** react with **1** in tetrahydrofuran to give enaminoimine hydrochlorides, which are thermally transformed *in situ* into the corresponding quinolines **4** (Scheme 1) in high yields *via* a tandem cyclization-elimination process [1]. More recently, we found (Scheme 1) that reactions between iminium salt **1** and dienamino compounds **3** can be used for a highly regioselective synthesis of pyridines **5** [4]. The high regioselectivity achieved in these two cases encouraged us to investigate the regioselective synthesis of 3,4-substituted pyrazoles from ketones, hydrazine and the Vilsmeier type reagent **1**. Pyrazoles are widely used in agrochemistry as insecticides, herbicides, and fungicides [5].

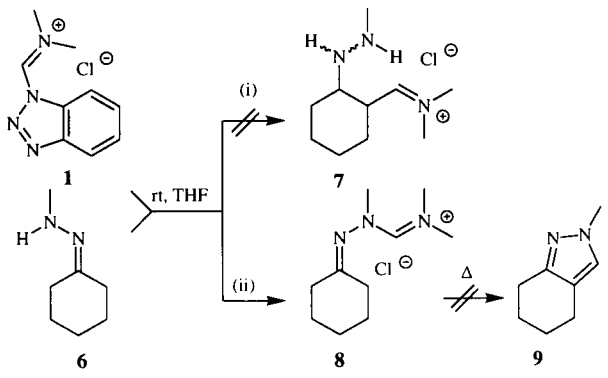
Scheme 1



Results and Discussion.

Initial reactions between the Vilsmeier type reagent **1** and hydrazone **6** (Scheme 2) performed at various temperatures up to 180° in a sealed tube gave complex mixtures. Literature comparison suggests that reagent **1** could attack *a priori* (i) at the α-C-atom [1,6,7] to yield pyrazoles *via* intermediates **7** [8], or (ii) at the NH group to give form-

Scheme 2

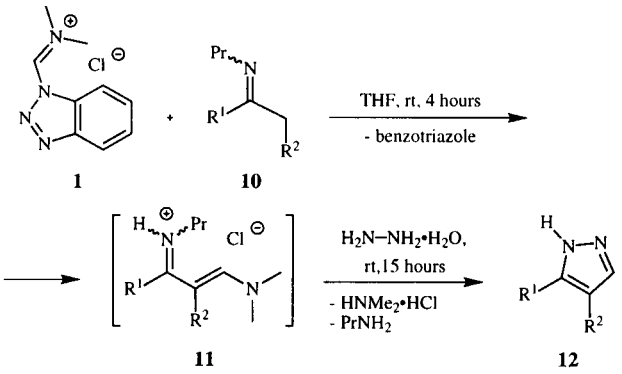


amidrazones **8** [9] (Scheme 2). Monitoring by nmr spectroscopy indicated that the reaction provides the formamidrazonium salt **8** at room temperature in virtually quantitative yield, which we did not cyclize into **9**.

An alternative approach utilized imines **10** prepared directly from the amines and ketones. The imines **10a-l** were characterized by nmr and used without purification. An experiment performed in an nmr tube revealed that iminium salt **1** reacts with *N*-propylimine **10a** (*via* the corresponding tautomeric secondary enamine) in the same manner [1] as *N*-arylimines providing the enaminoimine hydrochloride (vinamidium salt) **11a** at room temperature in virtually quantitative yield (Scheme 3). In the case of unsymmetrically substituted imine **10i**, the reagent **1** attacks the sterically less hindered α-position with high regioselectivity (higher than 95% as estimated by nmr). Although preliminary attempts to isolate **11a,i** as hydroperchlorates (by addition of aqueous sodium perchlorate solution) or as enaminoimine (by addition of dilute sodium hydroxide) failed, the variety of enaminoimine hydrochlorides **11a-l** can be transformed *in situ* into the corresponding pyrazoles **12a-l** by addition of hydrazine hydrate at ambient temperature (Scheme 3).

However, in comparison with the reaction described above for **10i**, three other nonsymmetrical *N*-propylimines **10j**, **10k** and **10l** are transformed into the corresponding pyrazoles **12j**, **12k** and **12l** with less selectivity. Cyclic imine **10j**, with a branched methyl group in the β-position, showed 83% selectivity as determined by the nmr spectra of the crude reaction mixture. The regioisomer ratios for **12k** and **12l** were about 60:40 and 55:45, respectively, as judged for the crude reaction mixtures. High reversed regioselectivity was obtained for imine **10f**, where electronic factors dictate that the sterically more hindered tautomeric enamine is virtually the exclusive intermediate (Table, entry 6). The moderate yields obtained for some pyrazoles is due to the formation of considerable amounts of by-products, mainly starting ketones. Another limitation was found regarding the structure of the starting *N*-propylimines **10**; attempts to

Scheme 3



1 **10** **11** **12**

Table

Synthesis of Pyrazoles **12** by Addition of Benzotriazole Iminium Salt **1** to Imines **10**

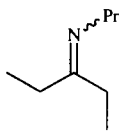
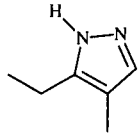
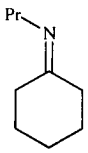
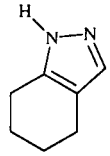
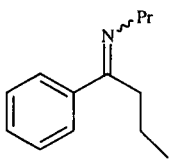
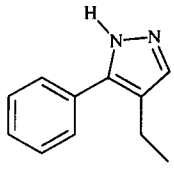
Entry	Imines **10**	Pyrazoles **12**	Yield (%) [a]	Regioselectivity [b]
1	 **10a**	 **12a**	31	-
2	 **10b**	 **12b**	66	-
3	 **10c**	 **12c**	38	-

Table (continued)

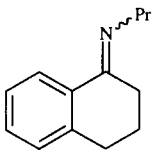
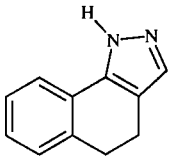
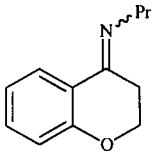
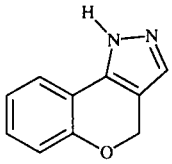
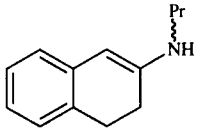
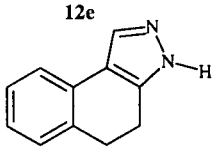
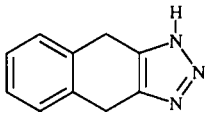
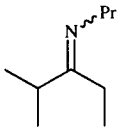
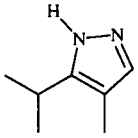
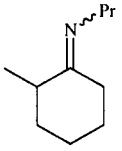
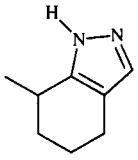
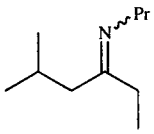
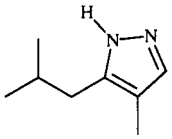
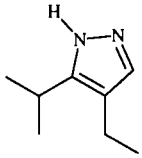
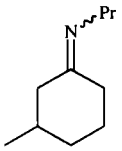
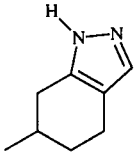
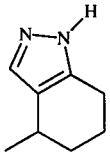
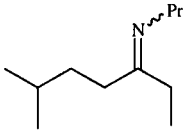
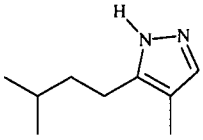
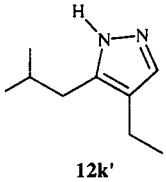
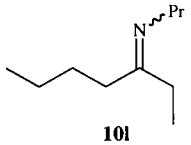
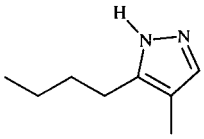
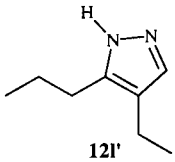
Entry	Imines **10**	Pyrazoles **12**		Yield (%) [a]	Regioselectivity [b]
4	 **10d**	 **12d**		54	-
5	 **10e**	 **12e**		31	-
6	 **10f**	 **12f**	 **12f'**	34	>95:<5
7	 **10g**	 **12g**		34	100
8	 **10h**	 **12h**		20	100
9	 **10i**	 **12i**	 **12i'**	83	>95:<5
10	 **10j**	 **12j**	 **12j'**	19	83:17
11	 **10k**	 **12k**	 **12k'**	31	60:40

Table (continued)

Entry	Imines **10**	Pyrazoles **12**	Yield (%) [a]	Regioselectivity [b]
12	 **10l**	 **12l**  **12l'**	15	55:45

[a] Isolated yields after column chromatography; [b] The ratio of the regioisomers was determined by ^{1}H nmr spectra of the crude reaction mixture.

transform imines **10** derived from methyl ketones such as acetophenone to the corresponding pyrazoles have so far failed.

Conclusions.

In summary, we have developed a straightforward synthesis of pyrazoles from ketones. Its broad scope, as well as the easy access to the starting materials, makes this method widely applicable in organic synthesis. Our method provides an efficient pathway for the synthesis of pyrazoles under mild conditions and should also be suitable for sensitive substrates.

EXPERIMENTAL

Melting points were determined on a Koefler hot-stage apparatus and were not corrected. The ^{1}H and ^{13}C nmr spectra were recorded on a Varian Gemini spectrometer at 300 and 75 MHz, respectively, in deuteriochloroform referenced to tetramethylsilane for the proton spectra, and to the solvent for the carbon spectra. The benzotriazole iminium salt **1** was prepared by refluxing a tetrahydrofuran solution of equimolar amounts of *N*-trimethylsilylbenzotriazole, dimethylformamide and thionyl chloride [2]. Tetrahydrofuran was distilled under nitrogen from Na/benzophenone prior to use. The *N*-propylimines **10** were prepared using a modification of a literature procedure [10]. Column chromatography was conducted with silica gel 230-400 mesh.

General Procedure for the Synthesis of Imines (**10**).

A solution of titanium (IV) chloride (3.3 ml, 30 mmoles) in dichloromethane (40 ml) is added slowly, under stirring, to a cooled (with an ice bath) solution of propylamine (5 ml, 60 mmoles) and triethylamine (15.3 ml, 110 mmoles) in dichloromethane (60 ml). Subsequently, the ketone (50 mmoles) is added at once. After stirring the mixture for 24 hours at room temperature the solvent is removed on the rotary evaporator. The residue is crushed with a spatula. Then diethyl ether (200 ml) is added and the resulting mixture is stirred vigorously until the residue is ground to a fine powder. Subsequently, the powder is sucked off and washed with diethyl ether (200 ml). Evaporation of ether yielded the crude imine **10**, which was used for the synthesis of pyrazoles without prior purification. The nmr data for the minor isomer are given in square brackets.

N-(Pentylidene-3)-1-propanamine (**10a**).

Compound **10a** was obtained as an oil [6] (yield 65%); ^{1}H nmr: δ 3.26 (t, J = 7.3 Hz, 2H), 2.30-2.26 (m, 4H), 1.69-1.57 (m, 2H), 1.12-1.00 (m, 6H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C nmr: δ 174.3, 51.9, 32.3, 24.0, 23.3, 11.6, 10.8, 10.5.

(*E*)- and (*Z*)-*N*-(Cyclohexylidene)-1-propanamine (**10b**).

Compound **10b** was obtained as an oil [11] (yield 80%), (diastereomeric mixture 7:1); ^{1}H nmr: δ 3.25 (t, J = 7.1 Hz, 2H), 2.39-2.22 (m, 4H), [1.90-1.80 (m, 8H)], 1.80-1.52 (m, 8H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C nmr: δ 171.9, 51.5, [41.4], 39.5, 28.2, 27.3, 26.5, 25.6, 23.7, 11.5.

(*E*)- and (*Z*)-*N*-(1-Phenylbutylidene)-1-propanamine (**10c**).

Compound **10c** was obtained as an oil (yield 92%), (diastereomeric mixture 3:1); ^{1}H nmr: δ [7.87 (d, J = 7.4 Hz, 1H)], 7.72-7.57 (m, 2H), [7.36 (d, J = 7.6 Hz, 1H)], 7.33-7.15 (m, 3H), [6.98 (d, J = 6.9 Hz, 1H)], 3.40 (t, J = 7.2 Hz, 2H), [3.05 (t, J = 6.9 Hz, 2H)], [2.85 (t, J = 7.4 Hz, 2H)], 2.58 (t, J = 7.9 Hz, 2H), [2.43 (t, J = 7.5 Hz, 2H)], 1.75-1.61 (m, 2H), 1.49-1.33 (m, 2H), [1.12 (t, J = 7.1 Hz, 2H)], 0.97-0.78 (m, 6H), [0.75 (t, J = 7.4 Hz, 3H)]; ^{13}C nmr: δ 168.5, 140.3, [132.7], 129.0, [128.4], [128.2 (2C)], 128.1 (2C), [127.9], [127.7], 126.8 (2C), [126.3 (2C)], [54.8], 53.3, [44.1], 30.6, 24.4, [24.3], 20.4, [19.7], 14.1, [13.7], 12.1, [11.8].

N-[3,4-Dihydro-1(2*H*)-naphthalenylidene]-1-propanamine (**10d**).

Compound **10d** was obtained as an oil which solidified on cooling (yield 90%), (diastereomeric mixture 4:1); ^{1}H nmr: δ 8.09 (d, J = 8.0 Hz, 1H), [7.95 (d, J = 8.0 Hz, 1H)], [7.40-7.30 (m, 2H)], 7.21-7.09 (m, 2H), 7.01 (d, J = 7.3 Hz, 1H), 3.30 (t, J = 7.1 Hz, 2H), [2.84 (t, J = 6.0 Hz, 2H)], 2.69 (t, J = 6.0 Hz, 2H), [2.54 (t, J = 6.3 Hz, 2H)], 2.46 (t, J = 6.3 Hz, 2H), [2.02 (t, J = 6.3 Hz, 2H)], 1.83 (t, J = 6.3 Hz, 2H), 1.75-1.58 (m, 2H), [1.40-1.31 (m, 2H)], 0.93 (t, J = 7.4 Hz, 3H), [0.81 (t, J = 7.4 Hz, 3H)]; ^{13}C nmr: δ 163.9, 140.1, 134.8, 129.2, 128.1, 126.1, 125.4, 52.6, 29.7, 27.6, 24.2, 22.5, 12.1.

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.36; H, 9.17. Found: C, 83.12; H, 9.04.

N-(2,3-Dihydro-4*H*-chromen-4-ylidene)-1-propanamine (**10e**).

Compound **10e** was obtained as an oil which solidified on cooling (yield 68%); ^{1}H nmr: δ 8.10 (d, J = 6.4 Hz, 1H), 7.28 (t, J = 8.3 Hz, 1H), 6.97 (t, J = 7.7 Hz, 1H), 6.88 (d, J = 8.2 Hz, 1H), 4.31 (t, J = 6.0 Hz, 2H), 3.42 (t, J = 7.1 Hz, 2H), 2.74 (t, J =

6.0 Hz, 2H), 1.81-1.69 (m, 2H), 1.01 (t, J = 7.3 Hz, 3H); ^{13}C nmr: δ 158.0, 157.7, 131.4, 125.6, 123.0, 121.2, 117.2, 65.7, 52.6, 27.0, 24.1, 12.1.

(*E*)- and (*Z*)-*N*-Propyl-3,4-dihydro-2-naphthalenamine (**10f**).

Compound **10f** was obtained as an oil (yield 86%), (diastereomeric mixture 6:1); ^{1}H nmr: δ [7.22-7.15 (m, 2H)], 7.11-6.94 (m, 2H), 6.90-6.79 (m, 2H), 5.21 (s, 1H), [3.55 (s, 1H)], 3.00 (t, J = 7.1 Hz, 2H), 2.78 (t, J = 7.5 Hz, 2H), [2.51 (t, J = 7.1 Hz, 2H)], 2.23 (t, J = 7.5 Hz, 2H), 1.59 (dd, J = 7.2, 7.4 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C nmr: δ 146.3, 137.6, 130.9, [126.8], 126.7, [126.7 (2C)], 126.4, 123.2, 122.1, 92.3, 45.0, [38.1], 29.2, 28.5, 22.2, 11.6.

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.36; H, 9.17. Found: C, 82.97; H, 9.01.

(*E*)- and (*Z*)-*N*-(2-Methylpentylidene-3)-1-propanamine (**10g**).

Compound **10g** was obtained as an oil [6] (yield 78%), (diastereomeric mixture 5:1); ^{1}H nmr: δ 3.29 (t, J = 7.1 Hz, 2H), 2.55-2.43 (m, 1H), 2.27-2.17 (m, 2H), 1.69-1.54 (m, 2H), 1.11-0.99 (m, 9H), 0.92 (t, J = 7.4 Hz, 3H); ^{13}C nmr: δ 177.4, 51.9, [51.2], 37.8, [29.0], [26.3], [24.2], 24.1, 22.0, 20.1 (2C), [19.3 (2C)], 11.7, 11.1.

(*E*)- and (*Z*)-*N*-(2-Methylcyclohexylidene)-1-propanamine (**10h**).

Compound **10h** was obtained as an oil [6] (yield 78%), (diastereomeric mixture 5:1); ^{1}H nmr: δ 3.30 (t, J = 7.2 Hz, 2H), 2.62-2.52 (m, 1H), 2.40-2.27 (m, 1H), 2.02-1.83 (m, 2H), 1.80-1.69 (m, 2H), 1.67-1.43 (m, 4H), 1.43-1.30 (m, 1H), 1.07 (d, J = 6.7 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C nmr: δ 174.5, [176.0], 51.7, [51.2], 41.8, 35.7, [35.3], [32.5], [30.6], 27.3, 27.2, 24.2, [24.1], 24.0, [20.1], 17.1, [16.6], [11.8], 11.7.

(*E*)- and (*Z*)-*N*-(5-Methylhexylidene-3)-1-propanamine (**10i**).

Compound **10i** was obtained as an oil [6] (yield 66%), (diastereomeric mixture 1:1); ^{1}H nmr: δ 3.28 (t, J = 6.7 Hz, 2H), 2.28-2.16 (m, 2H), 2.12 (d, J = 7.4 Hz, 2H), 2.04-1.92 (m, 1H), 1.68-1.59 (m, 2H), 1.10-1.01 (m, 3H), 0.95-0.90 (m, 9H); ^{13}C nmr: δ 173.2, 173.0, 52.6, 52.2, 48.7, 39.2, 33.2, 26.4, 26.1, 24.2, 23.9, 22.7, 22.4, 11.9, 11.8, 11.2, 10.7.

(*E*)- and (*Z*)-*N*-(3-Methylcyclohexylidene)-1-propanamine (**10j**).

Compound **10j** was obtained as an oil (yield 84%), (diastereomeric mixture 1:1); ^{1}H nmr: δ 3.26 (t, J = 7.1 Hz, 2H), 2.74-2.67 (m, 1H), 2.39-2.30 (m, 1H), 2.18-1.17 (m, 9H), 1.01-0.90 (m, 6H); ^{13}C nmr: δ 172.0, 171.9, 51.9, 51.8, 47.9, 39.1, 36.4, 34.2, 34.1, 34.1, 33.2, 27.7, 25.9, 25.4, 24.0, 21.9, 21.8, 11.7.

(*E*)- and (*Z*)-*N*-(6-Methylheptylidene-3)-1-propanamine (**10k**).

Compound **10k** was obtained as an oil (yield 83%), (diastereomeric mixture 1:0.8); ^{1}H nmr: δ 3.25 (t, J = 7.2 Hz, 2H), 2.29-2.15 (m, 4H), 1.71-1.49 (m, 3H), 1.47-1.36 (m, 1H), 1.36-1.26 (m, 1H), 1.12-1.00 (m, 3H), 0.97-0.86 (m, 9H); ^{13}C nmr: δ 174.3, [174.0], 52.4, [52.3], 38.0, 35.9, 35.3, 33.2, 28.7, 28.5, [28.2], 24.3, [24.3], 23.7, [22.4 (2C)], 22.3 (2C), 12.0, [12.0], 11.2, [10.9].

(*E*)- and (*Z*)-*N*-(Heptylidene-3)-1-propanamine (**10l**).

Compound **10l** was obtained as an oil (yield 72%), (diastereomeric mixture 1:1); ^{1}H nmr: δ 3.26 (t, J = 7.1 Hz, 2H), 2.31-2.17 (m, 4H), 1.71-1.24 (m, 6H), 1.11-0.99 (m, 3H), 0.99-0.78 (m, 6H); ^{13}C nmr: δ 173.8, 173.5, 52.4, 52.3, 39.7, 33.1, 30.4, 29.1, 28.6, 24.3 (2C), 23.7, 23.0, 22.7, 13.9, 13.8, 12.0 (2C), 11.2, 10.8.

Monitoring of the Formation of *N*-[1-(Dimethylamino)-2-methyl-1-pentenylidene-3]-propanaminium Chloride (**11a**) by NMR.

To a solution of the imine **10a** (0.100 g, 0.79 mmole) in water-free deuteriochloroform (1 ml) the benzotriazole iminium salt **1** (0.170 g, 0.82 mmole) was added in one portion at ambient temperature. Significant self-heating was observed. The solution was transferred quickly to an nmr tube. The spectra was taken within 1 hour after the mixing of reagents and showed that a mixture of two isomeric salts **11a** (probably *cis*- and *trans*-isomers) along with free benzotriazole formed. However the spectra recorded after 24 hours show that one isomer now strongly dominates in the mixture; ^{1}H nmr: δ 8.97 (br s, NH), 7.47 (s, 1H), 3.42-3.22 (m, CH_2-N), 3.22-2.88 (m, $N(CH_3)_2$), 2.62-2.40 (m, CH_2-C), 1.86 (br s, CH_3-C), 1.66-1.46 (CH_2), 1.24-1.09 (m, CH_3), 1.09-0.62 (m, CH_3); ^{13}C nmr: δ 175.9 (C=N$^+$), 156.1 (CH), 96.1 (C), 45.6 (CH_2-N$^+$), 44.0 (br, $N(CH_3)_2$), 22.6 (CH_2), 20.2 (CH_2), 13.2 (CH_3), 12.2 (CH_3), 10.3 (CH_3) (signals of free benzotriazole are excluded).

General Procedure for the Synthesis of Pyrazoles (**12**).

The reactions were conducted in water-free conditions under argon. To a solution of the imine (4 mmoles) in absolute tetrahydrofuran (20 ml), the benzotriazole iminium salt **1** (1.05 g, 5 mmoles) was added in one portion. The mixture was stirred for 4 hours at ambient temperature. Subsequently, hydrazine monohydrate (0.3 g, 6 mmoles) was added and the mixture was stirred overnight. Then dilute aqueous sodium hydroxide (2 *N*, 40 ml) was added and the resulting mixture was stirred vigorously for approximately 5 minutes. The organic phase was decanted off and the aqueous phase was washed with diethyl ether (3 x 50 ml). The combined organic phases were dried over sodium sulfate and the solvent removed on a rotary evaporator. Flash column chromatography of the crude product on silica gel using ethyl acetate/hexanes (3:1) provided the pyrazole **12**. The nmr data for minor isomer are given in square brackets.

3-Ethyl-4-methyl-1*H*-pyrazole (**12a**).

Compound **12a** was obtained as an oil (lit. bp 212-222° [12]), (yield 66%); ^{1}H nmr: δ 9.98 (br s, 1H), 7.27 (s, 1H), 2.62 (q, J = 7.6 Hz, 2H), 2.00 (s, 3H), 1.22 (t, J = 7.6 Hz, 3H); ^{13}C nmr: δ 146.4, 134.2, 111.7, 18.4, 13.3, 8.00.

Anal. Calcd. for $C_6H_{10}N_2$: N, 25.44. Found: N, 25.21.

4,5,6,7-Tetrahydro-1*H*-indazole (**12b**).

Compound **12b** was obtained in 31% yield, mp 68-70° (lit. mp 83-84° [13]); ^{1}H nmr: δ 9.52 (br s, 1H), 7.23 (s, 1H), 2.60 (t, J = 5.8 Hz, 2H), 2.46 (t, J = 5.7 Hz, 2H), 1.82-1.56 (m, 4H); ^{13}C nmr: δ 143.5, 131.8, 114.9, 23.4, 23.1, 22.0, 20.4.

4-Ethyl-3-phenyl-1*H*-pyrazole (**12c**).

Compound **12c** was obtained as an oil (yield 38%); ^{1}H nmr: δ 11.28 (br s, 1H), 7.66-7.52 (m, 1H), 7.44-7.22 (m, 4H), 7.39 (s, 1H), 2.62 (q, J = 7.5 Hz, 2H), 1.20 (t, J = 7.5 Hz, 3H); ^{13}C nmr: δ 144.6, 133.2, 132.4, 128.5 (2C), 127.6 (2C), 125.6, 120.0, 17.5, 14.9.

Anal. Calcd. for $C_{11}H_{12}N_2$: N, 16.27. Found: N, 16.48.

4,5-Dihydro-1*H*-benzo[*g*]indazole (**12d**).

Compound **12d** was obtained in 54% yield, mp 105-110° (lit. mp 123° [14]); ^{1}H nmr: δ 7.69 (d, J = 7.1 Hz, 1H), 7.32 (s, 1H), 7.22-7.16 (m, 4H), 2.89 (dd, J = 6.9, 7.6 Hz, 2H), 2.73 (dd, J = 7.6, 6.9 Hz, 2H); ^{13}C nmr: δ 146.2, 136.8, 129.0, 128.4, 127.9 (br), 127.6, 126.8, 121.9, 116.1, 29.8, 19.2.

Anal. Calcd. for $C_{11}H_{10}N_2$: N, 16.46. Found: N, 16.15.

1,4-Dihydrochromeno[4,3-*c*]pyrazole (**12e**).

Compound **12e** was obtained in 31% yield, mp 162-165° (lit. mp 162° [15]); ^{1}H nmr: δ 7.69 (d, J = 7.7 Hz, 1H), 7.38 (s, 1H), 7.27-7.17 (m, 1H), 6.99 (t, J = 8.0 Hz, 2H), 5.32 (s, 2H); ^{13}C nmr: δ 154.0, 142.1, 129.5, 125.6, 122.1, 121.8, 117.6, 117.2, 111.5, 63.7.

4,5-Dihydro-3*H*-benzo[*e*]indazole (**12f**).

Compound **12f** was obtained in 34% yield, mp 120-124° (lit. mp 134-136° [16]); ^{1}H nmr: δ 11.4 (br s, 1H), 7.77 (s, 1H), 7.39 (d, J = 7.4 Hz, 1H), 7.20 (dd, J = 7.1, 6.6 Hz, 2H), 7.10 (dd, J = 7.7, 6.6 Hz, 1H), 3.30-2.65 (m, 4H); ^{13}C nmr: δ 147.0, 134.1, 130.3, 128.4, 126.8 (2C), 125.8, 122.8, 117.1, 29.6, 21.2.

3-Isopropyl-4-methyl-1*H*-pyrazole (**12g**).

Compound **12g** was obtained as an oil, (yield 34%); ^{1}H nmr: δ 8.92 (br s, 1H), 7.29 (s, 1H), 3.12-2.95 (m, 1H), 2.04 (s, 3H), 1.28 (d, J = 6.9 Hz, 6H); ^{13}C nmr: δ 150.0, 135.1, 111.2, 25.5, 21.8, 8.4.

Anal. Calcd. for $C_7H_{12}N_2$: C, 67.69; N, 22.56. Found: C, 67.93; N, 22.46.

3-Methyl-4,5,6,7-tetrahydro-1*H*-indazole (**12h**).

Compound **12h** was obtained as an oil [17], (yield 20%); ^{1}H nmr: δ 8.69 (br s, 1H), 7.28 (s, 1H), 2.94-2.80 (m, 1H), 2.61-2.41 (m, 2H), 2.03-1.81 (m, 2H), 1.70-1.54 (m, 1H), 1.47-1.33 (m, 1H), 1.21 (d, J = 6.9 Hz, 3H); ^{13}C nmr: δ 147.9, 132.2, 114.5, 32.3, 28.2, 22.3, 20.6, 20.1.

Anal. Calcd. for $C_8H_{12}N_2$: N, 20.57. Found: N, 20.56.

3-Isobutyl-4-methyl-1*H*-pyrazole (**12i**).

Compound **12i** was obtained as an oil, (yield 83%); ^{1}H nmr: δ 11.37 (br s, 1H), 7.31 (s, 1H), 2.48 (d, J = 7.1 Hz, 2H), 2.01 (s, 3H), 1.99-1.89 (m, 1H), 0.92 (d, J = 6.7 Hz, 6H); ^{13}C nmr: δ 143.3, 135.4, 112.6, 34.0, 28.9, 22.4, 8.4.

Anal. Calcd. for $C_8H_{14}N_2$: C, 69.52; H, 10.23; N, 20.27. Found: C, 69.51; H, 10.30; N, 19.94.

4,5,6,7-Tetrahydro-6-methyl-1*H*-indazole (**12j**) and 4,5,6,7-tetrahydro-4-methyl-1*H*-indazole (**12j'**).

Compounds **12j** and **12j'** (mixture ~5:1) were obtained as an oil which solidifies on cooling (lit. mp 99-100° for **12j** [18]), (yield 19%); ^{1}H nmr: δ 10.45 (br s, 1H), [7.36 (s, 1H)], 7.29 (s, 1H), 2.84-2.73 (m, 1H), 2.63-2.56 (m, 1H), 2.56-2.42 (m, 1H), 2.29-2.16 (m, 1H), 1.97-1.77 (m, 2H), 1.44-1.26 (m, 1H), [1.20 (d, J = 6.7 Hz, 3H)], 1.08 (d, J = 6.6 Hz, 3H); ^{13}C nmr: δ 143.8, 131.6, 114.5, 31.8, 30.2, 29.6, 21.5, 19.8; hrms: Calcd. for $C_8H_{13}N_2$ (M+1): 137.1079. Found: 137.1082

Anal. Calcd. for $C_8H_{12}N_2$: C, 70.54. Found: C, 70.22.

3-Isopentyl-4-methyl-1*H*-pyrazole (**12k**) and 4-Ethyl-3-isobutyl-1*H*-pyrazole (**12k'**).

Compounds **12k** and **12k'** (mixture 1.5:1) were obtained as an oil, (yield 31%); ^{1}H nmr: δ 10.35 (br s, 1H), 7.30 (s, 1H), 2.68-2.57 (m, 2H,), 2.27 (d, J = 6.9 Hz, 2H), 2.02 (s, 3H), 1.82-1.67 (m, 1H), 1.65-1.45 (m, 3H), 1.25 (t, J = 7.5 Hz, 3H), 0.92 (t, J = 6.8 Hz, 6H); ^{13}C nmr: δ 146.0, 145.7, 136.1, 116.0, 112.0, 38.1, 32.7, 29.7, 27.8, 23.0, 22.3 (4C), 18.4, 13.7.

Anal. Calcd. for $C_9H_{16}N_2$: N, 18.41. Found: N, 18.13.

3-Butyl-4-methyl-1*H*-pyrazole (**12l**) and 4-Ethyl-3-propyl-1*H*-pyrazole (**12l'**).

Compounds **12l** and **12l'** (mixture ~2:1) were obtained as an oil, (yield 15%); ^{1}H nmr: δ 10.05 (br s,1H), [7.32 (s, 1H)], 7.30 (s, 1H), 2.71-2.55 (m, 2H), [2.38 (t, J = 7.7 Hz, 2H)], 2.02 (s, 3H), 1.68-1.50 (m, 2H), 1.45-1.32 (m, 2H), [1.25 (t, J = 7.7 Hz, 3H)], [0.94 (t, J = 6.9 Hz, 3H)], 0.92 (t, J = 7.2 Hz, 3H); ^{13}C nmr: δ 144.9, [140.8], 134.9, [134.0], [117.3], 112.2, 31.2, [25.5], 24.8, [23.9], 22.4, [18.5], [13.9], 13.8, [13.6], 8.2.

Anal. Calcd. for $C_8H_{14}N_2$: N, 20.27. Found: N, 19.98.

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