Pseudo-Cross-Conjugated Mesomeric Betaines and *N*-Heterocyclic Carbenes of Indazole

Andreas Schmidt,* Ariane Beutler, Tobias Habeck, Thorsten Mordhorst, Bohdan Snovydovych

Clausthal University of Technology, Institute of Organic Chemistry, Leibnizstrasse 6, 38678 Clausthal-Zellerfeld, Germany
Fax +49(5323)723861; E-mail: schmidt@ioc.tu-clausthal.de

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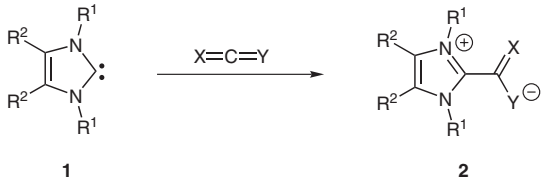
Abstract: 1,2-Dimethylindazolium-3-carboxylates are pseudo-cross-conjugated mesomeric betaines (PCCMB) and derivatives of the indazole alkaloid Nigellicin. They decarboxylate on heating to give intermediary *N*-heterocyclic carbenes of indazole that can be trapped with iso(thio)cyanates to amidates. Alternatively, 1,2-dimethylindazolium-3-amidates can be prepared starting from the corresponding 1*H*-indazol-3-carboxylic acid which is converted into its chloride, reacted with anilines and deprotonated on anion exchange resin. The heterocumulene moieties of these amidates, which are new representatives of pseudo-cross-conjugated mesomeric betaines, can be exchanged to 3,5-dichlorophenyl isocyanate via the *N*-heterocyclic carbene.

Key words: carbenes, nigellicin, nitrogen heterocycles, indazolium salts, decarboxylation

Introduction

Obviously, there is a strong relationship between the chemistry of *N*-heterocyclic carbenes (NHC) and the phenomenon of pseudo-cross-conjugation, which was defined in 1985 by Ollis, Stanforth, and Ramsden in order to classify the properties of heterocyclic mesomeric betaines (HMB).[1] Representatives of the latter-mentioned class of compounds are neutral conjugated molecules which can exclusively be represented by dipolar canonical formulae. They delocalize an even number of charges within a common π-electron system. According to the comprehensive classification accepted today, heterocyclic mesomeric betaines are divided into four major classes, i.e. heterocyclic *N*-ylides (1,2-dipoles), conjugated (CMB), cross-conjugated (CCMB) and pseudo-cross-conjugated (PCCMB) mesomeric betaines.[1] The chemical consequences of these distinct types of conjugation – insofar investigated to date – have been surveyed recently.[2] The chemistry of *N*-ylides and conjugated mesomeric betaines (CMB), which also include mesoions[3] such as sydnones,[4] münchnones,[5] and isothiomünchnones,[6] have been explored intensively. They are versatile key intermediates in heterocyclic as well as natural product synthesis,[7] mainly due to their capability to undergo 1,3-dipolar cycloadditions.

Very few information, however, is available on pseudo-cross-conjugated systems. It is known that pseudo-cross-conjugated mesomeric betaines of imidazole can be formed on interception of imidazol-2-ylidene or other nucleophilic carbenes with singlet oxygen,[8] or heterocumulenes such as CO_2 (X = Y = O),[9] CS_2 (X = Y = S),[9a,10,11] isocyanates (X = NR, Y = O),[11] isothiocyanates (X = NR, Y = S),[12] and carbodiimides (X = Y = NR)[12a] (Scheme 1). The intramolecular reaction of imidazol-2-ylidene with a ketene moiety leads to pseudo-cross-conjugated pyrrolo[1,2-*a*]imidazoliumolates.[13] Pseudo-cross-conjugated intermediates were also proposed in the reaction of thiazolium salts with isocyanates and isothiocyanates.[14]



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Scheme 1 Pseudo-cross-conjugated mesomeric betaines by interception of imidazol-2-ylidene with heterocumulenes

Literature gives some hints that the reverse process, the formation of *N*-heterocyclic carbenes from pseudo-cross-conjugated mesomeric betaines is also possible. Thus, decarboxylation of heteroarenium carboxylates[2,9c,d,10d,15] are only observed if the structures fulfill the definitions of pseudo-cross-conjugation (*vide infra*), and calculations support this assumption.[16] Cross-conjugated mesomeric betaines are stable under analogous reaction conditions.[2] Extrusion reactions would supplement widely applied syntheses of *N*-heterocyclic carbenes, i.e. the deprotonations of cationic precursors with potassium *tert*-butoxide,[17] sodium, or potassium hydride in the presence of catalytic amounts of either *t*-BuOK or the dimethyl sulfoxide anion,[18] or the reactions of imidazole thiones with potassium in boiling THF.[19] 1,2,4-Triazol-5-ylidenes form by thermal elimination of 5-methoxytriazoles in vacuo.[20]

An additional impetus for our work was the finding that all classes of heterocyclic mesomeric betaines have been isolated from natural sources, among them pseudo-cross-conjugated systems. A recent review article summarizes the surprisingly broad variety of betainic structures in nature.[21] In continuation of our interest in hetarenium salts,[22] mesomeric betaines[23] and natural products,[24] we therefore focused our interest on model compounds of the alkaloid nigellicin (**3**, Figure 1) from *Nigella sativa* Linn. as precursors for the formation of first *N*-heterocyclic carbenes

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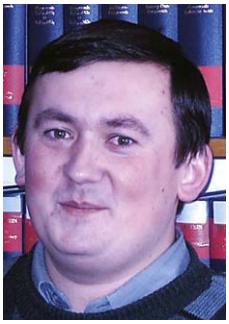
Biographical Sketches

Andreas Schmidt was born in 1964 in Wuppertal (Germany) and studied chemistry at the universities of Wuppertal and Bonn, Germany. He obtained his Dr. rer. nat. degree from the University of Bonn in 1992, by working under the guidance of Professor Heinrich Wamhoff. Then, he started his independent research at the University of Greifswald and completed his habilitation in 2000. Between 1999 and 2000 he undertook postdoctoral investigations with Professor Albert Padwa at Emory University, Atlanta (Georgia, USA). Since 2000 he is Privatdozent at the Institute of Organic Chemistry of the Clausthal University of Technology. His research interests include natural product and heterocyclic chemistry, especially heteroaromatic polycations, modified nucleobases, and mesomeric betaines.

Ariane Beutler was born in 1978 in Hannover (Germany) and studied chemistry at the Clausthal University of Technology. After studies at the University of Cardiff (UK) working on aza-Diels–Alder reactions, she received her Diploma from the TU Clausthal in 2005. Her thesis deals with pseudo-cross-conjugated heterocyclic mesomeric betaines and their conversion into nucleophilic carbenes.

Tobias Habeck, born in 1976 in Marne (Germany), studied chemistry at the Clausthal University of Technology. After studies at the Consejo Superior de Investigaciones Cientificas (CSIC) in Sevilla (Spain) in the group of Professor Ernesto Carmona, he joined the group of Andreas Schmidt in 2002 and received his Diploma in 2003. He is currently working on Nigellicin analogues as representatives of pseudo-cross-conjugated mesomeric betaines. During the years 2003–2004 he was the first speaker of the Jungchemiker-Forum Harz (JCF).

Thorsten Mordhorst was born in 1976 in Cuxhaven (Germany) and studied chemistry at the Clausthal University of Technology. He joined the group of Andreas Schmidt in 2002 and worked on betainic alkaloids from *Punica granatum*. Following his Diploma degree in 2003, he started his doctoral studies working on polycationic heteroaromatics and the synthesis of highly functionalized heterocycles.



Bohdan Snovydovych was born 1980 in Pidhorodystsche (Ukraine). He studied chemistry at the University of Lviv and received his diploma degree in 2002 in the group of Prof. Dr. Mykola Hanushchak. From 2002 to 2005 he was aspirant at the institute of Organic Chemistry of the University of Lviv and joined the group of Andreas Schmidt at Clausthal University of Technology in 2005. He is currently working on Nigellicin analogues.

of indazole. Only few reports have been published about derivatives or biological properties of this alkaloid.[25] We reported syntheses and properties of some model compounds, i.e. pyrazolium-3-carboxylates[26] and indazolium-3-carboxylates[27] and performed mass spectrometric investigations and gas phase reactions of these systems.[28]

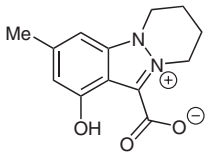


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Figure 1 Nigellicin

Nigellicin (**3**) from *Nigella sativa* belongs to the class of pseudo-cross-conjugated heterocyclic mesomeric betaines. Characteristic features of this type of conjugation are as follows. First, in the valence bond approach the charges are 'effectively, but not exclusively' (Ollis et al.[1]) delocalized in separated parts of the common π-electron system. Thus, pseudo-cross-conjugated mesomeric betaines can be *recognized* by canonical formulae which are electron sextet structures without internal electron octet stabilization (**I** in Figure 2). These canonical formulae delocalize the positive charge into the anionic partial structure, although their contribution to the weighted average of all canonical formulae which describe the structure is of course negligible.

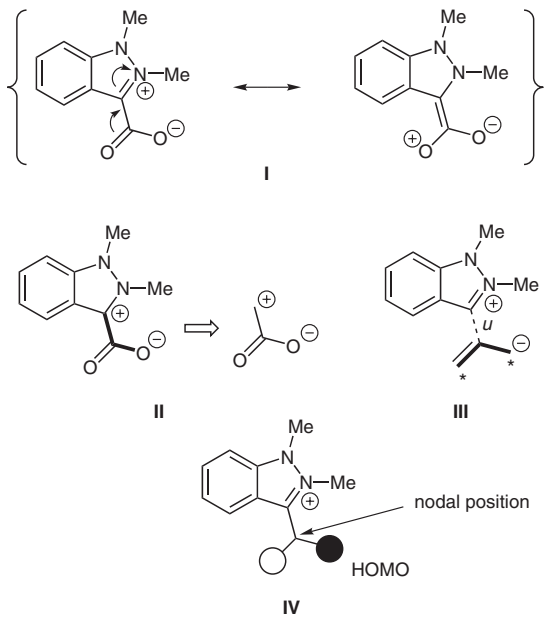


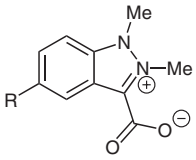
Figure 2 Characteristic features of pseudo-cross-conjugation

Second, the distinct classes of heterocyclic mesomeric betaines possess characteristic dipole increments which can be dissected from the canonical formulae.[1] Among them, the masked 2-oxyallyl 1,3-dipole **II** which is present in **3** and in its model compounds is characteristic for pseudo-cross-conjugated mesomeric betaines.[1]

Third, Potts and co-workers realized that the anionic partial structure of pseudo-cross-conjugated mesomeric betaines is always isoconjugate with an odd, alternant hydrocarbon anion[13] as exemplified by **III** (Figure 2). In the sense of Dewar, cation and anion are joined by a *union bond* ('*u*') through an unstarred position of the anionic partial structure. This atom, the carboxylate carbon atom of **3**, is a nodal position of the highest molecular orbital (HOMO) of the molecule **IV** and thus causes a charge-separated ground state of the molecule. As a consequence, the first excited state has a smaller permanent dipole moment than the ground state in CCMB and PCCMB.[29] Indeed, the effect of negative solvatochromism[30] is observable in model compounds: With increasing solvent polarity the UV/Vis absorption maxima shift to shorter wavelengths.[31] We presented results of *ab initio* calculations, spectroscopy and X-ray analyses which confirm these theoretically predicted features of pseudo-cross-conjugated systems.[26b,27]

Does pseudo-cross-conjugation translate into chemistry? In contrast to these theoretical characterizations of pseudo-cross-conjugated mesomeric betaines, very few information is available about the chemistry of these molecules.

We present here syntheses and properties of 1,2-dimethyl-5-dimethylaminoindazolium-3-carboxylate (**4**), 1,2-dimethyl-indazolium-3-carboxylate (**5**), as well as its 5-nitro derivative **6** as potential precursors for the formation of new pseudo-cross-conjugated mesomeric betaines and *N*-heterocyclic carbenes (Figure 3).



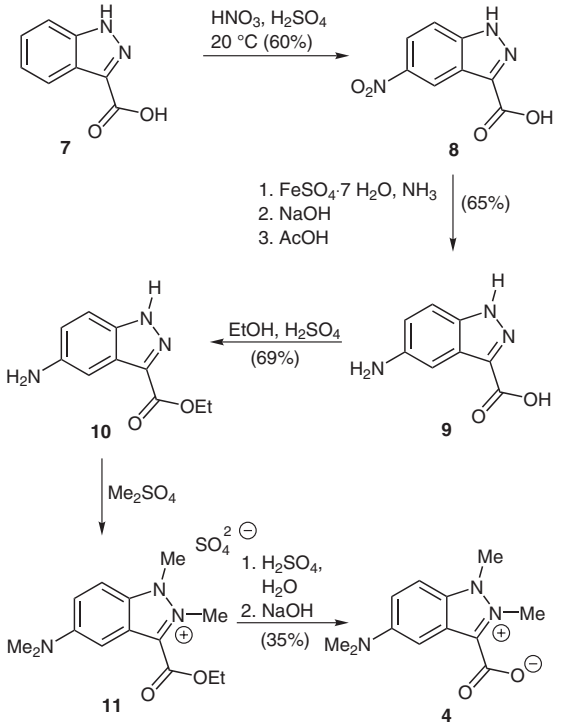
4: R = NMe_2
5: R = H
6: R = NO_2

Figure 3 Pseudo-cross-conjugated heterocyclic mesomeric betaines of indazole

Results and Discussion

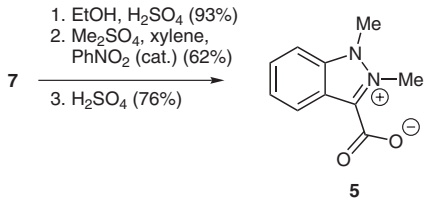
The syntheses of the indazolium betaines **4**, **5**, and **6** were accomplished as follows. Indazole-3-carboxylic acid (**7**) was converted according to modified literature procedures[32] into its 5-nitro derivative **8** by nitration (Scheme 2). Reduction of **8** using iron(II) sulfate and ammonia gave 5-amino-1*H*-indazole-3-carboxylic acid (**9**).[33] Esterification to **10**, followed by methylation with dimethyl sulfate in xylene gave the indazolium ester **11**, which was subjected without purification to hydrolysis in dilute sulfuric acid. The target compound, 1,2-dimethyl-5-di-

methylaminoindazolium-3-carboxylate (**4**) was obtained as a yellow solid. The betaine gives intense peaks at m/z = 256.1 (60%) $[M + Na]^+$ and 489.1 (100%) $[2 M + Na]^+$ in electrospray ionization mass spectrometry at 0 V fragmentor voltage. At 20 V the decarboxylated product can be detected at m/z = 190.1.



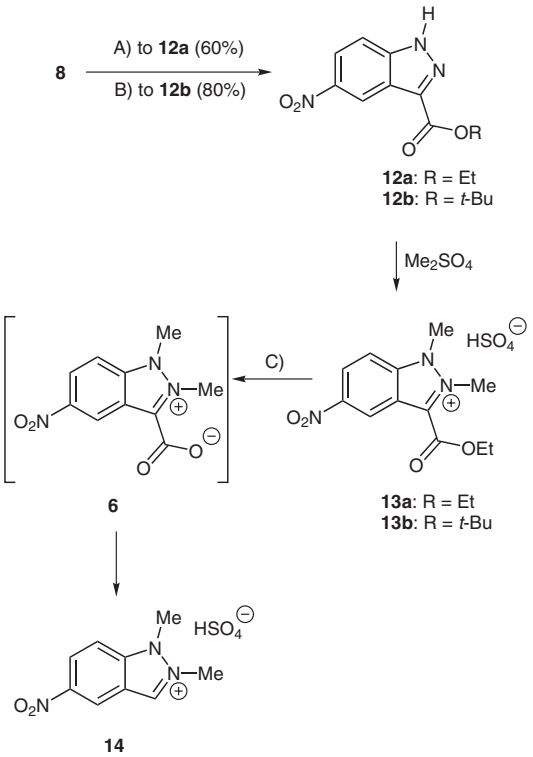
Scheme 2 Formation of the target betaine **4**

1,2-Dimethylindazolium-3-carboxylate (**5**) was prepared starting from indazole-3-carboxylic acid (**7**) as reported earlier[27] (Scheme 3). Acid **7** was first converted into the ethyl ester and then methylated by dimethyl sulfate in xylene in the presence of catalytic amounts of nitrobenzene. Saponification of the resulting 3-ethoxycarbonyl-1,2-dimethylindazolium salt with sulfuric acid yielded the pseudo-cross-conjugated mesomeric betaine **5**.



Scheme 3 Synthesis of mesomeric betaine **5**

Attempts to perform analogous series of reactions starting from the 5-nitro derivative **8** proved to be challenging. Methylation of **12a**, which was obtained on esterification of 5-nitro-1*H*-indazole-3-carboxylic acid (**8**) with ethanol in the presence of sulfuric acid,[33] yielded mixtures of intensely colored compounds which were chromatographically inseparable (Scheme 4). This approach to synthesize the 5-nitro derivative **6** was therefore abandoned.

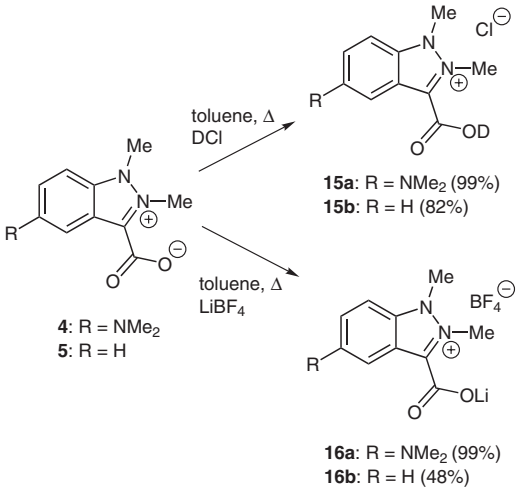


Scheme 4 Attempts to prepare the 5-nitro derivative **6**. *Reagents and conditions*: A) EtOH, H_2SO_4; B) 1. $SOCl_2$, dioxane; 2. *t*-BuOK; C) H_2SO_4, H_2O

We then synthesized the *t*-butyl ester **12b** by subsequent treatment of **8** with sulfuryl chloride in dioxane, and, after evaporation to dryness, potassium *tert*-butoxide in dioxane. Reaction of **12b** with dimethyl sulfate in xylene in the presence of catalytic amounts of nitrobenzene gave a brown solid which was treated with dilute sulfuric acid, neutralized with aqueous sodium hydroxide, and carefully evaporated in vacuo to dryness. The residue was dissolved in methanol to give a yellow solution, which was chromatographed on silica gel. The product finally obtained, however, proved to be the indazolium salt **14**. Presumably **14** was formed by decarboxylation of the target betaine **6**. No traces of the mesomeric betaine were detectable by ESI mass spectrometry.

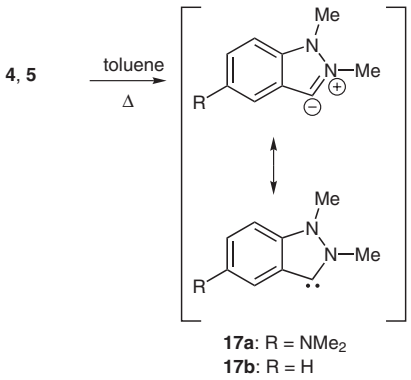
We next systematically investigated decarboxylations and trapping experiments. In contrast to betaine **6**, the compounds **4** and **5** were stable in boiling water over several hours. No trace of decomposition could be observed in acidic or basic solution, respectively. Most probably, hydration of the betaine stabilizes the molecule and prevents decarboxylation. The same effect was observed in toluene on addition of DCl, HCl or $LiBF_4$. Precipitations of colorless solids from mixtures in toluene were due to the formation of the acids **15a**,**b** and the lithium salts **16a**,**b**, respectively (Scheme 5).

Without these stabilizations, heating the betaines in toluene results in decarboxylation and formation of the *N*-het-



Scheme 5 Addition of DCl and $LiBF_4$ to betaines **4** and **5**: Stabilizing effects

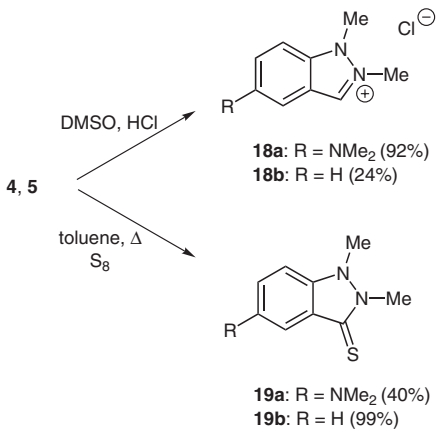
erocyclic carbenes **17a**,**b** (Scheme 6). The carbene **17b** was identified and its reactions in the gas phase were studied by high-resolution electrospray ionization mass spectrometry (HRESIMS). The carbene was detected as sodium adduct at $m/z = 169.0738$, and its dimeric form was identified as protonated species at $m/z = 293.1767$.[28] Gas phase reactions have also been studied by us.[28]



Scheme 6 *N*-Heterocyclic carbenes by decarboxylation of PCCMB

The suspensions of **4** and **5** in toluene, respectively, clear at temperatures above 60 °C, changing the color from yellowish to orange and red. Seemingly, the nucleophilic carbenes **17a**,**b** are not stable in solution under these conditions. Without trapping agents the TLC shows a diversity of spots which could not be separated. The most simple trapping agent is a proton. Thus, heating a sample of **4** in DMSO in the presence of traces of HCl results in the formation of the indazolium salt **18a** in 92% yield. Likewise, **5** reacted to give **18b** (Scheme 7).

The thermal conversion of the betaines **4** and **5** into the indazolium salts was examined by simple VTNMR experiments. Thus, DMSO-d_6 solutions of **4** and **5** were warmed stepwise from 20 °C to 70 °C, respectively. After ten minutes at these temperatures, ^{1}H NMR spectra were measured and the ratios of the betaines **4** and **5** to the



Scheme 7 Formation of indazolium salts and thiones from mesomeric betaines

indazolium salts **18a**,**b** were determined. As illustrated in Figure 4, decarboxylation of betaine **4** starts at approximately 45 °C (dashed line), yielding increasing concentrations of the indazolium salt **18a** with increasing temperature. The betaine **5** is less stable under these conditions. Considerable amounts of **18b** form at temperatures >30 °C, in addition to yet unidentified by-products. Source of the protons for salt formation is the water of crystallization of the betaines. According to the elemental analyses, **4** crystallizes with four molecules of H_2O, and **5** with 1 molecule of water.

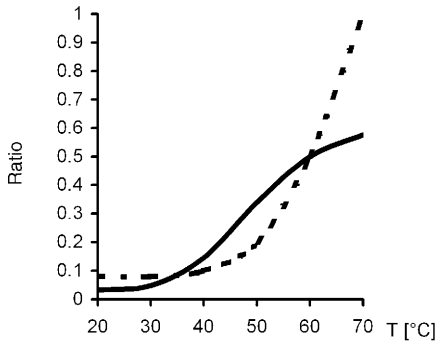


Figure 4 Results of VTNMR experiments to determine the stabilities of **4** and **5**. Ratio of **4/18a** (dashed line) and **5/18b** as function of temperature in DMSO-d_6.

Trapping the in situ generated nucleophilic carbenes **17a**,**b** with sulfur gave the thiones **19a**,**b** (Scheme 7). Whereas **19a** had to be chromatographed, **19b** was obtained in analytical purity. Simple filtration of excessive sulfur and evaporation of the solvent gave the thione **19b** in quantitative yield. According to a patent, **19b** was already synthesized by reaction of 1,2-dimethyl-3-chloroindazolium salts with alkali sulfide.[34]

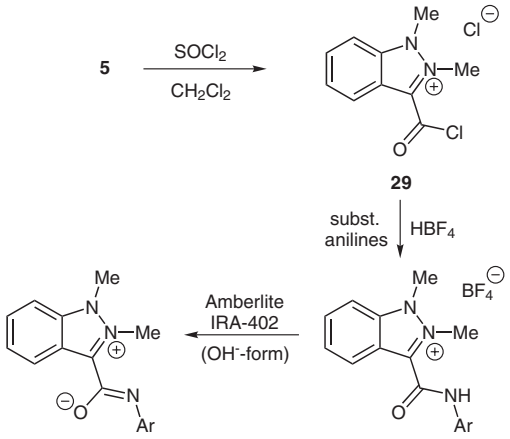
Next, we turned our attention to reactions of betaine **5** with isocyanates and isothiocyanates, respectively. Heating the betaine in toluene in the presence of 3,5-dichlorophenyl isocyanate, 2,4-dichlorophenyl isocyanate, and 4-acetylphenyl isocyanate, respectively, lead to the new

mesomeric betaines **20**–**22**, which precipitated as bright-yellow solids (Scheme 8). Filtration and drying in vacuo gives the pure compounds. Phenyl isocyanate, however, failed to undergo this reaction under the conditions applied. Mixtures of yet unidentified products were obtained. This observation is in accordance to Kröhnke's rule, which predicts increasing stability of ylides and related compounds with increasing stabilization and delocalization of the negative charge.[35]

Protonation of the amidates **20** and **21** lead to the amides **23** and **24**, which are colorless and water-soluble. On silica gel, however, the amide **25** is not stable. Although MS studies proved its formation (HRESIMS: *m*/*z* calcd for $C_{18}H_{18}N_3O_2$: 308.1399; found: 308.1401), cleavage to the *p*-substituted aniline and the starting material 1,2-dimethylindazolium-3-carboxylic acid occurred on chromatographic work-up. One molecule of water is necessary for this cleavage, which in the simplest case is the water of crystallization of the betaine. In addition, some amounts of amidate could be recovered.

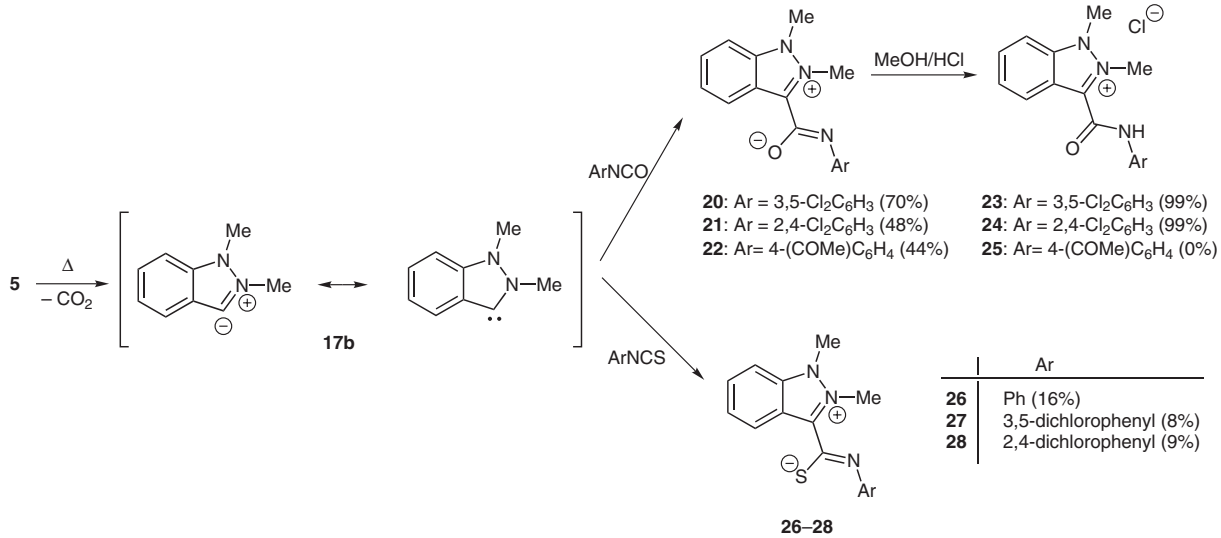
Phenyl isothiocyanate, however, was able to intercept the nucleophilic carbene **17b**. Thus, the adduct **26** was isolated and characterized, although in low yield. Analogously, the reaction with 3,5-dichlorophenyl isothiocyanate and 2,4-dichlorophenyl isothiocyanate, respectively, lead to the thioamidates **27** and **28** (Scheme 8). The thioamidates are orange to bright-yellow solids that are stable in air, slightly hygroscopic, but not sensitive to water. They show a poor solubility in organic solvents and water, and only DMSO gives satisfactory solutions for spectroscopic examinations. The thioamidates **26**–**28** underwent decomposition upon addition of acid, giving mixtures of yet unidentified products.

In order to study the possible extrusion of isocyanates from the amidates as a possible source of the *N*-heterocyclic carbene **17b**, we chose an alternative approach to synthesize more temperature-sensitive derivatives of pseudo-cross-conjugated mesomeric betaines. We started by chlorination of indazolium-3-carboxylate **5** to the corresponding chloride which we have described earlier.[27] Substitution with amines in the presence of HBF_4 gave the indazolium-amides **30**–**33** as stable compounds. Deprotonation can be accomplished by the anion exchange resin Amberlite IRA-402 in its hydroxy form, which produced the pseudo-cross-conjugated mesomeric betaines **34**–**37** under smooth conditions (Scheme 9).



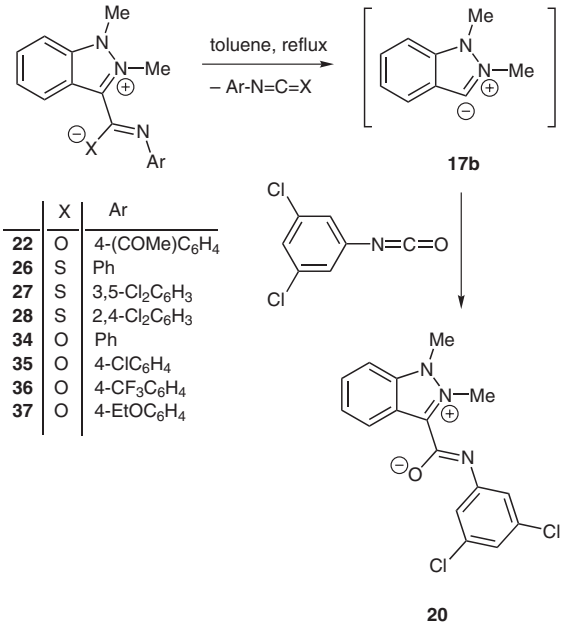
Scheme 9 Synthesis of amidates

Thus, the phenyl-substituted amidate **30**, which was not available by interception of the nucleophilic carbene **17b** with phenyl isocyanate, proved to be a stable compound at room temperature. Obviously, heating above a specific temperature breaks the *union bond* between the indazolium moiety and the isocyanate. To estimate this temperature we performed VTNMR-experiments which showed that the amidates are stable up to 70 °C. Using this infor-



Scheme 8 Formation of pseudo-cross-conjugated mesomeric betaines by interception of *N*-heterocyclic carbenes

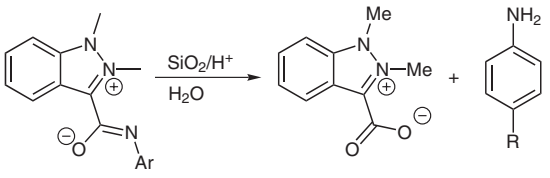
mation, and to prove the aforementioned assumption, we tried successfully to exchange the heterocumulene moieties of the pseudo-cross-conjugated amidates **22**, **34**–**37**, and the corresponding thioamidates **26**–**28** with 3,5-dichlorophenyl isocyanate, most probably via the *N*-heterocyclic carbene **17b**. Thus, heating the starting materials in toluene at reflux temperature for one hour in the presence of stoichiometric amounts of 3,5-dichlorophenyl isocyanate yielded the 3,5-dichloroamidate **20** in up to 28% yield (Scheme 10). Only the 2,4-dichloroamidate failed to undergo this exchange reaction. Obviously, the formation of *N*-heterocyclic carbenes is not restricted to decarboxylation reactions, but can be extended to a broad variety of heterocumulenes.



	X	Ar
22	O	4-(COMe)C_6H_4
26	S	Ph
27	S	3,5-$Cl_2C_6H_3$
28	S	2,4-$Cl_2C_6H_3$
34	O	Ph
35	O	4-ClC_6H_4
36	O	4-$CF_3C_6H_4$
37	O	4-$EtOC_6H_4$

Scheme 10 Reaction of amidates and thioamidates with 3,5-dichlorophenyl isocyanate to **20**

The pseudo-cross-conjugated mesomeric betaines **22** and **34**–**37** can furthermore be converted into the starting betaine **5** in yields up to 35%. As shown in Scheme 11, cleavage to anilines **38** and the indazolium carboxylate **5** was accomplished with silica gel and some traces of water. Under analogous conditions, the thioamidates **26**–**28**, however, undergo decomposition, giving mixtures of yet unidentified products.



22, **34**–**37** **5** **38a**–**e**

	R
38a	H
38b	Cl
38c	CF_3
38d	COMe
38e	OEt

Scheme 11 Cleavage of amidates under acidic conditions

Conclusion

In summary, we have presented the formation of *N*-heterocyclic carbenes from pseudo-cross-conjugated mesomeric betaines of indazole and vice versa. Extrusion reactions forming indazol-3-ylidene are not restricted to decarboxylations from indazolium-carboxylates, but can be also applied to amidates which exchange heterocumulene moities.

The ^1H and ^{13}C NMR spectra were recorded on Bruker Digital FT-NMR Avance 400 and Avance 200 spectrometers in DMSO-d_6 at 20 °C, unless otherwise noted. The chemical shifts are reported in ppm relative to internal TMS (δ = 0.000). FT-IR spectra were obtained on a Bruker Vektor 22 in the range of 400–4000 cm^{-1} (2.5% pellets in KBr). The electrospray ionization mass spectra (ESIMS) were measured with an Agilent LCMSD Series HP1100 with APIES (direct inlet). Samples were dissolved in MeOH and sprayed from MeOH at 0 V fragmentor voltage, 300 °C drying gas temperature, 4000 V capillary voltage, and 0.6 mL of solvent flow unless otherwise noted. Melting points are uncorrected.

The analytical and spectroscopic data for the indazole derivatives prepared are assembled in Table 1.

Table 1 Indazole Derivatives **4**, **10**, **12**, **14**–**16**, **18**–**28**, **30**–**37** Prepared

Product	Mp (°C)	^1H NMR (DMSO-d_6) δ, *J* (Hz)	^{13}C NMR (DMSO-d_6) δ, *J* (Hz)	ESI-MS[a] *m/z*
4	54–56[b]	7.69 (d, *J* = 9.5 Hz, 1 H), 7.51 (d, *J* = 9.2 Hz, 1 H), 7.34 (s, 1 H), 4.57 (s, 3 H), 4.13 (s, 3 H), 2.93 (s, 6 H)	158.3, 147.6, 137.8, 133.8, 123.5, 120.8, 110.7, 101.5, 34.6, 32.6	256.1
10	72	13.48 (s, 1 H), 7.35 (d, *J* = 8.8 Hz, 1 H), 7.13 (s, 1 H), 6.85 (dd, *J* = 8.8 Hz, 2.0, 1 H), 5.20 (s, 1 H), 4.35 (q, *J* = 7.1 Hz, 2 H), 1.36 (t, *J* = 7.1 Hz, 3 H)	162.7, 144.7, 135.2, 132.9, 124.0, 118.4, 111.2, 100.5, 59.6, 14.3	228.1
12b	178	9.11 (d, *J* = 2.1 Hz, 1 H), 8.38 (dd, *J* = 9.2 Hz, 2.1, 1 H), 8.10 (dd, *J* = 9.2 Hz, 1 H), 1.81 (m, 9 H)	161.6, 144.1, 143.5, 140.1, 122.1, 121.1, 119.5, 112.9, 83.8, 28.4	286.0

Table 1 Indazole Derivatives **4**, **10**, **12**, **14**–**16**, **18**–**28**, **30**–**37** Prepared (continued)

Product	Mp (°C)	^{1}H NMR (DMSO-d_6) δ, *J* (Hz)	^{13}C NMR (DMSO-d_6) δ, *J* (Hz)	ESI-MS[a] *m*/*z*
14	n.d.[c]	9.53 (s, 1 H), 9.21 (d, *J* = 2.1 Hz, 1 H), 8.60 (dd, *J* = 9.6 Hz, 2.1, 1 H), 8.25 (d, *J* = 9.6 Hz, 1 H), 4.47 (s, 3 H), 4.43 (s, 3 H)	n.d.[c]	192.1
15a	194[b,d]	8.09 (d, *J* = 9.6 Hz, 1 H), 7.78 (dd, *J* = 9.6 Hz, 1.8, 1 H), 7.21 (s, 1 H), 4.57 (s, 3 H), 4.38 (s, 3 H), 3.06 (s, 6 H)	159.4, 148.3, 134.4, 127.7, 124.5, 121.4, 112.4, 112.2, 36.6, 34.1	234.1
15b	167	8.31 (m, 1 H), 8.16 (m, 1 H), 7.93 (m, 1 H), 7.64 (m, 1 H), 4.63 (s, 3 H, CH_3), 4.40 (s, 3 H, CH_3)	158.7, 139.2, 133.0, 131.9, 126.8, 123.2, 119.5, 111.6, 36.8, 34.0	191.1
16a	135[b]	7.76 (d, *J* = 9.7 Hz, 1 H), 7.54 (d, *J* = 9.7 Hz, 1 H), 7.40 (s, 1 H), 4.61 (s, 3 H), 4.16 (s, 3 H), 2.96 (s, 6 H)	158.4, 147.7, 134.0, 133.8, 123.5, 120.8, 110.7, 101.4, 34.6, 32.6	234.1
16b	148–151	8.33 (m, 1 H), 8.02 (m, 1 H), 7.92 (m, 1 H), 7.62 (m, 1 H), 4.63 (s, 3 H, CH_3), 4.36 (s, 3 H, CH_3)	158.7, 139.1, 132.9, 132.8, 126.4, 123.4, 119.4, 111.3, 36.4, 33.7	197.1
18a	186–188	8.86 (s, 1 H), 7.84 (d, *J* = 9.5 Hz, 1 H), 7.63 (dd, *J* = 9.5 Hz, 2.0, 1 H), 6.96 (d, *J* = 2.0 Hz, 1 H), 4.32 (s, 3 H), 4.21 (s, 3 H), 2.97 (s, 6 H)	147.9, 134.6, 130.0, 124.1, 120.2, 111.4, 98.5, 37.3, 33.0	190.1
19a	136–137	7.19 (m, 3 H), 3.94 (s, 3 H), 3.48 (s, 3 H), 2.99 (s, 6 H)	147.88, 138.94, 128.25, 121.02, 110.80, 109.18, 106.02, 41.60, 36.43, 32.45	222.1
19b	118	8.05 (m, 1 H), 7.56 (m, 1 H), 7.27–7.15 (m, 2 H), 3.97 (s, 3 H, CH_3), 3.62 (s, 3 H, CH_3)	171.0, 144.2, 132.0, 126.7, 125.2, 122.5, 109.7, 35.3, 32.3	179.1
20	208–211[b]	8.71 (m, 1 H), 7.94 (m, 1 H), 7.80 (m, 1 H), 7.68 (d, *J* = 1.9 Hz, 2 H), 7.46 (m, 1 H), 6.90 (t, *J* = 1.9 Hz, 1 H), 4.77 (s, 3 H, CH_3), 4.24 (s, 3 H, CH_3)	159.0, 154.3, 139.1, 132.9, 132.1, 126.0, 124.3, 122.4, 119.0, 118.7, 110.4, 110.4, 35.5, 32.8	334.2
21	212–214[b]	8.93 (d, *J* = 8.5 Hz, 1 H), 8.32 (d, *J* = 8.8 Hz, 1 H), 7.94 (d, *J* = 8.70 Hz, 1 H), 7.80 (dd, *J* = 7.4 Hz, 7.2, 1 H), 7.47 (dd, *J* = 7.4 Hz, 7.6, 1 H), 7.39 (d, *J* = 2.4 Hz, 1 H), 7.17 (dd, *J* = 8.8 Hz, 2.4, 1 H), 4.85 (s, 3 H, CH_3), 4.25 (s, 3 H, CH_3)	158.0, 147.4, 141.9, 139.1, 132.1, 128.4, 127.9, 126.3, 126.2, 125.7, 124.2, 122.8, 119.3, 110.3, 35.5, 32.8	334.2
22	175–178[b]	8.66 (m, 1 H), 7.96 (m, 1 H), 7.83 (m, 1 H), 7.82 (m, 2 H), 7.69 (m, 2 H), 7.48 (m, 1 H), 4.76 (s, 3 H, CH_3), 4.26 (s, 3 H, CH_3), 2.49 (s, 3 H, CH_3)	201.3, 163.4, 160.4, 146.4, 144.3, 137.4, 134.5, 134.1, 130.8, 129.6, 128.5, 124.1, 115.7, 40.8, 38.1, 31.5	308.1
23	238[b]	8.12 (m, 1 H), 8.02 (m, 1 H), 7.93 (m, 1 H), 7.81 (d, *J* = 1.8 Hz, 2 H), 7.61 (m, 1 H), 7.46 (t, *J* = 1.8 Hz, 1 H), 4.43 (s, 3 H, CH_3), 4.33 (s, 3 H, CH_3)	155.8, 140.0, 139.8, 135.0, 134.3, 127.0, 125.5, 12.8, 119.9, 118.1, 112.4, 111.9, 37.5, 34.4	334.2
24	193[b]	8.26 (m, 1 H), 8.16 (m, 1 H), 7.20–8.04 (m, 3 H), 7.55–7.75 (m, 2 H), 4.53 (s, 3 H, CH_3), 4.43 (s, 3 H, CH_3)	155.3, 139.1, 134.5, 133.4, 132.2, 132.1, 130.0, 129.3, 129.3, 128.0, 126.2, 122.1, 117.5, 111.5, 36.9, 33.9	334.2
26	168–170[b]	8.21 (m, 1 H), 7.91 (m, 1 H), 7.81 (m, 1 H), 7.43 (m, 1 H), 7.23–7.32 (m, 4 H), 6.96 (m, 1 H), 4.40 (s, 3 H, CH_3), 4.23 (s, 3 H, CH_3)	169.3, 152.4, 145.7, 139.2, 132.3, 127.9, 123.9, 123.7, 122.2, 121.9, 117.2, 110.3, 34.8, 32.7	304.2
27	180–183	8.24 (m, 1 H), 7.92 (m, 1 H), 7.81 (m, 1 H), 7.44 (m, 1 H), 7.29 (m, 1 H), 7.14 (m, 1 H), 4.40 (s, 3 H, CH_3), 4.24 (s, 3 H, CH_3)	172.7, 155.3, 145.2, 139.2, 133.3, 132.5, 124.0, 123.9, 121.0, 121.0, 117.2, 110.5, 35.2, 32.9	350.2
28	172–174[b]	8.25 (m, 1 H), 7.93 (m, 1 H), 7.82 (m, 1 H), 7.52 (m, 1 H), 7.46 (m, 1 H), 7.32 (m, 2 H), 4.48 (s, 3 H, CH_3), 4.25 (s, 3 H, CH_3)	172.6, 149.3, 145.2, 139.2, 132.4, 128.3, 126.9, 126.0, 125.7, 124.5, 123.9, 123.8, 117.2, 110.4, 35.1, 32.8	350.2
30	200–202[b]	11.39 (s, 1 H), 8.16 (m, 2 H), 7.98 (m, 1 H), 7.80 (m, 2 H), 7.65 (m, 1 H), 7.47 (m, 2 H), 7.26 (m, 1 H), 4.49 (s, 3 H, CH_3), 4.42 (s, 3 H, CH_3)	154.6, 139.1, 137.4, 135.2, 133.4, 129.0, 125.9, 125.4, 122.5, 120.8, 117.3, 111.4, 36.9, 33.8	266.1

Table 1 Indazole Derivatives **4**, **10**, **12**, **14**–**16**, **18**–**28**, **30**–**37** Prepared (continued)

Product	Mp (°C)	^{1}H NMR (DMSO-d_6) δ, *J* (Hz)	^{13}C NMR (DMSO-d_6) δ, *J* (Hz)	ESI-MS[a] *m*/*z*
31	230–232[b]	11.67 (s, 1 H), 8.16 (m, 2 H), 7.98 (m, 1 H), 7.85 (m, 2 H), 7.64 (m, 1 H), 7.53 (m, 2 H), 4.50 (s, 3 H, CH_3), 4.41 (s, 3 H, CH_3)	154.7, 139.2, 136.6, 135.1, 133.5, 129.1, 129.0, 126.0, 122.6, 122.5, 117.4, 111.5, 37.1, 34.0	300.1
32	251–254[b]	11.71 (s, 1 H), 8.18 (m, 2 H), 8.07–7.93 (m, 3 H), 7.84 (m, 2 H), 7.66 (m, 1 H), 4.51 (s, 3 H, CH_3), 4.43 (s, 3 H, CH_3)	155.2, 141.2, 139.2, 134.8, 133.5, 126.4, 126.3, 126.1, 124.9, 122.6, 121.0, 117.4, 111.5, 37.0, 34.0[e]	334.1
33	205–208[b]	11.25 (s, 1 H), 8.15 (m, 2 H), 7.98 (m, 1 H), 7.71 (m, 2 H), 7.64 (m, 1 H), 7.01 (m, 2 H), 4.48 (s, 3 H, CH_3), 4.41 (s, 3 H, CH_3), 4.05 (q, *J* = 7.0 Hz, 2 H) 1.34 (t, *J* = 7.0 Hz, 3 H)	156.0, 154.2, 139.2, 135.5, 133.5, 130.4, 126.0, 122.6, 122.5, 117.3, 114.6, 111.4, 63.3, 36.9, 33.9, 14.7	310.2
34	149[b]	8.72 (m, 1 H), 7.90 (m, 1 H), 7.78 (m, 1 H), 7.58 (m, 2 H), 7.44 (m, 1 H), 7.15 (m, 2 H), 6.78 (m, 1 H), 4.80 (s, 3 H, CH_3), 4.22 (s, 3 H, CH_3	157.1, 151.6, 143.0, 139.0, 131.9, 127.6, 126.2, 124.2, 123.8, 119.9, 119.0, 110.1, 35.1, 32.6	266.1
35	180[b]	8.71 (m, 1 H), 7.90 (m, 1 H), 7.77 (m, 1 H), 7.65 (m, 2 H), 7.43 (m, 1 H), 7.16 (m, 2 H) 4.78 (s, 3 H, CH_3), 4.22 (s, 3 H, CH_3)	157.8, 150.6, 142.6, 139.1, 132.0, 127.5, 126.1, 125.8, 124.0, 123.1, 119.0, 110.3, 35.3, 32.7	300.1
36	177[b]	8.72 (m, 1 H), 7.93 (m, 1 H), 7.84–7.70 (m, 3 H), 7.40–7.51 (m, 3 H), 4.79 (s, 3 H, CH_3), 4.24 (s, 3 H, CH_3)	158.5, 155.6, 142.2, 139.1, 132.1, 126.0, 125.9 (*J* = 277.3 Hz) 124.9, 124.8, 124.8, 124.2, 119.2, 119.1, 110.4, 35.4, 32.8	334.1
37	150[b]	8.71 (m, 1 H), 7.89 (m, 1 H), 7.77 (m, 1 H), 7.60 (m, 2 H), 7.43 (m, 1 H), 6.73 (m, 2 H), 4.79 (s, 3 H, CH_3), 4.21 (s, 3 H, CH_3), 3.96 (q, *J* = 7.0 Hz, 2 H) 1.31 (t, *J* = 7.0 Hz, 3 H)	156.6, 152.5, 144.7, 143.1, 139.1, 131.9, 126.3, 125.0, 123.8, 119.0, 113.7, 110.2, 62.9, 35.2, 32.6, 14.9	310.2

[a] $[M]^+$, $[M + H]^+$ or $[M + Na]^+$.
[b] Decomposition.
[c] Not determined, as product was obtained in impure form.
[d] At >175 °C color changes.
[e] CF_3 not detectable due to insufficient solubility.

1,2-Dimethyl-5-dimethylamino-1*H*-indazolium-3-carboxylate (4)

A sample of indazole ester **10** (1.00 g, 4.3 mmol) was heated in a mixture of xylene (15 mL) and nitrobenzene (5 mL) to 140 °C. Then, dimethyl sulfate (10 mL) was added. Heating was continued for an additional hour. After evaporation of the solvent in vacuo, the brown oil was treated with H_2O (15 mL) and concd H_2SO_4 (13 mL) and refluxed over a period of 6–7 h. After cooling, the solution was neutralized with aq 2 N NaOH, and the H_2O was distilled off in vacuo. The residue was then extracted with EtOH (5 × 50 mL), the combined EtOH extracts were concentrated. The crude product obtained was purified by chromatography (silica gel, MeOH); yield: 35%.

IR (KBr): 3424, 1638, 1572, 1523, 1425, 1340, 1251, 1120, 963 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{12}H_{15}N_3O_2 + H^+$: 234.1243; found: 234.1188.

Anal. Calcd for $C_{12}H_{15}N_3O_2 \cdot 4H_2O$: C, 47.20; H, 7.59; N, 13.76. Found: C, 47.81, H, 6.47; N, 13.47.

5-Nitro-1*H*-indazole-3-carboxylic Acid (8)

At 10 °C, a sample of 1*H*-indazole-3-carboxylic acid (**7**; 3.32 g, 0.02 mol) was dissolved in concd H_2SO_4 (10 mL). Then, a mixture of concd H_2SO_4 (10 mL) and 64% HNO_3 (1.6 mL) was added and the mixture was allowed to warm to r.t. After 1 h, the mixture was poured onto ice and water (200 mL). The resulting precipitate was filtered off and washed with cold H_2O (2 × 50 mL). The crude product was recrystallized from AcOH to yield 2.5 g (60%) of **8**. Spectroscopic data are in agreement with literature values.[32]

Preparation of 5-Amino-1*H*-indazole-3-carboxylic Acid (9)

A solution of $FeSO_4 \cdot 7H_2O$ (10.6 g, 38 mmol) in H_2O (25 mL) was added to **8** (1.03 g, 0.5 mmol). Then, 25% aq NH_4OH (20 mL) was added at 80 °C within 15 min, and the solution was stirred for an additional hour at that temperature. After filtration, the precipitate was extracted with 1% aq NaOH (3 ×). The combined extracts were then adjusted to pH 6 with glacial AcOH whereupon a precipitate formed, which was filtered off and washed with cold H_2O (2 × 20 mL); yield: 65%. All spectroscopic data are in agreement with those reported.[33]

5-Amino-3-ethoxycarbonyl-1*H*-indazole (10)

A mixture of 5-aminoindazole-3-carboxylic acid (**9**; 1.77 g, 10.0 mmol) in EtOH (120 mL) and concd H_2SO_4 (20 mL) was refluxed for 12 h. Then, the mixture was neutralized with aq 2 N NaOH and extracted with Et_2O (3 × 50 mL). After drying (Na_2SO_4), the solvent was removed by distillation; yield: 69%.

IR (KBr): 3578, 3322, 1712, 1636, 1463, 1421, 1389, 1340, 1291, 1234, 1156, 1050, 1018, 926 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{10}H_{11}N_3O_2$: 206.0930; found: 206.0998.

Anal. Calcd for $C_{10}H_{11}N_3O_2 \cdot 2H_2O$: C, 49.79; H, 6.27; N, 17.42. Found: C, 49.11; H, 5.04; N, 17.42.

3-Ethoxycarbonyl-5-nitro-1*H*-indazole (12a)
A sample of 5-nitro-1*H*-indazole-3-carboxylic acid (**8**; 2.68 g, 13.0 mmol) was dissolved in EtOH (80 mL) and concd H_2SO_4 (10 mL) and then refluxed over a period of 9 h. Then, the mixture was neutralized with aq 2 N NaOH and extracted with Et_2O (4 × 40 mL). After drying (Na_2SO_4), the solvent was removed by distillation; yield: 1.85 g (60%). All spectroscopic data are in agreement with those reported earlier.[33]

5-Nitro-1*H*-indazole-3-carboxylic Acid *tert*-Butyl Ester (12b)
A mixture of **8** (2.0 g, 10.0 mmol) in dioxane (10 mL) and $SOCl_2$ (10 mL) was refluxed over a period of 2 h, whereupon the indazole dissolved. Then, the solvent was distilled off and the residue was treated with *t*-BuOK (1.12 g, 10.0 mmol) in dioxane (50 mL) and stirred with gentle warming for 2 h. The precipitate was collected by filtration and washed with Et_2O (2 ×). The combined organic layers were evaporated and the crude product was chromatographed (silica gel, EtOAc); yield: 2.0 g (80%).

IR (KBr): 3274, 2977, 1722, 1626, 1532, 1484, 1413, 1370, 1343, 1267, 1169, 1125, 970 cm^{-1}.

Anal. Calcd for $C_{12}H_{13}N_3O_4$: C, 54.75; H, 4.98; N, 15.96. Found: C, 54.49; H, 4.61; N, 15.67.

1,2-Dimethyl-5-nitro-1*H*-indazolium Hydrogensulfate (14)
The ester **12b** (160.0 mg, 0.6 mol) was heated in a mixture of xylene (10 mL) and nitrobenzene (3 mL) to 140 °C. Then, dimethyl sulfate (2 mL) was added and the mixture was heated for an additional hour. After cooling to r.t., the solvent was distilled off in vacuo. The brown residue was then treated with H_2O (12 mL) and concd H_2SO_4 (10 mL) and warmed to 40 °C. The saponification was monitored by TLC. After approximately 2 h, the ester was consumed quantitatively. After cooling, the acid was neutralized with aq 2 N NaOH and evaporated to dryness. The residue was extracted with EtOH (4 × 10 mL), the EtOH was evaporated and the residue chromatographed (silica gel, MeOH). The intense yellow solution changed the color to brown on evaporation of the solvent at 30 °C. The indazolium salt was finally obtained in impure form according to ^1H NMR analyses.

Protonation of Betaine 4 to 1,2-Dimethyl-5-dimethylamino-1*H*-indazolium-3-carboxylic Acid Chloride (15a)
A solution of betaine **4** (46.6 mg, 0.2 mmol) in MeOH (1 mL) was treated with concd HCl (1 mL). Then, the solution was evaporated to give the salt **15a**; yield: 61 mg (quant.).

IR (KBr): 3428, 2423, 1704, 1627, 1571, 1533, 1434, 1349, 1219, 1188, 1123, 938 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{12}H_{15}N_3O_2$: 234.1243; found: 234.1243.

Protonation of Betaine 5 to 1,2-Dimethyl-1*H*-indazolium-3-carboxylic Acid Chloride (15b)
The betaine **5** (0.5 mmol, 95 mg) was suspended in toluene (10 mL) and a drop of concd HCl was added. The mixture was refluxed for 30 min. The colorless precipitate was collected by filtration and dried in vacuo; colorless solid; yield: 91 mg (82%).

IR (KBr): 3163, 1706, 1513, 773 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{10}H_{11}N_2O_2$: 191.0821; found: 191.0825.

3-Lithiocarboxy-1,2-dimethyl-1*H*-indazolium Tetrafluoroborates 16a,b
The betaines **4** (51 mg, 0.22 mmol) and **5** (0.25 mmol, 48 mg) were suspended in MeOH (10 mL) and 1,4-dioxane (10 mL), respectively, and stoichiometric amount of $LiBF_4$ was added to each mixture. In dioxane, voluminous colorless solid precipitated immediately which was filtered off and dried in vacuo. The MeOH solution was evaporated.

3-Lithiocarboxy-1,2-dimethyl-5-dimethylamino-1*H*-indazolium Tetrafluoroborate (16a)
Yield: 72 mg (quant).

IR (KBr): 3428, 1673, 1537, 1525, 1433, 1358, 1301, 1256, 1063, 837 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{12}H_{15}N_3O_2$: 234.1243; found: 234.1247.

3-Lithiocarboxy-1,2-dimethyl-1*H*-indazolium Tetrafluoroborate (16b)
Colorless solid; yield: 35 mg (48%).

IR (KBr): 3566, 1727, 1519, 1065, 790, 768 cm^{-1}.

Indazolium Salts 18a,b by Decarboxylation
The betaines **4** (40 mg, 0.17 mmol) and **5** (48 mg, 0.25 mol) were dissolved in DMSO (10 mL). Then, concd HCl (100 μL) was added to each solution and the solution was heated to 100 °C for 2 h. After evaporation in vacuo, the indazolium salts were obtained; **18a**: 48 mg (92%); **18b**: 12 mg.

18a
IR (KBr): 3424, 1540, 1458, 1297, 1222, 1141, 1017, 920, 804, 608, 523 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{11}H_{16}N_3$: 190.1344; found: 190.1343.

18b
Salt **18b** is a known compound.[36]

1,2-Dimethyl-1,2-dihydroindazole-3-thione (19a) and 1,2-Dimethyl-5-dimethylamino-1,2-dihydroindazole-3-thione (19b)
The respective betaine **4** (120 mg, 0.81 mmol) and **5** (0.5 mmol, 95 mg) each was suspended in toluene (10 mL) and neat sulfur (200 mg) was added. The mixture was refluxed for 1.5 h. After filtration, the yellow solution was evaporated to dryness. Finally, the thione **19a** was chromatographed (silica gel, EtOAc); yield: 40%.

19a
IR (KBr): 2927, 1728, 1633, 1572, 1514, 1445, 1374, 1325, 1276, 1215, 1176, 1126, 1070, 954 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{11}H_{15}N_3S$: 222.1065; found: 222.1082.

Anal. Calcd for $C_{11}H_{15}N_3S$: C, 59.69; H, 6.83; N, 18.99. Found: C, 61.51; H, 7.66; N, 16.97.

19b
Thione **19b** was obtained in quantitative yield (89 mg) and analytical purity. This compound was described in a patent.[34]

New Mesomeric Betaines 20–22 and 26–28; General Procedure
Betaine **5** was suspended in toluene (10 mL) and the appropriate isocyanate/isothiocyante was added. The mixture was then heated to 100 °C for 20 min to 1 h. During the reaction, the color of the suspension changed from pale yellow to orange/red, whereupon a yellowish solid precipitated. The solids were filtered off and dried in vacuo. Amounts and reaction times are given below.

1,2-Dimethyl-1*H*-indazolium-3-(*N*-3,5-dichlorophenyl)amidate (20)
Betaine **5** (0.5 mmol, 95 mg), 3,5-dichlorophenyl isocyanate (0.5 mmol, 94 mg), toluene (10 mL), 30 min; bright-yellow solid; yield: 132 mg (70%).

IR (KBr): 1556, 1421, 752 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{16}H_{14}Cl_2N_3O$: 334.0514; found: 334.0513.

Anal. Calcd for $C_{16}H_{14}Cl_2N_3O$: C, 57.50; H, 3.92; Cl, 21.22; N, 12.57. Found: C, 57.12; H, 3.94; N, 12.58.

1,2-Dimethyl-1*H*-indazolium-3-(*N*-2,4-dichlorophenyl)amidate (21)
Betaine **5** (0.5 mmol, 95 mg), 2,4-dichlorophenyl isocyanate (0.5 mmol, 94 mg), toluene (10 mL), 40 min; bright-yellow solid; yield: 80 mg (48%).

IR (KBr): 3104, 1585, 1458, 1339 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{16}H_{14}Cl_2N_3O$: 334.0514; found: 334.0526.

Anal. Calcd for $C_{16}H_{14}Cl_2N_3O$: C, 53.35; H, 4.47; N, 11.67. Found: C, 53.30; H, 4.05; N, 11.79.

1,2-Dimethyl-1*H*-indazolium-3-(*N*-4-acetylphenyl)amidate (22)
Betaine **5** (0.26 mmol, 54 mg), 4-acetylphenyl isothiocyanate (0.26 mmol, 42 mg), toluene (5 mL), 60 min; orange–yellow solid; yield: 35 mg (44%).

IR (KBr): 3032, 1680, 1603, 1537, 758 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{18}H_{18}N_3O_2$: 308.1399; found: 308.1400.

1,2-Dimethyl-1*H*-indazolium-3-(*N*-phenyl)thioamidate (26)
Betaine **5** (0.5 mmol, 95 mg), phenyl isothiocyanate (0.5 mmol, 0.06 mL), toluene (10 mL), 60 min; orange solid; yield: 52 mg (16%).

IR (KBr): 3015, 1499, 756 cm^{-1}.

HRESIMS: *m*/*z* calcd 282.1065; found 282.1063.

1,2-Dimethyl-1*H*-indazolium-3-(*N*-3,5-dichlorophenyl)thioamidate (27)
Betaine **5** (0.5 mmol, 95 mg), 3,5-dichlorophenyl isothiocyanate (0.5 mmol, 102 mg), toluene (10 mL), 60 min; orange solid; yield: 33 mg (8%).

IR (KBr): 3045, 1553, 1501, 966 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{16}H_{14}Cl_2N_3S$: 350.0285; found: 350.0293.

1,2-Dimethyl-1*H*-indazolium-3-(*N*-2,4-dichlorophenyl)thioamidate (28)
Betaine **5** (0.5 mmol, 95 mg), 2,4-dichlorophenyl isothiocyanate (0.5 mmol, 102 mg), toluene (10 mL), 60 min; orange solid; yield: 37 mg (9%).

IR (KBr): 3037, 1496, 754 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{16}H_{14}Cl_2N_3S$ [M + 1]: 350.0285; found: 350.0274.

Anal. Calcd for $C_{16}H_{13}Cl_2N_3S{\cdot}0.5H_2O$: C, 53.68; H, 3.94; N, 11.73. Found: C, 53.30; H, 4.05; N, 11.79.

Indazolium Amides 23 and 24 by Protonation of the Corresponding Amidates; General Procedure
The amidates were suspended in MeOH and concd HCl was added. Immediate loss of color was observed. The solutions were evaporated to dryness to give the amides.

3-(*N*-3,5-Dichlorophenylcarbonyl)-1,2-dimethyl-1*H*-indazolium Chloride (23)
Amidate **5** (0.12 mmol, 40 mg) gave the amide **23** as colorless solid; yield: 44 mg (quant).

IR (KBr): 3455, 1681, 1512 cm^{-1}.

ESIMS: *m*/*z* = 334.2 (M^+, 100%).

HRESIMS: *m*/*z* calcd for $C_{16}H_{14}Cl_2N_3O$: 334.0514; found: 334.0516.

3-(*N*-2,4-Dichlorophenylcarbonyl)-1,2-dimethyl-1*H*-indazolium Chloride (24)
Amidate **6** (0.12 mmol, 40 mg) gave the amide **24** as colorless solid; yield: 44 mg (quant).

IR (KBr): 3451, 3382, 1679, 1531 cm^{-1}.

ESIMS: *m*/*z* = 334.2 (M^+, 100%).

HRESIMS: *m*/*z* calcd for $C_{16}H_{14}Cl_2N_3O$: 334.0514; found: 334.0518.

Indazolium Amides 30–33 from the Corresponding Anilines; General Procedure
The betaine **5** was suspended in CH_2Cl_2–pyridine and was then treated with freshly distilled $SOCl_2$ under N_2. The mixture was refluxed for 15 min. The appropriate aniline was added to the hot solution, which was refluxed for additional 2 h. Evaporation to dryness in vacuo gave residues which were treated with H_2O. After distilling off the H_2O, the resulting oils were dissolved in MeOH and treated with 50% HBF_4 at 0 °C. After stirring for 30 min, the amides were isolated as solids.

1,2-Dimethyl-3-(*N*-phenylcarbonyl)-1*H*-indazolium Tetrafluoroborate (30)
Starting from **5** (0.6 g, 3.2 mmol), $SOCl_2$ (2.25 g, 19 mmol), and aniline (0.88 g, 9.5 mmol, 0.86 mL), amide **30** was obtained as a colorless solid; yield: 59%.

IR (KBr): 3278, 3072, 1661, 1054 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{16}H_{16}N_3O$: 266.1293; found: 266.1305.

Anal. Calcd for $C_{16}H_{16}BF_4N_3O{\cdot}0.5H_2O$: C, 53.07; H, 4.73; N, 11.60. Found: C, 53.06; H, 4.17; N, 11.70.

3-(*N*-4-Chlorophenylcarbonyl)-1,2-dimethyl-1*H*-indazolium Tetrafluoroborate (31)
Starting from **5** (0.3 g, 1.58 mmol), $SOCl_2$ (1.69 g, 14.2 mmol), and 4-chloroaniline (0.6 g, 4.73 mmol), amide **31** was obtained as a colorless solid; yield: quant.

IR (KBr): 3338, 1681, 1541, 1068 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{16}H_{15}ClN_3O$: 300.0904; found: 300.0902.

Anal. Calcd for $C_{16}H_{15}BClF_4N_3O{\cdot}H_2O$: C, 49.58; H, 3.90; N, 10.84. Found: C, 51.73; H, 3.92; N, 11.35.

3-(*N*-4-Trifluoromethylphenylcarbonyl)-1,2-dimethyl-1*H*-indazolium Tetrafluoroborate (32)
Starting from **5** (0.3 g, 1.57 mmol), $SOCl_2$ (1.69 g, 14.2 mmol, 1.03 mL) and 4-trifluoromethylphenylaniline (0.76 g, 4.73 mmol, 0.6 mL), amide **32** was obtained as a colorless solid; yield: quant.

IR (KBr): 3339, 1689, 1543, 1119, 1067 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{17}H_{15}F_3N_3O$: 334.1167; found: 334.1173.

Anal. Calcd for $C_{17}H_{15}BF_7N_3O{\cdot}0.5H_2O$: C, 47.47; H, 3.75; N, 9.77. Found: C, 47.05; H, 2.83; N, 9.68.

3-(*N*-4-Ethoxyphenylcarbonyl)-1,2-dimethyl-1*H*-indazolium Tetrafluoroborate (33)
Starting from **5** (0.3 g, 1.57 mmol), $SOCl_2$ (1.67 g, 14.2 mmol, 11.03 mL) and 4-ethoxyphenylaniline (0.65 g, 4.73 mmol, 0.61 mL), amide **33** was obtained as a colorless solid; yield: quant.

IR (KBr): 3334, 2994, 1683, 1514, 1233, 1061 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{18}H_{20}N_3O_2$: 310.1556; found: 310.1543.

Indazolium Amidates 34–37 by Deprotonation of the Corresponding Amides; General Procedure

Amberlite IRA-402 was filled in a small column and subsequently treated with H_2O (400 mL) and aq 4% NaOH (50 mL). After 1 h, the resin was first washed with H_2O until the eluate was neutral, and then with EtOH–H_2O (1:1). A sample of the amide **30**–**33** was dissolved in the same solvent mixture and then given on the resin and eluted. Evaporation of the eluate gave the amidates.

1,2-Dimethyl-1*H*-indazolium-3-(*N*-phenyl)amidate (34)

Starting from amide **30** (0.54 g, 1.54 mmol), amidate **34** was obtained as a yellow solid; yield: 95%.

IR (KBr): 3045, 3015, 1556, 1313, 1245, 758 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{16}H_{16}N_3O$ [M + 1]: 266.1293; found: 266.1296.

Anal. Calcd for $C_{16}H_{15}N_3O·0.5H_2O$: C, 70.05; H, 5.88; N, 15.32. Found: C, 70.69; H, 5.78; N, 15.37.

1,2-Dimethyl-1*H*-indazolium-3-(*N*-4-chlorophenyl)amidate (35)

Starting from amide **31** (0.27 g, 0.69 mmol), amidate **35** was obtained as an orange solid; yield: quant.

IR (KBr): 3045, 1592, 1566, 1476, 1334, 1319, 749 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{16}H_{15}ClN_3O$ [M + 1]: 300.0904; found: 300.0917.

Anal. Calcd for $C_{16}H_{14}ClN_3O·H_2O$: C, 60.47; H, 5.08; N, 13.22. Found: C, 60.87; H, 4.75; N, 13.21.

1,2-Dimethyl-1*H*-indazolium-3-(*N*-4-trifluoromethylphenyl)amidate (36)

Starting from amide **32** (0.36 g, 0.86 mmol), amidate **36** was obtained as a yellow solid; yield: 85%.

IR (KBr): 3009, 1576, 1317, 1101, 1062 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{17}H_{15}F_3N_3O$ [M + 1]: 334.1167; found: 334.1172.

Anal. Calcd for $C_{17}H_{14}F_3N_3O·H_2O$: C, 59.65; H, 4.42; N, 12.28. Found: C, 59.44; H, 3.91; N, 12.25.

1,2-Dimethyl-1*H*-indazolium-3-(*N*-4-ethoxyphenyl)amidate (37)

Starting from amide **33** (0.24 g, 0.61 mmol), amidate **37** was obtained as an orange solid; yield: quant.

IR (KBr): 3032, 2977, 1578, 1566, 1499, 1234, 1045, 751 cm^{-1}.

HRESIMS: *m*/*z* calcd for $C_{18}H_{20}N_3O_2$ [M + 1]: 310.1556; found: 310.1563.

Anal. Calcd for $C_{18}H_{19}N_3O_2·2.5H_2O$: C, 61.18; H, 6.84; N, 11.89. Found: C, 61.22; H, 6.24; N, 11.66.

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