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N-Heterocyclic Carbene Induced Cycloaddition Reactions of Indazoles with Acetylenes To Form a New Ring System

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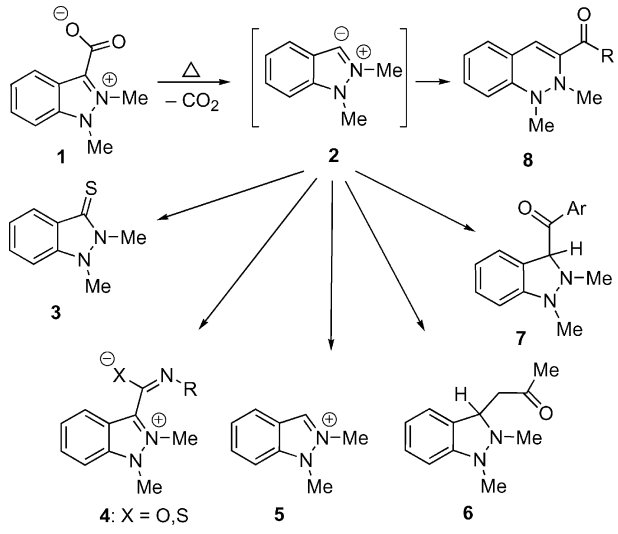
Keywords: Betaines / Decarboxylation / DMAD / 1,3-Dipoles / Carbenes / Cycloaddition

Thermal decarboxylation of the mesomeric betaine 1,2-dimethylindazolium-3-carboxylate resulted in the formation of the N-heterocyclic carbene indazol-3-ylidene which deprotonated a second molecule of the betaine to give an azomethine ylide. This 1,3-dipole underwent a cycloaddition/decarboxylation sequence on treatment with ethyl or methyl 3-phenylpropiolate to give the new ring system 3,5-dihydro-2*H*-pyrrolo[1,2-*b*]indazole. By contrast, dimethyl or diethyl but-2-ynedioate (DMAD, DEAD) as the activated triple bond yielded this ring system with an ester group at the 9b-position, which originates from the acetylene derivative. Model reactions were carried out to elucidate the mechanisms of these reactions, and some trapping products of the N-heterocyclic carbene have been characterized.

Introduction

The broad applicability of N-heterocyclic carbenes (NHC) of thiazole, triazole, imidazole, and imidazoline has been impressively demonstrated since the first stable N-heterocyclic carbene was described.[1] They are not only excellent ligands in organometallic chemistry,[2] but also versatile organocatalysts in Stetter reactions,[3] benzoin condensations,[4] umpolung reactions,[5] enantioselective syntheses of β-lactams by the Staudinger reaction,[6] highly diastereo- and enantioselective additions of homoenolates to nitrones,[7] and many other reactions.[8] Among these, their reactions with triple bonds have also been reported.[9] Some books and review articles dealing with the development of N-heterocyclic carbene chemistry have been published recently.[10] Less attention has been focussed on the N-heterocyclic carbenes of indazole.[11] These can be generated by decarboxylation of indazolium-3-carboxylates, which belong to the class of pseudo-cross-conjugated heterocyclic mesomeric betaines.[12,13] The N-heterocyclic carbenes of indazole undergo typical trapping reactions with sulfur to give indazolethione **3**,[13] with isocyanates to give indazol-3-amidates **4** (X = O), with isothiocyanates to give indazole-3-thioamidates **4** (X = S), and with protons to give indazolium salts **5** (Scheme 1). Ketones form stable 1:1 adducts **6**.[14] Few examples of the reactions of aromatic aldehydes have been found that form adducts **7**, which are tautomers of Breslow intermediates. The trapping of NHC **2** with α-halo ketones results in the formation of cinnolines **8**.[15]



Scheme 1.

In the presence of N-heterocyclic carbene **2** and alcohols, aromatic aldehydes undergo redox esterification reactions to give benzoates ArCOOR and indazoline **9** (Scheme 2).[14]

Furthermore, NHC **2** effectively induces debromination of vicinal dibromides to give alkenes (Scheme 3). The 3-bromoindazolium ion **10** is formed as the second product of this reaction.[15]

Likewise, 1,2-dibromoethene derivatives give acetylenes in very high yields (Scheme 4).[15]

As a continuation of an ongoing project dealing with the chemistry of mesomeric betaines and the N-heterocyclic

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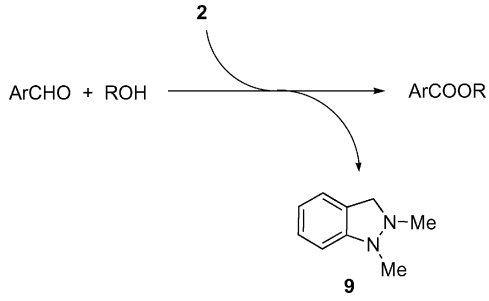
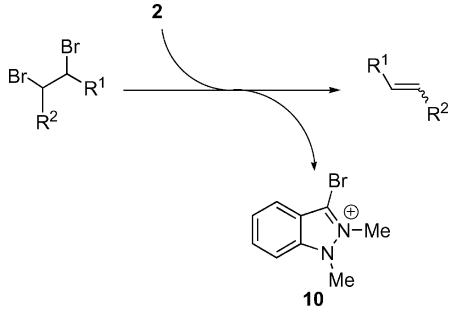
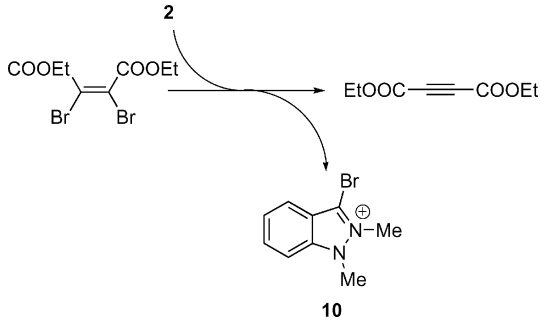


Scheme 2.



Scheme 3.

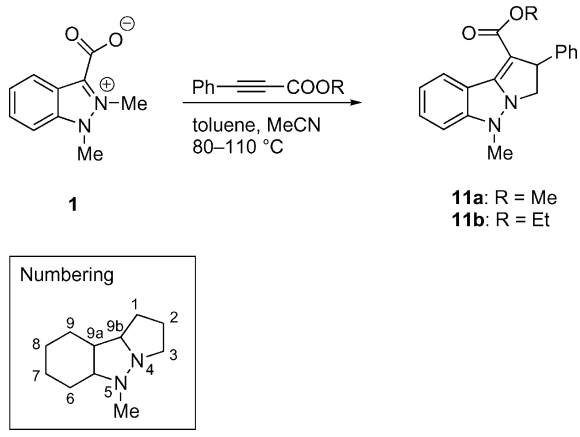


Scheme 4.

carbenes of indazoles, we report herein the unprecedented reactions of the pseudo-cross-conjugated heterocyclic mesomeric betaine **1** with activated carbon–carbon triple bonds.

Results and Discussion

Surprisingly, the reaction of indazolium-3-carboxylate **1** with methyl 3-phenylpropiolate in a mixture of toluene and acetonitrile at 80 °C, or in pure acetonitrile at 40–50 °C, resulted in the formation of the new ring system methyl 2*H*-pyrrolo[1,2-*b*]indazole-1-carboxylate **11a**, the structure of which was elucidated by HSQC, HMBC, and H–H COSY NMR spectroscopy (Scheme 5). Thus, the multiplet at δ = 6.01 ppm and the signal at δ = 75.8 ppm were assigned to 2-H and C-2, respectively. The signal of the C-3-H_2 group appears at δ = 68.6 ppm in the ^{13}C NMR spectrum and displays all the expected couplings. Conclusions concerning the regiochemistry of this reaction were drawn from the HMBC spectra, which revealed strong interactions of the C-2-H and C-3-H_2 groups with the phenyl ring, but only weak interactions between C-3-H_2 and the carbonyl group. A similar reaction was observed starting from ethyl 3-phenylpropiolate, which gave **11b**. Analogous spectroscopic results were obtained.



Scheme 5.

Formally, compounds **11a**,**b** are tautomers of the cycloadduct **11A** of the azomethine ylide **12a** and the acetylene derivative (Figure 1).

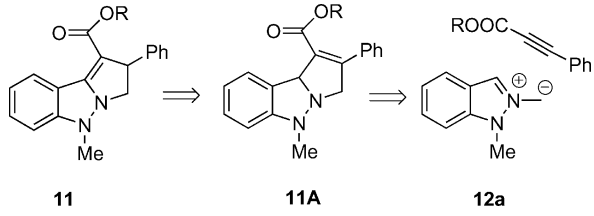


Figure 1. Retrosynthesis of ring system **11**.

To gain some insight into the mechanism, we performed model reactions and calculations.[17] First, we calculated the frontier orbital profiles of the NHC and the ylide. The HOMO and LUMO of the N-heterocyclic carbene **2** are shown in Figure 2. As expected, the HOMO is essentially located on the carbene lone pair, whereas the LUMO is located over the whole π-electron system. Figure 3 presents the frontier orbital profile of the 1,3-dipole **12a**.

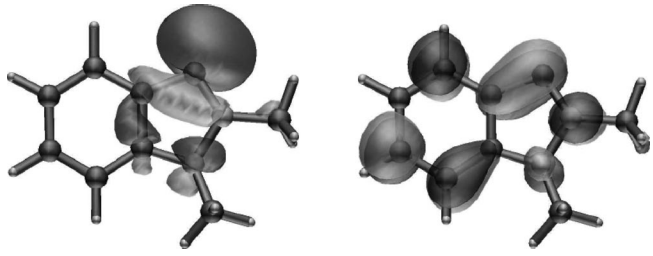


Figure 2. HOMO (left) and LUMO (right) of **2**.

We next performed calculations for the conversion of N-heterocyclic carbene **2** into 1,3-dipole **12a** (Scheme 6). The dipole **12a** is 18.61 kJ mol^{-1} more stable than **2** according to the calculations. However, as expected, the calculations show the intramolecular conversion **2** → **12a** to have a prohibitively large activation barrier of 180 kJ mol^{-1}.

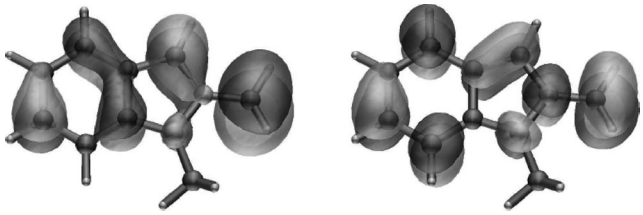
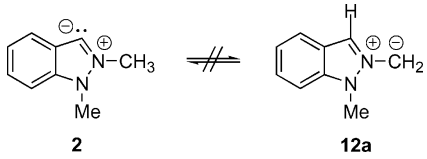
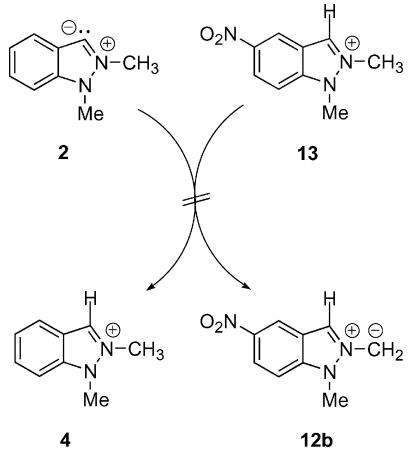


Figure 3. HOMO (left) and LUMO (right) of ylide **12a**.



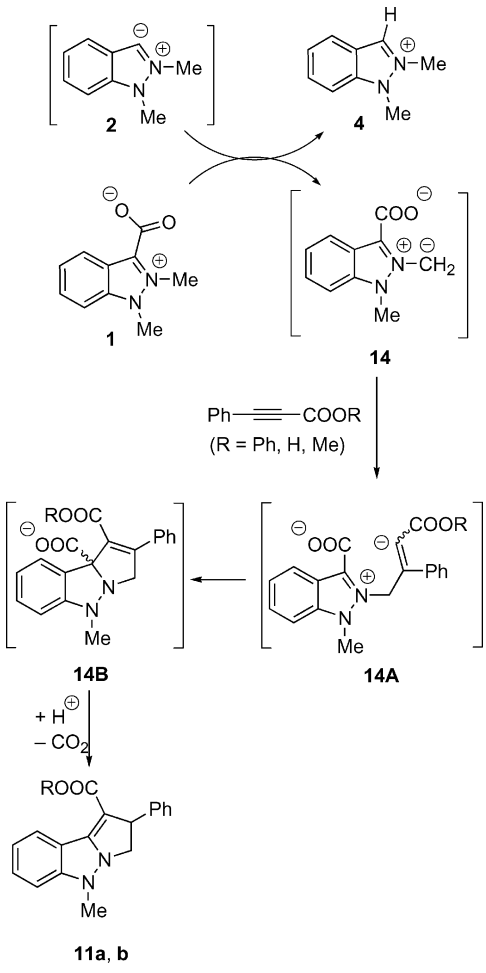
Scheme 6.

Model reactions have then been performed to examine the intermolecular processes. No experimental evidence was found for the in situ generated carbene **2** to deprotonate the 5-nitroindazolium salt **13** to give the 1,3-dipole **12b** along with the indazolium salt **4** (Scheme 7). In accordance with this, a 1:1:1 mixture of **1**, **13**, and methyl 3-phenylpropiolate exclusively yielded cycloadduct **11a**, but no traces of the 5-nitro derivative. Indazolium salt **4** was nonetheless isolated, which, it was concluded, could not be the source of the 1,3-dipoles.



Scheme 7.

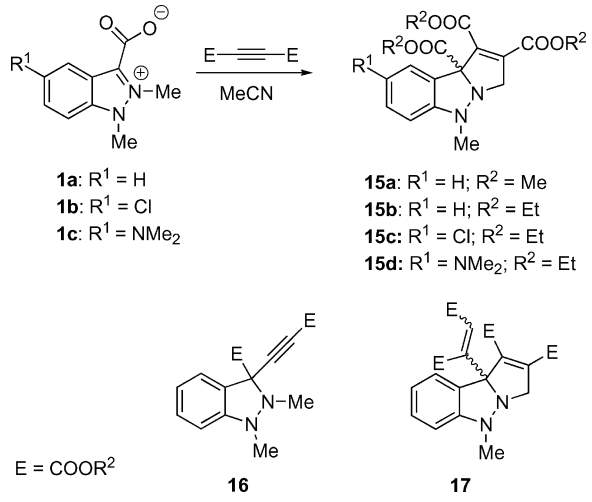
In view of these results and the regiochemistry of the reactions we propose the following mechanism. The unambiguous starting point is the N-heterocyclic carbene **2**, which forms on decarboxylation of **1** under the reaction conditions described here and which can indeed be trapped by numerous heterocumulenes and sulfur. The in situ generated indazol-3-ylidene **2** deprotonates betaine **1** to give the 1,3-dipole **14** and indazolium salt **4** (Scheme 8). The former species then undergoes 1,3-dipolar cycloaddition reactions with triple bonds. Decarboxylation of **14B** and protonation lead to the formation of the β-enaminocarbonyl chromophores in **11a**,**b**. If nucleophilic attack of C-3 of the N-heterocyclic carbene **2** on the activated triple bond took place, as reported for imidazol- and imidazolin-2-ylidenes,[9] regioisomers of **11a**,**b** would be formed, which we did not detect in our reaction mixtures.



Scheme 8.

Surprisingly, an analogous series of reactions starting from the betaines **1a**–**c** and dimethyl but-2-ynedioate (DMAD) and diethyl but-2-yndioate (DEAD) in toluene at 80 °C or in acetonitrile/toluene at 40 °C yielded the triesters **15a**–**d** as yellow oils (Scheme 9). The derivatives **16** and **17** were isolated as byproducts on slight modification of the reaction conditions and careful separation of the reaction mixture.

Mass spectra as well as NMR spectroscopic data unambiguously indicate the presence of a third ester functionality attached to the new ring system. In accordance with H–H COSY, HSQC, and HMBC NMR measurements, the ^{1}H NMR signal at δ = 7.45 ppm was assigned to 9-H of **15d** (for the numbering, cf. Scheme 5). The HMBC measurements show a coupling with a chemical shift at δ = 87.6 ppm, which is a quaternary atom according to DEPT experiments. The connectivities and assignments are presented in Figure 4. Signals of the C-3-H_2 group appear at δ = 4.62 and 4.30 ppm, and for C-3 at δ = 65.9 ppm. The 2,5-dihydropyrrole moiety is proved by couplings to C-2, C-1,



Scheme 9.

and C-9b, and to three carbonyl signals at δ = 163.2, 163.3, and 169.8 ppm. Coupling between the methyl group and C-9b prove the structure as shown. All derivatives **15a**–**d** display closely related features in the NMR spectra.

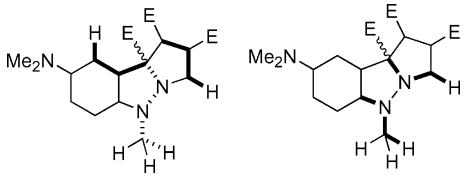
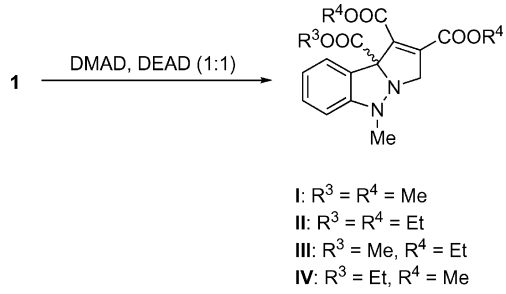


Figure 4. Some characteristic couplings in the HMBC measurements of **15d**.

The signal of the quaternary atom of **16** appears at δ = 70.3 ppm in the ^{13}C NMR spectrum, and displays couplings to 4-H and to a CH_2 group of an ester in the HMBC measurements. The methyl group attached to N-2 shows a small coupling to one of the acetylenic carbon atoms and a strong coupling to C-3. The signals of the sp carbon atoms appear at δ = 80.3 and 80.8 ppm in the ^{13}C NMR spectrum, and an absorption band can be seen at 2232 cm^{-1} in the IR spectrum.

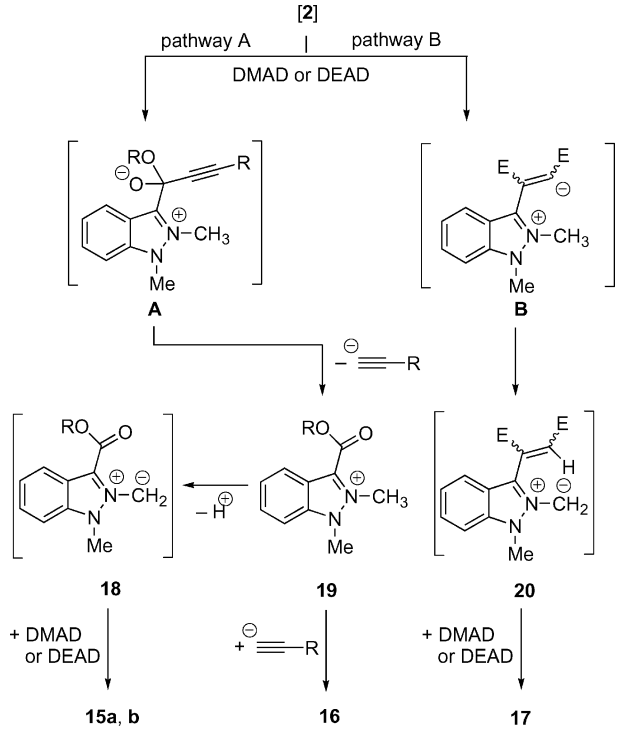
The vinylic proton of **17** was assigned to a singlet with chemical shift δ = 6.53 ppm. According to the structure, it couples to two ester groups, to C-9b, as well as to C-1 and C-9a. The signals of the protons of the CH_2 group of the 2,5-dihydropyrrole moiety appear at δ = 4.34 and 3.98 ppm and display a geminal coupling constant of 17.1 Hz.

We next performed several model reactions to clarify the origin of the ester group. We first conducted the carbene formation in the presence of a 1:1 mixture of DMAD and DEAD, which resulted in the formation of all possible substitution patterns **I**–**IV** (Scheme 10), as evidenced by chromatographic separation followed by electrospray ionization mass spectrometric analysis.



Scheme 10.

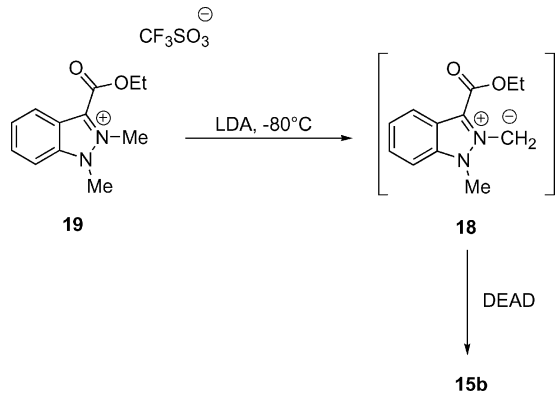
We concluded that the presence of an ester group at C-9b in **15a**–**d** is the result of nucleophilic attack of the carbene atom of **2** on the carbonyl group of the acetylene derivative to give adduct **A** (pathway A, Scheme 11). This resulted in methyl or ethyl indazolium-3-carboxylate **19** after elimination of the acetylenide moiety and prevents the system from undergoing decarboxylation, as observed in the formation of **11a**,**b**. Deprotonation then yielded 1,3-dipole **18**, which undergoes cycloaddition to give **15a**,**b**. The byproduct **16** can be explained by nucleophilic attack of the acetylenide on the iminium bond of **19**. Evidence for pathway B is the isolation of **17** from the reaction mixture. Its formation can be rationalized by a nucleophilic attack of the carbene atom of **2** on the triple bond to form adduct **B**, formal 1,5-H shift to yield 1,3-dipole **20**, and cycloaddition to give **17**.



Scheme 11.

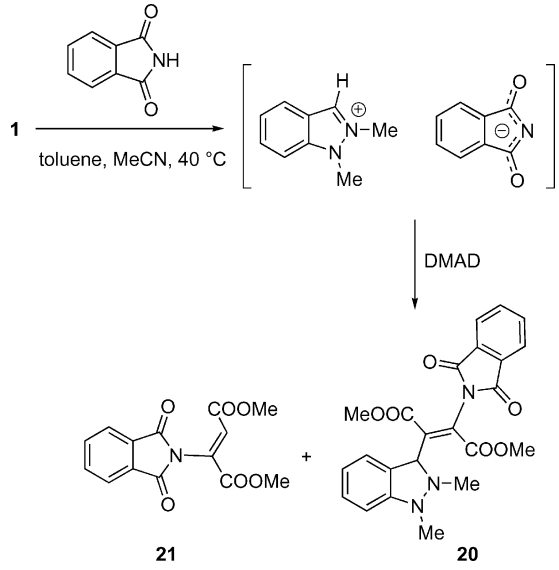
In accordance with the proposed mechanism, 3-(ethoxycarbonyl)-1,2-dimethyl-1*H*-indazolium triflate **19** could indeed be deprotonated to azomethine ylide **18**, which was trapped by DEAD to give **15b** (Scheme 12). By contrast,

1,2-dimethyl-1*H*-indazolium hydrogen sulfate gave no product under analogous reaction conditions.



Scheme 12.

The effect of protic reagents was tested as follows: The presence of a weak acid such as isoindoline-1,3-dione in the reaction of mesomeric betaine **1** with DMAD led to the immediate formation of the Michael adducts **20** and **21** (Scheme 13).



Scheme 13.

Conclusions

We have presented herein new cycloaddition reactions between 1,3-dipoles of indazoles and activated triple bonds. These cycloadditions are either induced by the N-heterocyclic carbene indazol-3-ylidene or result from an attack of this nucleophilic carbene on the triple bond of an acetylene derivative. The indazol-3-ylidene is generated in situ by thermal decarboxylation of the pseudo-cross-conjugated mesomeric betaine indazolium-3-carboxylate. These reactions differ considerably from those reported between the N-heterocyclic carbenes of other ring systems and activated triple bonds.

Experimental Section

General: 5-Nitroindazole was prepared according to a literature procedure.[16] ^{1}H and ^{13}C NMR spectra were recorded with Bruker Digital FT-NMR Avance 400 and Avance 200 spectrometers in [D_6]-DMSO at 20 °C unless otherwise noted. Chemical shifts are reported in ppm relative to internal TMS (δ = 0.000 ppm). Multiplicities are described by using the following abbreviations: s = singlet, d = doublet, t = triplet, m = multiplet. Peak assignments were made on the basis of HMBC, HSQC, and H–H NOESY measurements. FTIR spectra were obtained with a Bruker Vector 22 in the range of 400–4000 cm^{-1} (2.5% pellets in KBr). Electrospray ionization mass spectra (ESIMS) were measured with an Agilent LCMSD Series HP1100 spectrometer with APIES (direct inlet). Samples were dissolved in methanol and sprayed from methanol with a 0 V fragmenting voltage, 300 °C drying gas temperature, 4000 V capillary voltage, and 0.6 mL solvent flow unless otherwise noted. Mass spectra were recorded with a Varian GC3900/SAT2100T mass spectrometer. All samples were dried in vacuo at room temp. for 5 h prior to CHN analysis. Melting points were determined with a Boëtius melting point apparatus and are uncorrected. Yields were not optimized.

General Procedure for the Synthesis of the Pyrrolo[1,2-*b*]indazole-1-carboxylates 11a,b and Tricarboxylates 15a,b: Under an inert gas, a sample of 1,2-dimethyl-1*H*-indazolium-3-carboxylate in the solvent specified below was treated with the acetylene derivative and then heated at 90 °C for 2–4 h. Then, the solvent mixture was distilled off in vacuo. The residue was purified by chromatography (silica gel, petroleum ether/ethyl acetate = 4:1). Details are given below.

Methyl 5-Methyl-2-phenyl-3,5-dihydro-2*H*-pyrrolo[1,2-*b*]indazole-1-carboxylate (11a): A sample of 1,2-dimethyl-1*H*-indazolium-3-carboxylate (150 mg, 0.75 mmol) in acetonitrile (0.5 mL) and toluene (3.5 mL) was treated with methyl 3-phenylpropiolate (240 mg, 1.5 mmol). Yellow oil; yield 77 mg (32%). ^{1}H NMR ($CDCl_3$): δ = 7.40–7.31 (m, 6 H), 7.29–7.15 (m, 1 H), 6.93–6.85 (m, 1 H), 6.65 (d, J = 7.9 Hz, 1 H), 6.02–6.00 (m, 1 H), 4.42 (dd, J = 17.4, 2.2 Hz, 1 H), 4.29 (dd, J = 17.4, 2.4 Hz, 1 H), 3.69 (s, 3 H), 2.94 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 164.6, 151.0, 150.7, 133.5, 129.8, 128.8, 128.6, 128.5, 128.1, 128.0, 127.7, 126.6, 124.0 121.3, 110.8, 75.9, 68.5, 51.3, 43.4 ppm. IR (NaCl): $\tilde{\nu}$ = 3057, 2949, 2900, 1703, 1482, 1436, 910 cm^{-1}. MS (EI): m/z (%) = 306 (15), 304 (100), 247 (10), 246 (45). HRMS (ESI): calcd. for $C_{17}H_{19}N_2O_6$ 307.1447; found 307.1445.

Ethyl 5-Methyl-2-phenyl-3,5-dihydro-2*H*-pyrrolo[1,2-*b*]indazole-1-carboxylate (11b): A sample of 1,2-dimethyl-1*H*-indazolium-3-carboxylate (150 mg, 0.75 mmol) in acetonitrile (0.5 mL) and toluene (3.5 mL) was treated with ethyl 3-phenylpropiolate (262 mg, 1.5 mmol). Yellow oil; yield 61 mg (25%). ^{1}H NMR ($CDCl_3$): δ = 7.42–7.32 (m, 6 H), 7.21–7.17 (m, 1 H), 6.91–6.87 (m, 1 H), 6.66 (d, J = 7.8 Hz, 1 H), 6.02–6.01 (m, 1 H), 4.40 (dd, J = 17.4, 2.1 Hz, 1 H), 4.31 (dd, J = 17.4, 2.6 Hz, 1 H), 4.16 (q, J = 7.0 Hz, 2 H), 2.95 (s, 3 H), 1.17 (t, J = 7.04 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 164.2, 151.1, 150.4, 133.7, 129.9, 128.7, 128.6 (2 C), 128.1, 127.9, 127.6, 127.1, 124.1 121.3, 110.8, 75.9, 68.7, 60.5, 43.5, 14.0 ppm. IR (NaCl): $\tilde{\nu}$ = 3057, 2981, 2901, 1701, 1481, 1447, 911 cm^{-1}. MS (EI): m/z (%) = 320 (9), 317 (100), 245 (90), 146 (25). HRMS (ESI): calcd. for $C_{20}H_{20}N_2O_2$ 321.1603; found 321.1600.

Trimethyl 5-Methyl-5,9b-dihydro-3*H*-pyrrolo[1,2-*b*]indazole-1,2,9b-tricarboxylate (15a): A sample of the betaine (95 mg, 0.5 mmol) and dimethyl but-2-ynedioate (145 mg, 1 mmol) in acetonitrile (5 mL) was used. Yellow oil; yield 46 mg (27%). ^{1}H NMR ($CDCl_3$): δ = 7.45–7.41 (m, 1 H), 7.29–7.21 (m, 1 H), 7.93 (ddd, J = 7.5, 7.4,

1.0 Hz, 1 H), 6.68 (d, J = 7.9 Hz, 1 H), 4.45 (d, J = 17.2 Hz, 1 H), 4.23 (d, J = 17.2 Hz, 1 H), 3.81 (s, 3 H), 3.79 (s, 6 H), 2.95 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 169.5, 163.7, 163.1, 150.8, 139.5, 136.6, 129.7, 125.3, 124.8, 121.6, 111.0, 86.6, 64.8, 53.2, 52.4 (2 C), 43.6 ppm. IR (NaCl): $\tilde{\nu}$ = 3001, 2954, 2911, 1739, 1483, 1436, 916 cm^{-1}. MS (EI): m/z (%) = 346 (9) $[M]^+$, 288 (80), 257 (100). HRMS (ESI): calcd. for $C_{17}H_{18}N_2O_6Na$ 369.1063; found 369.1062. $C_{17}H_{18}N_2O_6$ (346.3): calcd. C 58.96, H 5.24, N 8.09; found C 58.94, H 4.70, N 8.01.

Triethyl 5-Methyl-5,9b-dihydro-3*H*-pyrrolo[1,2-*b*]indazole-1,2,9b-tricarboxylate (15b). Method A: A sample of the betaine (285 mg, 1.5 mmol) and acetonitrile (5 mL) were stirred at room temp. for 15 min. Then DEAD (0.29 mL, 1.6 mmol) was added. Stirring at 35 °C was continued for 24 h. Yellow oil; yield 128 mg (22%). ^{1}H NMR ($CDCl_3$): δ = 7.46 (dd, J = 7.6, 0.6 Hz, 1 H), 7.26–7.22 (m, 1 H), 6.92 (ddd, J = 7.6, 7.4, 0.8 Hz, 1 H), 6.66 (d, J = 8 Hz, 1 H), 4.43 (d, J = 17.2 Hz, 1 H), 4.28–4.19 (m, 7 H), 2.96 (s, 3 H), 1.32–1.27 (m, 9 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 169.0, 163.3, 162.9, 150.9, 138.9, 136.8, 129.6, 125.3, 125.0, 121.4, 111.0, 86.8, 64.7, 62.1, 61.5, 61.4, 43.6, 14.0 (3 C) ppm. IR (NaCl): $\tilde{\nu}$ = 2983, 2906, 1734, 1482 cm^{-1}. MS (EI): m/z (%) = 388 (5), 315 (100), 269 (44). HRMS (ESI): calcd. for $C_{20}H_{25}N_2O_6$ 389.1713; found 389.1937. $C_{20}H_{24}N_2O_6$ (388.4): calcd. C 61.84, H 6.23, N 7.21; found C 61.83, H 5.81, N 7.15. **Method B:** A suspension of 3-(ethoxycarbonyl)-1,2-dimethyl-1*H*-indazolium triflate (185 mg, 0.5 mmol) was treated at –80 °C with a 1 M solution of LDA in THF (0.64 mL) and stirred for 45 min at that temperature. Then DEAD (0.15 mL) was added and the solution was warmed to room temp. over a period of 4 h. A small amount of silica gel was then added, the solvent mixture was evaporated, and the residue was purified by chromatography. Yellow oil; yield 38 mg (20%).

Triethyl 8-Chloro-5-methyl-5,9b-dihydro-3*H*-pyrrolo[1,2-*b*]indazole-1,2,9b-tricarboxylate (15c): A sample of the 5-chlorobetaine (120 mg, 0.53 mmol) and DEAD (0.15 mL) were used. Pale-yellow oil; yield 47 mg (21%). ^{1}H NMR (C_6D_6): δ = 8.00 (d, J = 2.2 Hz, 1 H), 6.99 (dd, J = 8.4, 2.2 Hz, 1 H), 6.05 (d, J = 8.4 Hz, 1 H), 4.46 (d, J = 17.1 Hz, 1 H), 4.12 (d, J = 17.1 Hz, 1 H), 3.97–3.87 (m, 6 H), 2.57 (s, 3 H), 0.92–0.85 (m, 9 H) ppm. ^{13}C NMR (C_6D_6): δ = 169.5, 163.2, 162.4, 150.1, 140.9, 136.0, 129.6, 126.5, 126.2, 112.0, 86.7, 65.3, 61.9, 61.3, 61.2, 43.2, 13.6 ppm. IR (NaCl): $\tilde{\nu}$ = 2983, 2937, 2911, 1736, 1479 cm^{-1}. MS (EI): m/z (%) = 423 (8) $[M + H]^+$, 348 (100), 303 (45). HRMS (ESI): calcd. for $C_{20}H_{24}ClN_2O_6$ 423.1317; found 423.1323. $C_{20}H_{23}ClN_2O_6$ (422.9): calcd. C 56.81, H 5.48, N 6.62; found C 57.22, H 5.16, N 6.34.

Triethyl 8-(Dimethylamino)-5-methyl-5,9b-dihydro-3*H*-pyrrolo[1,2-*b*]indazole-1,2,9b-tricarboxylate (15d): A sample of the (dimethylamino)-substituted betaine (150 mg, 0.64 mmol), acetonitrile (2 mL), and THF (4 mL) were used. This mixture was stirred at room temp. for 15 min. Then DEAD (0.29 mL, 1.6 mmol) was added, and the mixture was heated at reflux for 6 h. Workup was carried out as described above. Yellow oil; yield 58 mg (21%). ^{1}H NMR (C_6D_6): δ = 7.45 (d, J = 2.4 Hz, 1 H), 6.59 (dd, J = 8.7, 2.4 Hz, 1 H), 6.54 (d, J = 8.7 Hz, 1 H), 4.62 (d, J = 17.1 Hz, 1 H), 4.30 (d, J = 17.1 Hz, 1 H), 4.06 (q, J = 7.1 Hz, 2 H), 4.05 (q, J = 7.1 Hz, 2 H), 3.90 (q, J = 7.1 Hz, 2 H), 2.85 (s, 3 H), 2.59 (s, 6 H), 0.97 (t, J = 7.1 Hz, 3 H), 0.90 (t, J = 7.1 Hz, 3 H), 0.85 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (C_6D_6): δ = 169.8, 163.3, 163.2, 147.6, 143.6, 139.9, 136.9, 115.4, 112.8, 110.9, 87.6, 65.9, 61.5, 61.0, 60.9, 45.8, 41.2 (2 C), 13.7 (3 C) ppm. IR (NaCl): $\tilde{\nu}$ = 2983, 2938, 2906, 2871, 1732, 1502 cm^{-1}. MS (EI): m/z (%) = 432 (37) $[M + H]^+$, 431 (2) $[M]^+$, 358 (21), 357 (100), 285 (31). HRMS (ESI): calcd. for $C_{22}H_{30}N_3O_6$ 432.2129; found 432.2139. $C_{22}H_{29}N_3O_6$ (431.5): calcd. C 61.24, H 6.77, N 9.74; found C 60.67, H 6.25, N 8.73.

Reaction of Mesomeric Betaine 1 and DEAD in Toluene: A suspension of the betaine (500 mg, 2.5 mmol) and DEAD (1.05 mL, 6.5 mmol) in toluene (30 mL) was heated at 90–100 °C over a period of 6 h. The solvent mixture was then removed in vacuo, and the residue was purified by chromatography to yield **15b**, **16**, and **17**.

Ethyl 3-(3-Ethoxy-3-oxoprop-1-ynyl)-1,2-dimethyl-2,3-dihydro-1*H*-indazole-3-carboxylate (16): Yellow oil; yield 87 mg (11%) ^{1}H NMR ($CDCl_3$): δ = 7.42–7.37 (m, 1 H), 7.30–7.22 (m, 1 H), 6.99–6.91 (m, 1 H), 6.68 (d, J = 7.9 Hz, 1 H), 4.39–4.28 (m, 2 H), 4.20 (q, J = 7.1 Hz, 2 H), 2.91 (s, 3 H), 2.88 (s, 3 H), 1.35 (t, J = 7.1 Hz, 3 H), 1.28 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 166.8, 153.1, 150.3, 129.9, 125.6, 124.0, 121.8, 110.9, 80.8, 80.3, 70.3, 62.8, 62.2, 40.4, 38.2, 14.0, 13.9 ppm. IR (NaCl): $\tilde{\nu}$ = 2981, 2906, 2232, 1737, 1714, 1482 cm^{-1}. MS (EI): m/z (%) = 316 (1) $[M]^+$, 243 (100). HRMS (ESI): calcd. for $C_{17}H_{21}N_2O_4$ 317.1501; found 317.1502. $C_{17}H_{20}N_2O_4$ (316.4): calcd. C 64.54, H 6.37, N 8.86; found C 63.41, H 5.70, N 7.95.

Diethyl 9b-(1,4-Diethoxy-1,4-dioxobut-2-en-2-yl)-5-methyl-5,9b-dihydro-3*H*-pyrrolo[1,2-*b*]indazole-1,2-dicarboxylate (17): Yellow oil; yield 136 mg (11%). ^{1}H NMR (C_6D_6): δ = 7.80–7.78 (m, 1 H), 7.00–6.96 (m, 1 H), 6.79–6.75 (m, 1 H), 6.53 (s, 1 H), 6.37 (d, J = 7.9 Hz, 1 H), 4.34 (d, J = 17.1 Hz, 1 H), 4.28–4.15 (m, 3 H), 3.97 (q, J = 7.1 Hz, 2 H), 3.91 (q, J = 7.1 Hz, 2 H), 3.84 (q, J = 7.1 Hz, 2 H), 1.05 (t, J = 7.2 Hz, 3 H), 0.90 (t, J = 7.1 Hz, 3 H), 0.86 (t, J = 7.1 Hz, 3 H), 0.79 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (C_6D_6): δ = 166.1, 164.5, 163.4, 162.8, 151.9, 151.2, 141.2, 136.7, 129.5, 127.0, 125.9, 122.4, 121.7, 111.8, 86.0, 63.4, 61.1, 61.0 (2 C), 60.5, 43.4, 13.8, 13.7 (2 C), 13.6 ppm. IR (NaCl): $\tilde{\nu}$ = 2984, 2939, 2906, 1728, 1479 cm^{-1}. MS (EI): m/z (%) = 486 (14) $[M]^+$, 314 (100), 269 (30). HRMS (ESI): calcd. for $C_{25}H_{31}N_2O_8$ 487.2080; found 487.2088. $C_{25}H_{30}N_2O_8$ (486.5): calcd. C 61.72, H 6.22, N 5.76; found C 61.06, H 5.85. N 5.34.

3-(Ethoxycarbonyl)-1,2-dimethyl-1*H*-indazolium Triflate (19): A solution of ethyl 1,2-dimethyl-1*H*-indazolium-3-carboxylate (1.9 g, 0.01 mol) and a catalytic amount of nitrobenzene in xylene (30 mL) was heated at reflux with methyl triflate (2.5 mL, 0.022 mol) over a period of 45 min. The solvent mixture was then distilled off, and the residue was recrystallized from acetone/diethyl ether (3:1). White solid; m.p. 136–138 °C; yield 1.6 g (43%). ^{1}H NMR ($CDCl_3$): δ = 8.36 (d, J = 8.6 Hz, 1 H), 8.03–7.89 (m, 2 H), 7.72–7.64 (m, 1 H), 4.69 (s, 3 H), 4.64 (q, J = 7.1 Hz, 2 H), 4.41 (s, 3 H), 1.54 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 157.4, 130.4 (q, J = 315 Hz, 1 C), 124.5, 123.4, 122.8, 120.9, 119.7, 117.0, 110.8, 63.3, 36.0, 32.9, 12.8 ppm. IR (KBr): $\tilde{\nu}$ = 3109, 3059, 3023, 2909, 1735, 765 cm^{-1}. MS (EI): m/z (%) = 219 (55) $[M]^+$, 204 (63), 159 (100). HRMS (ESI): calcd. for $C_{12}H_{15}N_2O_2$ 219.1134; found 219.1133.

Dimethyl 2-(1,2-Dimethyl-2,3-dihydro-1*H*-indazol-3-yl)-3-(1,3-dioxoisoindolin-2-yl)fumarate (20): A sample of 1,2-dimethyl-1*H*-indazolium-3-carboxylate (**1**; 100 mg, 0.5 mmol) and phthalimide (75 mg, 0.5 mmol) in acetonitrile (0.5 mL) and toluene (3.5 mL) was treated with DMAD (150 mg, 1.05 mmol). The mixture was heated at reflux for 45 min. The solvent mixture was then distilled off, and the residue was purified by chromatography. Yellow solid; m.p. 134–137 °C, yield 57 mg (26%). ^{1}H NMR ($CDCl_3$): δ = 7.92–7.90 (m, 2 H), 7.79–7.77 (m, 2 H), 7.21–7.13 (m, 2 H), 6.92 (dt, J = 7.5, 1.0 Hz, 1 H), 6.61 (d, J = 7.5 Hz, 1 H), 5.95 (s, 1 H), 3.80 (s, 3 H), 3.47 (s, 3 H), 2.80 (s, 3 H), 2.76 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 171.1, 166.1, 165.1, 162.8, 151.0, 149.0, 134.5, 131.8, 128.6, 127.5, 124.0, 123.0, 121.7, 121.4, 110.2, 69.6, 53.1, 51.9, 43.3, 41.9 ppm. IR (KBr): $\tilde{\nu}$ = 3433, 2953, 1727, 1249, 722 cm^{-1}. MS

(ESI): *m*/*z* (%) = 436.2. HRMS (ESI): calcd. for $C_{23}H_{21}N_2O_6Na$ 458.1328; found 458.1338.

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[17] All calculations were carried out by using the projector-augmented wave method[18] as implemented in the CP-PAW program. The wavefunctions were expanded into augmented plane waves up to a cut-off energy of 30 Ry (408 eV) and a density up to 60 Ry (816 eV). The number of projector functions of (s,p,d) type were as follows: H: (1,0,0); C,N: (2,2,0). The frozen-core approximation was employed for the corresponding next-lower noble gas shell, that is, an [He] core for C and N. Periodic boundary conditions were used with an fcc unit cell spanned by the lattice vectors (0.0 9.5 9.5), (9.5 0.0 9.5), (9.5 9.5 0.0) (in Å). To prevent electrostatic interactions between the periodic images, the Blöchl charge decoupling scheme[19] was used. The calculations were performed with the local-density approximation as parametrized by Perdew and Wang[20] with Perdew, Burke and Ernezerhof gradient corrections used for exchange and correlation.[21]

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