Oxidation of *N*-Aminophthalimide in the Presence of Conjugated Azoalkenes: Azimines, Azoaziridines, and [1,2,3]Triazoles

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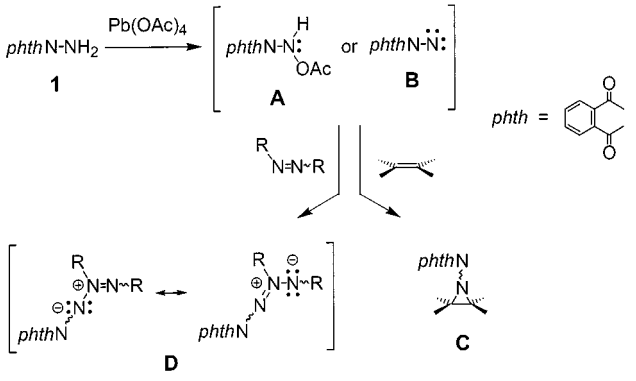
The oxidation of *N*-aminophthalimide (**1**) with lead tetraacetate in the presence of the phenylazoalkenes **2** afforded 2-phenylazo-1-(*N*-phthalimido)aziridines **3** or 2-phenyl[1,2,3]-triazoles **7**, as well as phthalimide (**4**). The reaction of 2-phenylazo-1-propene (**2d**) produced 5-methyl-2-phenyl-[1,2,3]triazole (**7d**) and *N*-[2-(phenylhydrazono)propylidene-amino]phthalimide (**8d**). The cyclic azoalkene 3,3,5-trimethyl-3*H*-pyrazole (**11**) gave a mixture of (*Z*)-3,3,5-trimethyl-1-[*N*-(phthalimido)amino]-3*H*-pyrazol-1-ium-2*N*-ide [(*Z*)-**12**] together with the regioisomers (*E*)- and (*Z*)-3,3,5-trimethyl-1-[*N*-(phthalimido)amino]-3*H*-pyrazol-2-ium-1*N*-ides [(*E*)- and (*Z*)-**13**].

Introduction

The oxidation of *N*-amino heterocycles such as *N*-aminophthalimide (**1**) with lead tetraacetate in the presence of substrates containing an olefinic double bond provides a general method for the synthesis of the *N*-aminoaziridines **C** ("oxidative aminoaziridination" of olefins)[1−5] (Scheme 1). In this amination reaction an aminonitrene **B** is thought to be involved as intermediate.[1,2] More recently, it has been shown that aziridine formation proceeds via the corresponding *N*-acetoxyhydrazine intermediate **A**, at least at temperatures below 0 °C, and does not necessarily involve the participation of an aminonitrene.[2−5] Furthermore, the oxidative addition of *N*-aminophthalimide (**1**) to diazenes (azo compounds) has been reported to provide the phthalimidoazimines **D** as isolable 1,3-dipolar species.[2,6]



Scheme 1

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Regardless of the actual intermediate involved in the course of the oxidation of *N*-aminophthalimide (**1**) and in the subsequent reaction with olefins or diazenes, it seemed interesting to explore the chemoselectivity of this reaction with substrates containing both types of π-bond functionalities. Thus, the conjugated systems of phenylazoalkenes **2**[7−9] and 3,3,5-trimethyl-3*H*-pyrazole (**11**)[10] a cyclic azoalkene, were subjected to the reaction with *N*-aminophthalimide (**1**) and lead tetraacetate.

Results and Discussion

The reaction of conjugated azoalkenes **2** with *N*-aminophthalimide (**1**) and lead tetraacetate gave rise to a mixture of products. Beside variable amounts of recovered starting material **2**, phthalimide (**4**) was isolated in all cases as a typical product of the oxidation of *N*-aminophthalimide (**1**) in the absence of another suitable reagent.[11] Formation of **4** possibly results from the attack of the putative reactive intermediate (*N*-acetoxyaminophthalimide **A** or *N*-phthalimidonitrene **B**) on *N*-aminophthalimide (**1**), followed by the loss of dinitrogen.[11] This process competes with the oxidative addition of *N*-aminophthalimide (**1**) to olefins or azo compounds.[2,6,11] Thus, the yield of phthalimide (**4**) obtained in the course of the oxidation of *N*-aminophthalimide **1** in the presence of a substrate may be considered an approximate measure of the substrate's reluctance to react with *N*-acetoxyaminophthalimide **A** or *N*-phthalimidonitrene **B**. However, this does not apply when phthalimide (**4**) is the complementary product originating from the reaction with the substrate (vide infra).

From the reaction of β-phenylazostyrene (**2a**) with *N*-aminophthalimide (**1**) and lead tetraacetate some starting material **2a** (41%) was recovered, and the aminoaziridine **3a** (38%) together with the side product **4** (31%) were isolated (Scheme 2).

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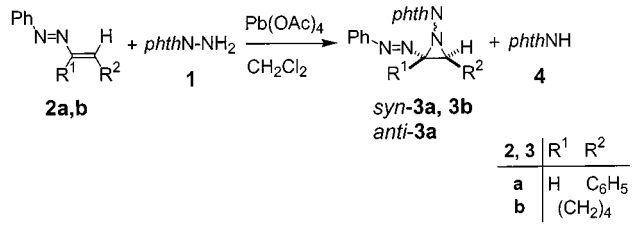
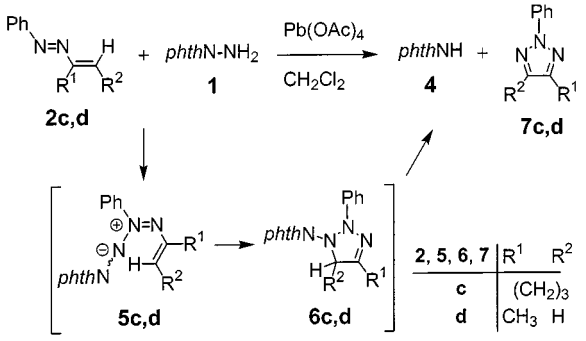


Scheme 2

Product **3a**, which resembles the cycloadduct to the olefinic bond of **2a**, was obtained as a mixture (revealed by ^{1}H NMR integral ratio 10:1) of *syn*- and *anti*-isomers (*syn* and *anti* refer to the relative orientation of the heteroatom substituents, the phenylazo and phthalimido groups). This is attributed to a slow inversion at the ring nitrogen atom, a phenomenon well documented for *N*-aminoaziridine derivatives.[12] Evidence for the stereospecific formation of *N*-phthalimidoaziridines *syn*- and *anti*-**3a** (with retention of substituent configuration at the ring carbon atoms) is provided by the magnitude of the vicinal coupling constants of the aziridine protons of both invertomers, $^3J_{2,3\text{-H}} = 4.4$ and 3.9 Hz for the *anti* and *syn* invertomers, respectively. These values are indicative of *trans* vicinal coupling, whereas $^3J_{cis}$ is expected to be on the order of 6−8 Hz.[12] The minor product isomer **3a** exhibits a well-separated AX quadruplet for the aziridine methine protons ($\Delta\delta_{2,3\text{-H}} = 1.79$ ppm). The pronounced downfield shift of one of the AX proton signals ($\delta = 6.27$) is attributed to deshielding both by the electronegative phenylazo substituent and by the anisotropy of the 1-phthalimido moiety exerted on 3-H (the phenylazo-substituted aziridine methine group) and is taken as evidence for the *anti* orientation of the 3-phenylazo and 1-phthalimido substituents in the invertomer (1*S**,2*S**,3*S**)-**3a** (*anti*-**3a**). Conversely, the close AB quadruplet ($\Delta\delta_{2,3\text{-H}} = 0.14$ ppm) of the aziridine methine protons of the major component **3a** is envisioned as the result of the *syn* orientation of the 1,3-hetero substituents in the invertomer (1*R**,2*S**,3*S**)-**3a** (*syn*-**3a**), the 1-phthalimido group giving rise to the downfield shift of 2-H (the phenyl-substituted aziridine methine group). For steric reasons, *syn*-**3a** (with a *trans* orientation of the sterically demanding 1-phthalimido and 2-phenyl substituents) is considered to be the favored invertomer.

Similarly, the reaction of 1-phenylazocyclohexene (**2b**) with *N*-aminophthalimide (**1**) and lead tetraacetate afforded the corresponding adduct to the olefinic bond. A single isomer was obtained, and the structure (1*R**,1a*S**,5a*R**)-**3b** (*syn*-**3b**) (51%) was tentatively assigned on the basis of the chemical shift of 5a-H (the fusion methine proton) and stereochemical considerations (vide supra; Scheme 2). The adducts **3a**,**b** appear to be the first representatives of *C*-azo-substituted aziridines, novel species both with respect to general aminal-type azo compounds[13−17] and, in particular, to α-azoalkylhydrazines.[1,2]

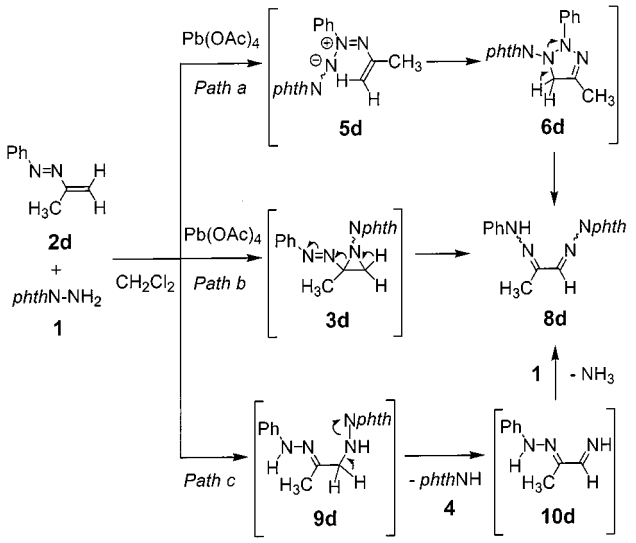
By contrast, and quite remarkably, the reaction of phenylazocyclopentene (**2c**) with *N*-aminophthalimide (**1**) and lead tetraacetate took a different course (Scheme 3). The major product is the [1,2,3]triazole derivative **7c** (70%), which lacks the phthalimido moiety of the reagent. Obviously, the amino nitrogen atom of **1** has been incorporated into the heterocyclic ring in product **7c**. The formation of triazole **7c** can be viewed as a result of the initial formation of the azimine intermediate **5c**; subsequent 1,5-electrocyclization gives rise to the [1,2,3]triazoline intermediate **6c** and is followed by 1,2-elimination of phthalimide (**4**) affording the aromatic [1,2,3]triazole **7c**. Thus, phthalimide (**4**) (48%) is the product originating from this reaction and is not just a side product.



Scheme 3

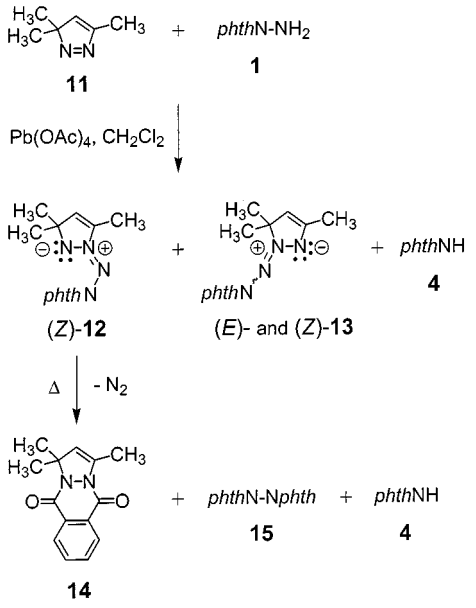
Similarly, the reaction of 2-phenylazopropene (**2d**) yielded the corresponding [1,2,3]triazole derivative **7d**[18] (41%) together with phthalimide (**4**) (46%). Presumably, both products were formed via intermediates **5d** and **6d** (Scheme 3). In addition, the bishydrazone derivative **8d** (39%) was obtained (the hydrazone configurations are undetermined, Scheme 4). It is not clear how **8d** was formed. Following *path a* (Scheme 4), the triazoline intermediate **6d** may be regarded as the common precursor of both products **7d** and **8d**. In competition with the fission of the *exo* N−N bond of **6d** (elimination of phthalimide **4** and concomitant formation of **7d**, Scheme 3), ring-opening by internal 1,2-elimination of the phenylhydrazone moiety by fission of the *endo* N−N bond (1,2-positions of the ring) of **6d** (Scheme 4) may afford the bishydrazone **8d**. Alternatively, the bishydrazone **8d** may arise via *path b* upon ring opening of the conceivably first-formed azoaziridine intermediate **3d**. Another possible reaction, *path c*, is the initial 1,4-addition of *N*-aminophthalimide (**1**) to 2-phenylazopropene (**2d**) giving rise to the α-hydrazinohydrazone **9d**. Subsequent elimination of phthalimide followed by the reaction of the resulting 1-iminopropan-2-one 2-phenylhydrazone (**10d**) with another molecule of **1** (an excess of **1** was provided, see Experimental Section), with displacement of ammonia, furnishes the bishydrazone **8d**. The latter reaction sequence does not involve lead tetraacetate, and the formal oxidation of the terminal carbon atom of **2d** is brought about by the reduction (N−N bond fission) of **9d** with concomitant formation of **10d** and **4**. This reaction (*path c*) is reminiscent of the formation of osazones from α-hydrazinohydrazone precursors.[19,20]

Another type of product was furnished by the reaction of the cyclic azoalkene 3,3,5-trimethyl-3*H*-pyrazole (**11**) with *N*-aminophthalimide (**1**) and lead tetraacetate. Beside



Scheme 4

phthalimide (**4**), the typical product of the reaction without involvement of the substrate **11**,[11] a mixture of three *N*-phthalimidoazimine isomers **12** (40%), (*E*)- and (*Z*)-**13** (17%) was obtained (Scheme 5).



Scheme 5

Because of the partial double bond character of both N−N bonds of the azimine function, the acyclic functional group can adopt four stereoisomeric forms (cf. structure **D**, Scheme 1). Several examples of (*ZZ*)-, (*ZE*)- and (*EZ*)-azimines have been reported in the literature as crystalline and isolable compounds, stable at room temperature in the solid state, but slowly equilibrating in solution.[2,6] The unsymmetrical azo compound **11** can give rise to the formation of two azimine regioisomers. Since one N−N bond of the resultant azimine is embedded in the heterocyclic ring (with an implicit (*E*) configuration of the endocyclic azimine moiety) each of the two conceivable azimine regioisomers is anticipated to form two stereoisomers (with *E*- and *Z*-configurations of the exocyclic azimine N−N bond).

One of the azimine products from the reaction of the pyrazole **11** was isolated as a pure single isomer, and its structure was unambiguously established by X-ray structure analysis as (*Z*)-3,3,5-trimethyl-1-[*N*-(phthalimido)amino]-3*H*-pyrazol-1-ium-2*N*-ide [(*Z*)-**12**] (Figure 1).

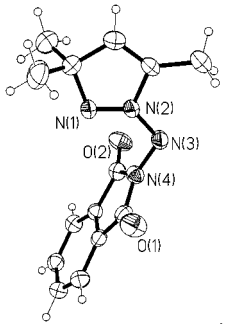


Figure 1. Molecular structure of (*Z*)-**12**

In addition, a mixture of two azimine stereoisomers **13** (ratio 6:1) was obtained. The major component of this mixture was isolated and is tentatively assigned the structure (*E*)-3,3,5-trimethyl-1-[*N*-(phthalimido)amino]-3*H*-pyrazol-2-ium-1*N*-ide [(*E*)-**13**]. Since no crystals suitable for X-ray structure analysis could be obtained, the assignment is tentative: The significant ^{1}H NMR downfield shift of the 3,3-dimethyl signal [$\delta = 1.51$ as compared to $\delta = 1.38$ of the stereoisomer (*Z*)-**13** and $\delta = 1.31$ of the regioisomer (*Z*)-**12**] is taken as evidence of anisotropic deshielding exerted by the phthalimido group (in close vicinity by virtue both of its position and the azimine configuration) on the *gem* dimethyl groups in (*E*)-**13**.

This tentative structure assignment receives support from the relative thermodynamic stability of both geometrical azimine isomers (*E*)- and (*Z*)-**13**; like (*Z*)-**12**, (*Z*)-**13** also appears to be the sterically less congested and thermodynamically more stable isomer. When a solution of (*E*)-**13** was kept at elevated temperature (in $CDCl_3$ at 55 °C for 40−60 h or in 1,2-dichlorobenzene at 100 °C for several hours) an equilibrium mixture of isomers (*E*)- and (*Z*)-**13** (ratio 0.7:1) was formed. The original reaction mixture of the configurational isomers **13** [containing (*E*)-**13** as the major component] also slowly equilibrated at room temperature, and the proportion of (*Z*)-**13** increased indicating that (*Z*)-**13** is the thermodynamically favored stereoisomer. Furthermore, the thermolysis of isomers **13** at 140 °C gave a very complex product mixture, but no trace of azimine (*Z*)-**12** could be detected. These results provide evidence that the azimines **13** are regioisomers of (*Z*)-**12**, and under these conditions the regioisomers **12** and **13** do not undergo interconversion. On the other hand, heating (*Z*)-**12** at 100 °C for 20 h did not change its ^{1}H NMR spectrum. However, heating a solution of (*Z*)-**12** in 1,2-dichlorobenzene or chloroform (in a sealed tube) at 150 °C for 65 h converted the azimine (*Z*)-**12** into the corresponding phthalazinedione derivative **14** (Scheme 5). This type of transformation with concomitant extrusion of dinitrogen is

a typical reaction of phthalimidoazimines;[2,6] phthalimide (**4**) and 2-(2,3-dihydro-1,3-dioxo-1*H*-isoindol-2-yl)-1*H*-isoindole-1,3(2*H*)-dione (**15**)[21] were also formed.

Conclusion

We have shown that the oxidation of *N*-aminophthalimide (**1**) with lead tetraacetate in the presence of the conjugated azoalkenes **2** follows different pathways in response to subtle modifications of the substrate structure. The products obtained from the phenylazoalkenes **2a**,**b** are the 3-phenylazo-1-aminoaziridine derivatives **3a**,**b** resembling formal cycloadducts of *N*-phthalimidonitrene to the olefinic bond of the azoalkenes **2**. Because of slow inversion at the aziridine nitrogen atom, 1-aminoaziridine (**3a**) exists as two equilibrating invertomers *syn*- and *anti*-**3a**. In contrast, the phenylazoalkenes **2c**,**d** furnished phthalimide (**4**) and the 2-phenyl-2*H*-[1,2,3]triazole derivatives **7c**,**d**, presumably via the azimine intermediates **5c**,**d**. The reaction of azoalkene **2d** also afforded the bishydrazone **8d**. Several alternative reaction paths have been considered to explain the formation of this product; the feasibility of these reactions is currently under investigation. The cyclic azoalkene **11** gave *N*-phthalimidoazimines as a mixture of regio- and stereoisomers (*Z*)-**12**, (*E*)- and (*Z*)-**13**. The structure of (*Z*)-**12** has been confirmed by X-ray analysis, but the configurational assignment of the equilibrating isomers **13** is tentative. Ongoing research focuses on the reasons for these dramatic changes in the reactivity of azoalkenes **2** and **11** with *N*-aminophthalimide (**1**) and lead tetraacetate.

Experimental Section

General Remarks: The phenylazoalkenes **2** were prepared according to literature procedures[7−10] and were stored in a refrigerator; 2-phenylazopropene (**2d**)[9] was prepared as a solution in dichloromethane immediately before use.

Thin-layer chromatography (TLC) was performed on precoated silica gel sheets (Macherey−Nagel, Polygram® SIL G/UV$_{254}$) and was employed to monitor reactions and separations, and to check the purity of the products. Product separations were carried out by column chromatography on silica gel 60 (Merck, 0.04−0.063 mm, 230−400 mesh) with freshly distilled solvents. PE refers to petroleum ether (boiling rage 40−60 °C).

Melting points (m.p.) were determined with a Reichert-Kofler hot stage microscope. − IR spectra were recorded on a Matson Galaxy FTIR 3020 spectrometer. − NMR spectra are referenced to internal TMS or to solvent signals, and were obtained on a Varian Gemini 200 (^{1}H at 200 MHz, ^{13}C at 50.3 MHz) or on a Bruker AM-300 spectrometer (^{13}C at 75.4 MHz). − Mass spectra were measured with a Finnigan MAT 95 spectrometer. − Elemental analyses were determined with an HP 185B C,H,N analyser.

2-{(1*R,2*S**,3*S**)-2-Phenyl-3-[(*E*)-phenyldiazenyl]aziridin-1-yl}-1*H*-isoindole-1,3(2*H*)-dione (*syn*-3a) and 2-{(1*S**,2*S**,3*S**)-2-Phenyl-3-[(*E*)-phenyldiazenyl]aziridin-1-yl}-1*H*-isoindole-1,3(2*H*)-dione (*anti*-3a). − Typical Procedure:** A solution of lead tetraacetate (580 mg of 85% reagent, 1.1 mmol) in dichloromethane (15 mL) was added dropwise during 40 min. to a vigorously stirred suspension of K_2CO_3 (1 g, 7 mmol) in a solution of **2a**[8] (208 mg, 1 mmol) and *N*-aminophthalimide (**1**; 162 mg, 1 mmol) in dichloromethane (10 mL) at −10 °C. The mixture was stirred for a further 40 min. and kept at room temp. for 10 min. before it was filtered through a sintered glass filter covered with silica gel and K_2CO_3 (5 mm layers each). The sticky residue of inorganic salts was washed with dichloromethane (100−120 mL) until the filtrate became colorless. The filtrate was evaporated in vacuo at ambient temperature. The residue (314 mg) was dissolved in a minimum volume of chloroform and chromatographed on silica gel (30 g, PE/diethyl ether, 5:1 followed by diethyl ether) to recover the starting material **2a** (86 mg, 41%); R_f = 0.74 (diethyl ether). Subsequent fractions contained *syn*- and *anti*-**3a** (10:1; 139 mg, 38%); R_f = 0.64 (diethyl ether) and **4** (45 mg, 31%[22]); R_f = 0.58 (diethyl ether), m.p. 230−234 °C (EtOH) (ref.[23] m.p. 232−235 °C).

Syn- and *anti*-**3a** (10:1): Yellow crystals, m.p. 120−124 °C. − IR (KBr): $\tilde{\nu}$ = 3059 cm^{-1}, 3028, 2922, 1771, 1721 (vs, C=O), 1713 (vs, C=O), 1377 (s), 1154 (s), 1138 (s), 706 (vs), 689. − ^{1}H NMR ($CDCl_3$; two sets of signals attributed to *syn*- and *anti*-**3a**, ratio 10:1):[24] δ = 4.48 (d, *J* = 4.4 Hz, 1 H, 2-H, *anti*-**3a**), 4.83 (d, *J* = 3.9 Hz, 1 H, 2-H$^{\#}$ *syn*-**3a**), 4.97 (d, *J* = 3.9 Hz, 1 H, 3-H$^{\#}$ *syn*-**3a**), 6.27 (d, *J* = 4.4 Hz, 1 H, 3-H *anti*-**3a**), 7.25−8.05 (m, 14 H, 2 C_6H_5 and C_6H_4). − ^{13}C NMR of *syn*-**3a** (50.3 MHz, $CDCl_3$):[24] δ = 51.06 (2-C), 74.29 (3-C), 134.06, 130.45, 122.50 (5,6-, 3a,7a-, 4,7$^{\#}$-C C_6H_4), 134.22, 128.68, 128.54, 127.40 (1-, 3,5-, 4-, 2,6-C 2-C_6H_5), 151.91, 131.33, 129.01, 123.15 (1-, 4-, 3,5-, 2,6$^{\#}$-C 3-$N_2C_6H_5$), 164.67 (1,3-C=O). − MS (70 eV, EI): *m*/*z* (%) = 368 (2) [M$^{+\cdot}$], 222 (20) [M − C_6H_4(CONCO)], 221 (100) [M − C_6H_4(CONHCO)], 220 (39), 194 (15), 147 (28) [C_6H_4(CONHCO)], 118 (16), 105 (17), 104 (28) [C_6H_4CO], 103 (24), 92 (7), 91 (88) [C_6H_5N], 77 (17) [C_6H_5], 76 (25. − $C_{22}H_{16}N_4O_2$ (368.40): calcd. C 71.73, H 4.38, N 15.21; found C 71.38, H 4.50, N 15.18.

2-{(1*R,1a*S**,5a*R**)-1a-[(*E*)-Phenyldiazenyl](perhydro-1-benzaziren-1-yl)}-1*H*-isoindole-1,3(2*H*)-dione (*syn*-3b):** Following the Typical Procedure the reaction of **2b**[8] (373 mg, 2 mmol) gave, after evaporation of the solvent, a partly oily and crystalline residue (663 mg), which was dissolved in diethyl ether/chloroform (1:1, 10 mL) and subjected to chromatography on silica gel (50 g). Elution with PE/diethyl ether (9:1) followed by diethyl ether furnished the pure starting material **2b** (39 mg), R_f = 0.57 (PE/diethyl ether 9:1), a fraction containing **2b**, **3b** and **4** (540 mg), and phthalimide (**4**) (63 mg), R_f < 0.03 (PE/diethyl ether 9:1). This latter fraction upon repeated chromatography on silica gel (48 g, PE/diethyl ether, 3:1 → 2:1) afforded more starting material **2b** (102 mg; total recovery 141 mg, 38%), **3b** (347 mg, 51%), R_f = 0.07 (PE/diethyl ether, 9:1), and **4** (9 mg; total yield 72 mg, 24%[22]).

***Syn*-3b:** Isolation of **3b** first gave a yellow glassy liquid, which formed a voluminous foam upon evaporation in vacuo. Stirring with PE (2−3 mL) turned the foam into lemon-yellow crystals, which were recrystallized from methanol, m.p. 89−95 °C; after melting, new crystals formed, m.p. 180−190 °C. When a drop of a solution of **3b** was placed on a TLC plate (silica gel) the spot after drying exhibited a bright blue fluorescence under the UV lamp (254 nm); R_f = 0.33 (PE/diethyl ether, 9:1). − ^{1}H NMR ($CDCl_3$): δ = 1.3−1.8 (m, 4 H), 2.02−2.29 (m, 2 H), 2.47 (ddd, *J* = 13, 7, 6 Hz, 1 H), 2.95 (ddd, *J* = 14.6, 7, 6 Hz, 1 H), 3.89 (dd, *J* = 5.3, 1.4 Hz, 1 H, 5a-H), 7.27−7.36 (m, 3 H, 3,4,5-H C_6H_5), 7.40−7.50 (m, 2 H, 2,6-H C_6H_5), 7.60−7.79 (m, 4 H, C_6H_4). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.04, 20.34, 23.45, 23.50 (2,3,4,5-C), 50.76 (6-C), 72.94 (1-C), 122.10, 128.82, 130.52, 151.82 (2,6-, 3,5-, 4-, 1-C 1-$N_2C_6H_5$), 122.75, 130.64, 133.73 (4,7-, 3a,7a-, 5,6-C

C_6H_4), 164.98 (1,3-C=O). − $C_{20}H_{18}N_4O_2$ (346.39): calcd. C 69.35, H 5.24, N 16.17; found C 69.08, H 5.24, N16.01.

2,4,5,6-Tetrahydro-2-phenylcyclopenta[*d*][1,2,3]triazole (7c): Following the same protocol, the reaction of **2c**[8] (487 mg, 2.83 mmol) gave a solid product mixture (775 mg), which was stirred with chloroform (10 mL). The resultant precipitate of **4** (198 mg, 48%[22]) was filtered off, and the filtrate was separated by chromatography on silica gel (50 g, chloroform) affording recovered starting material **2c** (57 mg, 12%), R_f = 0.55 ($CHCl_3$) and **7c** (368 mg, 70%) as colorless crystals; m.p. 64−66 °C; R_f = 0.38 ($CHCl_3$). − ^{1}H NMR ($CDCl_3$): δ = 2.48−2.70 (m, 2 H, 5-H), 2.86 (t, *J* = 7 Hz, 4 H, 4,6-H), 7.26 (tt, *J* = 7.4, 1.2 Hz, 1 H, 4-H C_6H_5), 7.43 (tm, *J* = 7.6 Hz, 2 H, 3,5-H C_6H_5), 7.98 (dm, *J* = 7.4 Hz, 2 H, 2,6-H C_6H_5). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 22.20 (4,6-C), 28.74 (5-C), 118.16, 126.35, 129.14, 140.74 (2,6-, 4-, 3,5-, 1-C C_6H_5), 156.77 (3a,6a-C). − MS (FAB, NOBA): *m*/*z* (%) = 187 (15), 186 (100) [M + 1], 185 (42) [$M^{\cdot+}$]. − $C_{11}H_{11}N_3$ (185.23): calcd. C 71.33, H 5.99, N 22.69; found C 71.37, H 6.08, N 23.18.

4-Methyl-2-phenyl-2*H*-[1,2,3]triazole[18] (7d) and 2-[2-(Phenylhydrazono)propylideneamino]-1*H*-isoindole-1,3(2*H*)-dione (8d): A 0.1 M solution of **2d**[9] in dichloromethane was prepared from 1-(2-phenylhydrazonopropyl)pyridinium iodide[9] (1.06 g, 3 mmol) and was employed for the reaction following the typical procedure. The partly oily and solid reaction mixture (795 mg) was dissolved in chloroform (50 mL) and subjected to chromatography on silica gel (100 g, diethyl ether). Repeated chromatographic separations afforded **4** (202 mg, 46%[22]), **7d** (161 mg, 41%) and **8d** (362 mg, 39%).

7d:[18] Viscous, colorless liquid rapidly turning brown on standing; R_f = 0.68 (diethyl ether). − ^{1}H NMR ($CDCl_3$): δ = 2.40 (s, 3 H, CH_3), 7.30 (tt, *J* = 7.4, 1.2 Hz, 1 H, 4-H C_6H_5), 7.45 (tm, *J* = 7.6 Hz, 2 H, 3,5-H, C_6H_5), 7.55 (s, 1 H, 5-H), 8.03 (dm, *J* = 7.6 Hz, 2 H, 2,6-H C_6H_5). − ^{13}C NMR (75.4 MHz; $CDCl_3$): δ = 10.71 (CH_3), 118.49, 126.94, 129.14, 139.89 (2,6-, 4-, 3,5-, 1-C C_6H_5), 134.91 (5-C), 145.34 (4-C). − MS (70 eV, CI, NH_3): *m*/*z* (%) = 160 (100) [M + 1].

8d: Red needles, m.p. 250−253 °C (methanol); R_f = 0.45 (diethyl ether); only slightly soluble in common organic solvents. − ^{1}H NMR ($CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 6.97 (tt, *J* = 7.1, 1.2 Hz, 1 H, 4-H C_6H_5), 7.17−7.25 (m, 2 H, 2,6-H C_6H_5), 7.26−7.39 (m, 2 H, 3,5-H C_6H_5), 7.72−7.82 (m, 2 H, 5,6-H C_6H_4), 7.87−7.97 (m, 3 H, NH and 4,7-H C_6H_4), 9.05 (s, 1 H, N=CH). − ^{1}H NMR ([D_6]DMSO): δ = 2.19 (s, 3 H, CH_3), 6.91 (m, 1 H, 4-H C_6H_5), 7.25−7.36 (m, 4 H, 2,3,5,6-H C_6H_5), 7.85−7.96 (m, 4 H, C_6H_4), 8.85 (s, 1 H, N=CH), 10.08 (br.s, 1 H, NH). − ^{13}C NMR (50.3 MHz, [D_6]DMSO): δ = 9.79 (CH_3), 113.62, 120.86, 129.12, 139.60 (2,6-, 4-, 3,5-, 1-C C_6H_5), 123.36, 130.16, 134.85 (4,7-, 3a,7a-, 5,6-C C_6H_4), 144.27 (2-C), 160.41 (1-C), 164.56 (1,3-C=O). − MS (70 eV, CI, NH_3): *m*/*z* (%) = 308 (19) [M + 2], 307 (100) [M + 1], 306 (13) [$M^{\cdot+}$]. −$C_{17}H_{14}N_4O_2$ (306.33): calcd. C 66.66, H 4.61, N 18.29; found C 66.02, H 4.73, N 18.24.

(*Z*)-1-{[1,3(2*H*)-Dioxo-1*H*-isoindol-2-yl]amino}-3,3,5-trimethyl-3*H*-pyrazol-1-ium-2*N*-ide [(*Z*)-12], (*E*)- and (*Z*)-2-{[1,3(2*H*)-Dioxo-1*H*-isoindol-2-yl]amino}-3,3,5-trimethyl-3*H*-pyrazol-2-ium-1*N*-ide [(*E*)- and (*Z*)-13]: Following the typical procedure, compound **11**[10] (550 mg, 5 mmol) afforded a solid product mixture (1.124 g). Chromatography on silica gel (120 g, dichloromethane followed by dichloromethane/diethyl ether, 9:1 → 1:2) gave a mixture (6:1) of (*E*)- and (*Z*)-**13** (230 mg, 17%), (*Z*)-**12** (546 mg, 40%), and **4** (213 mg, 29%[22]).

(*Z*)-12: Yellowish crystals, m.p. 169−171 °C (ethanol); R_f = 0.18 (benzene/ethyl acetate, 9:1). − ^{1}H NMR ($CDCl_3$): δ = 1.31 (s, 6 H, 3,3-$(CH_3)_2$], 2.37 (d, *J* = 1.4 Hz, 3 H, 5-CH_3), 6.60 (br s, 1 H, 4-H), 7.68−7.75 (m, 2 H, 5,6-H C_6H_4), 7.80−7.87 (m, 2 H, 4,7-H C_6H_4). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 11.10 (5-CH_3), 23.43 (3,3-$(CH_3)_2$], 75.24 (3-C), 123.20, 131.24, 133.75 (4,7-, 3a,7a-, 5,6-C C_6H_4), 141.23 (4-C), 141.29 (5-C), 164.55 (1,3-C=O). − MS (70 eV, CI, NH_3): *m*/z (%) = 272 (24) [M + 2], 271 (100) [M + 1], 270 (8) [$M^{\cdot+}$], 228 (9), 227 (69), 104 (6), 96 (73). − $C_{14}H_{14}N_4O_2$ (270.29): calcd. C 62.21, H 5.22, N 20.73; found C 62.77, H 5.29, N 21.14.

X-ray Crystallographic Structure Analysis of (*Z*)-12: Crystal size 0.65 × 0.4 × 0.3 mm, monoclinic, space group *C*2/*c* (no. 15), *a* = 2095.6(7), *b* = 802.4(2), *c* = 1674.6(4) pm, β = 93.29(2)°, *V* = 2.8112(14) nm^3, *Z* = 8, *F*(000) = 1136, $\rho_{calcd.}$ = 1.277 g·m^{-3}, *T* = 223(2) K; Siemens P4 diffractometer, Mo-K_α (λ = 71.073 pm), μ = 0.081 mm^{-1}. Data were measured with ω scans and corrected for Lorentz and polarization effects; of 2219 reflections collected, 1724 were independent and 1388 with $I > 2\sigma(I)$; structure solution by direct methods (SHELXS-86) and refinement against F^2 (SHELXS-93)[25] of 198 parameters with GOF = 1.046. The hydrogen atoms at C(2) and C(301) were refined isotropically, the others were placed in calculated positions. *R*1 = 0.0419 (against |*F*|), *wR*2 = 0.1062 (against |F^2|).[26]

(*E*)-13: Recrystallization of the mixture of stereoisomers from ethanol afforded the major component (*E*)-**13** as yellowish crystals; m.p. 83−85 °C (ethanol); R_f = 0.52 (benzene/ethyl acetate, 9:1). − ^{1}H NMR ($CDCl_3$): δ = 1.51 [s, 6 H, 3,3-$(CH_3)_2$], 2.21 (d, *J* = 1.3 Hz, 3 H, 5-CH_3), 5.56 (q, *J* = 1.3 Hz, 1 H, 4-H), 7.69−7.79 (m, 2 H, 5,6-H C_6H_4), 7.82−7.92 (m, 2 H, 4,7-H C_6H_4). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 16.89 (5-CH_3), 27.93 [3,3-$(CH_3)_2$], 60.11 (3-C), 123.37, 131.70, 134.08 (4,7-, 3a,7a-, 5,6-C C_6H_4), 129.91 (5-C), 134.60 (4-C), 166.78 (1,3-C=O). − MS (70 eV, CI, NH_3): *m*/*z* (%) = 272 (24) [M + 2], 271 (100) [M + 1], 227 (69), 104 (6), 96 (73). − $C_{14}H_{14}N_4O_2$ (270.29): calcd. C 62.21, H 5.22, N 20.73; found C 62.56, H 5.32, N 21.14.

(*Z*)-13 was characterized in a mixture with (*E*)-**13**. ^{1}H NMR ($CDCl_3$): δ = 1.38 [s, 6 H, 3,3-$(CH_3)_2$], 2.00 (d, *J* = 1.3 Hz, 3 H, 5-CH_3), 5.69 (q, *J* = 1.3 Hz, 1 H, 4-H), 7.69−7.79 (m, 2 H, 5,6-H C_6H_4), 7.82−7.92 (m, 2 H, 4,7-H C_6H_4). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 22.89 (5-CH_3), 26.75 [3,3-$(CH_3)_2$], 60.46 (3-C), 123.48, 132.18, 134.02 (4,7-, 3a,7a-, 5,6-C C_6H_4), 126.59 (5-C), 133.74 (4-C), 167.00 (1,3-C=O). − MS (70 eV, CI, NH_3): *m*/*z* (%) = 288 (4), [M + 18], 229 (45), 228 (100), 227 (4), 210 (11), 186 (7).

1,1,3-Trimethyl-5,10-dihydro-1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione : A solution of (*Z*)-**12** (54 mg, 0.2 mmol) in $CDCl_3$ (0.4 mL) in a sealed glass tube was placed in a steel autoclave partially filled with chloroform and was heated at 140 °C for 40 h. The ^{1}H NMR spectrum of the solution showed the presence of the starting material (*Z*)-**12** (25%); continued heating of the sample at 150 °C for 40 h led to complete conversion of (*Z*)-**12**. The ^{1}H NMR spectrum revealed a mixture of three products: **14**, **4**, and 2-(2,3-dihydro-1,3-dioxo-1*H*-isoindol-2-yl)-1*H*-isoindole-1,3(2*H*)-dione (**15**) in a ratio of 5:3:2; the latter product was identified by comparison with an authentic sample.[21] After the solvent was removed in vacuo, the residue (49 mg) was chromatographed (silica gel, PE/diethyl ether, 1:1) to yield **14** (25 mg, 85% purity). Repeated recrystallisation from ethanol gave colorless crystals of **14**; m.p. 190−194 °C. ^{1}H NMR ($CDCl_3$): δ = 1.80 [s, 6 H, 1,1-$(CH_3)_2$], 2.49 (d, *J* = 1.5 Hz, 3 H, 3-CH_3), 5.15 (q, *J* = 1.5 Hz, 1 H, 2-H), 7.73−7.83 (m, 2 H, 7,8-H C_6H_4), 8.24−8.36 (m, 2 H, 6,9-H C_6H_4). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.77 (3-CH_3), 24.68 [1,1-$(CH_3)_2$], 69.34 (1-C), 116.88 (2-C), 126.94, 127.30 (6-, 9-C), 129.57, 129.98 (5a-,

9a-C), 132.90, 133.21 (7-, 8-C), 134.45 (3-C), 154.62, 155.25 (5-, 10-C=O). − MS (70 eV, EI): *m/z* (%) = 242 (15) [$M^{\cdot+}$], 228 (67), 227 (100), 104 (14), 77 (11), 76 (19), 28 (12). − $C_{14}H_{14}N_2O_2$ (242.28): calcd. C 69.41, H 5.82, N 11.56; found C 69.70, H 5.65, N 11.68.

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