Regioselective Reactions of Ambident Dianions, 4[◇]

Reaction of Ambident Dianions with Oxalic Acid Dielectrophiles − Effect of the Heteroatoms of the Dinucleophile on the Regiochemistry of Cyclization

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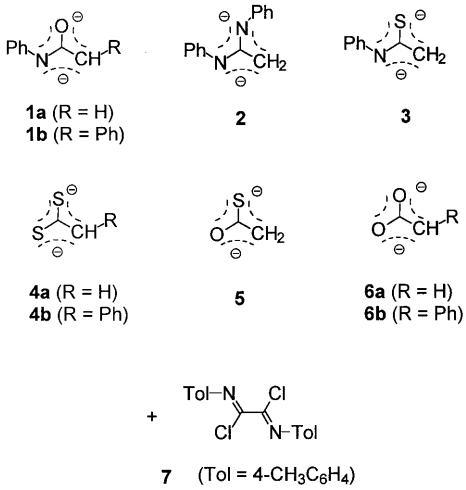
Y-Shaped ambident dianions **1-6** were reacted with dielectrophilic oxalic acid-bis(imidoyl)dichlorides **7** providing a convenient access to novel N-heterocycles **8–13** containing a heteroanalogous oxalic acid unit. The cyclization reactions generally proceeded with good regioselectivity which is controlled by the heteroatoms of the dianion reagents.

Polymetalation has been developed as a valuable tool for regioselective carbon−carbon bond formation in organic synthesis.[1] Previous attention has been mainly focused on reactions of dianions with monofunctional electrophiles after which the resultant monoanion is simply quenched with water following the initial reaction. Much less interest has been directed towards cyclization reactions with dielectrophiles involving *two* nucleophilic atoms of the dianion.[2] Recently, we have reported the first examples of cyclization reactions of dianions with dielectrophiles containing the oxalic acid subunit.[3][4][5] The latter is contained in a variety of compounds of pharmaceutical interest,[6a] NIR dyes[6b], and novel ligands.[6c] To the best of our knowledge, no systematic study on the parameters controlling the regiochemistry of cyclization reactions involving ambident dianions has been reported so far. Based on our previous work we have, thus, studied the regioselectivity of the cyclization reactions of different Y-shaped dianions with oxalic acid dielectrophiles and herein we wish to report the results of our efforts.

For 1,3-dianions containing a terminal carbon atom and two heteroatoms (O, S, N) six different hetero-analogues of bislithiated trimethylenemethane are possible.[7a][7b] Reaction with symmetric dielectrophiles, in principle, can afford three regioisomeric 1:1-cyclization products (due to the ambident character of the dianion), macrocycles, or polymers. All attempts to induce cyclization by treatment of a THF solution of amide dianions with oxalic acid dichloride or diesters resulted in formation of polymeric material only.[3] However, regioselective cyclization[8] was obtained using oxalbis(*p*-tolylimidoyl) dichloride $Cl_2C_2(NTol)_2$ **7**

Scheme 1. Hetero-analogues of Y-shaped dianions (the Li^+ counterions were omitted for clarity)



(BTIOC), a C_2-building block of moderate reactivity.[9] Treatment of a THF solution of BTIOC with the dianions of acetanilide[10a] **1a** and of (*N*-phenyl)phenylacetic acid amide **1b** (generated from the corresponding amides by means of two equivalents of *n*BuLi) afforded iminotetramic acid amides **8a**, **b** (40 and 42%, respectively).[3][10b] The cyclization involved the carbon and the nitrogen atom of the dianion. Similarly, employment of the dianion of *N,N′*-diphenylacetamidine **2** resulted in a *C,N* cyclization mode to give bis-amidine **9** (38%).

Reaction of the dianion of thioacetanilide **3**[11] with BTIOC gave an inseparable mixture of isomeric 4-amino-5-

[◇] Part 3: Ref.[5].

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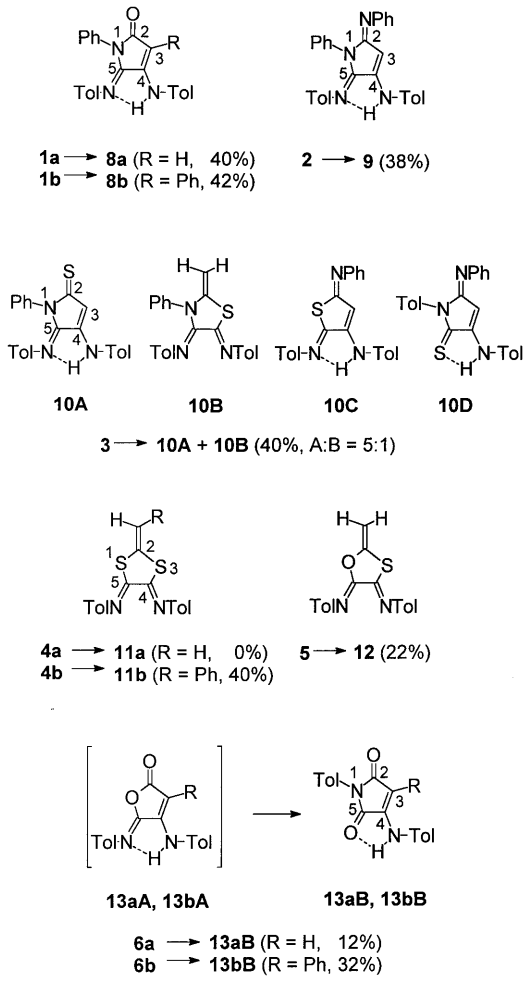
Scheme 2. Regioselectivity in the reactions of dianions **1-6** with dielectrophile **7**



imino-2*H*-pyrrole-2-thione **10A** and of azathiolane **10B** (40%, A/B = 5:1) arising from *C*,*N*- and *S*,*N*-cyclization, respectively. Two heteroatoms are involved in the cyclization of BTIOC with the dianion of dithiophenylacetic acid **4b**, and dithiolane **11b** was obtained in 40% yield. Dimers of **11b** are of interest as unsymmetrical π donors.[12] However, no cyclization was induced starting with the dianion of dithioacetic acid **4a**. Reaction of the dianion of thioacetic acid **5** resulted in a complex reaction mixture from which **12** (formed by *S*,*O* cyclization) was separated by chromatography (22%). Derivatives of (2-methylen-1,3-oxathiolane-4,5-diylidene)bisamine **12** have, to our knowledge, not been previously prepared. Further varying the heteroatoms of the Y-shaped dianions the cyclization reactions of carboxylic acid dianions were studied next. Reaction of the dianions of acetic acid **6a** and of phenylacetic acid **6b**[13] with BTIOC afforded amino-substituted maleimides **13aB** and **13bB** via *C*,*O*-cyclization of the dianions with BTIOC and subsequent *Dimroth* rearrangement of the *iso*maleimides **A** initially formed.[14]

Several isomeric and tautomeric forms are, in principle, possible for all heterocycles described herein due to Dimroth rearrangements and imin−enamine tautomerism, respectively. Compounds **8a,b** are vinylogous ureas and, thus, exhibit amide absorptions in their IR spectra.[3] As expected, two ν_{CO} bands (IR) and two carbonyl resonances (^{13}C NMR) are observed for maleimides **13aB** and **13bB**. Signal splitting of a variety of signals (^{13}C NMR) is detected for bis-amidine **9** which indicates that (*E*/*Z*) isomerism of the C-2 phenylimino group is slow on the NMR time-scale. This effect is not observed for arylimino groups located within the oxalic acid subunit and the ^{13}C-NMR spectra of **8**, **10A**, **13aB**, and **13bB**, thus, display only one set of signals. Due to the relatively symmetric structure of **11b** similar values (^{13}C NMR) are observed each for the two imine and for the two CH_3 carbon atoms. The low field shift of carbon atom C-2 is indicative for the structure of oxathiolane **12** and a *Dimroth* rearrangement similar to **13aA** → **13aB** and **13bA** → **13bB** can be excluded. Whereas the structure of **10B** can be easily recognized by the presence of the CH_2 group the assignment of structure **10A** is more difficult: A *C*,*S*-cyclization mode (isomer **C**) and a subsequent Dimroth rearrangement (**C** → **D**) have to be envisaged. The presence of a quaternary aryl carbon atom attached to N-1 (δ = 136.51) is in agreement with structures **A** and **D**. The resonance of C-3 is shifted to lower field (with respect to **8a** and **9**) which suggests that a neighboring thiocarbonyl group is present (isomer **A**). No (*E*/*Z*) isomerism of an arylimino group is detected which also speaks in favor of structure **A**. Heterocycles **8**, **9**, **10A**, **13aB**, and **13bB** exclusively adopt tautomers containing intramolecular hydrogen bonds which are located within the oxalic acid subunit (as indicated by the respective low field ^{1}H-NMR resonances).

Mostly the carbon center of the dianions (which is deprotonated last and, thus, represents the most nucleophilic center) is involved in cyclization. For dianions containing a sulfur atom, the latter competes with the carbon atom and regiochemistry appears to depend on the second heteroatom of the dianion.[15] The cyclization proceeds more readily via a nitrogen than via an oxygen atom, presumably due to the lower nucleophilicity of the latter. If cyclization does proceed via the oxygen atom (which is true for carboxylic acid dianions), the initially formed condensation products are unstable and undergo a Dimroth rearrangement. AM1-Calculations suggest that the transformation **13bA** → **13bB** proceeds under thermodynamic control.[16] Similar to the reactions of **1a** and **6a**, regioselective *C*,*N*- and *C*,*O*-cyclizations are observed for phenyl-substituted dianions **1b** and **6b**, respectively. These results suggest that the regioselectivity is controlled by electronic rather than by steric effects.[17]

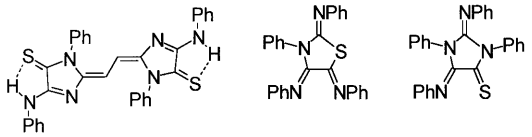
We have recently reported that reaction of $C_2Cl_2(NPh)_2$ with thioamide $CH_3(CS)NH_2$ in the presence of triethylamine results in *S*,*N*-cyclization, subsequent Dimroth rearrangement and oxidative dimerization to give **14**.[18a] When PhNH(CS)NHPh was refluxed with $C_2Cl_2(NPh)_2$ in the presence of DABCO, a 1:1 mixture of heterocycles **15A** and **15B** has been obtained.[18b] The latter was formed from **15A** via a Dimroth rearrangement. Thus, the regiochemistry of cyclization with oxalic acid bis(imidoyl)dichlorides is strikingly different for dianions and for electroneutral re-

Table 1. Diagnostic chemical shifts (^{13}C NMR, [ppm]) of heterocycles prepared from Y-shaped dianions

	8a[a]	**8b**[a]	**9**[b]	**10A**[b]	**11b**[c]	**12**[a]	**13bB**[c]
C-2	172.33	171.70	159.95	160.94	160.01	179.03	171.43
C-3	88.39	101.80	85.28	105.53	–	–	102.20
C-4	138.29	136.47	138.78	138.74	158.78	145.39	138.13
C-5	148.53	146.75	151.42	152.83	158.78	153.41	167.85
C-Tol	144.38	142.51	145.28	148.24	149.01	140.36	137.14[d]
(to N)	146.83	144.76	147.86	150.98	149.49	140.86	
C-Ph	135.32	135.55	136.75	136.51	–	–	–
(to N)			145.20				

[a] $CDCl_3$ – [b] [D_8]THF – [c] CD_2Cl_2. – [d] Only a single signal was observed.

Scheme 3



14 **15A** **15B**

agents. However, sulfur generally tends to be involved in cyclization. The occurrence of a Dimroth rearrangement for intermediates containing an endocyclic sulfur atom adjacent to an imino group seems to depend on the reaction conditions and on the specific substrate employed since such a rearrangement was observed for formation of **15B**, but not for **10B**, **11**, and **12**.

In summary, we have studied the effect of the heteroatoms of Y-shaped 1,3-dianions on the regioselectivity of cyclization with oxalbis(imidoyl) dichlorides. Our dianion methodology provides a convenient route to a variety of heterocycles containing a heteroanalogous oxalic acid unit. Present work is directed towards extending the concept presented to ambident dianions other than 1,3-dianions.[19]

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Experimental Section

General. All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. Petroleum ether (b.p. 40−70°C) and ether were distilled prior to use. − BTIOC was prepared by literature procedures.[9] − IR: Perkin Elmer 2000 FT-IR. − NMR: Bruker AC 200 F. 200 MHz and 50 MHz (for ^1H and ^{13}C, respectively), if not quoted otherwise. For ^1H NMR, $CDCl_3$ and CD_2Cl_2 as solvent, TMS was used as internal standard, for [D_8]THF as solvent, δ = 1.73, 3.58; for ^{13}C NMR, $CDCl_3$ and CD_2Cl_2 as solvents, TMS was used as internal standard, for [D_8]THF, δ = 25.5, 67.7. The multiplicity of the C atoms was determined by the DEPT 135 technique. − MS: Finnigan Mat SSQ 710 spectrometer (70 eV; CI, H_2O: chemical ionization with water). − Preparative scale chromatography: J. T. Baker silica gel (60-200 mesh). − Elemental analyses: Microanalytical laboratory of the University of Hannover.

General Procedure for the Preparation of Heterocycles **8−10** *and* **12**: To a THF solution (20 ml) of the substrate (6 mmol) was added *n*BuLi (8.25 ml, 2.2 equiv., 1.6 M solution in hexane) at 0°C. The color of the solution became yellow. After stirring for 45 min at 0°C, the solution containing the dilithiated amide was transferred within 10 min to a THF solution (80 ml) of BTIOC (1.8 g, 6 mmol) using a metal cannula at 0°C. The color of the solution changed to deep red. The solution was stirred at 0°C for 15 min and at room temperature for 2 h. THF was removed using a rotary evaporator and the crude product obtained was purified by chromatography (petroleum ether/ether = 3:1) without prior filtration of the LiCl formed in the reaction. For preparation of **12**, 2.0 ml of abs. TMEDA was added to the solution before *n*BuLi was added.

1,5-Dihydro-4-[(4-methylphenyl)amino]-5-[(4-methylphenyl)-imino]-1-phenyl-2H-pyrrole-2-phenylimine **9**: Starting with 1.26 g of *N,N′*-diphenylacetamidine, 1.0 g (38%) of **9** was isolated, yellow solid, m.p. 124−126°C. Peak splitting is observed for a variety of carbon atoms indicating *E*/*Z* isomerization of the C-2 phenylimino group. The difference in chemical shifts of these signals is very small (ca. 0.5 Hz). − ^1H NMR ([D_8]THF): δ = 2.10, 2.27 (s, 6 H, CH_3), 5.79 (s, 1 H, H-3), 6.40−7.25 (m, 18 H, Ar), 8.22 (br, 1 H, NH). − ^{13}C NMR ([D_8]THF): δ = 20.72, 20.73 (CH_3), 85.28 (CH, C-3), 119.85, 121.65, 122.47, 123.34, 126.67, 128.12, 128.90, 129.21, 129.51, 130.46 (CH, Ar), 132.36, 133.08 (C, Tol-C to CH_3), 136.75, 138.78 (C, C-4, Ph-C to N-1), 145.20, 145.28, 147.86 (C, Ar-C to N), 151.42 (C, C-5), 159.95 (C, C-2). − MS (CI, H_2O); *m*/*z* (%): 443 (100) [M^+ + 1]. − $C_{30}H_{26}N_4$ (442.5): calcd. C 81.42, H 5.92, N 12.65; found C 80.94, H 5.65, N 12.80.

1,5-Dihydro-4-[(4-methylphenyl)amino]-5-[(4-methylphenyl)-imino]-1-phenyl-2H-pyrrole-2-thione **10A** *and N,N′-(2-Methylen-1-phenyl-1,3-azathiolane-4,5-diylidene)bis[4-methylbenzenamine]* **10B**: Starting with 906 mg of thioacetanilide, 919 mg (40%) of an inseparable mixture of **10A** and **10B** was isolated (**A**/**B** = 5:1, respectively). − **10A**: IR (KBr): ν = 3335 (w) cm^{-1}, 3023 (w), 2920 (w), 1600 (s), 1578 (s), 1525 (s), 1368 (w), 1195 (m), 1150 (m). − ^1H NMR ([D_8]THF): δ = 2.30, 2.37 (s, 6 H, CH_3), 6.56 (s, 1 H, H-3), 6.80-7.40 (m, 13 H, Ar), 8.31 (br, 1 H, NH). − ^{13}C NMR ([D_8]THF): δ = 20.78, 20.89 (CH_3), 105.53 (CH, C-3), 120.55, 121.12, 124.92, 128.84, 129.03, 130.41, 130.48 (CH, Ar), 131.05, 133.91 (C, Tol-C to CH_3), 136.51 (C, Ph-C to N), 138.74 (C, C-4), 148.24, 150.98 (C, Tol-C to N), 152.83 (C, C-5), 160.94 (C, C-2). − MS (CI, H_2O); *m*/*z* (%): 384 (100) [M^+ + 1]. − **10B**: ^1H NMR ([D_8,]THF): 2.20, 2.30 (s, 6 H, CH_3), 4.21, 4.28 (d, *J* = 3 Hz, 2 H, CH_2), 6.50−7.50 (m, 13 H, Tol). − $C_{24}H_{21}N_3S$ (383.4) (mixture of isomers): calcd. C 75.17, H 5.52, N 10.95; found C 75.25, H 5.58, N 10.77.

N,N′-(2-Methylen-1,3-oxathiolane-4,5-diylidene)bis[4-methylbenzenamine] **12**: Starting with thioacetic acid (0.43 ml, 6 mmol), 404 mg (22%) of slightly yellow **12** was isolated. − ^1H NMR ($CDCl_3$): δ = 2.36, 2.43 (s, 6 H, CH_3), 3.81, 4.32 (d, *J* = 4.5 Hz, 2 H, CH_2), 7.15−7.60 (m, 8 H, Tol). − ^{13}C NMR ($CDCl_3$): δ = 21.13, 21.27 (CH_3), 70.77 (CH_2), 124.83, 126.91, 129.63, 130.56 (CH, Tol), 131.48, 136.76 (C, Tol-C to CH_3), 140.36, 140.86 (C,

Tol-C to N), 145.39 (C, CSN), 153.41 (C, CON), 179.03 (COS). – MS (CI, H_2O); *m/z* (%): 309 (100) [M^+ + 1]. – $C_{18}H_{16}N_2SO$ (308.5): calcd. C 70.10, H 5.23, N 9.08; found C 70.47, H 5.16, N 8.64.

Procedure for the Preparation of Dithiolane **11b**: To a THF solution (20 ml) of CS_2 (1.27 g, 16.63 mmol) was added benzylmagnesium chloride (5.5 ml, 11 mmol, 2 M solution in THF) at −50°C. The temperature was allowed to rise to 20°C within 2 h. After stirring for 2 h, LDA (6 ml, 12 mmol, 2 M solution in THF) was added by syringe. The temperature was allowed to rise to 20°C within 2 h and the solution was stirred at 20°C for 30 min. The solution was transferred to a THF solution (50 ml) of BTIOC (3.05 g, 10 mmol) at −78°C. The solution was stirred for 12 h during which time the temperature was allowed to rise to 20°C. The solvent was removed in vacuo and to the residue was added CH_2Cl_2 (50 ml). The solution was filtered and the solvent of the filtrate was removed in vacuo. The crude product obtained was purified by chromatography (toluene).

N,N′-(2-Phenylmethylene-1,3-dithiolane-4,5-diylidene)bis[4-methylbenzenamine] **11b**: Starting with 11 mmol of benzylmagnesium chloride and 10 mmol of BTIOC, 1.6 g (40%) of **11b** was isolated, yellow solid. – IR (Nujol): ν = 1616 (m) cm^{-1}, 1582 (m), 1500 (m), 1463 (s), 1377 (m), 1213 (m). – ^1H NMR (CD_2Cl_2): δ = 2.41 (s, 6 H, CH_3), 6.69 (s, 1 H, =CH), 7.00−7.35 (m, 13 H, Ar). – ^{13}C NMR (CD_2Cl_2): δ = 21.19 (CH_3), 119.92 (=CH), 120.09, 123.37, 123.96, 128.62, 129.12, 130.38 (CH, Tol), 130.46, 136.44, 136.47 (C, Ph-C to C, Tol-C to CH_3), 149.01, 149.49 (C, Tol-C to N), 158.78 (C, CSN), 160.01 (CS_2). – MS (CI, H_2O); *m/z* (%): 401 (100) [M^+ + 1]. – $C_{24}H_{20}N_2S_2$ (400.6): calcd. C 71.97, H 5.03, N 6.99; found C 71.72, H 5.25, N 7.32.

General Procedure for the Preparation of N,N′-Diarylaminomaleic Acid Imides **13aB** *and* **13bB**: To a THF solution (30 ml) of the respective carboxyclic acid (10 mmol) was added LDA (22 mmol, 11 ml, 2 M solution in THF) at −50°C. The temperature was allowed to rise to 20°C within 2 h and the solution was stirred at 20°C for 30 min and was transferred to a THF solution (50 ml) of BTIOC (3.05 g, 10 mmol) at −78°C. The solution was stirred for 12 h during which time the temperature was allowed to rise to 20°C. The solvent was removed in vacuo and the residue was purified by chromatography (toluene) without prior filtration of the LiCl formed in the reaction.

N,N′-Di-[(4-methylphenyl)amino]maleic Acid Imide **13aB**. Starting with 6 mmol of acetic acid, 350 mg (12%) of **13aB** was isolated. The melting point and the spectroscopic data were identical with those reported in the literature.[14]

N,N′-Di-[(4-methylphenyl)amino]phenylmaleic Acid Imide **13bB**: Starting with 10 mmol of phenylacetic acid, 1.18 g (32%) of **13bB** was isolated. – IR (Nujol) ν = 3292 (m) cm^{-1}, 1758 (m), 1703 (s), 1644 (s). – ^1H NMR (CD_2Cl_2): δ = 2.22, 2.42 (s, 6 H, CH_3), 6.61, 6.85 (d, *J* = 8.5 Hz, 4 H, Tol), 7.05−7.35 (m, 9 H, Ar), 7.48 (br, 1 H, NH). – ^{13}C NMR (CD_2Cl_2): δ = 19.54, 20.91 (CH_3), 102.20 (C, C-3), 122.08, 126.44, 127.56, 127.60, 129.13, 129.93, 130.23 (CH, Ar), 129.81 (C, Ph), 134.29, 135.03, 137.14, 138.13 (C, Tol-C to CH_3, Tol-C to N-1, C-4), 167.85, 171.43 (CO). – MS (CI, H_2O); *m/z* (%): 369 (100) [M^+ + 1], 234 (15). – $C_{24}H_{20}N_2O_2$ (368.42): calcd. C 78.24, H 5.47, N 7.60; found C 78.62, H 5.80, N 7.94.

[1] Reviews: [1a] A. Maercker, *Methoden Org. Chem.* (Houben-Weyl) 4th ed., vol. *E19d*, **1993**, 448−566. – [1b] C. M. Thompson, D. Green, *Tetrahedron* **1991**, *47*, 4223−4285.

[2] For recent work on cyclization reactions of dianions with dielectrophiles: [2a] D. Seebach, M. Pohmakotr, *Tetrahedron* **1981**, *37*, 4047−4058. – [2b] J. Vollhardt, H.-J. Gais, L. Lukas, *Angew. Chem.* **1985**, *97*, 609−610. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 610−611. – [2c] A. Maercker, A. Groos, *Angew. Chem.* **1996**, *108*, 216−218; *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 210−212. – [2d] D. Seyferth, T. Wang, P. Langer, R. L. Ostrander, A. L. Rheingold, *Organometallics* **1997**, *16*, 2413−2426. – [2e] J. F. K. Müller, M. Neuburger, M. Zehnder, *Helv. Chim. Acta*, **1997**, *80*, 2182−2195. – [2f] S. Baskaran, E. Nagy, M. Braun, *Liebigs Ann./Receuil* **1997**, 311−312.

[3] P. Langer, M. Döring, H. Görls, R. Beckert, *Liebigs Ann.* **1997**, 2553−2561.

[4] P. Langer, M. Döring, *Synlett* **1998**, 396−398.

[5] P. Langer, M. Döring, *Synlett* **1998**, 399−401.

[6] [6a] C. C. Chiu, F. Jordan, *J. Org. Chem.* **1994**, *59*, 5763−5766. – [6b] J. Fabian, H. Nakazumi, M. Matsuoka, *Chem. Rev.* **1992**, *92*, 1197−1226. – [6c] C. M. Killian, L. K. Johnson, M. Brookhart, *Organometallics* **1997**, *16*, 2005−2007.

[7] [7a] We refer to ambident dianions as to systems bearing two delocalized negative charges, in the generation of which at least one abstraction of a proton attached to a carbon atom is involved. – For a review on Y-aromaticity: [7b] J. Klein, *Tetrahedron* **1983**, *39*, 2733−2759.

[8] For all dianion cyclizations reported herein (except for formation of **12**), virtually no heterocyclic side products, but some ether-insoluble polymeric material, were formed from which the product was readily separated by flash-chromatography. In some cases small amounts of TolNC (< 10% yield) were isolated, which derive from reductive cleavage of the carbon−carbon bond of BTIOC. The yields generally dropped when the dianion was reacted with a low concentrated (10^{-3} mol/l) solution of BTIOC and when the dianion solution was added within 1.5 h rather than within 10 min).

[9] D. Lindauer, R. Beckert, M. Döring, P. Fehling, H. Görls, *J. Prakt. Chem.* **1995**, *337*, 143−152 and literature cited herein.

[10] [10a] I. T. Barnish, C. R. Hauser, *J. Org. Chem.* **1968**, *33*, 2116−2118. – For preparation of an iminotetramic acid amide by a different approach: [10b] A. Roedig, W. Ritschel, D. Scheutzow, H. J. Hecht, *Chem. Ber.* **1982**, *115*, 2652−2663.

[11] Y. Tamaru, M. Kagotani, Y. Farukawa, Y. Amino, Z. Yoshida, *Tetrahedron Lett.* **1981**, *22*, 3413−3416.

[12] G. C. Papavassiliou, S. Y. Yiannopoulos, J. S. Zambounis, *J. Chem. Soc., Chem. Commun.* **1986**, 820−821.

[13] E. M. Kaiser, J. D. Petty, P. L. A. Knutson, *Synthesis* **1977**, 509−550.

[14] For amino-substituted *iso*maleimides and maleimides prepared by a different approach: F. E. Herkes, *J. Org. Chem.* **1975**, *40*, 423−428 and literature cited herein.

[15] The first attack of the 2-mercaptoacetic acid ester dianion on monofunctional alkylhalides has been reported to occur at the sulfur atom: E. Vedejs, M. J. Arnost, J. P. Hagen, *J. Org. Chem.* **1979**, *44*, 3230−3238.

[16] The structures were generated and the energies were subsequently minimized using the MM+ force field which is implemented in release 3.0 of HyperChem®. MM+ supplements the standard MM2 parameters (N. L. Allinger, *J. Am. Chem. Soc.* **1977**, *99*, 8127−8134). All input geometries were taken from the molecule editor and optimized using the Polak-Ribiere algorithm. Non-bonded electrostatic interactions were calculated as bond dipoles without cut-offs. The minima obtained from the search were further optimized using the AM1 wavefunction (M. J. S. Dewar, E. G. Zoebisch, E. F. Healy, J. J. P. Stewart, *J. Am. Chem. Soc.* **1985**, *107*, 3902−3909) and the RHF approximation.

[17] The dianion of phenylacetone was reported to be attacked by monofunctional alkyl halides at the methine rather than at the methylene site: G. B. Trimitsis, J. M. Hinkley, R. TenBrink, A. L. Faburada, M. Anderson, M. Poli, B. Christian, G. Gustafson, J. Erdman, D. Rop, *J. Org. Chem.* **1983**, *48*, 2957−2962.

[18] [18a] R. Beckert, W. Bauer, *J. Prakt. Chem.* **1991**, *333*, 555−559. – [18b] R. Beckert, M. Gruner, *J. Prakt. Chem.* **1992**, *334*, 611−620.

[19] For reactions of BTIOC with monoanions, see: [19a] J. Wuckelt, M. Döring, P. Langer, R. Beckert, H. Görls, *Tetrahedron Lett.* **1997**, 5269−5272. – [19b] J. Wuckelt, M. Döring, P. Langer, H. Görls, R. Beckert, *Tetrahedron Lett.* **1998**, 1135−1138.

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