Efficient Synthesis of Nitrogen Heterocycles by Cyclization of Bis(nucleophiles) with Oxaldiimidoyl Dichlorides

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The reaction of ambident dianions and bis-nucleophiles with oxaldiimidoyl dichlorides offers a new strategy for the regio- and diastereoselective synthesis of a variety of biologically relevant N-heterocycles. This includes cyclization, domino, one-pot, and double-anion-capture reactions.

Introduction

Nitrogen heterocycles are of considerable pharmacological relevance and the development of new methods to synthesize them efficiently is an important field in organic chemistry.[1a,1b] Because of their nitrogen lone pairs, many N-heterocycles form inter- and intramolecular hydrogen bonds and thus have defined stereochemical orientations; this plays an important role in biochemistry and supramolecular chemistry. Many N-heterocycles have interesting redox properties and represent versatile ligands for metal ions. General approaches to N-heterocyclic systems mainly involve cycloaddition reactions, ring transformations, and cyclizations catalyzed by acids, bases, or transition metals. In this context, sequential[1c] and domino[1d] reactions have proven particularly efficient.

Despite the simplicity of the idea, cyclization reactions between 1,2-dielectrophiles and strong carbon nucleophiles (such as dianions) are often problematic, due to the lability of many 1,2-dielectrophiles and the high reactivity of the carbanions. Poor reactivity matching of the starting materials often gives rise to a number of drawbacks, such as polymerization, formation of open-chain products, overaddition, SET processes, or decomposition.[2] Oxalic acid dielectrophiles are known to be particularly prone to such side reactions. We have recently developed a number of cyclization reactions between free or masked 1,3-dicarbonyl dianions and 1,2-dielectrophiles, which permit efficient syntheses of oxa- and carbacyclic systems. The success of these transformations relies on the application of two concepts:

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Peter Langer was born in Hannover (Germany) in 1969. He studied chemistry at the University of Hannover and at the Massachusetts Institute of Technology (MIT) and received his Diplom under the guidance of Prof. D. Seyferth in March 1994. In February 1997 he obtained his Dr. rer. nat. for synthetic work on Cinchona alkaloids under the supervision of Prof. H. M. R. Hoffmann at the University of Hannover (summa cum laude). During a postdoctoral period with Prof. S. V. Ley (Cambridge, UK) he worked on the synthesis of oligosaccharides. In 1998 he moved to the University of Göttingen, where he started his independent research associated to Prof. A. de Meijere. He completed his habilitation in July 2001 and is currently working as a Privatdozent at the University of Göttingen. His research is focussed on the development of new synthetic methods and their application to the synthesis of biologically relevant natural products. This includes regio- and stereoselective cyclization reactions of dianions and electroneutral dianion equivalents, transition metal and Lewis acid catalysis, and the application of allenes in organic synthesis. Awards and scholarships: Studienstiftung des deutschen Volkes (1992–94), Fonds der Chemischen Industrie (1995–96), Feodor-Lynen-Stipendium (1997–98), Liebig-Stipendium (1999–2001), Heisenberg-Stipendium (2001).

Manfred Döring was born in Sömmerda, Germany in 1954. He studied chemistry at the University of Jena, where he received his PhD degree with Egon Uhlig in 1984. After several years as a manager at the same university and after postdoctoral studies at the University of Erlangen/Nürnberg and the Massachusetts Institute of Technology, his habilitation was completed in 1994. In the following years he worked as a Privatdozent at the University of Jena. Since 2000 he has held a professorship in technical catalysis at the University of Heidelberg and at the Forschungszentrum Karlsruhe. His current research includes bioinorganic chemistry and homogeneous catalysis using heterocyclic ligands.

MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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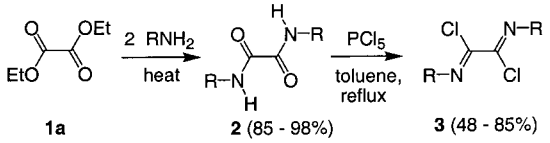
a) proper reactivity tuning of the starting materials and b) the use of electroneutral dianion equivalents (masked dianions) in Lewis acid catalyzed reactions.[3−5]

Here we wish to report a new strategy for the synthesis of N-heterocyclic systems, base-mediated cyclization reactions between dianions or dinucleophiles and oxaldiimidoyl dichlorides **3**, which may be viewed as nitrogen analogues of oxalyl dichloride.[6] The chemistry of oxaldiimidoyl dichlorides (**3**) differs greatly from that of oxalyl dichloride and diethyl oxalate. Unlike these, oxaldiimidoyl dichlorides exhibit excellent reactivity matching with a great variety of nucleophiles and are readily available from diethyl oxalate (**1a**) in only two steps (Scheme 1). The cyclization products contain imine or enamine functions that can in many cases be hydrolyzed to carbonyl and enol groups.



Scheme 1. Synthesis of oxaldiimidoyl dichlorides **3**; R = aryl, SO_2Ph, $CH(CH_3)Ph$

Four categories of cyclization reactions between oxaldiimidoyl dichlorides **3** and nucleophiles can be identified.

Type 1: Cyclization Reactions

The reaction between **3** and a dianion or an electroneutral bis(nucleophile) affords a ring system (1:1 stoichiometry). The formation of carbon−carbon bonds requires the use of dianions, produced with 2 equiv. of strong base (such as *n*BuLi or LDA). Use of a weak base is sufficient for cyclizations of electroneutral bis(nucleophiles), which are limited in most cases to the formation of carbon−nitrogen, carbon−oxygen, or carbon−sulfur bonds. An example of a cyclization of a dianion with oxalbis(*p*-tolylimidoyl) dichloride (**3a**) is given in Figure 1 (for details see Scheme 5).

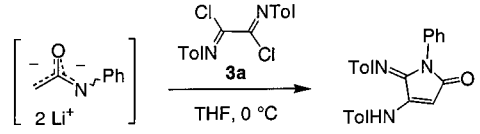


Figure 1. Cyclization of dilithiated acetanilide with **3a**

Type 2: Domino Reactions

Some cyclization products are unstable under the reaction conditions and are transformed in situ into another product. The Dimroth rearrangement is often observed in these circumstances. The driving force of the process is the conversion of an imino ether or imino thioether group into a thermodynamically more stable amide or thioamide group, respectively. An example is given in Figure 2 (for details see Scheme 5).

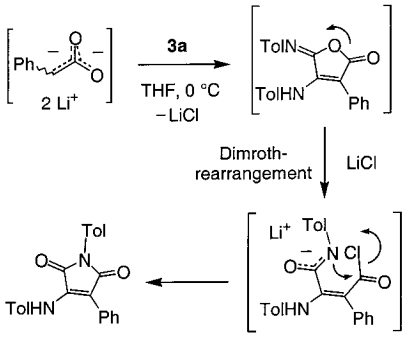


Figure 2. Domino reaction of dilithiated phenylacetic acid with **3a**

Type 3: One-Pot Reactions

One-Pot reactions of oxaldiimidoyl dichlorides rely on the use of dianions and involve the coupling of three different compounds in one synthetic operation. The reagents are added sequentially. An example is given in Figure 3 (for details see Scheme 31).

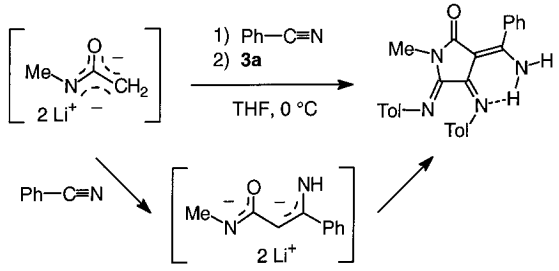


Figure 3. One-pot reaction of dilithiated *N*-methylacetic amide with benzonitrile and **3a**

Type 4: Double-Anion-Capture Reactions

Double-anion-capture reactions proceed by attack of a monofunctional nucleophile (such as an ester enolate) onto the oxaldiimidoyl dichloride **3** and subsequent cyclization through the nitrogen atoms of **3**. An example is given in Figure 4 (for details see Scheme 34).

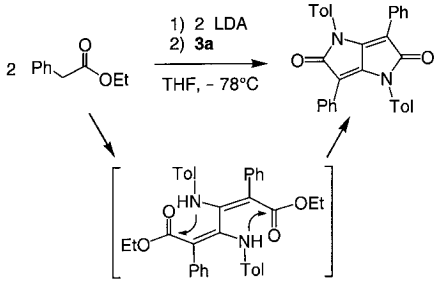
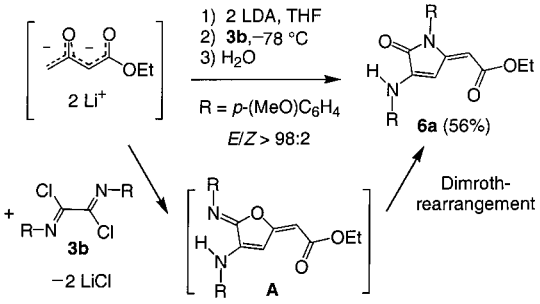


Figure 4. Double-anion-capture reaction of lithiated ethyl phenylacetate with **3a**

The cyclization reactions reported in this review are ordered systematically according to the type of reaction and the type of nucleophile (distance between the nucleophilic centers).



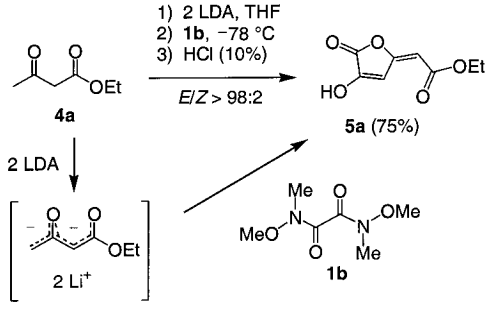
Scheme 3. Domino reaction between the dianion of ethyl acetoacetate and oxaldiimidoyl dichloride **3b** (reaction type 2)

1. Cyclization and Domino Reactions

1.1 Cyclization Reactions of 1,3-Dinucleophiles

1,3-Dicarbonyl Dianions

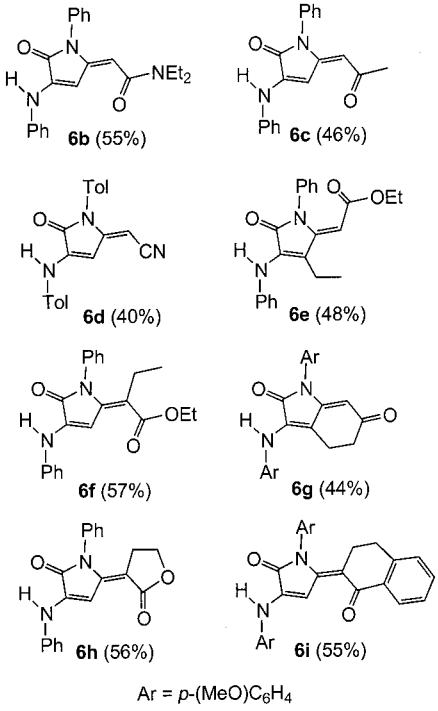
We have recently reported an efficient synthesis of γ-alkylidene-α-hydroxybutenolides by direct cyclization of 1,3-dicarbonyl dianions[7] with *N*,*N*′-dimethoxy-*N*,*N*′-dimethylethanediamide (**1b**) (Scheme 2).[8] This transformation proceeded by regioselective attack of the terminal carbon atom of the dianion onto **1b** and subsequent cyclization through the oxygen atom of the dianion. The *O*-regioselectivity can be explained by stereoelectronic considerations,[9] while the (*E*) diastereoselectivity is a result of the electrostatic repulsion of the oxygen atoms.



Scheme 2. Cyclization of the dianion of ethyl acetoacetate with *N*,*N*′-dimethoxy-*N*,*N*′-dimethylethanediamide **1b**

The reaction between the dianion of **4a** and oxalbis(*p*-methoxyphenylimidoyl) dichloride (**3b**) afforded the 5-alkylidene-5*H*-pyrrol-2-one **6a**, which can be regarded as an aza analogue of **5a** (Scheme 3).[10] The formation of **6a** can be explained by regioselective attack of the terminal carbon atom of the dianion onto **3b** and subsequent cyclization through the oxygen atom to give intermediate **A**, which undergoes a Dimroth rearrangement to give **6a** (reaction type 2). The product was formed not only with very good regioselectivity, but also with very good (*E*) diastereoselectivity, due to the steric interaction between the *N*-aryl moiety and the ester group.

5-Alkylidene-5*H*-pyrrol-2-ones are present in a number of biologically relevant natural products,[11] and so we studied the preparative scope of the cyclization reaction (Scheme 4). Variation of the starting materials allowed the preparation of a great variety of 5-alkylidene-5*H*-pyrrol-2-ones (30 examples), including not only esters, but also amides, ketones, and nitriles (such as **6b**−**d**). 5-Alkylidene-5*H*-pyrrol-2-ones containing a substituent at the exocyclic double bond were also efficiently prepared (**6e**, for example). All products were formed with very good (*E*) diastereoselectivity. A change from (*E*) to (*Z*) diastereoselectivity was observed for products containing a heterocyclic substituent (such as **6f**). Bicyclic products, such as **6g**, were prepared from dilithiated cyclohexane-1,3-diones. Treatment of bis(imidolyl) dichlorides with the dianions of α-acetyl-γ-butyrolactone and α-acetyltetralone afforded the dinuclear products **6h** and **6i**, respectively.

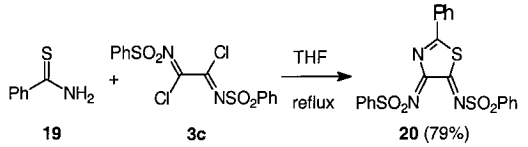


Scheme 4. Selected 5-alkylidene-5*H*-pyrrol-2-ones 6 prepared

Amides and Related 1,3-Dinucleophiles

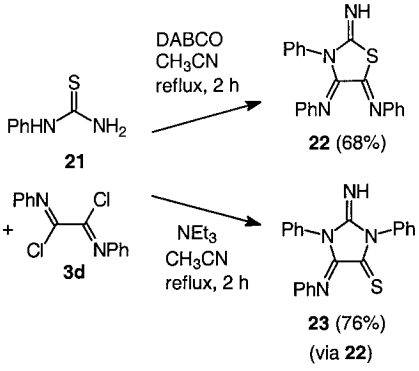
The regioselectivity of cyclization reactions between oxaldiimidoyl dichlorides **3** and ambident dianions has been studied (Scheme 5).[12] These reactions generally proceed by initial attack of the atom X of the dianion onto **3** and subsequent cyclization through a second atom Y. We define these transformations as "*X*,*Y*-cyclizations" (*X*, *Y* = C, N O, S). Treatment of oxaldiimidoyl dichlorides **3** with dilithiated amides[13] (such as acetanilide **7**) afforded iminotetramic amides such as **8** by regioselective attack of the carbon atom of the dianion on **3** and subsequent cyclization through the nitrogen atom (*C*,*N*-cyclization, reaction type 1).[14] The cyclization of the dianion of *N*,*N*′-diphenylacetamidine (**9**) and **3a** again resulted in *C*,*N*-cyclization and formation of the bis(amidine) **10**. Treatment of the dianion of thioacetanilide (**11**)[15] with **3a** gave an inseparable mixture of 4-amino-5-imino-2*H*-pyrrole-2-thione (**12-A**) and the isomeric azathiolane **12-B**, arising from *C*,*N*- and *S*,*N*-cyclization, respectively (40%, **A**/**B** = 5:1). Two heteroatoms are involved in the cyclization of **3a** and the dianion of dithiophenylacetic acid (**13**) to give dithiolane **14** (*S*,*S*-cyclization). Treatment of **3a** with the dianion of thioacetic acid (**15**) resulted in formation of a complex mixture, from which **16** was isolated in low yield (*S*,*O*-cyclization). Treatment of the dianion of phenylacetic acid (**17**)[16] with **3a** afforded the aminomaleic imide **18**, produced by *C*,*O*-cyclization and subsequent Dimroth rearrangement (reaction type 2).[12]

Heating of a THF solution of oxalbis(phenylsulfonylimidoyl) dichloride (**3c**) with thiobenzoic amide (**19**) afforded the expected cyclization product **20** (Scheme 6).[17a] In contrast, use of oxalbis(phenylimidoyl) dichloride (**3d**) gave an open-chain product.



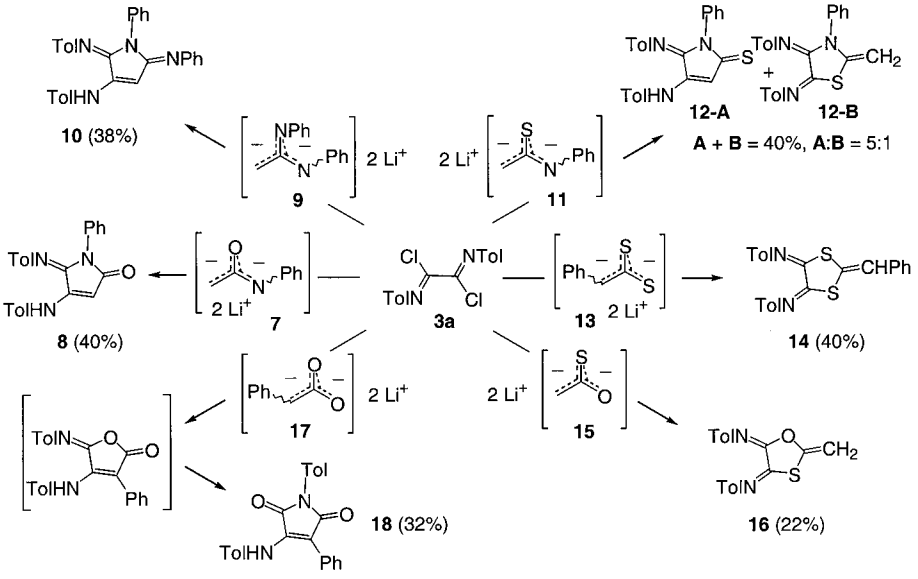
Scheme 6. Cyclization of thiobenzamide and **3c** (reaction type 1)

The DABCO-mediated reaction between **3d** and thiourea **21** afforded heterocycle **22** by regioselective *S*,*N*-cyclization (Scheme 7). The use of triethylamine (NEt_3) resulted in formation of the regioisomeric product **23**, produced by Dimroth rearrangement of **22**.[17b]



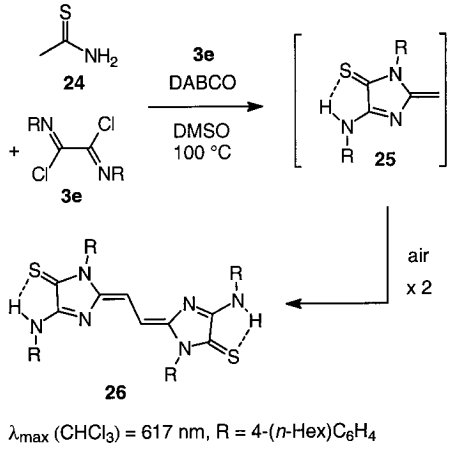
Scheme 7. Domino reaction between thiourea **21** and **3d** (reaction type 1 and 2)

The DABCO-mediated reaction between oxalbis(*n*-hexylphenylimidoyl) dichloride (**3e**) and thioacetamide (**24**) afforded the tetramethine-bridged, deeply blue-colored thiazoline **26** by *S*,*N*-cyclization, Dimroth rearrangement, and



Scheme 5. Cyclization of ambident 1,3-dianions with **3a** (reaction type 1 and 2)

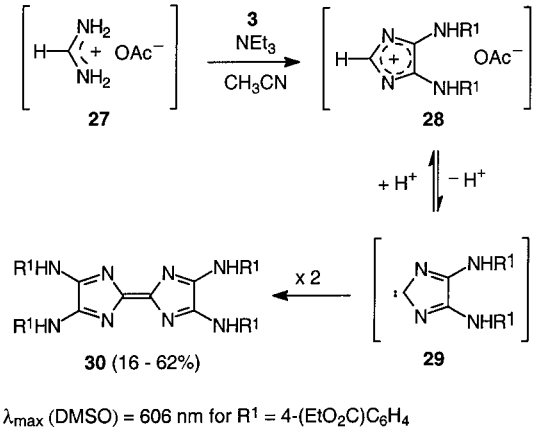
subsequent oxidative dimerization of intermediate **25** (Scheme 8).[17c] (The hexyl substituents were necessary in order to increase the solubility of the product for NMR spectroscopy.)



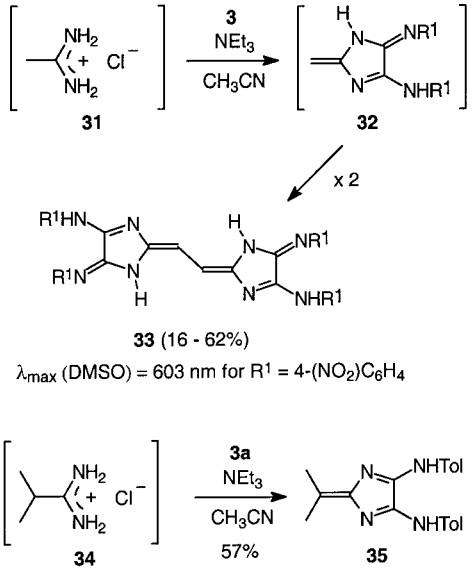
Scheme 8. Domino reaction between thioacetamide and **3e** (reaction type 2)

Regioselectivity − Concluding Remarks

In summary, the first attack of dianions onto oxaldiimidoyl dichlorides **3** generally occurs at the carbon atom of the dianion, which is the most nucleophilic center. In the case of dilithiated amides, *C*,*N*-cyclization rather than *C*,*O*-cyclization is observed, due to the higher nucleophilicity of nitrogen compared to oxygen. An exception is represented by the dianion of **13**, which undergoes *S*,*S*-cyclization. In the case of thioureas, *S*,*N*-cyclization rather than *N*,*N*-cyclization is observed, which can be explained by the higher nucleophilicity of sulfur in comparison to that of nitrogen. For intermediates containing an endocyclic *sulfur* atom adjacent to an imino group, a Dimroth rearrangement may occur, depending on the reaction conditions and on the specific substrate employed. The Dimroth rearrangement is more generally observed when an endocyclic *oxygen* atom is located next to an imino group, due to the high thermodynamic stability of the amide group produced.



Scheme 9. Domino reactions between oxaldiimidoyl dichlorides and formamidinium acetate (reaction type 2); R^1 = aryl



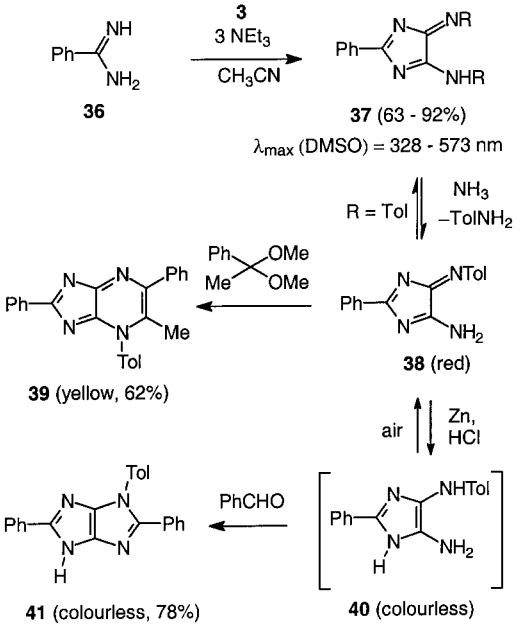
Scheme 10. Domino reactions between oxaldiimidoyl dichlorides and acetamidinium chloride (reaction type 2) or isobutylamidinium chloride (reaction type 1); R^1 = aryl

Amidinium Salts

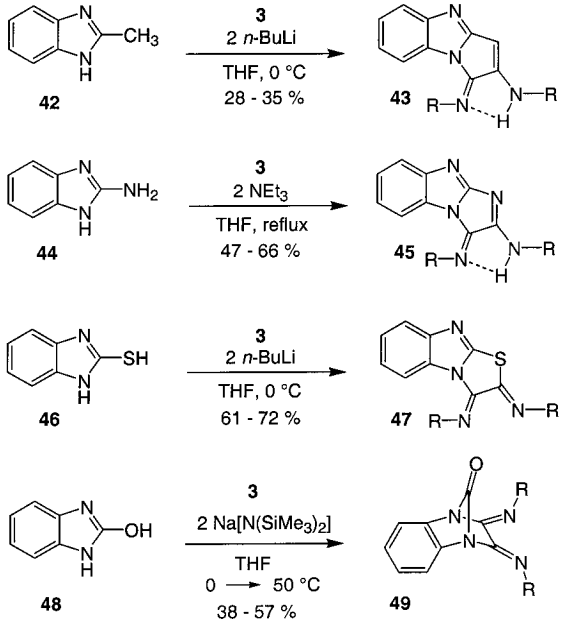
R. Beckert and co-workers have reported an efficient synthesis of 1,4,5,8-tetraazafulvalenes **30** by treatment of oxaldiimidoyl dichlorides **3** with formamidinium acetate (**27**) (Scheme 9).[18a] The formation of **30** can be explained by base-mediated cyclization, deprotonation of the C−H-acidic imidazolinium salt **28** to give the carbene **29**, and subsequent dimerization of this. The UV/Vis absorption (λ_{max}) of **30** varies from 528 to 606 nm.

Treatment of **3** with acetamidinium chloride (**31**) afforded the vinylogous tetraazafulvalenes **33** by base-mediated cyclization, deprotonation, and subsequent dimerization of intermediate **32** (Scheme 10).[18b] The UV/Vis absorption (λ_{max}) varies from 556 to 603 nm. For steric reasons, no dimerization was possible in the reaction between amidinium chloride **34** and **3a**, which gave the diazafulvene **35**.

Treatment of **3a** with benzamidine **36** afforded the red 4*H*-imidazole **37** (Scheme 11).[18c] The UV/Vis absorption (λ_{max}) varies from 328 nm [R = 4-$O_2NC_6H_4$] to 573 nm [R = 4-$Me_2NC_6H_4$]. Transamination of **37** with ammonia afforded **38**, which could be transformed into heterocycle **39** by treatment with acetophenone dimethylacetal. Reduction of **38** with Zn/HCl afforded the colorless imidazole **40**, which was treated in situ with benzaldehyde to give the leuko compound **41** in good yield.[18d] Heterocycle **40**, containing an electron-rich tetraaminoethylene moiety, was oxidized by air to give **38**.



Scheme 11. Cyclization of **3** and benzamidine (reaction type 1); R = aryl

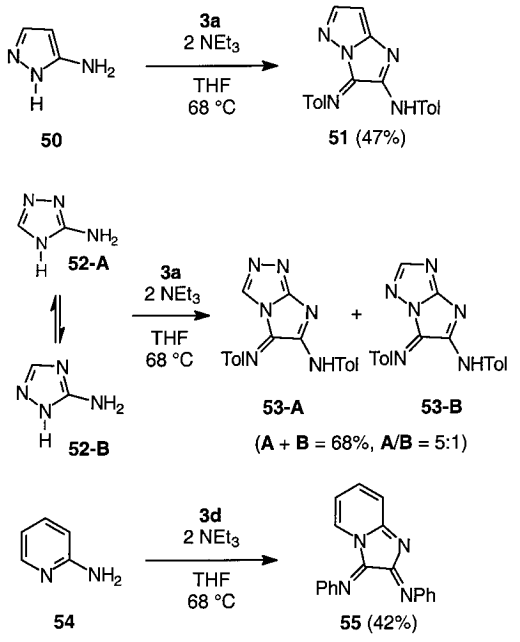


Scheme 12. Cyclization of functionalized benzimidazoles and oxaldiimidoyl dichlorides (reaction type 1); R = aryl

Heterocyclic 1,3-Dinucleophiles

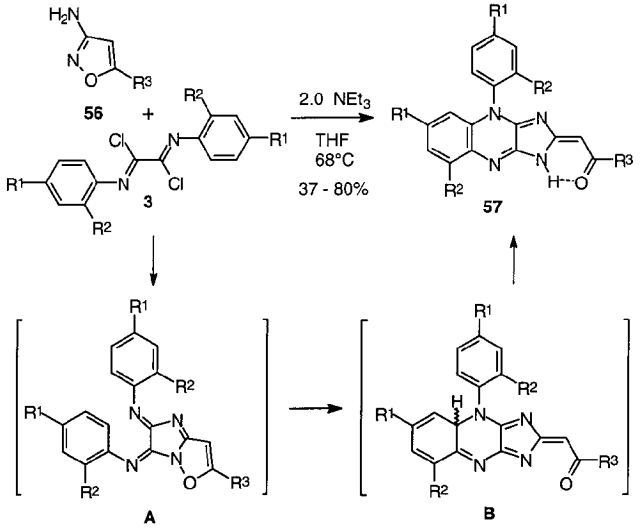
Regioselective *C*,*N*-cyclization and formation of 1*H*-pyrrolo[1,2-*a*]benzimidazoles **43** was observed on treatment of the dianion of 2-methylbenzimidazole (**42**) with oxaldiimidoyl dichlorides (Scheme 12).[19] The triethylamine-mediated cyclization of oxaldiimidoyl dichlorides with 2-aminobenzimidazole (**44**) afforded the 3*H*-imidazo[1,2-*a*]benzimidazoles **45**.[20] Regioselective *S*,*N*-cyclization and formation of the 2,3-dihydrothiazolo[3,2-*a*]benzimidazoles **47** was observed on treatment of oxaldiimidoyl dichlorides with the dianion of 2-mercaptobenzimidazole (**46**) (generated by *n*BuLi).[20,21] In contrast, the novel diazabicyclo[2.2.1]heptanones **49** were regioselectively formed by *N*,*N*-cyclization of oxaldiimidoyl dichlorides with the dianion of 2-hydroxybenzimidazole **48** (generated with $Na[N(SiMe_3)_2]$).[20] This unexpected regioselectivity is presumably kinetically controlled, as according to AM1 calculations the isomeric *O*,*N*-cyclization product is thermodynamically favored by 22.2 kcal/mol. The different reaction conditions employed were crucial for obtaining the products in optimal yields.

The cyclization of oxaldiimidoyl dichloride **3a** and 3-aminopyrazole (**50**) afforded the 3*H*-imidazo[1,2-*b*]pyrazole **51** (Scheme 13).[20] Use of 3-amino-1,2,4-triazole (**52**) resulted in regioselective formation of the 5*H*-imidazo[2,1-*c*]-1,2,4-triazoles **53-A** and **53-B** (**A**/**B** = 5:1).[22] The regioselectivity can be explained by the higher thermodynamic stabilities of **52-A** and **53-A** relative to **52-B** and **53-B**, respectively. Treatment of 2-aminopyridine (**54**) with **3d** gave the deep purple 2,3-diimino-2,3-dihydroimidazo[1,2-*a*]pyridine **55**. The cyclization proceeded through the pyridine nitrogen atom. In contrast, the reaction between 2-aminopyridine and oxalyl dichloride resulted in formation of an open-chain product.



Scheme 13. Cyclization of heterocyclic amines and oxaldiimidoyl dichlorides (reaction type 1)

Treatment of 3-aminoisoxazoles **56** with oxaldiimidoyl dichlorides **3** afforded the novel 2,4-dihydroimidazo[4,5-*b*]quinoxalines **57**, which can be regarded as analogues of riboflavine (vitamin B_2) and of the antibiotic clofazimine (Scheme 14).[22,23] The formation of **57** can be explained by cyclization of the starting materials to give intermediate **A**, cleavage of the N–O bond, attack of the nitrogen atom onto the aryl group (intermediate **B**), and a subsequent proton shift. The exocyclic double bond is formed in (*E*)-diastereoselective fashion, due to formation of a stable intramo-

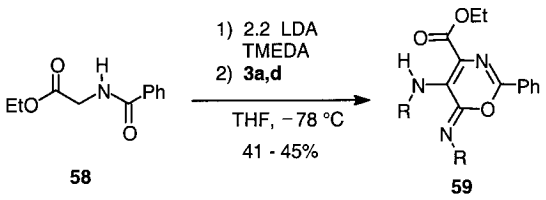


Scheme 14. Domino reaction between 3-aminoisoxazoles and oxaldiimidoyl dichlorides (reaction type 2); R^1, R^2 = H, Me, OMe; R^3 = Me, *t*Bu

lecular N−H···O hydrogen bond. Treatment of 3-aminoisoxazole with oxalyl dichloride resulted in formation of open-chain products rather than cyclic compounds.

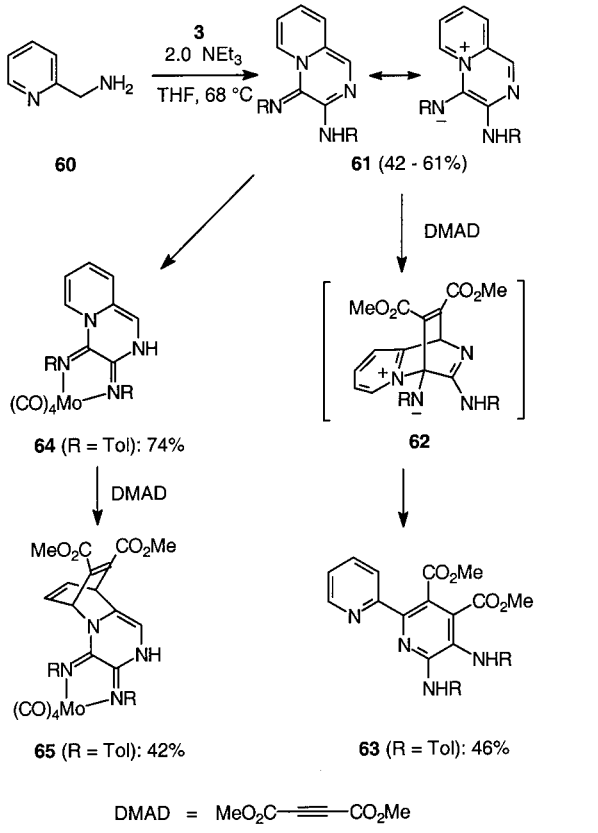
1.2 Cyclization Reactions of 1,4-Dinucleophiles

The reactions between oxaldiimidoyl dichlorides **3** and the ambident dianion of ethyl hippurate (**58**)[24] afforded the 6-imino-6*H*-[1,3]oxazines **59** by regioselective cyclization through the carbon and the oxygen atom of the dianion (Scheme 15).[25] The regioselectivity can be explained by the higher electron density at the oxygen atom, relative to that at the nitrogen atom in the dianion, or alternatively by initial formation of a four-membered ring and subsequent ring-expansion.



Scheme 15. Cyclization of dilithiated ethyl hippurate and oxaldiimidoyl dichlorides (reaction type 1); R = Tol, Ph

The cyclization of 2-aminopicoline **60** and oxaldiimidoyl dichlorides permitted efficient syntheses of a variety of pyrido[1,2-*a*]pyrazines **61** (Scheme 16).[26] Treatment of **61** with dimethyl acetylenedicarboxylate (DMAD) afforded the bipyridine derivatives **63**. This transformation proceeded through a hetero-Diels−Alder (HDA) reaction between DMAD and the zwitterionic mesomeric structure of **61** to give the bridged intermediate **62**, which was subsequently cleaved with formation of the pyridine ring. The pyrazine moiety of **61** could be efficiently protected by preparation of the 1,4-diazadiene molybdenum complex **64**. The



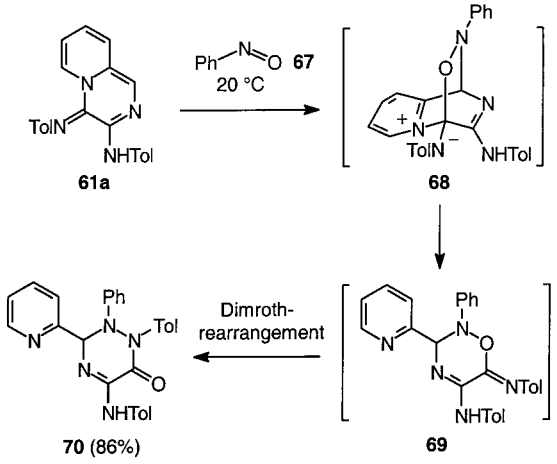
Scheme 16. Cyclization of 2-aminopicoline and oxaldiimidoyl dichlorides (reaction type 1) and hetero-Diels−Alder reactions of the products; for **61**: R = 4-MeC_6H_4 (Tol), Ph, 3-$F_3CC_6H_4$, 3-Me-OC_6H_4, 4-$EtO_2CC_6H_4$, 4-$O_2NC_6H_4$

Diels−Alder reaction between **64** and DMAD occurred exclusively at the pyridine moiety, to give the bridged product **65** rather than bipyridine **63**.

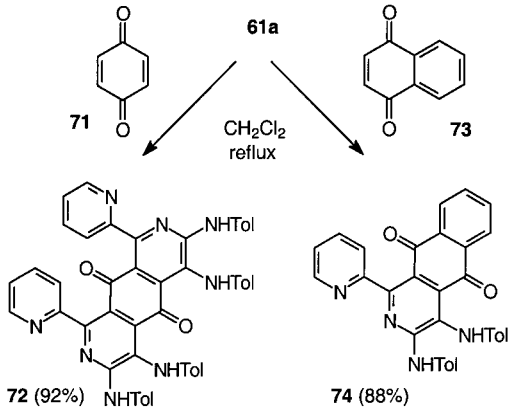
Diels−Alder reactions between pyrido[1,2-*a*]pyrazines **61** and other dienophiles were studied next.[27] Treatment of **61** with nitrosobenzene (**67**) afforded the 2,3-dihydro-1,2,4-triazin-6(1*H*)-one **70** in 86% yield through regioselective formation of the bridged intermediate **68**, subsequent ring-opening (intermediate **69**), and Dimroth rearrangement (Scheme 17).[27a]

Treatment of 2 equiv. of pyrido[1,2-*a*]pyrazines **61** with 1 equiv. of quinone **71** afforded the large heterocyclic systems **72** through Diels−Alder reaction and subsequent oxidation.[27b] It is interesting to note that the cyclization proceeded with high regioselectivity to give the isomer containing two pyridine substituents at the same site in the molecule. The 1,4-dihydro[1,2,4]triazino[1,2-*b*]phthalazine-6,11-diones **74** were prepared from phthalazinedione **73** (Scheme 18).[27a]

Reactions between heterocycles **61** and singlet oxygen afforded the 6-(2-pyridinyl)-2*H*-1,2,5-oxadiazin-3(6*H*)-ones **76** by initial hetero-Diels−Alder reaction to give intermediates **75**, cleavage of these, and Dimroth rearrangement.[27a] In contrast, oxidation of **61** with H_2O_2 gave the 2,3-dihydroimidazol-4-ones **78**, presumably by initial oxidation of the bridgehead nitrogen atom, formation of the ox-

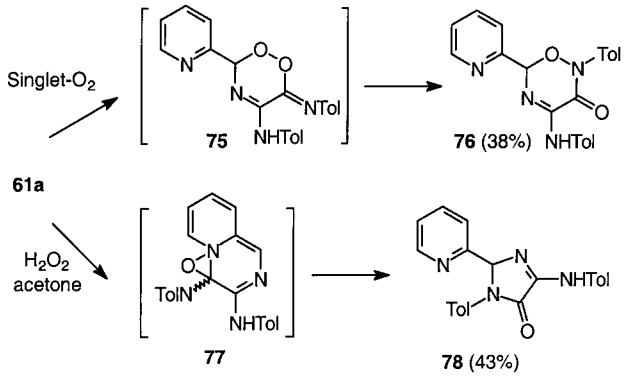


Scheme 17. Hetero-Diels–Alder reaction between pyrido[1,2-*a*]pyrazine **61a** and nitrosobenzene (**67**); R^1, R^2 = aryl



Scheme 18. Diels–Alder reactions between **61a** and quinone and naphthoquinone

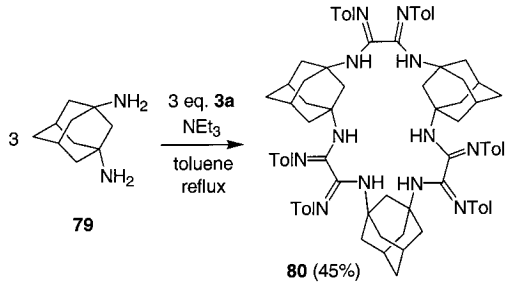
aziridine **77**, cleavage of the latter, and subsequent ring-transformation (Scheme 19).[28]



Scheme 19. Oxidation of **61a** with singlet oxygen and H_2O_2; R^1 = aryl

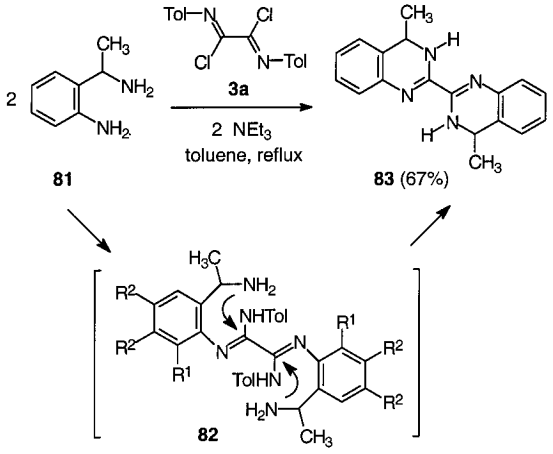
1.3 Cyclization Reactions of 1,5-Dinucleophiles

The cyclization of **3a** and 1,3-diaminoadamantane **79** afforded the macrocycle **80** in a 3:3 reaction (Scheme 20).[29] Because of the rigid character of **79**, formation of a 1:1 cyclization product was sterically not possible.



Scheme 20. Cyclization of 1,3-diaminoadamantane and **3a** (reaction type 1)

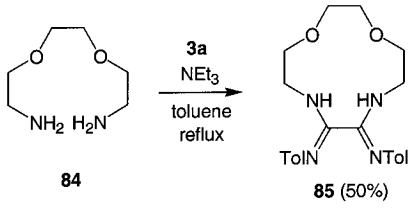
A completely different reaction path was observed in the cyclization of **3a** and 1,5-diamine **81**. Condensation of **81** (2 equiv.) with **3a** (1 equiv.) gave intermediate **82**. Twofold attack of the amino moieties onto the amidine groups and extrusion of toluidine afforded the bis(quinazoline) **83** in good yield (Scheme 21).



Scheme 21. Cyclization of 1,5-diamine **81** and **3a** (reaction type 1)

1.4 Cyclization Reactions of 1,10-Dinucleophiles

Treatment of **3a** with 1,2-bis(aminoethoxy)ethane (**84**) afforded the crown ether **85** (Scheme 22).[29] This compound might be useful for the simultaneous complexation of transition and alkali metal ions.

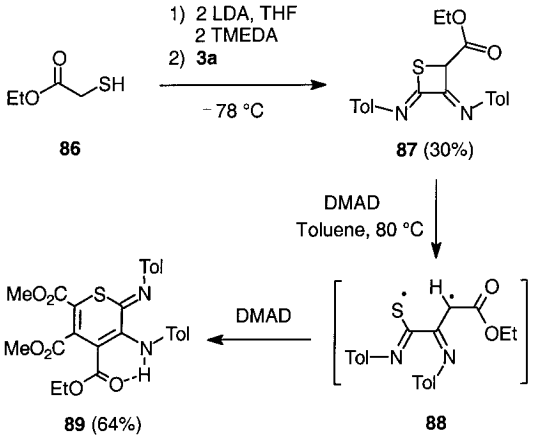


Scheme 22. Cyclization of 1,10-diamine **84** and **3a** (reaction type 1)

1.5 Cyclization Reactions of 1,2-Dinucleophiles

Four-membered ring lactams and lactones represent pharmacologically important compounds that, due to their

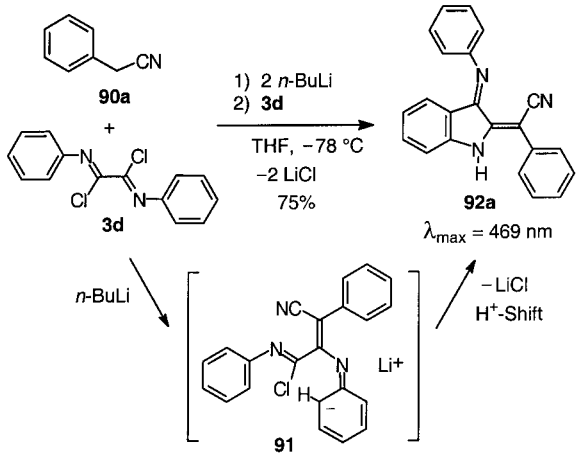
ring strain, readily undergo ring-expansion or ring-opening reactions. Treatment of **3a** with the dianion of ethyl thioglycolate **86** afforded the first (to the best of our knowledge) 2,3-diiminothietane **87** (Scheme 23).[25,30] Treatment of a toluene solution of **87** with dimethyl acetylenedicarboxylate (DMAD) at 80 °C afforded the yellow thioimino ether **89** in 64% yield. The formation of **89** can be explained by formation of the 1,4-zwitterion or diradical intermediate **88** and subsequent regioselective hetero-Diels–Alder reaction with DMAD.



Scheme 23. Cyclization of the 1,2-dianion of **86** and **3a** (reaction type 1)

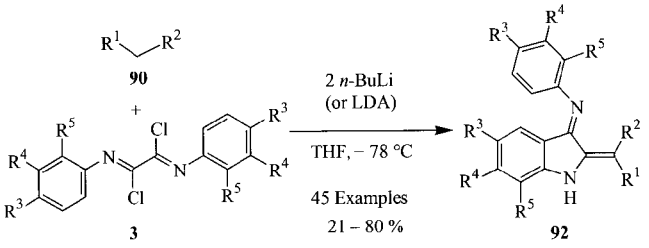
1.6 Cyclization Reactions of 1,1-Dinucleophiles

Many nitriles and sulfones are known to form dianions upon treatment with 2 equiv. of strong base.[31] The reaction between dilithiated phenylacetonitrile **90a** and oxaldiimidoyl dichloride **3d** afforded the 2-alkylidene-3-iminoindole **92a** in good yield and with very good regioselectivity and (*E*) diastereoselectivity (Scheme 24).[32] The product, which can be regarded as a protected 2-alkylidene-3-oxindole, was formed by attack of the dianion onto the first imidoyl chloride group to give the anionic intermediate **91**. The second imidoyl chloride moiety was subsequently attacked by the *ortho*-carbon atom of the phenylimino group, and a 1,3-proton shift finally afforded **92a**. The high (*E*) diastereoselectivity is a result of the steric interaction between the bulky phenylimino group and the phenyl moiety. 2-Alkylidene-3-oxindoles can be regarded as aza-analogous aurones and have recently been recognized as powerful dienophiles[33] in Diels–Alder reactions of normal electron demand[34] for synthesis of the spirocyclic *Aristotelia* alkaloid framework.[35] 2-Alkylidene-3-oxindoles have also been used as heterodienes in inverse electron demand hetero-Diels–Alder reactions for the preparation of δ-carbolines.[36] Because of their indigo-type structures, the colors of heterocycles **92** vary from orange to violet.



Scheme 24. Cyclization of phenylacetonitrile and **3d** (reaction type 1); acetonitrile was used for the UV/Vis measurement

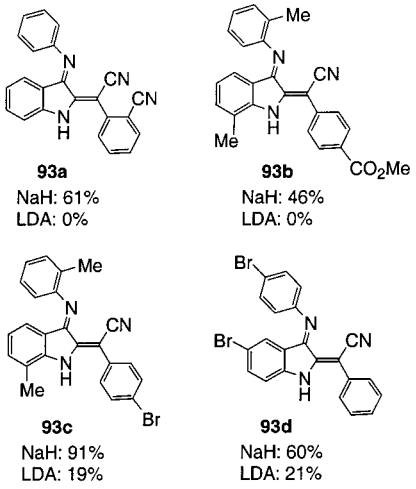
Cyclizations of dilithiated arylmethyl cyanides and sulfones **90** with oxaldiimidoyl dichlorides **3** enabled a great variety of 2-alkylidene-3-iminoindoles **92** to be synthesized efficiently (Scheme 25).[37,38] Substituents could be introduced both at the indole moiety and at the exocyclic double bond by variation of the substituents on **3** and **90**, respectively. The cyclizations proceeded with very good (*E*) diastereoselectivities for products with sterically distinct substituents R^1 and R^2. Amide-substituted indoles could be prepared with high (*E*) diastereoselectivity by treatment of **3** with monolithiated carboxylic amides.[38]



Scheme 25. Scope of cyclizations of lithiated cyanides, sulfones, and amides with oxaldiimidoyl dichlorides (reaction type 1); R^1 = Ar, SO_2Ph, $SiMe_3$; R^2 = CN, Ph, $CONR_2$; R^3, R^4, R^5 = H, Me, OMe; for all products, (*E*)/(*Z*) > 98:2, except R^1 = SO_2Ph, R^2 = Ph, (*E*)/(*Z*) = 2:1

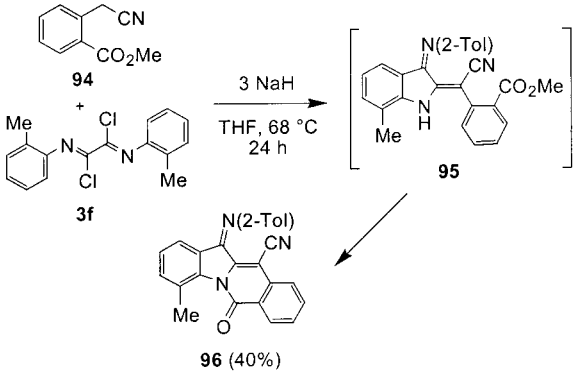
To extend the preparative scope of our methodology further, we systematically studied the reaction conditions and eventually developed a stepwise deprotonation procedure using sodium hydride (Scheme 26).[39] This procedure permitted successful cyclization of substrates containing functional groups unstable to strong bases (such as *n*BuLi or LDA). LDA-mediated reactions between oxaldiimidoyl dichlorides and 2-cyanophenylacetonitrile or methyl 4-(cyanomethyl)benzoate, for example, afforded only complex mixtures. In contrast, the ester- and cyano-substituted indoles **93a** and **93b** could be prepared in good yields if sodium hydride (NaH) in refluxing THF was used. LDA-mediated treatment of 4-bromophenylacetonitrile with **3** was unsuccessful, since metal/halide exchange occurred. In con-

trast, the desired indole **93c** could be prepared in good yield and with very good (*E*) diastereoselectivity if NaH was used. The NaH-mediated cyclization of phenylacetonitrile and oxalbis(*p*-bromophenylimidoyl) dichloride afforded **93d**, containing a brominated indole moiety.



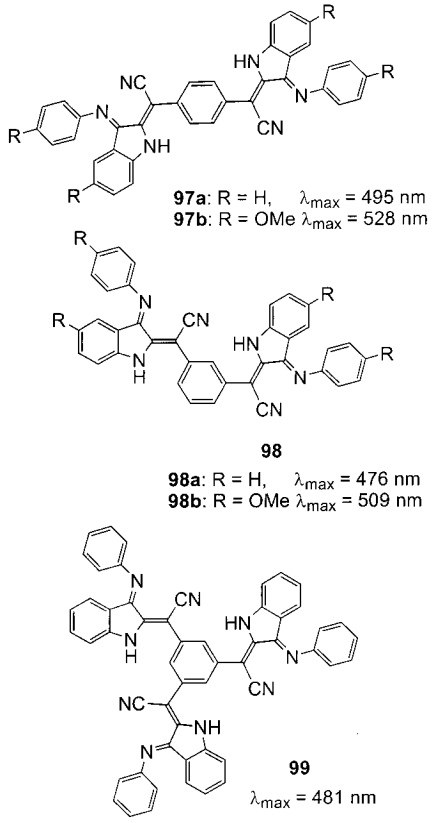
Scheme 26. Synthesis of functionalized 2-alkylidene-3-iminoindoles (reaction type 1)

Treatment of methyl 2-(cyanomethyl)benzoate (**94**) with **3f** afforded the tetracyclic product **96**, produced by a domino cyclization-lactamization reaction by way of intermediate **95** (Scheme 27).



Scheme 27. Domino cyclization-lactamization reaction (reaction type 2)

Large heterocyclic π-systems, merocyanines, and substituted benzenes play important roles in the field of material sciences, thanks to their NIR, photochromic, solvatochromic, electron-transfer, ferromagnetic, and nonlinear-optical properties.[40] Treatment of 1,4-phenylenebis(acetonitrile) with 4 equiv. of *n*BuLi or LDA and then with oxaldiimidoyl dichlorides **3** afforded the highly conjugated 1,4-bis(indolinylidenemethyl)benzenes **97** (Scheme 28).[51] Four carbon−carbon bonds were formed with very good regioselectivities and (*E*) diastereoselectivities. Starting with 1,3-phenylenebis(acetonitrile), the 1,3-bis(indolinylidenemethyl)benzenes **98** were prepared in good yields. Treatment of 3,5-bis(cyanomethyl)phenylacetonitrile with **3d** afforded the tris(indolinylidenemethyl)benzene **99**, with formation of six carbon−carbon bonds in one synthetic operation. Bathochromic shifts (relative to the parent compound **92a**) were observed for compounds **97** (Scheme 24), thanks to their *para* substitution and extended π-system, but not for the *meta* derivatives **98** and **99**. As expected, a greater shift was observed for the methoxy-substituted indole **97b** than for **97a**. The colors of heterocycles **97**−**99** vary from deep red to violet.



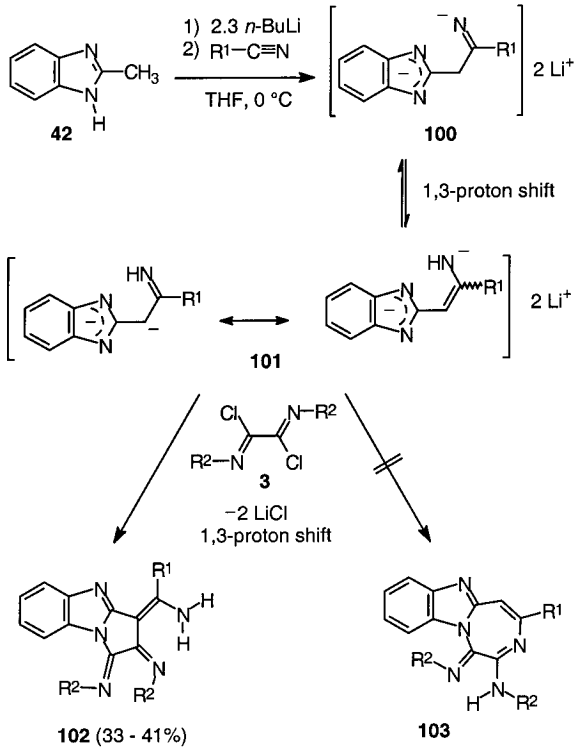
Scheme 28. Synthesis of bis- and tris(indolinylidenemethyl)benzenes (reaction type 1); for all products: (*E*)/(*Z*) > 98:2; acetonitrile was used for UV/Vis experiments

2. One-Pot Reactions

One-pot reactions have found widespread application in organic synthesis.[42] Carbanionic one-pot reactions of three components involve attack of a nucleophile onto a suitable relais species to form a reactive intermediate; this is subsequently trapped by addition of an electrophile. Recent examples include treatment of carbon nucleophiles with allenes and subsequent cyclization with acrylates,[43a] and reactions involving isocyanates,[43b] allenyl isothiocyanates,[43c] or ketones[44] as the relais species. In the course of our studies[45a,45b] into the development of a new method for the synthesis of allenes from silyl enol ethers, we have recently developed one-pot reactions of lithiated allenes with nitriles as the relais species.[45c]

The one-pot reaction of 1,3-dianions with non-enolizable nitriles and oxaldiimidoyl dichlorides allowed a variety of

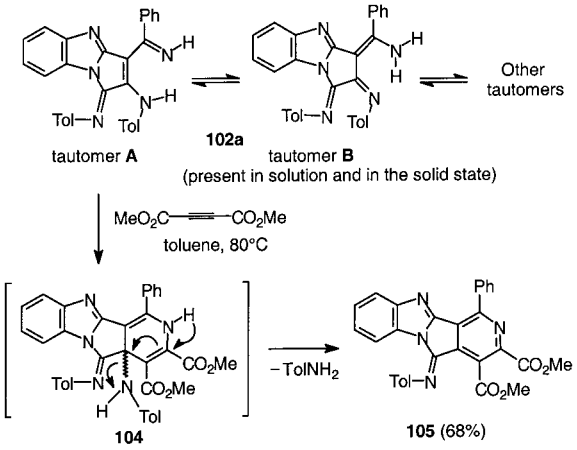
radialene-shaped pyrroles to be synthesized efficiently.[19,46] For example, the radialene-shaped pyrroles **102** could be regioselectively prepared, starting with the dianion of 2-methylbenzimidazole (**42**) (Scheme 29).[19,46] The formation of **102** can be explained by attack of the dianion onto the nitrile to give intermediate **100**, which subsequently underwent a 1,3-proton shift to give the ambident dianionic intermediate **101**. The addition of **3** resulted in regioselective *C*,*N*-cyclization rather than *N*,*N*-cyclization, to give the pyrroles **102** rather than the isomeric seven-membered ring products **103**.



Scheme 29. One-pot treatment of dilithiated 2-methylbenzimidazole with nitriles and oxaldiimidoyl dichlorides (reaction type 3); R^1 = Tol, Ph, *t*Bu; R^2 = Tol, Ph

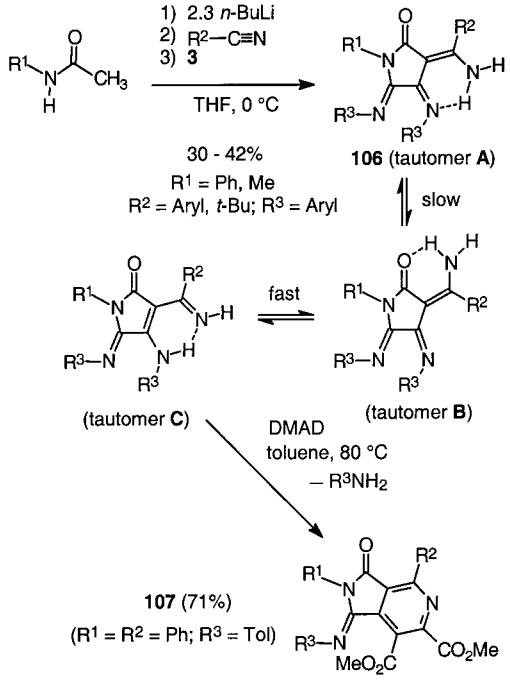
A number of tautomeric structures for pyrroles **102** are possible. The radialene-type structure **B**, the lowest-lying minimum structure at the B3LYP/3−21G//AM1 level of theory, was shown experimentally to be present both in solution and in the solid state. Treatment of pyrrole **102a** with DMAD afforded the imidazo[1′,2′:1,2]pyrrolo[3,4-*c*]pyridin-5-one **105**, presumably formed by an HDA reaction between DMAD and the 1-azadiene system of **102a** (tautomer **A**) and subsequent elimination of *p*-aminotoluene (Scheme 30).

Pyrroles **106** were prepared from dilithiated amides by a one-pot reaction related to that described for the synthesis of **102** (Scheme 31).[46] The cyclizations again proceeded with very good *C*,*N*-regioselectivities. The relevant tautomers of **106** are structures **A**−C, including radialenes **A** and **B**. The radialene-shaped tautomer **A** is present in solution and in the solid state and also represents the lowest-lying minimum structure at the B3LYP/3−21G//AM1 level of



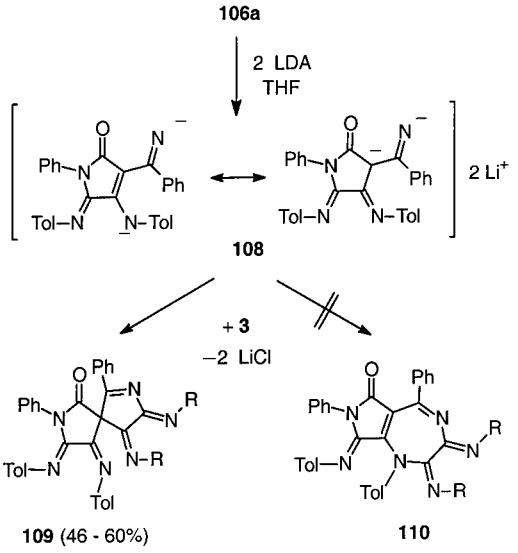
Scheme 30. Hetero-Diels−Alder reaction of radialene-shaped pyrrole **102a**

theory. In solution, slow **A**/**B** interconversion could be detected by low-temperature ^{1}H NMR experiments. Treatment of **106** with DMAD afforded the 2,3-dihydro-1-imino-3-oxo-1*H*-pyrrolo[3,4-*c*]pyridine **107**, by an HDA reaction and subsequent elimination of *p*-toluidine.



Scheme 31. One-pot treatment of dilithiated amides with nitriles and **3** (reaction type 3)

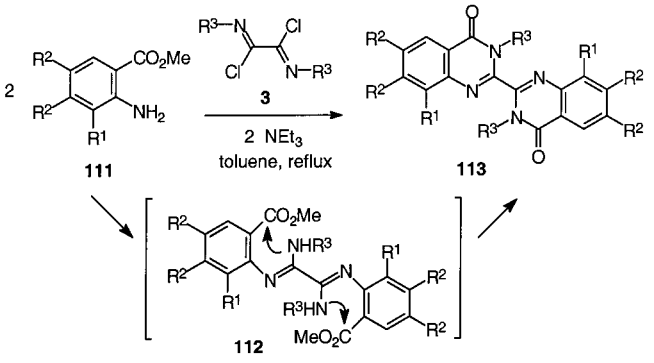
Deprotonation of the two N−H groups of **106a** afforded the ambident dianion **108** (Scheme 32). Similarly to the formation of pyrroles **106**, treatment of **108** with oxaldiimidoyl dichlorides resulted in regioselective *C*,*N*-cyclization rather than *N*,*N*-cyclization, to give the novel 3,4,8,9-tetraimino-2,7-diazaspiro[4.4]non-6-en-1-ones **109** rather than the isomeric seven-membered ring compounds **110** (Scheme 32).[12]



Scheme 32. Cyclization of dilithiated radialene-shaped pyrrole **106a** and **3** (reaction type 1); R = Tol, Ph

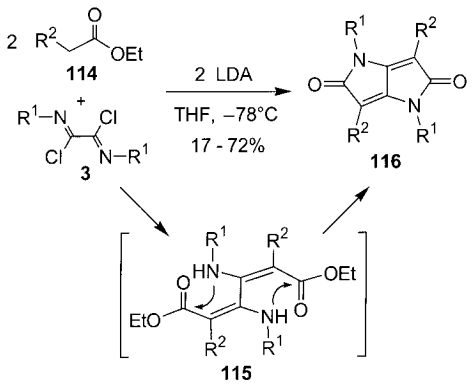
3. Double-Anion-Capture Reactions

Treatment of 2 equiv. of anthranilic esters **111** with 1 equiv. of oxaldiimidoyl dichlorides **3** afforded the novel 2,2′-bis(quinazolin-4-one)s **113** (Scheme 33).[47,48] The formation of **113** can be explained by formation of the open-chain intermediate **112** and subsequent cyclization by attack of the amidine nitrogen atoms onto the ester groups.



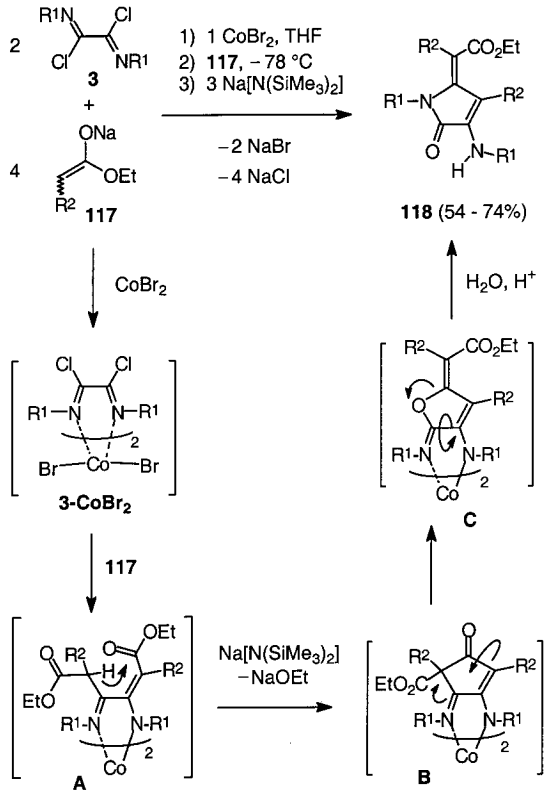
Scheme 33. Double-anion-capture reaction between anthranilic esters and **3** (reaction type 4); yields: 21−46%; R^1 = H, CH_3, R^2 = H, OCH_3, R^3 = aryl

Treatment of lithiated esters **114** with oxaldiimidoyl dichlorides afforded the pyrrolo[3,2-*b*]pyrrole-2,5-diones **116** (Scheme 34).[49] The formation of **116** proceeds by formation of the open-chain intermediate **115** and subsequent attack of the nitrogen atoms onto the ester groups. Besides their interesting electronic situation, heterocycles **116** represent useful synthetic pigments[50] and can be regarded as lactam analogues of pulvinic acids, a class of natural products.[51]



Scheme 34. Double-anion-capture reaction between ester carbanions and **3** (reaction type 4); R^1 = aryl, R^2 = H, alkyl, NMe_2, aryl, hetaryl

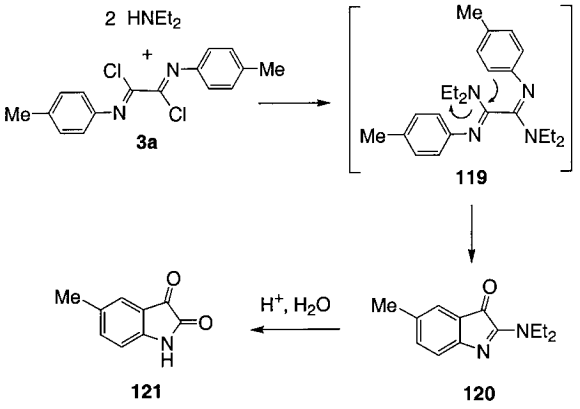
Treatment of **3** (1.0 equiv.) with sodium diethyl malonate or sodium ethyl cyanoacetate **117** (2.0 equiv.) in the presence of cobalt(II) or nickel(II) bromide and $Na[N(SiMe_3)_2]$ (1.5 equiv.) gave the 5-alkylidenepyrrol-2(5*H*)-ones **118** in good yields.[52] The formation of **118** can be explained by initial formation of a (1,4-diazadiene)cobalt(II) complex **3-CoBr$_2$** (Scheme 35). Attack of **117** onto **3-CoBr$_2$** afforded complex **A**, which underwent a regioselective ring-closure reaction to give intermediate **B**. Rearrangement of this gave intermediate **C**, and subsequent Dimroth rearrangement and decomplexation during the aqueous workup afforded



Scheme 35. Transition metal mediated cyclization of lithiated esters and **3** (reaction type 4); R^1 = aryl, R^2 = CO_2Et, CN

118. In contrast to the formation of pyrrolo[3,2-*b*]pyrrole-2,5-diones **116**, formation of heterocycles **118** involved attack of a carbon rather than a nitrogen atom onto the ester group, due to chelation of the nitrogen atoms to the metal center. The mechanism is supported by the observation that treatment of an independently prepared sample of intermediate **A** with $Na[N(SiMe_3)_2]$ afforded product **118** in good yield.

Treatment of primary amines with **3** afforded open-chain oxalyl amidines.[6] In contrast, treatment of **3a** with diethylamine resulted in formation of the isatin **121** (Scheme 36). The formation of **121** proceeds by formation of oxalyl amidine **119** and subsequent attack of the *ortho*-carbon atom of one of the tolyl groups onto the amidine to give intermediate **120**. The amidine group of **120** was hydrolyzed during the aqueous workup.



Scheme 36. Synthesis of isatine **121** (reaction type 4)

Conclusions

In summary, we have shown that cyclization reactions of oxaldiimidoyl dichlorides with dianions and electroneutral bis(nucleophiles) allow efficient and regioselective synthesis of a great variety of heterocyclic systems. As well as simple cyclization reactions, the general concept has also been extended to domino, one-pot, and double-anion-capture reactions. Recent and current work has been directed towards cyclization reactions of oxaldiimidoyl dichlorides containing *N*-protecting groups that can be selectively removed from the heterocyclic products. In this context, the phenylsulfonyl and phenylethyl groups represent particularly promising candidates. In future, the developed chemistry should be applied to the synthesis of natural and unnatural target molecules.

Acknowledgments

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[1] [1a] *Comprehensive Heterocyclic Chemistry II* (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven), Pergamon Press, Oxford, **1996**. [1b] S. Laschat, *Liebigs Ann./Receuil* **1997**, 1, and references cited therein; [1c] L. F. Tietze, U. Beifuss, *Angew. Chem.* **1993**, *105*, 137; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 131. [1d] L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115.

[2] For the extrusion of carbon monoxide in the reaction between glycols and oxalyl chloride, see: [2a] T. Iida, T. Itaya, *Tetrahedron* **1993**, *49*, 10511. [2b] M. P. Sibi, M. Marvin, R. Sharma, *J. Org. Chem.* **1995**, *60*, 5016.

[3] For a review, see: P. Langer, *Chem. Eur. J.* **2001**, *111*, 3858.

[4] For cyclizations of 1,3-dicarbonyl dianions: [4a] P. Langer, E. Holtz, *Angew. Chem.* **2000**, *112*, 3208; *Angew. Chem. Int. Ed.* **2000**, *39*, 3086. [4b] P. Langer, I. Karimé, *Synlett* **2000**, 743. [4c] P. Langer, I. Freifeld, E. Holtz, *Synlett* **2000**, 501. [4d] P. Langer, I. Freifeld, *Chem. Eur. J.* **2001**, *7*, 565. [4e]P. Langer, E. Holtz, N. N. R. Saleh, *Chem. Eur. J.*, in print.

[5] For cyclizations of electroneutral dianion equivalents: [5a] P. Langer, T. Eckardt, *Angew. Chem.* **2000**, *112*, 4503; *Angew. Chem. Int. Ed.* **2000**, *39*, 4343. [5b] P. Langer, T. Krummel, *Chem. Commun.* **2000**, 967. [5c] P. Langer, T. Eckardt, *Synlett* **2000**, 844. [5d] P. Langer, T. Schneider, *Synlett* **2000**, 497. [5e] P. Langer, V. Köhler, *Org. Lett.* **2000**, 1597. [5f] P. Langer, V. Köhler, *Chem. Commun.* **2000**, 1653. [5g] P. Langer, B. Kracke, *Tetrahedron Lett.* **2000**, 4545. [5h] P. Langer, I. Freifeld, *Synlett* **2001**, 523. [5i] P. Langer, U. Albrecht, *Synlett* **2001**, 526. [5j] P. Langer, T. Krummel, *Chem. Eur. J.* **2001**, *7*, 1720.

[6] D. Lindauer, R. Beckert, M. Döring, P. Fehling, H. Görls, *J. Prakt. Chem.* **1995**, *337*, 143.

[7] L. Weiler, *J. Am. Chem. Soc.* **1970**, *92*, 6702.

[8] [8a] P. Langer, M. Stoll, *Angew. Chem.* **1999**, *111*, 1919; *Angew. Chem. Int. Ed.* **1999**, *38*, 1803. [8b] P. Langer, T. Schneider, M. Stoll, *Chem. Eur. J.* **2000**, *6*, 3204.

[9] [9a] J. E. Baldwin, L. I. Kruse, *J. Chem. Soc., Chem. Commun.* **1977**, 233. For a review on the structure and reactivity of lithium enolates, see: [9b] D. Seebach, *Angew. Chem.* **1988**, *100*, 1685; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1624.

[10] P. Langer, M. Döring, *Synlett* **2001**, 1437.

[11] For Amaryllidaceae alkaloids, see: [11a] M. F. Grundon, *Nat. Prod. Rep.* **1987**, *4*, 89. [11b] J. R. Lewis, *Nat. Prod. Rep.* **1993**, *10*, 291. [11c] J. R. Lewis, *Nat. Prod. Rep.* **1994**, *11*, 329. [11d] J. H. Rigby, R. C. Hughes, M. J. Heeg, *J. Am. Chem. Soc.* **1995**, *117*, 7834. For pukeleimides, see: [11e] J. H. Rigby, *Tetrahedron* **1996**, *52*, 10569 and references cited therein. [11f] C. J. Simmons, F.-J. Marner, J. H. Cardellina, R. E. Moore, K. Seff, *Tetrahedron Lett.* **1979**, 2003. [11g] J. H. Cardellina, R. E. Moore, *Tetrahedron Lett.* **1979**, 2007.

[12] P. Langer, J. Wuckelt, M. Döring, R. Beckert, *Eur. J. Org. Chem.* **1998**, 1467.

[13] I. T. Barnish, C. R. Hauser, *J. Org. Chem.* **1968**, *33*, 2116.

[14] P. Langer, M. Döring, H. Görls, R. Beckert, *Liebigs Ann./Receuil* **1997**, 2553.

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

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

[17] [17a] J. Goerdeler, K. Brüning, *Tetrahedron Lett.* **1970**, 3781. [17b] R. Beckert, M. Gruner, *J. Prakt. Chem.* **1992**, *334*, 611. [17c] R. Beckert, W. Bauer, *J. Prakt. Chem.* **1991**, *333*, 555.

[18] [18a] C. Käpplinger, R. Beckert, W. Günther, H. Görls, *Liebigs Ann./Receuil* **1997**, 617. [18b] J. Brandenburg, C. Käpplinger, R. Beckert, *Synthesis* **1996**, 1302. [18c] J. Atzrodt, J. Brandenburg, C. Käpplinger, R. Beckert, W. Günther, H. Görls, J. Fabian, *J. Prakt. Chem.* **1997**, *339*, 729. [18d] J. Atzrodt, R. Beckert, W. Günther, H. Görls, *Eur. J. Org. Chem.* **2000**, 1661.

[19] P. Langer, M. Döring, *Synlett* **1998**, 399.

[20] P. Langer, J. Wuckelt, M. Döring, P. R. Schreiner, H. Görls, *Eur. J. Org. Chem.* **2001**, 2245.

[21] For related compounds, see: [21a] R. Beckert, M. Gruner, *J.*

Prakt. Chem. **1992**, *334*, 611. [21b] A. K. El-Shafei, H. S. Kashef, A.-B. A. G. Ghattas, *Gazz. Chim. Ital.* **1981**, *111*, 409.
[22] J. Wuckelt, M. Döring, R. Beckert, P. Langer, *Synlett* **1999**, 468.
[23] P. Langer, J. Wuckelt, M. Döring, P. R. Schreiner, H. Görls, *Eur. J. Org. Chem.* **2001**, 2257.
[24] A. P. Krapcho, E. A. Dundulis, *Tetrahedron Lett.* **1976**, 2205.
[25] P. Langer, M. Döring, *Chem. Commun.* **1999**, 2439.
[26] J. Brandenburg, R. Beckert, P. Fehling, M. Döring, H. Görls, *J. Prakt. Chem.* **1996**, *338*, 430.
[27] [27a] T. Billert, R. Beckert, P. Fehling, M. Döring, J. Brandenburg, H. Görls, P. Langer, *J. Heterocycl. Chem.* **1999**, *36*, 627. [27b] T. Billert, R. Beckert, P. Fehling, M. Döring, *Tetrahedron* **1997**, *53*, 5455.
[28] R. Beckert, M. Döring, H. Görls, F. Knoch, E. Uhlig, J. Wuckelt, *J. Prakt. Chem.* **1995**, *337*, 38.
[29] D. Lindauer, R. Beckert, T. Billert, *J. Prakt. Chem.* **1995**, *337*, 508.
[30] For the preparation of a triiminothietane, see: [30a] G. L'abbé, L. Huybrechts, *J. Chem. Soc., Chem. Commun.* **1979**, 161. For the preparation of a 2,4-diiminothietane, see: [30b] G. L'abbé, J.-P. Dekerk, *Tetrahedron Lett.* **1979**, 3213. [30c] H. J. Bestmann, *Angew. Chem.* **1977**, *89*, 370; *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 358.
[31] Lithiated nitriles and sulfones can exist as true dianions or as base-associated monoanions. For a review see: G. Boche, *Angew. Chem.* **1989**, *101*, 286; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 277.
[32] P. Langer, M. Döring, *Synlett* **1998**, 396.
[33] J. Y. Mérour, L. Chichereau, E. Desarbre, P. Gadonneix, *Synthesis* **1996**, 519.
[34] E. Wenkert, S. Liu, *Synthesis* **1992**, 323.
[35] R. Stahl, R. Galli, R. Güller, H.-J. Borschberg, *Helv. Chim. Acta* **1994**, *77*, 2125.
[36] [36a] A. Buzas, J. Y. Mérour, *Synthesis* **1989**, 458. [36b] J. Y. Mérour, A. Mérour, *Synthesis* **1994**, 767.
[37] P. Langer, J. Wuckelt, M. Döring, H. Görls, *J. Org. Chem.* **2000**, *65*, 3603.
[38] P. Langer, J. Anders, M. Döring, H. Görls, *Eur. J. Org. Chem.*, in print.
[39] P. Langer, J. Anders, manuscript submitted.
[40] [40a] R. Gompper, H.-U. Wagner, *Angew. Chem.* **1988**, *100*, 1492; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1437. [40b] F. Effenberger, H. Schlosser, P. Bäuerle, S. Maier, H. Port, H. C. Wolf, *Angew. Chem.* **1988**, *100*, 274; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 281; [40c] J. Fabian, H. Nakazumi, M. Matsuoka, *Chem. Rev.* **1992**, *92*, 1197.
[41] P. Langer, J. Anders, M. Döring, submitted.
[42] H. Bienaymé, C. Hulme, G. Oddon, P. Schmitt, *Chem. Eur. J.* **2000**, *6*, 3321.
[43] [43a] A. Padwa, P. E. Yeske, *J. Am. Chem. Soc.* **1988**, *110*, 1617. [43b] I. Khattak, R. Ketcham, E. Schaumann, G. Adiwidjaja, *J. Org. Chem.* **1985**, *50*, 3431. [43c] K. Banert, H. Hückstädt, K. Vrobel, *Angew. Chem.* **1992**, *104*, 72; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 90.
[44] [44a] P. Langer, M. Döring, D. Seyferth, *Synlett* **1999**, 135. [44b] P. Langer, M. Döring, H. Görls, *Eur. J. Org. Chem.* **2001**, 1511.
[45] [45a] P. Langer, *Chem. Commun.* **1999**, 1217. [45b] P. Langer, M. Döring, D. Seyferth, H. Görls, *Chem. Eur. J.* **2001**, *7*, 573. [45c] P. Langer, M. Döring, D. Seyferth, *Chem. Commun.* **1998**, 1927.
[46] P. Langer, M. Döring, P. R. Schreiner, H. Görls, *Chem. Eur. J.* **2001**, *7*, 2617.
[47] J. Wuckelt, M. Döring, R. Beckert, P. Langer, *Synlett* **1999**, 1100.
[48] P. Langer, J. Wuckelt, M. Döring, H. Görls, *Eur. J. Org. Chem.* **2001**, 1503.
[49] P. Langer, J. Wuckelt, M. Döring, *J. Org. Chem.* **2000**, *65*, 729.
[50] [50a] L. Casser, A. Iqbal, A. C. Rochat (Ciba−Geigy), *Eur. Pat. Appl.*, EP 98808, **1983**. [50b] W. Herbst, K. Hunger, *Industrial Organic Pigments*, VCH, Weinheim **1993**, p. 550.
[51] [51a] Y. S. Rao, *Chem. Rev.* **1976**, *76*, 625. [51b] G. Pattenden, *Prog. Chem. Nat. Prod.* **1978**, *35*, 133. [51c] M. Gill, W. Steglich, *Prog. Chem. Org. Nat. Prod.* **1987**, *51*, 1. [51d] D. W. Knight, *Contemp. Org. Synth.* **1994**, *1*, 287. [51e] M. Schweppe, *Handbuch der Naturfarbstoffe*, ecomed, Landsberg **1992**, p. 185, 525.
[52] J. Wuckelt, M. Döring, P. Langer, R. Beckert, H. Görls, *J. Org. Chem.* **1999**, *64*, 365.

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