Multicomponent Reaction of Aldehydes, Anhydrides, and Dienophiles: Synthesis of "Butterfly"-Like Diazatetradecenes

Dirk Strübing,[a] Axel Jacobi von Wangelin,[a] Helfried Neumann,[a] Dirk Gördes,[a] Sandra Hübner,[a] Stefan Klaus,[a] Anke Spannenberg,[a] and Matthias Beller*[a]

Keywords: Domino reactions / Multicomponent reactions / Diazatetradecenes / Diels−Alder reaction

An operationally simple one-pot synthesis of functionalized bicyclo[2.2.2]oct-2-ene derivatives has been developed using a novel multicomponent coupling of α,β-unsaturated aldehydes, carboxylic acid anhydrides, and dienophiles.

Introduction

The development and use of domino[1] and multicomponent[2] reactions for the preparation of natural products, biologically active compounds and building blocks for organic synthesis is becoming more and more attractive for synthetic organic chemists.[3] This is caused by the several advantages of such methods over the usual stepwise formation of individual bonds. The obviation of time- and cost-consuming separation steps and the high-atom economy are important attributes, and make these methods ideally suited for a sustainable chemistry. Numerous classical multicomponent reaction (MCR) classics use the in situ condensation of aldehydes, amines or amides to give reactive imine or enamine derivatives, which subsequently react with other different components. Typical examples include the Mannich[4] and Strecker[5] reaction, the Hantzsch pyrrole synthesis,[6] the Biginelli synthesis of dihydropyrimidines,[7] and the four-component Bucherer−Bergs reaction,[8] as well as the prominent Ugi-4CR.[9] Interestingly, the use of transition-metal catalysts, e.g. Pd complexes, enables the development of new variants of MCRs. Here, a prominent example is the amidocarbonylation of aldehydes to give *N*-acyl α-amino acids.[10]

More recently, we have developed mulicomponent reactions by taking advantage of the intermediacy of 1-(*N*-acylamino)-1,3-butadienes,[11] which are formed by the condensation of an amide with simple or α,β-unsaturated aldehydes. In the presence of electron-deficient dienophiles, a Diels−Alder reaction affords the three-component MCR product (Scheme 1).

To date, this AAD reaction (*a*mide, *a*ldehyde, *d*ienophile) has been developed as a powerful tool for the synthesis of highly substituted cyclohexene derivatives.[12] Further successful applications include the preparation of substituted alkyl phthalates,[13] anilines,[14] and luminols.[15]

Herein, we report an extension of our AAD reaction, which led to a novel method for the synthesis of "butterfly"-like bicyclo[2.2.2]oct-2-enes directly from ubiquitously available α,β-unsaturated aldehydes and dienophiles.

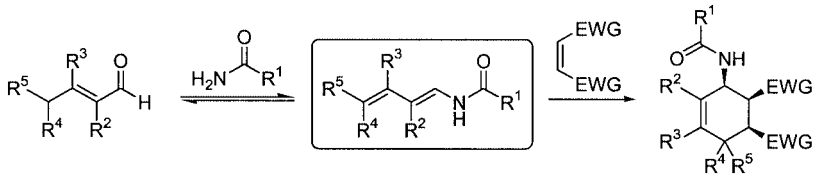
Results and Discussion

While studying the three-component reaction of acetamide, 2-methyl-2-pentenal and *N*-methyl maleimide in detail we observed the formation of small amounts (< 25% yield) of the diazatetradecene **1** as by-product at higher reaction temperatures (> 120 °C). As shown in Scheme 2, we assumed that **1** is formed by a remarkable sequence of enamide **1a** formation, an *endo*-selective Diels−Alder reaction to **1b**, and 1,4-elimination of acetamide from the resulting *cis*-4-(*N*-acetylamino)-5,7-dimethyl-1,3-dioxo-2,3,3a,4,7,7a-hexahydro-1*H*-isoindole to give the corresponding 1,3-cyclohexadiene **1c**, which then undergoes another selective Diels−Alder cycloaddition with maleimide to the final diazatetradecene **1**.

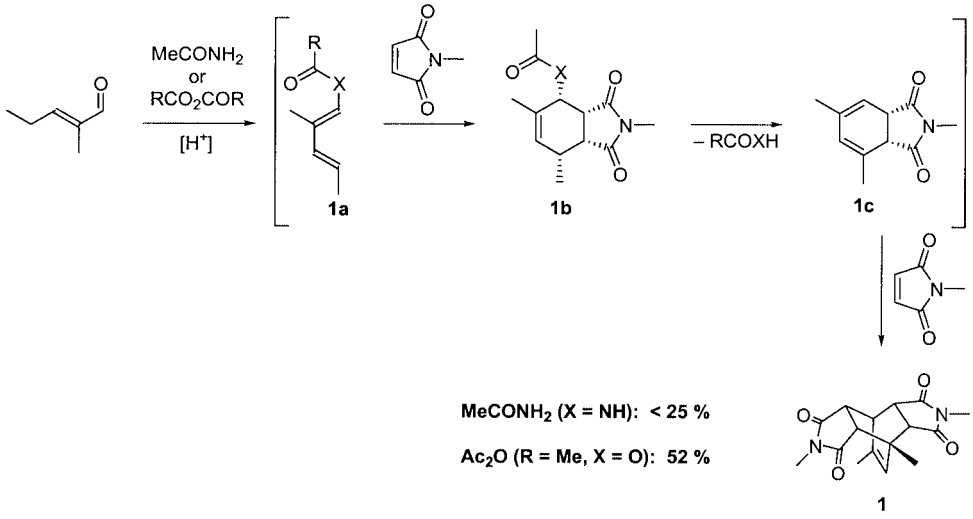
A literature search revealed that these tetracyclic compounds constitute interesting building blocks with promising biological activity. For example, several derivatives of the structurally related mitindomide, a 1:2 photoadduct of benzene and maleimide, were proven to exhibit high antitumor activity.[16] Furthermore, these structures provide the opportunity for chemical manipulation towards other attractive bicyclo[2.2.2]octane derivatives and cage molecules. Despite the interesting properties of the products, there are

[a] Leibniz-Institut für Organische Katalyse an der Universität Rostock e.V.,
Buchbinderstr. 5−6, 18055 Rostock, Germany
Fax: (internat) + 49-381-46693-24
E-mail: matthias.beller@ifok.uni-rostock.de

 DOI: 10.1002/ejoc.200400563



Scheme 1. Formation and Diels−Alder reaction of *N*-acylaminodienes

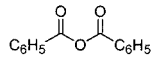
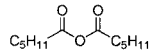
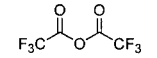


Scheme 2. Mechanism for the formation of the diazatetradecene **1** from 2-methyl-2-pentenal

only very few literature examples that report on the synthesis of related structures by Diels−Alder reactions with α,β-unsaturated aldehydes or pyrones or indoles.[17]

Thus, we decided to investigate this novel reaction sequence more closely. Based on our experience with the AAD reaction, we anticipated that elimination of acetamide towards the intermediate 1,3-cyclohexadiene is slow and therefore rate-determining. Obviously, oxygen nucleophiles such as carboxylate anions would constitute superior leaving groups under the (acidic) reaction conditions. Consistently, we studied the model reaction of 2-methyl-2-pentenal and *N*-methylmaleimide in the presence of various carboxylic acid anhydrides. Selected experiments of this optimization study are shown in Table 1. A primary solvent screening proved toluene to be a superior solvent with respect to the formation of the intermediate 1-acyloxy-1,3-butadienes. Hence, all of the following reactions were run in this solvent.

Table 1. Screening of reaction conditions for the synthesis of **1**

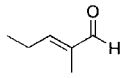
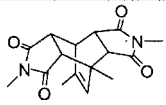
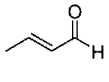
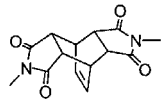
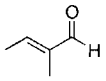
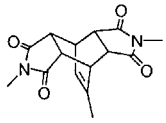
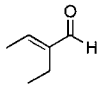
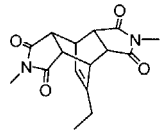
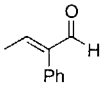
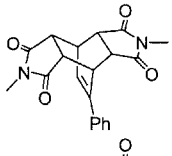
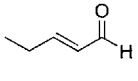
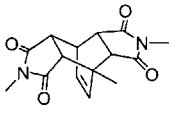
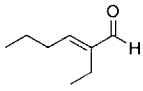
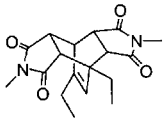
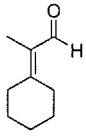
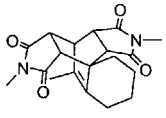
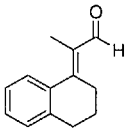
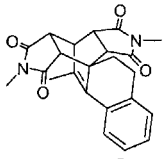
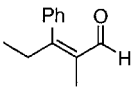
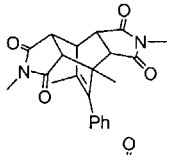
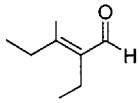
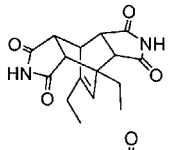
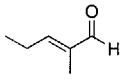
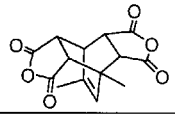
Entry	Anhydride	*T* [°C]	*T* [h]	Yield of **1** [%]
1		80	16	–
2		110	16	3
3		110	40	24
4		140	16	25
5		140	40	52
6		140	16	6
7		140	40	7
8		140	16	27
9		140	40	46
10		140	16	68
11		140	40	82
12		140	64	85

In the presence of acetic anhydride, low to moderate yields (up to 52%) were obtained (Table 1, Entries 1−5). In order to observe significant formation of **1** elevated temperature (> 120 °C) and long reaction times are required (24−40 h). The use of other alkane- and arenecarboxylic anhydrides was found to be inferior (Table 1, Entries 6−9). However, to our delight, the use of trifluoroacetic anhydride resulted in improved yields of **1** (up to 85%, Table 1, Entry 12). The selective 1-acyloxy-1,3-diene formation and the twofold Diels−Alder reaction with this high yield is especially remarkable when considering the numerous side reactions that are likely to proceed under these conditions (aldol condensations, oligomerizations, aromatization).

We then aimed at the diversification of the general "butterfly"-scaffold by employing various substituted α,β-unsaturated aldehydes to the optimized set of conditions (Table 2). The best results were obtained by employing 2-ethyl-2-butenal, which was smoothly converted into the desired product in 92% yield (Table 2, Entry 4). It is interesting to note that a clever choice of reactants can result in the generation of products with up to six annulated ring systems in one step (Table 2, Entry 9)! Apart from *N*-methylmaleimide, maleimide and maleic anhydride are also shown to be suitable dienophiles in this reaction sequence (Table 2, Entries 11 and 12).

Although several equilibrating cyclohexadiene isomers can be produced upon elimination of trifluoroacetic acid, the reactions selectively gave only one product. Thus, both

Table 2. Synthesis of substituted bicyclo[2.2.2]oct-2-ene derivatives; reaction conditions: trifluoroacetic anhydride (4.5 mmol), aldehyde (3.0 mmol), dienophile (9.0 mmol), *p*-TSA (4 mol %), toluene (20 mL), 140 °C, 40 h

Entry	Aldehyde	Dienophile X =	Product		Yield [%]
1		NMe		**1**	82
2		NMe		**2**	85
3		NMe		**3**	85
4		NMe		**4**	92
5		NMe		**5**	81
6		NMe		**6**	78
7		NMe		**7**	86
8		NMe		**8**	50
9		NMe		**9**	73
10		NMe		**10**	26[a]
11		NH		**11**	83
12		O		**12**	60

[a] 64 h.

cycloaddition reactions to the intermediate 1-acyloxy-1,3-diene and cyclohexadiene species proceed with high *endo* preference in all cases.

NMR spectra of **1**−**12** exhibit only one set of signals for the two dihydromaleimide/dihydromaleic anhydride moieties, and the ^{1}H resonances have double intensities. Consistently, the isolated tetracyclic adducts are symmetric with respect to an internal mirror plane. This structural assignment is proven by the X-ray analysis of **11** (Figure 1).[18] Here, suitable crystals were obtained by crystallization from ethyl acetate.

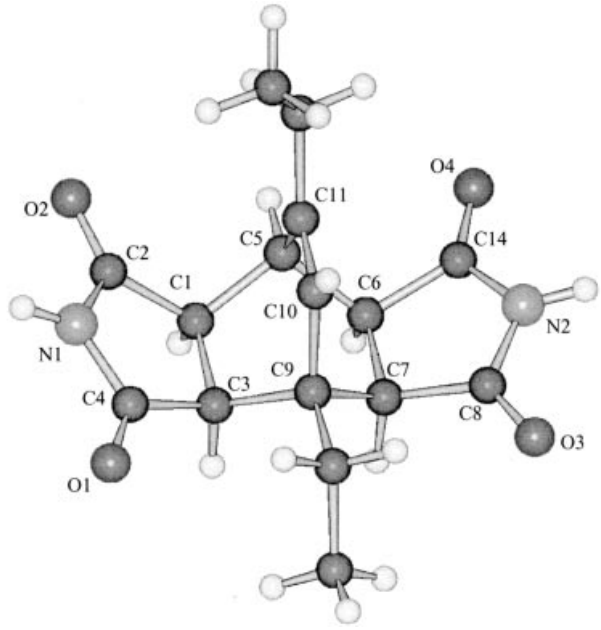


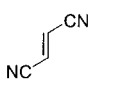
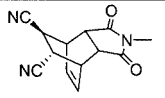
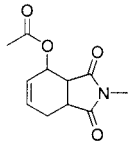
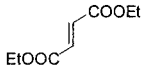
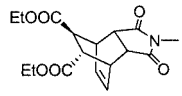
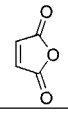
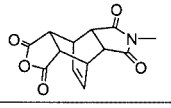
Figure 1. Crystal structure of **11**; selected bond lengths [Å]: C1−C2 1.511 (3); C2−N1 1.382 (2); C1−C3 1.546 (3); C1−C5 1.537(3); C5−C11 1.334(3); C10−11 1.334(3); C9−C10 1.518(2); C3−C9 1.560(3); selected bond angles [°]: C5−C1−C3 110.4(2); C11−C5−C1 107.74 (14); C10−C11−C5 112.9(2); C2−C1−C5 111.6(2); C2−C1−C3 104.92(15)

Enhanced structural diversification was realized by adoption of a two-step procedure with different dienophiles (Table 3). Exemplified by the reactions with crotonaldehyde, sequential condensations were performed that involved isolation of the *N*-methylmaleimide adduct in 61% yield.[19] Consumption thereof, by performing an additional reaction step in the presence of secondary dienophiles like maleic anhydride, fumarodinitrile, and diethyl fumarate, afforded the desired unsymmetrical bicyclo[2.2.2]oct-2-enes in good yield (60−74%, Table 3, Entries 1−3).

Conclusions

In summary, we developed a novel multicomponent reaction for the synthesis of highly functionalized bicyclo[2.2.2]-oct-2-enes, which provides an easy entry into this class of compounds and allows numerous further structural manipulations. The underlying domino condensation/

Table 3. Synthesis of mixed adducts by sequential AAD reaction, elimination and Diels−Alder reaction; reaction conditions: *cis*-4-acetoxy-1,3-dioxo-2,3,3a,4,7,7a-hexahydro-1*H*-isoindole (2.25 mmol), dienophile (6.75 mmol), *p*-TSA (2 mol %), toluene (10 mL), 140 °C, 72 h

Entry	Substrate	Secondary dienophile	Product		Yield [%]
1				**13**	74
2				**14**	73
3				**15**	60

Diels−Alder elimination/Diels−Alder reaction sequence with carboxylic anhydrides, aldehydes, and dienophiles exhibits a marked increase in structural complexity, as six stereogenic centers are formed in an operationally simple one-pot procedure.

Experimental Section

Procedure A: Trifluoroacetic anhydride (4.5 mmol), α,β-unsaturated aldehyde (3 mmol), dienophile (9 mmol) and *p*-toluenesulfonic acid monohydrate (4 mol %) were combined in a pressure tube, and toluene (20 mL) was added. The reaction mixture was stirred at 140 °C for 40−64 h. After cooling, all volatile compounds were removed under reduced pressure. Silica gel flash chromatography (*n*-heptane/EtOAc) afforded the corresponding products.

Procedure B: *cis*-4-Acetoxy-1,3-dioxo-2,3,3a,4,7,7a-hexahydro-1*H*-isoindole (2.25 mmol), dienophile (6.75 mmol) and *p*-toluenesulfonic acid monohydrate (2 mol %) were combined in a pressure tube, and toluene (10 mL) was added. The reaction mixture was stirred at 140 °C for 72 h. After cooling, all volatile compounds were removed under reduced pressure. Silica gel flash chromatography (*n*-heptane/EtOAc) afforded the corresponding products.

1,4,10,14-Tetramethyl-4,10-diazatetracyclo[5.5.2.0^{2,6}.0^{8,12}]tetradec-13-ene-3,5,9,11-tetraone (1): Procedure A. 40 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.11. Yield: 82%. Colorless solid. M.p. 212−214 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 5.36 [s, 1 H, C(CH$_3$)C*H*=C(CH$_3$)], 3.19 [d, *J* = 2.97 Hz, 1 H, HC=C(CH$_3$)C*H*CH], 3.15 (m, 2 H, 2 CHC*H*CO), 2.79 (m, 2 H, 2 CH$_3$CC*H*CO), 2.70 (s, 6 H, 2 CONC*H*$_3$), 1.64 (s, 3 H, C*H*$_3$C=CH), 1.49 (s, 3 H, C=CHCC*H*$_3$) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]DMSO): δ = 177.2 (2 *C*ONCH$_3$), 176.5 (2 *C*ONCH$_3$), 139.0 [CH*C*(CH$_3$)=CH], 126.7 [C(CH$_3$)=*C*HCH], 48.0 and 43.5 (*C*HCONCH$_3$), 38.2 (=CH*C*HCH), 36.2 [C=CH*C*(CH$_3$)CH], 24.2 (2 CONC*H*$_3$), 21.0 (HC=C*C*H$_3$), 19.2 (C=CHC*C*H$_3$) ppm. MS (EI, 70 eV): *m*/*z* (%) = 302 (52) [M]$^+$, 191 (48), 106 (100), 91 (29), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3445 (m), 3048 (w), 2936 (m), 1645 (s), 1418 (s) cm^{-1}. HR MS (EI): calcd. for $C_{16}H_{18}N_2O_4$: 302.12666; found 302.12464 [M]$^+$.

4,10-Dimethyl-4,10-diazatetracyclo[5.5.2.0^{2,6}.0^{8,12}]tetradec-13-ene-3,5,9,11-tetraone (2): Procedure A. 40 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.25. Yield: 85%. Colorless solid. M.p. 197 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 6.01 (dd, *J* = 1.18 Hz and *J* = 2.97 Hz, 2 H, *H*C=C*H*), 3.35 (m, 2 H, 2 HC=CHC*H*), 3.16 (s, 4 H, 4 CHC*H*CO), 2.71 (s, 6 H, 2 CONC*H*$_3$) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]DMSO): δ = 177.5 (4 *C*ONCH$_3$), 130.8 (*C*H=*C*H), 42.3 (4 CH*C*HCO), 33.3 (2 CH=CH*C*HCH), 24.3 (2 CONC*H*$_3$) ppm. MS (EI, 70 eV): *m*/*z* (%) = 274 (79) [M]$^+$, 163 (100), 104 (28), 78 (74), 40 (19), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3458 (m), 3087 (w), 2987 (m), 2976 (m), 2931 (m), 1697 (s), 1433 (s), 967 (s), 612 (s) cm^{-1}. HR MS (EI): calcd. for $C_{14}H_{14}N_2O_4$: 274.09536; found 274.09480 [M]$^+$.

4,10,14-Trimethyl-4,10-diazatetracyclo[5.5.2.0^{2,6}.0^{8,12}]tetradec-13-ene-3,5,9,11-tetraone (3): Procedure A. 40 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.12. Yield: 85%. Colorless solid. M.p. 213 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 5.57 [d, *J* = 5.9 Hz, 1 H, *H*C=C(CH$_3$)], 3.61 (m, 1 H, C=CHC*H*CH), 3.16 (m, 2 H, 2 CHC*H*CO), 3.09 [m, 1 H, HC=C(CH$_3$)C*H*CH], 2.70 (s, 6 H, 2 CONC*H*$_3$), 1.48 (d, *J* = 1.38 Hz, 3 H, HC=CC*H*$_3$) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]DMSO): δ = 177.6 (2 *C*ONCH$_3$), 177.4 (2 *C*ONCH$_3$), 140.2 [CH*C*(CH$_3$)=CH], 121.4 [C(CH$_3$)=*C*HCH], 43.0 and 42.2 (2 *C*HCONCH$_3$), 38.4 (C=CH*C*HCH), 34.1 [HC=C(CH$_3$)*C*HCH], 24.3 (2 CONC*H*$_3$), 21.0 (HC=C*C*H$_3$) ppm. MS (EI, 70 eV): *m*/*z* (%) = 288 (85) [M]$^+$, 177 (18), 112 (21), 92 (100), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3442 (m), 2954 (m), 2919 (m), 1709 (s), 1434 (s), 784 (s) cm^{-1}. HR MS (EI): calcd. for $C_{15}H_{16}N_2O_4$: 288.11101; found 288.10972 [M]$^+$.

14-Ethyl-4,10-dimethyl-4,10-diazatetracyclo[5.5.2.0^{2,6}.0^{8,12}]tetradec-13-ene-3,5,9,11-tetraone (4): Procedure A. 40 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.13. Yield: 92%. Colorless solid. M.p. 172−175 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 5.55 [dd, *J* = 1.38 Hz and *J* = 4.75 Hz, 1 H, C(Et)=C*H*CH], 3.29 [m, 1 H, HC=C(Et)C*H*CHCO], 3.20 (m, 1 H, C=CC*H*CH), 3.14 (m, 2 H, 2 CHC*H*CO), 2.71 (s, 6 H, 2 CONC*H*$_3$), 1.77 (m, 2 H, CH$_3$C*H*$_2$C=CH), 0.71 (t, *J* = 7.33 Hz, 3 H, C*H*$_3$CH$_2$C=CH) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]DMSO): δ = 177.6 (2 *C*ONCH$_3$), 177.4 (2 *C*ONCH$_3$), 145.5 [CH=*C*(Et)CH], 120.1 [C(Et)=*C*HCH], 43.0 [2 C(Et)CH*C*HCO], 42.4 (2 C=CHCH*C*H), 37.6 [C(Et)*C*HCHCO], 33.9 (C=CH*C*HCH), 27.5 (2 CONC*H*$_3$), 24.2 (CH$_3$*C*H$_2$C=CH), 11.3 (*C*H$_3$CH$_2$C=CH) ppm. MS (EI, 70 eV): *m*/*z* (%) = 302 (100) [M]$^+$, 287 (46), 191 (24), 112 (42), 106 (86), 91 (64), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3450 (m), 3062 (w), 2961 (m), 1700 (s), 1436 (s), 973 (s), 782 (s) cm^{-1}. HR MS (EI): calcd. for $C_{16}H_{18}N_2O_4$: 302.12666; found 302.12655 [M]$^+$.

4,10-Dimethyl-14-phenyl-4,10-diazatetracyclo[5.5.2.0^{2,6}.0^{8,12}]-tetradec-13-ene-3,5,9,11-tetraone (5): Procedure A. 40 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.21. Yield: 81%. Colorless solid. M.p. 247−249 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.45−7.28 (m, 5 H, *H*-Ar), 6.37 (m, 1 H, CHC*H*=CPh), 4.00 (m, 1 H, PhCC*H*CH), 3.63 (m, 1 H, PhC=CHC*H*CH), 3.46 (m, 2 H, 2 CHC*H*CON), 3.38 (dd, *J* = 2.77 Hz and *J* = 5.15 Hz, 2 H, 2 PhCCHC*H*CON), 2.76 (s, 6 H, 2 CONCH$_3$) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]DMSO): δ = 177.5 (2 *C*ONCH$_3$), 177.2 (2 *C*ONCH$_3$), 142.1 (*i*-*C*-Ar), 128.6 and 128.0 (2 *o*-*C*H-Ar and 2 *m*-*C*H-Ar), 125.2 (*p*-*C*H), 137.0 (Ph*C*=CH), 123.3 (CHC*H*=CPh), 42.7 and 42.6 (2 C*H*CON), 36.5 (PhC*C*HCH), 34.4 (CH*C*HCH), 24.3 (2 CONC*H*$_3$) ppm. MS (EI, 70 eV): *m*/*z* (%) = 350 (75) [M]$^+$, 239 (22), 154 (100), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3449 (m), 3054 (w), 3001 (w), 2967 (m), 2952 (m), 1697 (s), 1436 (s), 971 (s), 617 (m) cm^{-1}. HR MS (EI): calcd. for $C_{20}H_{18}N_2O_4$: 350.12666; found 350.12647 [M]$^+$.

1,4,10-Trimethyl-4,10-diazatetracyclo[5.5.2.0^{2,6}.0^{8,12}]tetradec-13-ene-3,5,9,11-tetraone (6): Procedure A. 40 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.13. Yield: 78%. Colorless solid. M.p. 228−230 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 5.89 [dd, J = 2.01 Hz and J = 6.14 Hz, 1 H, CHC*H*=CHC(CH$_3$)], 5.73 [d, J = 8.32 Hz, 1 H, C(CH$_3$)C*H*=CH], 3.23 (m, 1 H, CH=CHC*H*), 3.10 (dd, J = 2.97 Hz and J = 4.95 Hz, 2 H, 2 CHC*H*CO), 2.77 [m, 2 H, 2 C(CH$_3$)C*H*CO], 2.63 (s, 6 H, 2 CONC*H*$_3$), 1.63 (s, 3 H, CC*H*$_3$) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]DMSO): δ = 177.3 (2 *C*ONCH$_3$), 176.4 (2 *C*ONCH$_3$), 135.8 and 129.6 (C*H*=C*H*), 47.4 (2 CH*C*HCONCH$_3$), 43.7 (2 C(CH$_3$)*C*HCO), 40.1 (C=CH*C*HCH), 33.1 [C=CH*C*(CH$_3$)CH], 24.3 (2 CON*C*H$_3$), 19.3 (C=CHCH*C*H$_3$) ppm. MS (EI, 70 eV): *m*/*z* (%) = 288 (13) [M]$^+$, 177 (23), 112 (17), 92 (100), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3438 (m), 3051 (w), 2993 (m), 2949 (m), 1696 (s), 1437 (s), 779 (m) cm^{-1}. HR MS (EI): calcd. for $C_{15}H_{16}N_2O_4$: 288.11101; found 288.11106 [M]$^+$.

1,14-Diethyl-4,10-dimethyl-4,10-diazatetracyclo[5.5.2.0^{2,6}.0^{8,12}]-tetradec-13-ene-3,5,9,11-tetraone (7): Procedure A. 40 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.14. Yield: 86%. Colorless solid. M.p. 167−168 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 5.24 [s, 1 H, C(Et)=C*H*CH] 3.18 (m, 2 H, 2 CHC*H*CON), 3.14 [d, J = 2.97 Hz, 1 H, HC=C(Et)C*H*CH] 3.02 [m, 2 H, 2 CH(Et)C*H*CON] 2.69 (s, 6 H, 2 CONC*H*$_3$), 2.17 (m, 2 H, CH$_3$C*H*$_2$C=CH), 1.81 (m, 2 H, CC*H*$_2$CH$_3$), 1.13 (t, J = 7.23 Hz, 3 H, C*H*$_3$CH$_2$C=), 0.72 (t, J = 7.43 Hz, 3 H, C*H*$_3$CH$_2$CH) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]DMSO): δ = 177.4 (2 *C*ONCH$_3$), 176.2 (2 *C*ONCH$_3$), 144.3 [CH=*C*(Et)CH], 126.0 [C(Et)=*C*HCH], 43.7 (2 C(Et)CH*C*HCO), 43.3 (2 C=CHCH*C*H), 43.1 [C(Et)*C*HCHCO], 37.6 [C=CH*C*(Et)CH], 27.4 (2 CON*C*H$_3$), 24.2 (CH$_3$*C*H$_2$C=), 23.6 (CH$_3$*C*H$_2$CH), 11.3 (*C*H$_3$CH$_2$C=), 8.1 (*C*H$_3$CH$_2$CH) ppm. MS (EI, 70 eV): *m*/*z* (%) = 330 (75) [M]$^+$, 315 (17), 219 (100), 134 (86), 119 (32), 112 (24), 105 (48), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3439 (m), 3050 (w), 2979 (s), 2966 (s), 2939 (m), 2888 (w), 1701 (s), 779 (s) cm^{-1}. HR MS (EI): calcd. for $C_{18}H_{22}N_2O_4$: 330.15796; found 330.15737 [M]$^+$.

4,10,14-Trimethylcyclohexa[*m*]-4,10-diazatetracyclo[5.5.2.0^{2,6}.0^{8,12}]-tetradec-13-ene-3,5,9,11-tetraone (8): R_f (SiO_2; *n*-heptane/EtOAc, 1:1): 0.13. Yield: 50%. Colorless solid. M.p. 199−201 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.10 (m, 1 H, COCHC*H*CHCO), 3.07 (dd, J = 7.74 Hz and J = 3.17 Hz, 2 H, COC*H*CHC*H*CO), 2.80 (d, J = 7.73 Hz, 2 H, COC*H*CC*H*CO), 2.70 (s, 6 H, 2 CONC*H*$_3$), 2.57 (m, 2 H, C*H*$_2$), 1.93 (t, J = 5.94 Hz, 2 H, C*H*$_2$), 1.51 (m, 2 H, C*H*$_2$), 1.43 (s, 3 H, C=CC*H*$_3$), 1.25 (m, 2 H, C*H*$_2$) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]DMSO): δ = 177.3 (2 *C*ONCH$_3$), 177.2 (2 *C*ONCH$_3$), 131.7 and 129.2 (*C*=*C*), 49.3 (CO*C*HC*C*HCO), 43.0 (CO*C*HCH*C*HCO), 41.3 (COCH*C*HCHCO), 27.5 and 25.4 and 22.4 and 21.3 (4 *C*H$_2$), 24.3 (2 CON*C*H$_3$), 17.3 (C=C*C*H$_3$) ppm. MS (EI, 70 eV): *m*/*z* (%) = 342 (29) [M]$^+$, 231 (100), 146 (58), 131 (21), 118 (15), 112 (16), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3446 (m), 2931 (m), 2870 (m), 2827 (w), 1771 (m), 1701 (s), 1437 (m), 1286 (m), 1129 (m), 776 (m) cm^{-1}. HR MS (EI): calcd. for $C_{19}H_{22}N_2O_4$: 342.15796; found 342.15744 [M]$^+$.

4,10,14-Trimethyl-1,2,3,4-tetrahydronaphthaleno[1,2-*m*]-4,10-diazatetracyclo[5.5.2.0^{2,6}.0^{8,12}]tetradec-13-ene-3,5,9,11-tetraone (9): Procedure A. 40 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.11. Yield: 73%. Colorless solid. M.p. 162−163 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.09−7.06 (m, 4 H, C*H*-Ar), 3.35 (t, J = 3.2 Hz, 1 H, CH$_3$CC*H*), 3.27 (dd, J = 8.1, J = 3.2 Hz, 2 H, 2 COC*H*CH), 3.00 (d, J = 8.1 Hz, 2 H, 2 COC*H*C), 2.72 (t, J = 6.2 Hz, 2 H, C*H*$_2$), 2.62 (s, 6 H, 2 CONC*H*$_3$), 2.57 (t, J = 6.2 Hz, 2 H, C*H*$_2$), 1.94 (s, 3 H, C*H*$_3$C) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]DMSO): δ = 177.1 (2 *C*ONCH$_3$), 176.8 (2 *C*ONCH$_3$), 139.1 (*C*), 132.6 (*C*), 131.7 (*C*), 130.1 (*C*), 127.8 (*C*H-Ar), 127.4 (*C*H-Ar), 127.0 (*C*H-Ar), 125.6 (*C*H-Ar), 48.7 (2 CO*C*HC), 44.0 (COCH*C*), 43.6 (2 CO*C*HCH), 40.6 (COCH*C*H), 27.2 (*C*H$_2$), 26.2 (*C*H$_2$), 24.4 (2 CON*C*H$_3$), 21.6 (*C*H$_3$C) ppm. MS (EI, 70 eV): *m*/*z* (%) = 390 (100) [M]$^+$, 279 (43) [M − C$_5$H$_5$NO$_2$]$^+$, 278 (51), 264 (7), 219 (6), 194 (62) [M − C$_5$H$_5$NO$_2$ − C$_3$H$_3$NO$_2$]$^+$, 178 (56), 165 (12), 113 (71), 58 (12), 43 (15), 29 (11), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3442 (m), 3030 (w), 3015 (w), 2939 (s), 2879 (m), 1765 (s), 1697 (vs), 1481 (m), 1439 (vs), 1384 (s), 1315 (s), 1289 (vs), 1230 (s), 1178 (m), 1160 (s), 1133 (s), 1078 (w), 1047 (w), 1018 (w), 997 (m), 977 (s), 928 (w), 914 (w), 840 (w), 822 (w), 804 (w), 772 (vs), 744 (w), 699 (w), 685 (w), 644 (m), 615 (m), 595 (w), 540 (w), 482 (w), 446 (w), 408 (m) cm^{-1}. HR MS (EI): calcd. for $C_{23}H_{22}N_2O_4$: 390.15796; found 390.15506 [M]$^+$.

1,4,10,14-Tetramethyl-13-phenyl-4,10-diazatetracyclo-[5.5.2.0^{2,6}.0^{8,12}]tetradec-13-ene-3,5,9,11-tetraone (10): Procedure A. 64 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.16. Yield: 26%. Colorless solid. M.p. 255 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.32−7.19 and 6.54−6.46 (m, 5 H, *H*-Ar), 3.31 (d, J = 2.97 Hz, 1 H, CHC*H*CH), 3.28 (dd, J = 3.17, J = 7.92 Hz, 2 H, C*H*CHC*H*), 2.94 (d, J = 7.92 Hz, 2 H, C*H*CC*H*), 2.83 (s, 6 H, 2 CONC*H*$_3$), 1.42 (s, 3 H, C=CC*H*$_3$), 1.31 (s, 3 H, C*H*$_3$CCH) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]DMSO): δ = 177.3 (2 CONCH$_3$), 176.8 (2 CONCH$_3$), 138.0 and 136.4 (*C*=*C*), 133.3 (*i*-*C*-Ar), 128.3 and 128.1 (2 *o*-*C*H-Ar and 2 *m*-*C*H-Ar), 126.9 (*p*-*C*H-Ar), 48.7 (2 *C*HCC*C*H), 43.3 (2 *C*HCH*C*H), 42.8 (CH*C*CH), 39.2 (CH*C*HCH), 24.4 (2 CON*C*H$_3$), 19.1 (C=C*C*H$_3$), 18.9 (CHC*C*H$_3$) ppm. MS (EI, 70 eV): *m*/*z* (%) = 378 (73) [M]$^+$, 267 (60), 182 (100), 167 (37), 112 (15), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3442 (m), 3074 (w), 2994 (w), 2979 (w), 2953 (m), 2909 (w), 1767 (s), 1696 (s), 1433 (s), 972 (m) cm^{-1}. HR MS (EI): calcd. for $C_{22}H_{22}N_2O_4$: 378.15796; found 378.15317 [M]$^+$.

1,14-Diethyl-4,10-diazatetracyclo[5.5.2.0^{2,6}.0^{8,12}]tetradec-13-ene-3,5,9,11-tetraone (11): Procedure A. 40 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.15. Yield: 83%. Colorless solid. M.p. > 311 °C (dec). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 11.09 (s, 2 H, 2 CON*H*CO), 5.34 [s, 1 H, C(Et)=C*H*CH], 3.09 [q, J = 1.45 Hz, 1 H, C(Et)C*H*-CON], 3.06 [dd, J = 3.17 Hz and J = 4.75 Hz, 2 H, 2 C(Et)CHC*H*CO], 2.91 [d, J = 7.9 Hz, 2 H, 2 C(Et)C*H*CO], 2.15 (q, J = 7.3 Hz, 2 H, CH$_3$C*H*$_2$C=), 1.88 (dq, J = 1.6 Hz and J = 7.3 Hz, 2 H, CHC*H*$_2$CH$_3$), 1.07 (t, J = 7.3 Hz, 3 H, C*H*$_3$CH$_2$C=), 0.82 (t, J = 7.3 Hz, 3 H, C*H*$_3$CH$_2$CH) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]DMSO): δ = 178.7 (2 *C*ONCH$_3$), 177.8 (2 *C*ONCH$_3$), 144.1 [CH=*C*(Et)CH], 125.8 [C(Et)=*C*HCH], 45.0 [2 C(Et)CH*C*HCO], 44.4 (2 C=CHC*C*HCO), 42.9 [C(Et)*C*HCHCO], 37.4 [C=CH*C*(Et)CH], 27.5 (CH$_3$*C*H$_2$C=), 23.5 (CH$_3$*C*H$_2$CH), 10.9 (*C*H$_3$CH$_2$C=C), 8.0 (*C*H$_3$CH$_2$CH) ppm. MS (EI, 70 eV): *m*/*z* (%) = 302 (28) [M]$^+$, 205 (100), 134 (72), 105 (43), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3180 (br. m), 3077 (m), 2969 (m), 2924 (w), 2877 (w), 2775 (w), 1768 (s), 1704 (vs), 1461 (w), 1441 (w), 1353 (s), 1320 (s), 1205 (s), 1167 (s), 1136 (m), 1042 (m), 1005 (m), 828 (m), 709 (m), 633 (m) cm^{-1}. HR MS (EI): calcd. for $C_{16}H_{18}N_2O_4$: 302.12666; found 302.12682 [M]$^+$.

1,4,10,14-Tetramethyl-4,10-dioxatetracyclo[5.5.2.0^{2,6}.0^{8,12}]tetradec-13-ene-3,5,9,11-tetraone (12): Procedure A. 40 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.19. Yield: 60%. Colorless solid. M.p. 284 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 5.69 [s, 1 H, CH(CH$_3$)C*H*=C], 3.67 (dd, J = 3.17, J = 5.35 Hz, 2 H, 2 CHC*H*COO), 3.28 (m, 1 H, CHC*H*CH), 3.25 [m, 2 H, 2 C(CH$_3$)C*H*COO], 1.63 (m, 3 H, CC*H*$_3$), 1.62 (s, 3 H, C=CC*H*$_3$) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]DMSO): δ = 172.4 (2 CHCOO), 171.1 (2 CH*C*OO), 141.3

(CH_3C=CH), 128.3 [C(CH_3)CH=C), 48.4 [C(CH_3)CHCOO], 44.4 (CHCHCOO), 38.3 (CHCHCH), 21.2 (CH_3C=CH), 18.1 [CHC(CH_3)] ppm. MS (EI, 70 eV): *m/z* (%) = 276 (6) $[M]^+$, 178 (18), 150 (18), 106 (100), 91 (45), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3433 (m), 2968 (w), 2946 (w), 1854 (m), 1783 (s)1221 (s), 1094 (s), 935 (s), 755 (m) 414 (m) cm^{-1}. HR MS (EI): calcd. for $C_{17}H_{18}N_2O_3$: 276.06339; found 276.06393 $[M]^+$.

4-Methyl-3,5-dioxo-4-azatricyclo[5.2.2.0^{2,6}]undec-10-ene-8,9-dicarbonitrile (13): Procedure B. 72 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.4. Yield: 74%. Colorless solid. M.p. 138 °C. ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 6.31 (m, 2 H, CH=CH), 3.69 and 3.39 (both m, both 1 H, CHCHCON), 3.37 and 3.28 (both m, both 1 H, CHCHCN), 3.14 and 2.83 (both m, both 1 H, =CHCHCH), 2.73 (s, 3 H, CONCH_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D_6]DMSO): δ = 176.9 and 176.6 (2 CONCH_3), 133.0 and 130.8 (CH=CH), 120.0 and 119.2 (CHCN), 41.6 and 38.9 (CHCHCON), 33.8 and 33.5 (CHCHCN), 30.8 and 29.8 (HC=CHCHCH), 24.5 (CONCH_3) ppm. MS (EI, 70 eV): *m/z* (%) = 241 (17) $[M]^+$, 163 (100), 129 (25), 77 (22), 51 (18), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3464 (m), 3065 (w), 3006 (w), 2949 (w), 2949 (m), 2922 (m), 2242 (m), 1783 (s), 1699 (s), 1440 (s), 739 (m) cm^{-1}. HR MS (EI): calcd. for $C_{13}H_{11}N_3O_2$: 241.08513; found 241.08322 $[M]^+$.

Diethyl 4-methyl-3,5-dioxo-4-azatricyclo[5.2.2.0^{2,6}]undec-10-ene-8,9-dicarboxylate (14): Procedure B. 72 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.35. Yield: 73%. Colorless oil. ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 6.21 and 6.02 (both m, both 1 H, CH=CH), 4.14 and 4.04 (both m, both 2 H, CH_3CH_2O), 3.36 and 3.28 (both m, both 1 H, CHCON), 3.14 (dd, *J* = 1.98 Hz and *J* = 3.76 Hz, 1 H, CHCHCOO), 3.10 (dd, *J* = 2.97, *J* = 4.95 Hz, 1 H, CHCHCOO), 2.86 (dd, *J* = 3.17, *J* = 4.95 Hz, 1 H, CH=CHCHCH), 2.79 (q, *J* = 2.84 Hz, 1 H, CH=CHCHCH), 2.69 (s, 3 H, CONCH_3), 1.19 (t, *J* = 7.03 Hz, 3 H, CH_2CH_3), 1.14 (t, *J* = 7.13 Hz, 3 H, CH_2CH_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D_6]DMSO): δ = 177.9 and 177.5 (2 CONCH_3), 172.2 and 172.0 (2 COO), 132.8 and 130.6 (2 CH=CH), 61.0 and 60.8 (2 CH_3CH_2O), 44.2 and 43.7 (2 CHCHCON), 42.9 and 34.0 (2 CHCHCOO), 33.9 and 29.5 (2 CHCHCH), 24.3 (CONCH_3), 14.0 and 13.9 (2 OCH_2CH_3) ppm. MS (EI, 70 eV): *m/z* (%) = 335 (58) $[M]^+$, 289 (36), 262 (34), 216 (25), 163 (26), 151 (38), 131 (21), 123 (21), 105 (31), 78 (100), 29 (80), no other peaks > 10%. IR (KBr): $\tilde{\nu}$ = 3449 (m), 3054 (w), 2965 (m), 2952 (w), 1770 (m), 1697 (s), 1436 (m), 971 (m) cm^{-1}. HR MS (EI): calcd. for $C_{17}H_{21}NO_6$: 335.13689; found 335.13656 $[M]^+$.

4-Methyl-10-oxa-4-azatetracyclo[5.5.2.0^{2,6}.0^{8,12}]tetradec-13-ene-3,5,9,11-tetraone (15): Procedure B. 72 h. R_f (SiO_2, *n*-heptane/EtOAc, 1:1): 0.26. Yield: 60%. Colorless solid. M.p. 344−345 °C. ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 6.19 (m, 2 H, CH=CH), 3.55 (m, 2 H, 2 CHCHCON), 3.41 (m, 2 H, 2 CHCHCOO), 3.21 (m, 2 H, 2 CHCHCH), 2.72 (s, 3 H, CONCH_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D_6]DMSO): δ = 177.1 (CONCH_3), 172.8 (COO), 131.7 (CH=CH), 43.5 (2 CHCON), 41.7 (2 CHCOO), 33.3 (2 CHCHCH), 24.3 ($CONCH_3$) ppm. MS (EI, 70 eV): *m/z* (%) = 261 (4) $[M]^+$, 189 (22), 104 (13), 78 (100), 51 (11), no other peaks > 10%. IR (KBr): $\tilde{\nu} = 1/\lambda$ = 3461 (w), 2952 (w), 1842 (m), 1769 (s), 1697 (s), 1438 (m), 1226 (m), 949 (m) 765 (m), 604 (m) cm^{-1}. HR MS (ESI): calcd. for $C_{17}H_{18}N_2O_3$: 262.07166; found 262.07100 $[M + H]^+$.

Acknowledgments

The authors thank S. Giertz, S. Buchholz, Dr. C. Fischer, Dr. W. Baumann, and H. Baudisch (all IfOK) for excellent technical and analytical assistance. Generous financial support from the State of Mecklenburg-Vorpommern (Landesforschungsschwerpunkt), the BMBF and the Fonds der Chemischen Industrie is gratefully acknowledged.

[1] [1a] L. F. Tietze, *Chem. Rev.* **1996**, *96*. 115. [1b] L. F. Tietze, F. Haunert, in *Stimulating Concepts In Chemistry* (Eds.: M. Shibasaki, J. F. Stoddart, F. Vögtle), Wiley-VCH, Weinheim **2000**, p. 39. [1c]L. F. Tietze, A. Modi, *Med. Res. Rev.* **2000**, *20*, 304. [1d] G. H. Posner, *Chem. Rev.* **1986**, *86*, 831. [1e] R. W. Armstrong, A. P. Combs, P. A. Tempest, S. D. Brown, T. A. Keating, *Acc. Chem. Res.* **1996**, *29*, 123.

[2] Review: A. Dömling, I. Ugi, *Angew. Chem. Int. Ed.* **2000**, *39*, 3168. For selected recent examples see: [2a] D. J. Vugts, H. Jansen, R. F. Schmitz, F. J. J. de Kanter, R. V. A. Orru, *Chem. Commun.* **2003**, 2594. [2b] R. Frey, S. G. Galbraith, S. Guelfi, C. Lamberth, M. Zeller, *Synlett* **2003**, 1536. [2c] C. Hulme, V. Gore, *Curr. Med. Chem.* **2003**, *10*, 51. [2d] G. Dyker, K. Breitenstein, G. Henkel, *Tetrahedron: Asymmetry* **2002**, *13*, 1929. [2e] R. Gamez−Montano, E. Gonzalez−Zamora, P. Potier, J. P. Zhu, *Tetrahedron* **2002**, *58*, 6351. [2f] R. Zimmer, A. Ziemer, M. Gruner, I. Brudgam, H. Hartl, H. U. Reissig, *Synthesis* **2001**, 1649. [2g] B. Beck, S. Hess, A. Dömling, *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1701. [2h] S. Heck, A. Dömling, *Synlett* **2000**, *2*, 424. [2i] A. de Meijere, S. Bräse, *J. Organomet. Chem.* **1999**, *76*, 88. [2j] H. Bienaymé, C. Hulme, G. Oddon, P. Schmitt, *Chem. Eur. J.* **2000**, *6*, 3321.

[3] A literature search in the Science Citation Index in July 2004 revealed that since 2000 more than 300 references are listed for the keywords multicomponent reactions and domino reactions.

[4] [4a] T. Akiyama, J. Itoh, K. Yokota, K. Fuchibe, *Angew. Chem. Int. Ed.* **2004**, *43*, 1566. [4b] N. Gommermann, C. Koradin, K. Polborn, P. Knochel, *Angew. Chem. Int. Ed.* **2003**, *42*, 5763. [4c] W. Notz, F. Tanaka, S. Watanabe, N. S. Chowdari, J. M. Turner, R. Thayumanaran, C. F. Barbas, III, *J. Org. Chem.* **2003**, *68*, 9624. [4d] Y. Hayashi, W. Tsuboi, I. Ashimine, T. Urushima, A. Shoji, K. Sakai, *Angew. Chem. Int. Ed.* **2001**, *40*, 2995. [4e] C. Schneider, O. Reese, *Angew. Chem. Int. Ed.* **2000**, *39*, 2948.

[5] [5a] L. Yet, *Angew. Chem. Int. Ed.* **2001**, *40*, 875. [5b] M. Takamura, Y. Hamashima, H. Usuda, M. Kanai, M. Shibasaki, *Angew. Chem. Int. Ed.* **2000**, *39*, 1650. [5c] M. S. Sigman, P. Vachal, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2000**, *39*, 1279. [5d] J. Li, W. Y. Jiang, K. L. Han, G. Z. He, C. Li, *J. Org. Chem.* **2003**, *68*, 8786. [5e] F. A. Davis, K. R. Prasad, P. J. Carroll, *J. Org. Chem.* **2002**, *67*, 7802.

[6] [6a] A. Dondoni, A. Massi, E. Minghini, V. Bertolasi, *Tetrahedron* **2004**, *60*, 2311. [6b] S. J. Garden, C. R. W. Guimaraes, M. B. Correa, C. A. F. de Oliveira, A. D. Pinto, R. B. de Alencasto, *J. Org. Chem.* **2003**, *68*, 8815. [6c] G. Sabitha, G. S. K. K. Reddy, C. S. Reddy, N. Fatima, J. S. Yadav, *Tetrahedron Lett.* **2003**, *44*, 4129.

[7] [7a] J. Shimokawa, K. Shirai, A. Tanatani, Y. Hashimoto, K. Nagasawa, *Angew. Chem. Int. Ed.* **2004**, *43*, 1559. [7b] J. S. Yadav, B. V. S. Reddy, P. Sridar, J. S. S. Reddy, Nagaiah, N. Lingaiah, P. S. Saiprasad, *Eur. J. Org. Chem.* **2004**, *3*, 552. [7c] F. Cohen, S. K. Collins, L. E. Overman, *Org. Lett.* **2003**, *5*, 4485. [7d] V. R. Choudhary, V. H. Tillu, V. S. Narkhede, H. B. Borate, R. D. Wakhardar, *Catal. Commun.* **2003**, *4*, 449. [7e] A. Dondoni, A. Massi, E. Minghini, S. Sabbatini, V. Bertolasi, *J. Org. Chem.* **2003**, *68*, 6172.

[8] [8a] J. Micova, B. Steiner, M. Koos, V. Langer, D. Gyepesova, *Synlett* **2002**, *10*, 1715. [8b] F. J. C. Martins, A. M. Viljoen, H. G. Kruger, J. Roscher, A. J. Joubert, P. L. Wessels, *Tetrahedron* **2001**, *57*, 1601.

[9] [9a] P. Cristau, J. P. Vors, J. P. Zhu, *Tetrahedron Lett.* **2003**, *44*, 5575. [9b] P. Cristau, J. P. Vors, J. P. Zhu, *Org. Lett.* **2001**, *3*, 4079.

[10] [10a] A. Enzmann, M. Eckert, W. Ponikwar, K. Polborn, S. Schneiderbauer, M. Beller, W. Beck, *Eur. J. Inorg. Chem.* **2004**,

1330. [10b] D. Gördes, H. Neumann, A. Jacobi von Wangelin, C. Fischer, K. Drauz, H.-P. Krimmer, M. Beller, *Adv. Synth. Cat.* **2003**, *34*, 510. [10c] D. A. Freed, M. C. Kozlowski, *Tetrahedron Lett.* **2001**, *42*, 3403. [10d] M. Beller, M. Eckert, *Angew. Chem. Int. Ed.* **2000**, *39*, 1010. [10e] M. Beller, M. Eckert, H. Geissler, B. Napierski, H.-P. Rebenstock, E. W. Holla, *Chem. Eur. J.* **1998**, *4*, 935. [10f] M. Beller, M. Eckert, F. Vollmüller, S. Bogdanovic, H. Geissler, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1494. [10g] M. Beller, M. Eckert, W. Moradi, H. Neumann, *Angew. Chem. Int. Ed.* **1999**, *38*, 1454. [10h] M. Beller, M. Eckert, E. W. Holla, *J. Org. Chem.* **1998**, *63*, 5658. [10i] M. Beller, W. A. Moradi, M. Eckert, H. Neumann, *Tetrahedron Lett.* **1999**, *40*, 4523. [10j] M. Beller, M. Eckert, W. A. Moradi, *Synlett* **1999**, *1*, 108. [10k] M. Beller, M. Eckert, F. Vollmüller, *J. Mol. Catal.* **1998**, *135*, 23.

[11] [11a] D. Gördes, A. Jacobi von Wangelin, S. Klaus, H. Neumann, D. Strübing, H. Jiao, W. Baumann, M. Beller, *Org. Biomol. Chem.* **2004**, *2*, 845. [11b] J. M. Janey, T. Iwama, S. A. Kozmin, V. H. Rawal, *J. Org. Chem.* **2000**, *65*, 9059. [11c] M. B. Smith, *Org. Prep. Proced. Int.* **1990**, *22*, 315. [11d] L. E. Overman, R. L. Freerks, C. B. Petty, L. A. Clizbe, R. K. Ono, G. F. Taylor, P. J. Jessup, *J. Am. Chem. Soc.* **1981**, *103*, 2816. [11e] W. Oppolzer, L. Bieber, E. Francotte, *Tetrahedron Lett.* **1979**, *16*, 4537.

[12] [12a] H. Neumann, A. Jacobi von Wangelin, D. Gördes, A. Spannenberg, M. Beller, *J. Am. Chem. Soc.* **2001**, *123*, 8398. [12b] A. Jacobi von Wangelin, H. Neumann, D. Gördes, S. Klaus, D. Strübing, M. Beller, *Chem. Eur. J.* **2003**, *9*, 4286. [12c] A. Jacobi von Wangelin, H. Neumann, D. Gördes, A. Spannenberg, M. Beller, *Org. Lett.* **2001**, *3*, 2895. [12d] H. Neumann, A. Jacobi von Wangelin, D. Gördes, A. Spannenberg, W. Baumann, M. Beller, *Tetrahedron* **2002**, *58*, 2381. [12e] D. Strübing, H. Neumann, S. Klaus, A. Jacobi von Wangelin, D. Gördes, M. Beller, P. Braiuca, C. Ebert, L. Gardossi, U. Kragl, *Tetrahedron* **2004**, *60*, 683. [12f] S. Klaus, S. Hübner, H. Neumann, D. Strübing, D. Gördes, M. Beller, *Adv. Synth. Catal.*, in press.

[13] H. Neumann, A. Jacobi von Wangelin, D. Gördes, S. Klaus, H. Jiao, A. Spannenberg, M. Beller, T. Krüger, C. Wendler, K. Thurow, N. Stoll, *Chem. Eur. J.* **2003**, *9*, 2273.

[14] H. Neumann, A. Jacobi von Wangelin, S. Klaus, D. Strübing, D. Gördes, M. Beller, *Angew. Chem. Int. Ed.* **2003**, *42*, 4503.

[15] H. Neumann, S. Klaus, M. Klawonn, D. Strübing, S. Hübner, D. Gördes, A. Jacobi von Wangelin, M. Lalk, M. Beller, *Z. Naturforsch., Teil B* **2004**, *59*, 431.

[16] [16a] D. Bryce-Smith, in *Photochemistry* (Ed.: D. Bryce-Smith), The Royal Society of Chemistry, London, **1985**, vol. 16. [16b] H. M. Deutsch, L. T. Gelbaum, M. McLaughlin, T. J. Fleischmann, L. L. Earnhart, R. D. Haugwitz, L. H. Zalkow, *J. Med. Chem.* **1986**, *29*, 2164.

[17] A previous example of the condensation of an α,β-unsaturated aldehyde with dienophiles has been reported in a patent application: [17a] Lonza A. G., DE 1020626, **1953**. For other preparations see: [17b] T. Shimo, K. Matsuo, K. Somekawa, O. Tsuge, *J. Heterocycl. Chem.* **1991**, *28*, 549. [17c] W. E. Noland, M. J. Konkel, M. S. Tempesta, R. D. Cink, D. M. Powers, E. O. Schlemper, C. L. Barnes, *J. Heterocycl. Chem.* **1993**, *30*, 183. [17d] F. Effenberger, Z. Ziegler, *Chem. Ber.* **1987**, *120*, 1339. [17e] M. Koreeda, M. A. Ciufolini, *J. Am. Chem. Soc.* **1982**, *104*, 2308. [17f] M. J. Goldstein, G. L. Thayer, *J. Am. Chem. Soc.* **1972**, *94*, 5928.

[18] Crystal structure analysis of **11**: X-ray data of **11** were collected with a STOE-IPDS diffractometer using graphite-monochromated Mo-K_α radiation, $\lambda = 0.71069$ Å. The structure was solved by direct methods (SHELXS-86: G. M. Sheldrick, *Acta Crystallogr., Sect. A* **1990**, *46*, 467) and refined by full-matrix least-squares techniques against F^2 (G. M. Sheldrick, SHELXL-93, University of Göttingen, Germany, **1993**). XP (Bruker AXS) was used for structure representation. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms (except the hydrogen atom attached to a nitrogen atom) were included at calculated positions and refined by using the riding model. Crystal data: $0.4 \times 0.3 \times 0.2$ mm, colorless prism, space group $P2_1/c$, monoclinic, $a = 11.578(2)$, $b = 14.992(3)$, $c = 14.027(3)$ Å, $\beta = 113.56(3)°$, $V = 2231.8(8)$ Å^3, $Z = 4$, $\rho_{calcd.} = 1.365$ g·cm^{-3}, 6585 reflections measured, 3528 were independent of symmetry, of which 2791 were observed [$I > 2\sigma(I)$], $R1 = 0.0344$, wR^2 *(all data) = 0.0963, 303 parameters.*

[19] Unpublished results.

Received August 6, 2004

