Rhodium(II)-catalyzed intramolecular carbonyl ylide formation of α-diazo-β-ketoesters derived from *N*-phthaloyl-α-amino acids

Marc Enßle, Stefan Buck, Roland Werz, and Gerhard Maas*

Institute of Organic Chemistry I, University of Ulm, D-89069 Ulm, Germany
E-mail: gerhard.maas@uni-ulm.de

Dedicated to Professor Rainer Beckert on the occasion of his 60th birthday

DOI: http://dx.doi.org/10.3998/ark.5550190.0013.312

Abstract

Starting from L-alanine, L-phenylalanine, L-leucine, L-norleucine, or L-isoleucine, 2-diazo-3-oxo-4-phthalimido-alkanoates **8** were prepared in three steps. Considerable racemization occurred at the stage of the 3-oxo-4-phthalimido-alkanoates **7**. Dirhodium tetraacetate effectively catalyzed the intramolecular formation of carbonyl ylides **9**, which in the absence of a trapping reagent underwent a [3+3] cycloaddition reaction to form the dimers **10**. Carbonyl ylides **9** underwent [3+2] cycloaddition reactions with several electron-deficient alkenes and alkynes to give oxygen and nitrogen containing multicyclic systems **12**–**16**. The keto group of the α-oxy-β-ketoester moiety of cycloadducts **2** and **12** is easily hydrated to give the *gem*-diol.

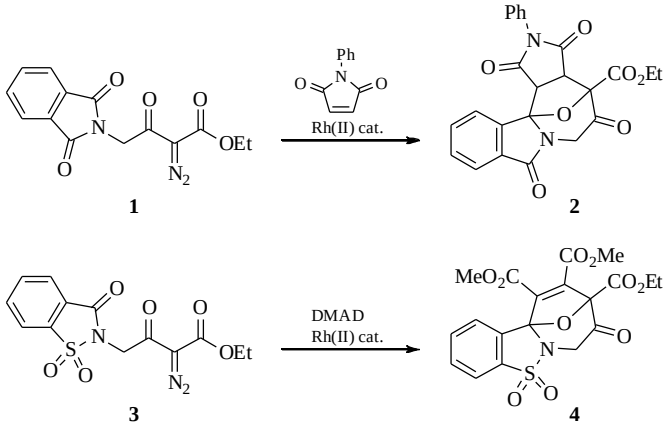
Keywords: Amino acids, carbonyl ylides, diazo compounds, dipolar cycloaddition reactions, rhodium(II)-catalyzed carbenoid reactions

Introduction

The intramolecular metallocarbenoid chemistry of α-diazocarbonyl compounds has attracted much attention in recent years.[1,2] While carbenoid C,H insertion and olefin cyclopropanation reactions give rise to carbocyclic frameworks, various heterocyclic ring systems become accessible in the presence of additional heteroatom-containing functional groups being able to participate in carbenoid reactions. Typcial examples are N–H and O–H insertion reactions as well as the formation and further transformation of various kinds of O-, S-, and N-ylides. Since α-diazoketones and α-diazo-β-ketoesters are frequently synthesized from carboxylic acids as starting materials, it is not far-fetched to consider amino acids as precursors for diazocarbonyl compounds incorporating an additional amine functional group and eventually a chiral center, if the naturally occurring α-amino acids are considered.

In fact, α-diazocarbonyl compounds derived from α-amino acids have already been employed for various synthetic transformations. N-protected α'-amino-α-diazoketones have been converted into β-amino acid derivatives by Wolff rearrangement[3] and into 3-aminoalkyl-azetidin-2-ones (β-lactams) by a Wolff rearrangement/[2+2] imine cycloaddition sequence.[4] Various intramolecular carbenoid insertion (C–H,[5] N–H[6]) and cyclopropanation[7] reactions have been achieved with α-diazoketones derived from α-amino acids. The Rh(II)-catalyzed dediazoniation of a diazoketone derived from *N*-Cbz-serine resulted mainly in an azetidin-3-one due to N–H insertion, the O–H insertion product and an oxonium ylide derived 1,3-oxazine-2,5-dione were formed as by-products.[8] A γ-amino-α-diazo-β-ketoester derived from Boc-tyrosine underwent Rh-catalyzed intramolecular aromatic C–H insertion.[9]

In the past two decades in particular, the tandem carbenoid carbonyl ylide formation/[3+2] cycloaddition sequence has been studied intensively.[10,11] This synthetic strategy can be employed for the fast assembly of complex oxamulticyclic molecular frameworks on the way to natural product targets.[12,13] Padwa and coworkers[11a,14] have also observed that amido-functionalized α-diazoketones can undergo Rh(II)-catalyzed carbenoid cyclization to form five-, six-, and seven-membered cyclic carbonyl ylides. In a related study, they found that the phthalimido-substituted α-diazo-β-ketoester **1** underwent Rh-catalyzed formation of a carbonyl ylide which was trapped with *N*-phenylmaleimide to give the polyheterocyclic adduct **2** (Scheme 1).[14] Similarly, the sacccharin-derived diazoester **3** gave cycloadduct **4**.[15] Both **1** and **3** can be considered as glycine derivatives, although they were assembled by alkylation of the phthalimide[16] and saccharinate[15] anion, respectively.



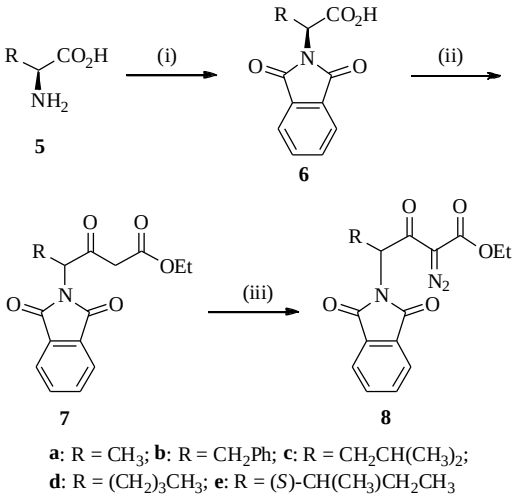
Scheme 1

In this paper, we report on the use of several α-alkyl-substituted, naturally occurring α-amino acids as starting materials for the preparation of the title compounds structurally related to **1**. The generation of six-membered cyclic carbonyl ylides by intramolecular metallocarbenoid cyclization and some typical trapping reactions of the carbonyl ylides are also described.

Results and Discussion

Synthesis of α-diazo-β-ketoesters 8

The synthesis of 2-diazo-3-oxo-4-phthalimido-alkanoates **8** is outlined in Scheme 2. α-Amino acids L-alanine, L-phenylalanine, L-leucine, L-norleucine, and L-isoleucine (**5a**–**e**) were converted into their N-phthalolyl derivatives **6a**–**e** by a published procedure[17] which uses a catalytic amount of triethylamine to lower the required reaction temperature. It was reported that for L-phenylalanine, no racemization occurs under these conditions. In the case of *N*-phthaloyl-L-isoleucine, however, the observation of two diastereomers in the ratio 97:3 by ^{1}H NMR analysis revealed a minor extent of epimerization at carbon atom C-2 ((2*S*,3*S*) isomer: δ(NCH) = 4.68 ppm, ^3J(H,H) = 8.4 Hz; (2*R*,3*S*) isomer: δ = 4.74 ppm and J = 7.6 Hz; for assignments, see lit.[18]).



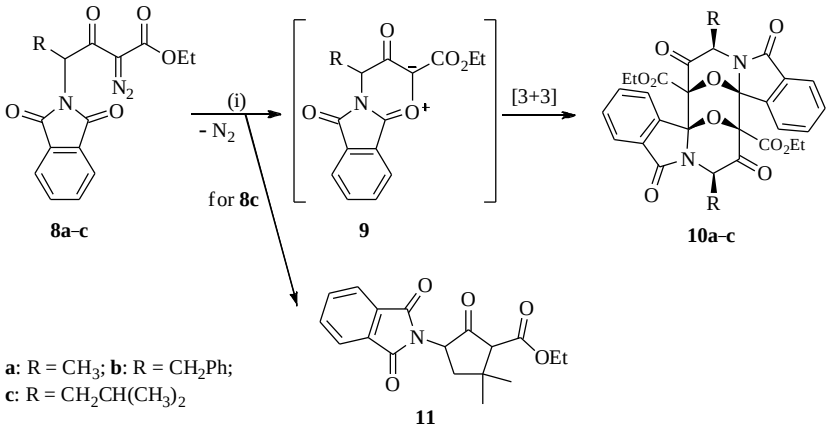
a: R = CH_3; **b**: R = CH_2Ph; **c**: R = $CH_2CH(CH_3)_2$;
d: R = $(CH_2)_3CH_3$; **e**: R = (*S*)-$CH(CH_3)CH_2CH_3$

Scheme 2. Conditions: (i) Phthalic anhydride, NEt_3 (10 mol%), toluene, reflux, 2 h, 76–98% yield; (ii) 1. carbonyldiimidazole, THF, 16 h; 2. $MgCl_2$, NEt_3, $HOOC–CH_2CO_2Et$, 3.5 h, 14–54% yield; (iii) imidazole-1-sulfonylazide.HCl, NEt_3, CH_2Cl_2, reflux, 16 h (82–90% yield, 14% of **8b**), or (for **8c**) *p*-TsN_3, NEt_3, CH_3CN, 16 h (67% yield).

N-Protected amino acids **6** were then converted into β-ketoesters **7a**–**e** according to a published procedure;[19] this method gave yields in the range 37–54% (14% for **7e**). Ketoesters **7** were transformed into α-diazo-β-ketoesters **8a**–**e** by standard diazo group transfer reactions using either *p*-tosyl azide or the recently introduced imidazole-1-sulfonylazide hydrochloride,[20] which allows for a simplified workup procedure. At the stage of β-ketoesters **7**, a considerable degree of racemization occurred. For ketoester **7e** derived from L-isoleucine, the presence of two diastereomers in 56:44 ratio was indicated by a ^{1}H NMR spectrum. HPLC analysis of ketoester **7a** and diazo esters **8a**–**e** revealed more or less complete racemization. Furthermore, the formation of diastereomers of the carbonyl ylide derived products (vide infra) clearly showed the racemization at the chiral center (N*C*H).

Rhodium-catalyzed decomposition of diazoesters 8a–c

The $Rh_2(OAc)_4$-catalyzed dediazoniation of diazoesters **8a,b** in boiling benzene produced one product in high yield according to the NMR spectra. Due to the limited stability of this product toward chromatographic conditions, even flash column chromatography over silica gel was accompanied by severe loss of material and complete purification was not possible, in particular the rhodium catalyst could not be removed completely. In the case of the product derived from alanine derivative **8a**, however, single crystals suited for an X-ray structure analysis could be grown which established the structure of the oxazapolycycle **10a**, the *syn*-dimer of carbonyl ylide intermediate **9a**. The analogous carbonyl ylide dimers **10b** and **10c** were formed from diazoesters **8b** and **8c**, as was confirmed by the similarity of the relevant NMR data and the molecular ion peaks in the mass spectra. In the latter case, the formation of **10c** was accompanied by intramolecular carbenoid insertion into the methine C–H bond giving rise to 2-oxocyclopentanecarboxylate **11**. Unfortunately, efforts toward chromatographic separation of the approximately 1:1 mixture of the two products were not successful.



Scheme 3. (i): $Rh_2(OAc)_4$ (3 mol-%), benzene, 80 ºC, 4 h.

Structure determination for carbonyl ylide dimer 10a

The molecular structure of **10a** in the solid state is shown in Figure 1. The molecule has a C_2 topology, which does not coincide, however, with a crystallographic twofold rotation axis; in fact it can be seen that the the two carboxylate groups occupy opposite positions with respect to the neighboring C–O bond of the epoxy bridge, one carbonyl group being almost *syn*-periplanar with that bond (O4–C13–C4–O1) and the other *anti*-periplanar (O9–C28–C19–O6). In this diastereomer, the two epoxy bridges are *syn* to each other, and the methyl groups occupy equatorial positions at the ring system. Since the compound crystallizes in a centrosymmetric space group, the two enantiomers are present, which confirms that racemization at the chiral center of the original α-amino acid has occurred. An interesting structural detail is given by the unusually long C–C bonds connecting the two carbonyl ylide subunits (1.597 and 1.600 Å).

In agreement with the solid-state structure of **10a**, the ^{1}H NMR signal of the ester-CH_3 groups in the carbonyl ylide dimers has undergone a significant upfield shift compared with the precursors **8** (e.g. **10a**: δ = 0.71 vs. 1.28 ppm) due to their position in the shielding area above the aromatic ring (as can be seen clearly in Figure 1 for the $COOCH_2CH_3$ group at the left-hand side). The formation of the *syn*-dimers **10a-c** results from a [3+3] cycloaddition with an *endo* transition state structure, in which the substituent R at each carbonyl ylide molecule for steric reasons is oriented *anti* to the approaching second carbonyl ylide molecule and therefore ends up in the equatorial position of the cycloadduct.

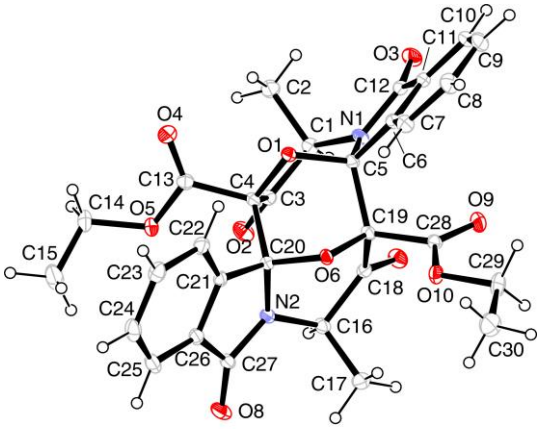


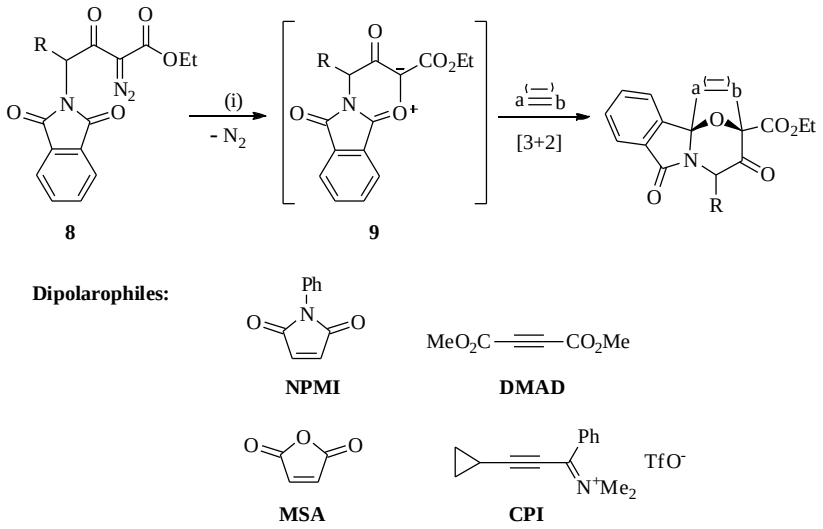
Figure 1. Structure of **10a** in the solid state (ORTEP plot). Selected bond distances (Å) and angles (deg): C4–C20 1.600(3), C5–C19 1.597(3), O1–C4 1.421(2), O1–C5 1.432(2), N1–C12 1.375(3), N1–C1 1.467(2), N1–C5 1.441(2); C4–O1–C5 108.67(13), C19–O6–C20 109.20(13). Torsion angles (deg): O1–C4–C13–O4 8.0(3), O6–C19–C28–O9 –175.8(2).

Several authors have mentioned earlier the formation of [3+3] carbonyl ylide dimers of the 2-benzopyrylium-4-olate type, but a rigorous structural proof has not been furnished.[21,22] In one case, the tentative assignment of a head-to-tail dimer had to be corrected, when an X-ray structure analysis revealed the formation of a dimer with different constitution.[23] Other studies have documented the complexity of dimerization reactions involving carbonyl ylides of this type.[24] As far as we know, only one crystal structure determination of a carbonyl ylide dimer has been published so far.[25] In that case, the dimer was derived from a five-membered cyclic carbonyl ylide and had the two epoxy bridges in *anti* orientation (i.e. the central 1,4-dioxane ring had an envelope conformation). The X-ray structure analysis of **10a**, on the other hand, shows the two epoxy bridges in *syn* orientation, with a twisted boat-like conformation of the central 1,4-dioxane ring.

Tandem carbonyl ylide formation / [3+2] cycloaddition reactions

The rhodium-catalyzed dediazoniation of diazoesters **8a** and **8d** was carried out in the presence of several electron-deficient olefinic and acetylenic dipolarophiles in order to intercept carbonyl

ylides **9** by a [3+2] cycloaddition (Scheme 4). Besides the standard dipolarophiles *N*-phenylmaleimide (NPMI), maleic anhydride (MSA) and dimethyl acetylenedicarboxylate (DMAD), we also applied a cyclopropyl-substituted propyne iminium triflate[26d] (CPI). In previous work, we have documented the reactivity of acetylenic iminium salts as dienophiles as well as dipolarophiles.[26] Here, this type of an electron-deficient alkyne was used for the first time to trap a carbonyl ylide.



Scheme 4. Generation and trapping of carbonyl ylides **9**; (i): $Rh_2(OAc)_4$ (3 mol-%), benzene, 80 °C, 2 h; see text for yields.

In all cases, the 1:1 cycloaddition products were formed in good yield according to the ^{1}H NMR spectra. However, in some cases efforts of purification by crystallization were unsuccessful and column chromatography was accompanied by a strong loss of product. The structures of the prepared cycloadducts **12**–**16** are shown in Figure 2. In the case of **16**, the regiochemistry of the cycloaddition reaction was established beyond doubt by NOESY correlations between an iminium *N*-methyl group (δ = 4.17 ppm) and the proton in ortho-position of the phthaloyl ring (δ = 7.76 ppm), this proton having been identified by 2D NMR experiments.

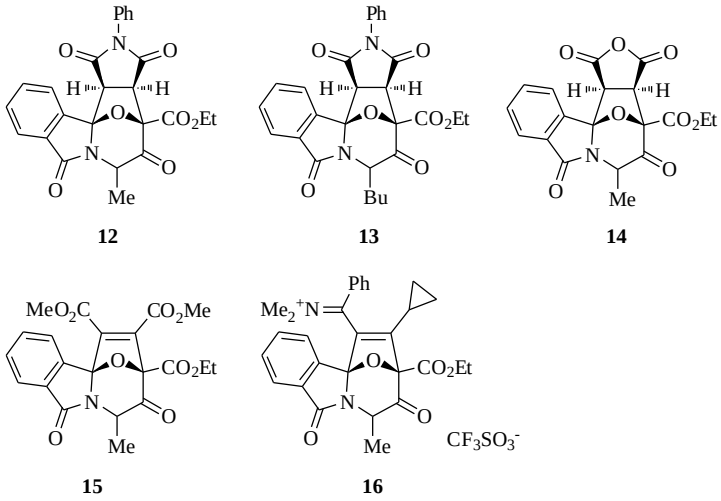


Figure 2. Cycloaddition products **12**–**16**.

For all cycloadducts **12**–**16**, a mixture of two diastereomers was formed (Table 1). The similarity of the ^{1}H NMR chemical shifts of the bridgehead protons (CHCH), the NCH proton and the NCH-methyl protons (Table 1) suggests the same stereochemical characteristics for **12**–**14** on one hand and for **15** and **16** on the other. For cycloadducts **12**–**14**, not only the configuration at the NCH carbon atom has to be assigned, but it is also of interest to know whether the dipolarophile has undergone an *exo* or an *endo* approch to the carbonyl ylide dipole. NOESY NMR studies for cycloadducts **12** and **13** clearly showed nuclear Overhauser effects between the two bridgehead protons and the methyl substituent in diastereomer **A**, and between the two bridgehead protons and the NCH proton in **B** (Figure 3; for **A** and **B**, see also Table 1). This means that the pyrrolidine ring occupies the *exo* position (*syn* to the epoxy bridge) in both diastereomers, and that diastereomer **A** has the methyl substituent in the *endo* position. By analogy, the same stereochemical assignments can be assumed for MSA adduct **14**. Although diastereomer **A**, with the alkyl substituent in *endo*-position, is not in all cases the major isomer resulting from the cycloaddition reaction (Table 1), it appears to be the thermodynamically favored one. For the crude norleucine-derived cycloadduct **13** an **A**:**B** molar ratio of 0.31 was observed, which was reversed to 2.66 after chromatographic purification on silica gel. Epimerization at the NCH carbon atom was also found for alanine-derived **12**; here, a solid containing only the epimer **12A** (besides impurities) was obtained from an acetonitrile solution of the crude reaction product by precipitation with water, but again, chromatography over silica gel caused epimerization (**A**:**B** = 1.16).

Table 1. Diastereomeric ratio (dr) and selected ^{1}H NMR data of cycloadducts **12**–**16** ($CDCl_3$, 400.13 MHz, δ/ppm)[a]

Compound	dr (**A**:**B**)	δ(C*H*C*H*)	δ(NCH)	δ(NCHCH_3)
12	1.07	4.00, 4.12 / 3.83, 4.06	4.80/4.69	1.73/1.80
13	[b]	4.02, 4.13/ 3.77, 4.01	4.75/4.64	1.93, 2.10/ 2.16, 2.44[c]
14	0.90	4.01, 4.24/ 3.88, 4.19	4.69/4.59	1.62/1.68
15	1.67		4.93/4.82	1.66/1.96
16	3.17		4.72/4.50	1.67/1.76

[a] Values are given in the order of isomer **A**/isomer **B**. [b] The **A**:**B** ratio was 0.31 in the crude product mixture, and 2.66 after chromatographic separation. [c] NCHCH^ACH^B.

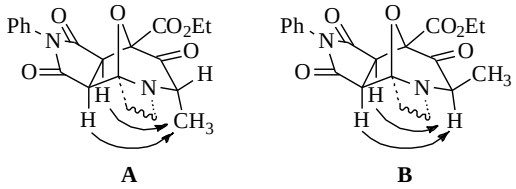


Figure 3. Major (**A**) and minor (**B**) diastereomer of alanine-derived cycloadduct **12** and NOESY relationships; the isoindoline ring has been omitted for clarity.

The two diastereomers of cycloadducts **15** and **16** must have the *exo*- or *endo*-methyl configuration, respectively. A single-crystal X-ray structure determination of **15** revealed the molecular structure of the major diastereomer **15A** (Figure 4). In contrast to the structure found for **10a**, the diastereomer with the methyl group in the pseudoaxial (*endo*) position at the ring was analyzed here. In the ^{1}H NMR spectra of both **15** and **16**, the methyl signal of the NCH-methyl group in the major diastereomer **A** appears at a lower δ-value than in the minor one; this could be explained by its position in the shielding area of the magnetic anisotropy cone of the neighboring olefinic C=C bond. Again, the presence of the racemate in the crystal indicates racemization of the chiral center of the α-amino acid during the synthesis.

The stereochemistry of cycloadduct **2** (Scheme 1) had not been assigned so far.[14] Therefore, we have also performed NOESY experiments with **2** and are now able to establish the *exo*-configuration for this compound, too.

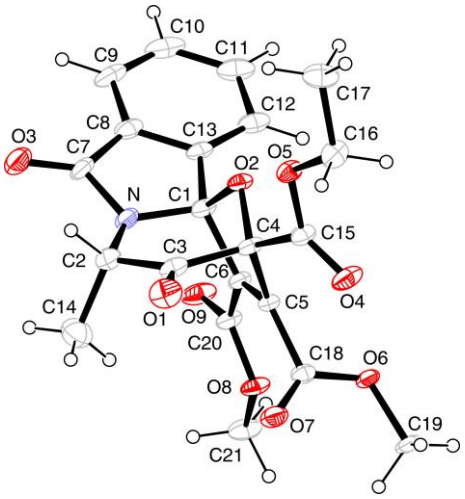
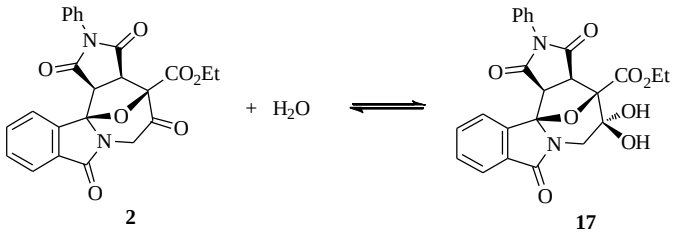


Figure 4. Structure of one diastereomer of **15** in the solid state (ORTEP plot). Selected bond distances (Å) and angles (deg): N–C1 1.471(4), N–C7 1.375(3), C1–C6 1.529(3), C5–C6 1.340(3), O2–C1 1.439(3), O2–C4 1.425(3); C1–O2–C4 103.75(18). Torsion angles (deg): C5–C6–C20–O9 176.4(3), C6–C5–C18–O7 –107.0(4), O2–C4–C15–O4 140.3(3).

Formation of *gem*-diols from ketones 2 and 12

As a side-result of our spectroscopic studies of cycloadduct **2**, we found that it forms a stable *gem*-diol (ketone hydrate) **17** (Scheme 5). While it has been reported[14b] that ketone **2** can be recrystallized from dichloromethane–hexane, we observed that our product precipitated after a few minutes from a chloroform solution. It was, however, soluble in more polar solvents such as DMSO, acetone, and acetonitrile. The identity of the precipitated product as the *gem*-diol **17** is in agreement with NMR and IR data and an elemental analysis. The mass spectrum (CI mode), on the other hand, showed the molecular ion peak corresponding to ketone **2**, but not that of hydrate **17**. In the ^{1}H NMR spectra, two singlets for OH protons are indicative; while one of them is observed in the range δ = 5.5–5.8 ppm irrespective of the solvent, the chemical shift of the second one is strongly solvent dependent (δ = 4.07 (in chloroform), 6.30 (acetone), 6.90 (dimethyl sulfoxide)), suggesting a higher propensity to hydrogen-bond formation with solvent molecules. In the ^{13}C NMR spectra, the absence of a signal for a keto carbon atom around δ = 192 ppm and the presence of an additional signal at δ = 90 ppm clearly distinguish *gem*-diol **17** from ketone **2**. In the IR spectrum of **17**, the O–H stretching vibration appears at ν = 3400–3140 cm^{-1}, while the C=O absorption at 1746 cm^{-1} exhibited by **2** is absent. The hydration of ketone **2** is reversible: *gem*-diol **17** is converted completely into **2** by dehydration at 130 °C in vacuo. When **2** was dissolved in [D$_6$]DMSO containing the unavoidable amount of water, the NMR spectra showed the exclusive presence of **17**, while the spectra of solutions of **2** in $CDCl_3$ or [D$_6$]acetone (both containing traces of water) displayed the signal sets of both **2** and **17**.



Scheme 5. Reversible hydration of ketone **2**.

We have also checked briefly the formation of a *gem*-diol from alanine-derived cycloadduct **12**. According to the complex ^{1}H and ^{13}C NMR spectra recorded for solutions of **12** in wet [D_6]DMSO or in CD_3CN to which increasing amounts of water are added, three major components are present. We tentatively assign the signal sets to the *gem*-diol forms of the two diastereomers of **12**, one of which is in equilibrium with the original, non-hydrated keto form. The two isomeric *gem*-diols give rise to ^{13}C NMR signals at $\delta(C(OH)_2)$ = 92.69 and 92.90 ppm in wet [D_6]acetone.

The equilibrium between a ketone and its hydrated form, the *gem*-diol, is generally on the side of the ketone.[27] Stable diols exist and can be isolated when strongly electron-withdrawing groups are attached to the *gem*-diol carbon atom (as in polyfluoro and polychloro ketones, in the bis(2-pyridyl)methanediol ligand,[28] but also in α-ketoacid derivatives[29]), and also when the transition from an sp^2- to an sp^3-hybridized carbon atom reduces the ring strain of cyclic ketones (such as in cyclopropanones and 7-norbornanones[30]). However, hydrated keto forms can exist also in less electron-withdrawing molecular environments. In particular, they have been observed in ketosugars[31,32] and related compounds.[33] In some cases,[32,33] the hydrates could be characterized in the solid state. The cycloadducts **2** and **12**–**16** reported here contain an α-oxy-β-ketoester moiety. We are aware of only one related structure, a 4-oxo-4,8-dioxabicyclo[3.2.0]octane-5-carboxylic ester, for which a *gem*-diol was also observed (albeit only in solution).[34]

Conclusions

Several α-amino acids featuring an unfunctionalized carbon chain have been converted into *N*-phthaloyl-4-amino-2-diazo-3-oxo-carboxylic esters in three steps. Starting with optically pure amino acids, racemization at the stage of the 4-amino-3-oxoesters could not be avoided. The Rh(II)-catalyzed carbenoid reactivity of these diazoesters is dominated by the intramolecular formation of carbonyl ylides involving a phthaloyl carbonyl group; only the intramolecular cyclopentane-forming insertion into a methine C–H bond could compete effectively with the ylide formation. These ylides could be trapped effectively with several electron-deficient dipolarophiles to give densely functionalized oxazapolycyclic ring systems which may be useful

for further synthetic transformations. In the absence of trapping reagents, the carbonyl ylides form head-to-tail dimers by [3+3] cycloaddition via an *endo* transition state that brings the two epoxy bridges in a *syn* orientation.

Experimental Section

General. NMR spectra: Bruker Avance 400 spectrometer (^{1}H: 400.13 MHz; ^{13}C: 100.62 MHz). The signal of the solvent ($CDCl_3$ or $[D]_6DMSO$) was used as the internal standard; δ values are reported in ppm. When necessary, ^{13}C signal assignments were derived from C,H COSY, HSQC and HMBC spectra. IR spectra: Bruker Vector 22; wavenumbers [cm^{-1}] are given. Elemental analyses: Elementar Vario Micro Cube. Mass spectra: Finnigan MAT SSQ 700 (CI spectra) and Bruker Daltonics micrOTOFQ and FT-ICR solariX spectrometers (HRMS-ESI spectra). Column chromatography was performed under hydrostatic pressure (silica gel Si 60, Macherey-Nagel, 0.063–0.2 mm).

Materials. L-Norleucine was purchased from Novabiochem, all other amino acids from Merck.

***N*-Phthaloylamino acids 6a–e.** They were prepared from L-alanine, L-phenylalanine, L-leucine, L-norleucine, and L-isoleucine (**5a–e**), respectively, phthalic anhydride (1 equiv.) and triethylamine (10 mol-%) in refluxing toluene as reported for *N*-phthaloyl-L-phenylalanine.[17] Yields: 94% (**6a**), 98% (**6b**), 88% (**6c**), 76% (**6d**), 84% (**6e**).

Synthesis of β-ketoesters 7. General procedure

The appropiate *N*-phthaloyl-amino acid **6** (1 equiv.) was dissolved in 100–200 mL of dry THF. *N*,*N*'-carbonyldiimidazole (1.1 equiv.) was added in portions, and the mixture was stirred for 16 h under argon at room temperature. In a separate flask purged with argon and cooled in an ice bath, a solution of malonic acid monoethyl ester (1.1 equiv.) in dry THF (100–200 mL) was prepared. To the stirred solution were added anhydrous $MgCl_2$ (0.6 equiv.) and triethylamine (1.2 equiv., gradual addition so as to keep the temperature below 10 °C), and the formed white slurry was stirred for 1 h at 0 °C. The ice bath was removed and the two mixtures were combined and stirred for 3.5 h at room temperature. Most of the solvent (90%) was evaporated, and diethyl ether and water (60–100 mL each) were added. The phases were separated, and the water phase was extracted with three portions (3 × 15–20 mL) of ether. The combined organic phases were extracted with three portions of water (3 × 15–20 mL) and once with brine. After drying with Na_2SO_4, the solvent was removed, and the crude product was purified by column chromatography. The eluent was evaporated, and the product was dried at 25 °C/10^{-3} bar.

Ethyl 3-oxo-4-phthalimido-pentanoate (7a). Prepared from **6a** (2.50 g, 11.41 mmol). After chromatography with ethyl acetate–cyclohexane (1:1), 1.64 g (5.67 mmol, 50%) of a yellow solid were obtained; m.p. 42–43 °C (lit.:[35] 43–44 °C). IR (KBr): ν = 2989 (w), 2904 (w), 1780

(s), 1718 (s), 1397 (m), 718 (w) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.21 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3), 1.63 (d, 3H, ^3J = 7.2 Hz, 3H, CH_3CHN), 3.49/3.54 (AB quartet, ^2J = 15.8 Hz, 2H, $COCH_2CO$), 4.13 (2 q, ^3J = 7.1 and 7.2 Hz, 2H, OCH_2CH_3), 5.00 (q, ^3J = 7.2 Hz, 1H, CH_3CHN), 7.74–7.77 (m, 2 H, H_{Ar}), 7.86–7.88 (m, 2 H, H_{Ar}) ppm; enol form (4%): δ = 5.18 (s, 1H, =CH), 12.27 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$): δ = 14.11 (OCH_2CH_3), 14.38 (CH_3CHN), 46.17 ($COCH_2CO$), 54.15 (CHN), 61.79 (OCH_2), 123.77 (CH_{Ar}), 131.96 (COC_{Ar}), 134.52 (CH_{Ar}), 166.58 (CO_2Et), 167.58 (NC=O), 198.13 ($COCH_2$) ppm. MS (CI): *m*/*z* (%) = 318 (14) $[M+C_2H_5]^+$, 290 (64) $[M + H]^+$, 244 (100) $[M – OC_2H_5]^+$. Anal. calcd. for $C_{15}H_{15}NO_5$ (289.29): C 62.28, H 5.23, N 4.84; found: C 62.45, H 5.16, N 4.79.

Ethyl 3-oxo-5-phenyl-4-phthalimidopentanoate (7b). Prepared from **6b** (10.00 g, 33.86 mmol). After chromatography with ethyl acetate–cyclohexane (1:2), 6.31 g (17.27 mmol, 51%) of an off-white solid were obtained; m.p. 94–96 °C (lit.:[36] 93–94 ºC). IR (KBr): ν = 3099, 3070, 3033, 2983, 2933, 2909 (all w), 1774 (m), 1750 (s), 1717 (s), 1383 (s), 725 (m) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.21 (t, ^3J = 7.2 Hz, 3H, OCH_2CH_3), 3.39/3.60 (AB part of ABX system, ^2J = 11.1 Hz, 2H, CH^AH^BCHN), 3.54/3.59 (AB quartet, ^2J = 15.8 Hz, 2H, $COCH_2CO$), 4.13 (q, ^3J = 7.1 Hz, 2H, OCH_2CH_3), 5.19 (X part of ABX system, ^3J = 11.1 and 5.0 Hz, 1H, $CH^AH^BCH^XN$), 7.09–7.18 (m, 5H, $PhCH_2$), 7.69–7.73 (m, 2 H, H_{Pht}), 7.76–7.80 (m, 2 H, H_{Pht}) ppm; enol form (3%): δ = 5.25 (s, 1H, =CH), 12.41 (s, 1H, OH). ^{13}C NMR ($CDCl_3$): δ = 14.08 (OCH_2CH_3), 33.80 ($PhCH_2$), 46.64 ($COCH_2CO$), 60.01 (NCH), 61.84 (OCH_2), 123.69 (CH_{Pht}), 127.02 (CH_{Ph}), 128.67 (CH_{Ph}), 129.00 (CH_{Ph}), 131.45 ($NCOC_{Pht}$), 134.47 (CH_{Pht}), 136.49 (C_{Ph}), 166.45 (CO_2Et), 167.56 (NC=O), 197.61 (CH_2C=O) ppm. MS (CI): *m*/*z* (%) = 394 (16) $[M + C_2H_5]^+$, 366 (92) $[M + H]^+$, 320 (100) $[M – OC_2H_5]^+$. Anal. calcd. for $C_{21}H_{19}NO_5$ (365.39): C 69.03, H 5.24, N 3.83; found: C 68.95, H 5.23, N 3.79.

Ethyl 6-methyl-3-oxo-4-phthalimidoheptanoate (7c). Prepared from **6c** (17.39 g, 66.56 mmol). After chromatography with ethyl acetate–cyclohexane (1:1), 11.93 g (36.04 mmol, 54%) of an orange oil were obtained. IR (film): ν = 2961 (m), 2873 (m), 1778 (m), 1717 (s), 1469 (s), 1386 (s), 723 (m) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.95 and 0.97 (2 d, ^3J = 6.5 and 6.6 Hz, 3H each, $CH(CH_3)_2$), 1.23 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3), 1.43–1.51 (m, 1H, 5-H^A), 1.87–1.94 (m, 1H, 5-H^B), 2.20–2.27 (m, 1H, $(CH_3)_2CH$), 3.47–3.55 (m, 2H, $COCH_2CO$), 4.14 (2 q, ^3J = 7.1 and 7.2 Hz, 2H, OCH_2), 4.99 (dd, ^3J = 11.3 and 4.2 Hz, 1 H, NCH), 7.75–7.77 (m, 2 H, H_{Ar}), 7.86–7.88 (m, 2 H, H_{Ar}) ppm; enol form (7%): δ = 5.18 (s, 1H, =CH), 12.29 (s, 1H, OH). ^{13}C NMR ($CDCl_3$): δ = 14.13 (OCH_2CH_3), 21.22/23.38 ($CH(CH_3)_2$), 25.28 ($CH(CH_3)_2$), 36.47 ($NCHCH_2$), 46.49 ($COCH_2CO$), 57.66 (NCH), 61.79 (OCH_2), 123.78 (CH_{Ar}), 131.85 ($NCOC_{Ar}$), 134.50 (CH_{Ar}), 166.52 (CO_2Et), 167.92 (NC=O), 198.21 (CH_2C=O) ppm. MS (CI): *m*/*z* (%) = 360 (10) $[M + C_2H_5]^+$, 332 (39) $[M + H]^+$, 286 (100) $[M – OC_2H_5]^+$.

Ethyl 3-oxo-4-phthalimido-octanoate (7d). Prepared from **6d** (8.42 g, 32.22 mmol). After chromatography with ethyl acetate–cyclohexane (1:4), 4.00 g (12.07 mmol, 37%) of an orange oil resulted. IR (film): ν = 2960, 2934, 2873 (all m), 1778 (m), 1717 (s), 1468 (m), 1385 (s), 723 (m) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.86 (t, ^3J = 7.1 Hz, 3H, $CH_2CH_2CH_3$), 1.22 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3), 1.25–1.39 (m, 4H, $CH_2CH_2CH_3$), 2.14–2.20 (m, 2H, $NCHCH_2$), 3.49/3.53 (AB

quartet, ^2J = 15.7 Hz, 2H, $COCH_2CO$), 4.14 (2 q, ^3J = 7.1 and 7.2 Hz, 2H, OCH_2), 4.87–4.91 (m, 1H, NCH), 7.76–7.78 (m, 2 H, CH_{Ar}), 7.88–7.90 (m, 2 H, CH_{Ar}) ppm; enol form (7%): δ = 5.19 (s, 1H, =CH), 12.28 (s, 1H, OH). ^{13}C NMR ($CDCl_3$): δ = 13.94 ($CH_2CH_2\mathit{C}H_3$), 14.12 ($OCH_2\mathit{C}H_3$), 22.22 ($CH_2\mathit{C}H_2CH_3$), 27.51 ($\mathit{C}H_2CH_2CH_3$), 28.44 ($NCH\mathit{C}H_2$), 46.53 ($CO\mathit{C}H_2CO$), 59.05 (NCH), 61.78 (OCH_2), 123.81 (CH_{Ar}), 131.81 ($NCO\mathit{C}_{Ar}$), 134.53 (CH_{Ar}), 166.57 ($\mathit{C}O_2Et$), 167.91 (NC=O), 197.99 ($CH_2\mathit{C}$=O) ppm. MS (CI): *m*/*z* (%) = 360 (16) $[M + C_2H_5]^+$, 332 (71) $[M + H]^+$, 286 (100) $[M – OC_2H_5]^+$. Anal. calcd. for $C_{18}H_{21}NO_5$ (331.37): C 65.24, H 6.39, N 4.23; found: C 65.16, H 6.51, N 4.09.

Ethyl (4*RS*, 5*S*)-5-methyl-3-oxo-4-phthalimidoheptanoate (7e). Prepared from **6e** (1.00 g, 3.83 mmol). After chromatography with ethyl acetate–cyclohexane (1:2), 0.18 g (0.54 mmol, 14%) of an orange oil was obtained; mixture of two diastereomers (56:44 by ^{1}H NMR integration). IR (Film): ν = 2968, 2935, 2878 (all m), 1776 (m), 1718 (s), 1465 (m), 1382 (s), 722 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$), major (**A**)/minor (**B**) isomer, keto form (90.6%): δ = 0.97/0.84 (2 t, ^3J = 7.4/7.3 Hz, $C\mathit{H}_3CH_2CH_2$, 3H total), 0.82/1.04 (2 d, ^3J = 6.9/6.7 Hz, $C\mathit{H}_3CH$, 3H total), 1.18/1.17 (2 t, ^3J = 7.1/7.1 Hz, 3H total, $OCH_2C\mathit{H}_3$), 1.21–1.47 (m, 1H, $CH_3C\mathit{H}^AH^B$, **A** and **B**), 1.51–1.71 (m, 1H, $CH_3CH^A\mathit{H}^B$, **A** and **B**), 2.50–2.62 (m, 1H, $CH_3C\mathit{H}$, **A** and **B**), 3.40/3.47 and 3.41/3.48 (2 AB quartets, 2H total, $COCH_2CO$), 4.04–4.13 (m, 2H, OCH_2 **A** and **B**), 4.68 (d, ^3J = 8.3 Hz, 0.44H, NCH, **B**), 4.75 (d, ^3J = 7.2 Hz, 0.56H, NCH, **A**), 7.76–7.80 (m, 2H, CH_{Ar}), 7.87–7.92 (m, 2H, CH_{Ar}); enol form (9.4%): δ = 5.35 (s, 1H, C=CHCO), 12.11 and 12.14 (2 s, 1H total, OH) ppm. ^{13}C NMR ($CDCl_3$): keto form major/minor diastereomer: δ = 11.53/11.14 ($\mathit{C}H_3CH_2CH$), 14.08 ($OCH_2\mathit{C}H_3$), 15.53/16.85 ($\mathit{C}H_3CH$), 27.46/25.44 ($CH_3\mathit{C}H_2$), 33.95/33.34 ($CH_3\mathit{C}H$), 46.99/47.08 ($CO\mathit{C}H_2CO$), 62.23/61.72 (NCH), 63.27 (OCH_2), 123.90/123.59 (CH_{Ar}), 131.62 ($NCO\mathit{C}_{Ar}$), 134.66/134.28 (CH_{Ar}), 166.78/166.73 ($\mathit{C}O_2Et$), 168.09/167.98 (NC=O), 197.07/196.89 (C=O) ppm. MS (CI): *m*/*z* (%) = 360 (15) $[M + C_2H_5]^+$, 332 (62) $[M + H]^+$, 286 (100) $[M – OC_2H_5]^+$. Anal. calcd. for $C_{18}H_{21}NO_5$ (331.37): C 65.24, H 6.39, N 4.23; found: C 65.31, H 6.43, N 4.19.

Synthesis of α-diazoesters 8. General procedure

The appropiate β-ketoester **7** (1 equiv.) was dissolved in dry CH_2Cl_2 (10–15 mL per mmol of **7**). Imidazole-1-sulfonylazide hydrochloride (1.2 equiv.) and triethylamine (5 equiv.) were added. The solution was stirred at 40 ºC for 16 h. After cooling, dichloromethane was added (10 mL per mmol of **7**), the solution was extracted twice with 1 M aqueous HCl and once with water, dried (Na_2SO_4), and the solvent was removed. The crude product was purified by column chromatography with ethyl acetate–cyclohexane (1:4) as eluent.

Ethyl 2-diazo-3-oxo-4-phthalimidopentanoate (8a). Prepared from **7a** (1.00 g, 3.46 mmol). After chromatography with ethyl acetate–cyclohexane (1:4), 0.90 g (2.85 mmol, 82%) of a yellow solid was obtained, m.p. 146–148 °C. IR (KBr): ν = 2998 (w), 2933 (w), 2160 (s), 1781 (m), 1707 (s), 1383 (s), 717 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 1.28 (t, ^3J = 7.1 Hz, 3H, $OCH_2C\mathit{H}_3$), 1.76 (d, ^3J = 7.3 Hz, 3H, $C\mathit{H}_3CHN$), 4.27 (q, ^3J = 7.1 Hz, 2H, OCH_2), 5.61 (q, ^3J = 7.3 Hz, 1H, $CH_3C\mathit{H}N$), 7.71–7.73 (m, 2 H, H_{Ar}), 7.84–7.86 (m, 2 H, H_{Ar}) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.38

(OCH_2CH_3), 14.82 (CH_3CHN), 53.02 (CHN), 61.91 (OCH_2), 75.99 (CN_2), 123.50 (CH_{Ar}), 131.97 ($NCOC_{Ar}$), 134.16 (CH_{Ar}), 160.68 (CO_2Et), 167.95 (NC=O), 188.28 (C=O) ppm. MS (CI): *m*/*z* (%) = 316 (44) $[M + H]^+$, 288 (100) $[M - N_2]^+$, 174 (69) $[M - COCN_2CO_2Et]^+$. Anal. calcd. for $C_{15}H_{13}N_3O_5$ (315.29): C 57.14, H 4.16, N 13.33; found: C 56.95, H 4.30, N 13.12.

Ethyl 2-diazo-3-oxo-5-phenyl-4-phthalimidopentanoate (8b). Prepared from **7b** (1.34 g, 3.67 mmol). After chromatography with ethyl acetate–cyclohexane (1:3), 0.20 g (0.51 mmol, 14%) of a yellow solid was obtained, m.p. 148–151 °C. IR (KBr): ν = 3112, 3055, 3029, 2979, 2960 (all w), 2147 (s), 1776 (s), 1706 (s), 1383 (s), 718 (s) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.34 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3), 3.45–3.79 (AB part of ABX system, ^2J = 13.7 Hz, 2H, $CH^AH^BCH^XN$), 4.33–4.39 (m, 2H, OCH_2), 5.19 (X part of ABX system, ^3J = 11.4 and 4.2 Hz, 1H, NCH), 7.11–7.15 (m, 1H, H_{Ph}), 7.19–7.23 (m, 2H, H_{Ph}), 7.35–7.37 (m, 2H, H_{Ph}), 7.64–7.69 (m, 2 H, H_{Pht}), 7.75–7.80 (m, 2 H, H_{Pht}) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.39 (OCH_2CH_3), 33.39 ($PhCH_2$), 59.27 (NCH), 61.98 (OCH_2), 75.97 (CN_2), 123.35 (CH_{Pht}), 126.80 (CH_{Ph}), 128.52 (CH_{Ph}), 129.05 (CH_{Ph}), 131.71 ($NCOC_{Pht}$), 133.99 (CH_{Pht}), 137.02 (C_{Ph}), 160.69 (CO_2Et), 168.11 (NC=O), 187.36 (C=O) ppm. MS (CI): *m*/*z* (%) = 420 (12) $[M + C_2H_5]^+$, 392 (100) $[M + H]^+$, 364 (97) $[M - N_2]^+$, 250 (86) $[M - COCN_2CO_2Et]^+$. Anal. calcd. for $C_{21}H_{17}N_3O_5$ (391.39): C 64.45, H 4.38, N 10.74; found: C 64.38, H 4.52, N 10.65.

Ethyl 2-diazo-3-oxo-4-phthalimidooctanoate (8d). Prepared from **7d** (4.00 g, 12.07 mmol). After chromatography with ethyl acetate–cyclohexane (1:4), 3.80 g (10.63 mmol, 88%) of a yellow oil were obtained. IR (film): ν = 2960 (m), 2873 (m), 2141 (s), 1780 (m), 1719 (s), 1468 (m), 1383 (s), 720 (s) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.84–0.88 (m, 3H, $CH_2CH_2CH_3$), 1.30 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3), 1.32–1.41 (m, 4H, $CH_2CH_2CH_3$), 1.99–2.07 (m, 1H, $NCHCH^A$), 2.43–2.53 (m, 1H, $NCHCH^B$), 4.29 (2 almost coinciding q, ^3J = 7.1 Hz, 2H, OCH_2), 5.57 (dd, ^3J = 11.1 and 4.0 Hz, 1H, $NCHCH^AH^B$), 7.70–7.72 (m, 2H, H_{Ph}), 7.83–7.85 (m, 2H, H_{Ph}) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.99 ($CH_2CH_2CH_3$), 14.41 (OCH_2CH_3), 22.20 ($CH_2CH_2CH_3$), 27.80 ($CH_2CH_2CH_3$), 29.08 ($NCHCH_2$), 58.00 (NCH), 61.91 (OCH_2), 76.04 (CN_2), 123.50 (CH_{Ar}), 131.98 ($NCOC_{Ar}$), 134.13 (CH_{Ar}), 160.74 (CO_2Et), 168.34 (NC=O), 188.17 (C=O) ppm. MS (CI): *m*/*z* (%) = 386 (9) $[M + C_2H_5]^+$, 358 (100) $[M + H]^+$, 330 (68) $[M - N_2]^+$, 216 (63) $[M - COCN_2CO_2Et]^+$. Anal. calcd. for $C_{18}H_{19}N_3O_5$ + 0.27 CH_2Cl_2 (357.37 + 22.93): C 57.70, H 5.18, N 11.05; found: C 57.99, H 5.45, N 10.76.

Ethyl (4*RS*, 5*S*)-2-diazo-5-methyl-3-oxo-4-phthalimido-heptanoate (8e). Prepared from **7e** (2.63 g, 7.94 mmol). After chromatography with ethyl acetate–cyclohexane (1:4), 2.56 g (7.16 mmol, 90%) of a yellow oil was obtained, which was a mixture of two diastereomers (56:44 according to ^1H NMR integration). IR (film): ν = 2928 (m), 2852 (m), 2138 (s), 1775 (m), 1726 (s), 1468 (m), 1386 (s), 718 (s) cm^{-1}. ^1H NMR ($CDCl_3$), major/minor diastereomer: δ = 0.97/0.89 (2 t, ^3J = 7.4/7.4 Hz, 3H, CH_2CH_3), 0.92/1.05 (2 d, ^3J = 6.8/6.8 Hz, 3H, CH_3CH), 1.18/1.22 (2 t, ^3J = 7.1/7.1 Hz, 3H, OCH_2CH_3), 1.13–1.31/1.42–1.57 (m, 1H, $CH_3CH^AH^B$), 2.60–2.78 (m, 1H, CH_3CH), 4.11–4.27 (m, 2H, OCH_2), 5.30/5.42 (2 d, ^3J = 7.1/8.8 Hz, 1H, NCH), 7.71–7.73 (m, 2H, H_{Ar}), 7.83–7.86 (m, 2H, H_{Ar}) ppm. ^{13}C NMR ($CDCl_3$), major/minor diastereomer: δ = 11.17/11.87 (CH_3CH_2CH), 14.33/14.36 (OCH_2CH_3), 15.69/16.21 (CH_3CH), 25.79/27.14

(CH_3CH_2CH), 34.22/34.79 (CH_3CH), 59.81/60.10 (NCH), 61.81/61.86 (OCH_2), 123.59/123.61 (CH_{Ar}), 131.76/131.79 ($NCOC_{Ar}$), 134.21 (CH_{Ar}), 160.75/160.77 (CO_2Et), 168.01/168.03 (NC=O), 187.30/187.71 (C=O) ppm; the CN_2 signal was not observed. MS (CI): *m*/*z* (%) = 386 (10) $[M + C_2H_5]^+$, 358 (97) $[M + H]^+$, 330 (80) $[M – N_2]^+$, 250 (100) $[M – COCN_2CO_2Et]^+$. Anal. calcd. for $C_{18}H_{19}N_3O_5$ (357.37): C 60.50, H 5.36, N 11.76; found: C 60.70, H 5.41, N 11.86.

Ethyl 2-diazo-6-methyl-3-oxo-4-phthalimidoheptanoate (8c). β-Ketoester **7c** (11.52 g, 34.76 mmol) was dissolved in dry acetonitrile (100 mL) and *p*-toluenesulfonyl azide (7.54 g, 38.2 mmol) as well as triethylamine (2.54 mL, 18.3 mmol) were added. The solution was stirred at room temperature for 16 h. Then the solvent was replaced by CH_2Cl_2. Upon addition of *n*-pentane, the by-product *p*-toluenesulfonyl amide was precipitated and was filtered off. The mother liquor was evaporated to dryness, and the residue was purified by column chromatography with ethyl acetate–cyclohexane (1:5) as eluent. A yellow oil was obtained (8.32 g, 23.28 mmol, 67%), which was dried at 25 °C/10^{-3} bar. IR (film): ν = 2960 (m), 2872 (m), 2139 (s), 1775 (m), 1721 (s), 1467 (m), 1383 (s) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.94/1.00 (2 d, ^3J = 6.6/6.6 Hz, 3H each, $CH(CH_3)_2$), 1.33 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3), 1.54–1.65 (m, 1H, $NCHCH^AH^B$), 1.75–1.81 (m, 1H, $NCHCH^AH^B$), 2.52–2.60 (m, 1H, $(CH_3)_2CH$), 4.14 (q, ^3J = 7.1 Hz, 2H, OCH_2), 5.75 (dd, ^3J = 11.9 and 4.0 Hz, 1H, NCH), 7.69–7.74 (m, 2H, H_{Ar}), 7.83–7.87 (m, 2H, H_{Ar}) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.33 (OCH_2CH_3), 20.62/23.17 ($CH(CH_3)_2$), 25.63 ($CH(CH_3)_2$), 35.94 ($NCHCH_2$), 56.51 (NCH), 61.75 (OCH_2), 75.70 (CN_2), 123.33 (CH_{Ar}), 131.85 ($NCOC_{Ar}$), 134.04 (CH_{Ar}), 160.44 (CO_2Et), 168.26 (NC=O), 188.45 (CN_2C=O) ppm. MS (CI): *m*/*z* (%) = 386 (8) $[M + C_2H_5]^+$, 358 (100) $[M + H]^+$, 330 (48) $[M – N_2]^+$, 216 (40) $[M – COCN_2CO_2Et]^+$. Anal. calcd. for $C_{18}H_{19}N_3O_5$ (357.37): C 60.50, H 5.36, N 11.76; found: C 60.45, H 5.38, N 11.71.

Catalytic decomposition of diazoesters 8a–c. General procedure

To a refluxing suspension of $Rh_2(OAc)_4$ (13 mg, 0.03 mmol) in dry benzene (20 mL) was added via a syringe pump a solution of 1.00 mmol of the appropriate diazo ester **8** in dry benzene (5 mL) during 1 h. After 2–4 h the diazo stretching vibration had disappeared (IR control), and the solvent was evaporated.

Decomposition of 8a. A ^1H NMR spectrum of the reaction crude indicated the formation of one major product (**10a**, ca. 63%) besides several unidentified minor ones. The residue was dissolved in a mixture of ethyl acetate–cyclohexane (1:1) and flushed over a short column filled with silica gel (20 g). This procedure did not allow to remove all of the catalyst. The greenish solid was dissolved in a minimum volume of acetone, and *n*-pentane was allowed to diffuse into this solution. After some time, crystals of carbonyl ylide dimer **10a** suited for X-ray analysis were formed. IR (KBr): ν = 3062 (w), 2982 (w), 2940 (w), 1762, 1725 (s), 1367 (s) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.71 (t, ^3J = 7.2 Hz, 3H, OCH_2CH_3), 1.59 (d, ^3J = 7.1 Hz, 3H, $CHCH_3$), 3.36–3.44 (m, 1H, OCH^AH^B), 3.67–3.75 (m, 1H, OCH^AH^B), 4.55 (q, ^3J = 7.2 Hz, 1H, $CHCH_3$), 7.63–7.68 (m, 2H, CH_{Ar}), 7.72–7.76 (m, 1H, CH_{Ar}), 7.89–7.93 (m, 1H, CH_{Ar}) ppm. ^{13}C NMR ($CDCl_3$): δ =

13.27 (OCH_2CH_3), 17.66 ($CHCH_3$), 61.50 ($NCHCH_3$), 63.45 (OCH_2), 86.50 (OC_q), 94.19 (OC_q); 122.48, 123.90, 131.58, 133.01 (CH_{Ar}); 134.26, 142.09 (C_{Ar}); 161.85 (CO_2Et), 166.68 (NC=O), 197.62 (CHC=O) ppm. MS (CI): *m*/*z* (%) = 575 (22) $[M + H]^+$, 288 (100) $[M/2 + H]^+$. HRMS (ESI): *m*/*z* = 575.1653; calcd. for ($C_{30}H_{26}N_2O_{10}$ + H): 575.1660.

Decomposition of 8b. Column chromatography (150 g of silica gel, ethyl acetate–cyclohexane (1:1)) furnished carbonyl ylide dimer **10b** as a colorless solid (0.11 g, 0.10 mmol, 14%), m.p. 200–205 °C. IR (KBr): ν = 3061 (w), 3029 (w), 2983 (w), 1720 (s), 1369 (s), 719 (m) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.64 (t, ^3J = 7.2 Hz, 3H, OCH_2CH_3), 2.61 (dd, ^3J = 14.0 and 11.6 Hz, 1H, $PhCH^A$), 3.38–3.46 (m, 1H, $OCH^AH^BCH_3$), 3.59–3.67 (m, 1H, $OCH^AH^BCH_3$), 4.15 (dd, 14.0 and 4.8 Hz, 1H, $PhCH^B$), 4.60 (dd, 1H, ^3J = 11.6 and 4.8 Hz, NCH), 6.88–6.90 (m, 2H, H_{Ph}), 7.14–7.17 (m, 3H, H_{Ph}), 7.63–7.70 (m, 2H, H_{Pht}), 7.81–7.89 (m, 1H, H_{Pht}), 7.90–7.94 (m, 1H, H_{Pht}) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.17 (OCH_2CH_3), 36.05 ($PhCH_2$), 63.26 (OCH_2), 67.07 (NCH), 86.75 (OC_q), 94.02 (OC_q), 122.64 (CH_{Pht}), 123.82 (CH_{Pht}), 127.39 (CH_{Ph}), 128.45 (CH_{Ph}), 128.93 (CH_{Ph}), 131.58 (CH_{Pht}), 133.02 (2 C, CH_{Pht}, C_{Ph}), 134.31 (C_{Pht}), 141.85 (C_{Pht}), 161.48 (CO_2Et), 166.33 (NC=O), 193.43 (CHC=O) ppm. MS (CI): *m*/*z* (%) = 727 (6) $[M + H]^+$, 364 (100) $[M/2 + H]^+$. A satisfactory elemental analysis was obtained for a sample that had been treated with dichloromethane. Anal. calcd. for $C_{42}H_{34}N_2O_{10}$ + 0.25 CH_2Cl_2 (726.74 + 21.23): C 67.85, H 4.65, N 3.75; found: C 67.44, H 4.76, N 3.79.

Decomposition of 8c. A greenish solid was obtained which consisted mainly of carbonyl ylide dimer **10c** and cyclopentanecarboxylate **11** in an approximately 1:1 molar ratio according to a ^1H NMR spectrum. The separation of the two products and removal of residual rhodium catalyst by column chromatography (silica gel) was not possible. The following NMR and MS data were recorded for the mixture. Dimer **10c**: ^1H NMR ($CDCl_3$): δ = 0.72–0.75 (m, 12H, 2 OCH_2CH_3, 2 $CHCH_3$), 0.97–0.99 (m, 6H, 2 $CHCH_3$), 1.09–1.14 (m, 2H, 2 $CH(CH_3)_2$), 1.48–1.52 (m, 2H, $NCHCH^AH^B$), 2.35–2.43 (m, 2H, $NCHCH^AH^B$), 3.33–3.41 and 3.36–3.71 (2 m, 2H each, $OCH^AH^BCH_3$), 4.54 (dd, ^3J = 11.9 and 4.3 Hz, 2H, NCH), 7.61–7.91 (m, 8H, CH_{Ar}) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.36 (OCH_2CH_3), 20.71 ($CHCH_3$), 23.40 ($CHCH_3$), 24.30 ($CH(CH_3)_2$), 38.31 ($NCHCH_2$), 61.46 (NCH), 63.26 (OCH_2), 86.66 (C_q), 94.22 (C_q), 161.74 (CO_2Et), 166.37 (NC=O), 195.73 (C=O) ppm. MS (CI): *m*/*z* (%) = 687 (13) $[M + C_2H_5]^+$, 659 (54) $[M]^+$. $C_{36}H_{38}N_2O_{10}$ (658.70).

Ethyl 2,2-dimethyl-5-oxo-4-phthalimidocyclopentanecarboxylate (11). ^1H NMR ($CDCl_3$): keto form: δ = 1.32–1.36 (t + 2 s, 9H, OCH_2CH_3, $C(CH_3)_2$), 2.03–2.08 (m, 1H, 3-H^A), 2.80 (virtual t, 1H, 3-H^B), 3.15 (s, 1H, 1-H), 4.26 (q, ^3J = 7.1 Hz, 2H, OCH_2), 4.95–5.00 (m, 1H, NCH), 7.61–7.91 (m, 4H, H_{Ar}) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.34 (OCH_2CH_3), 25.50 (2-CH_3), 30.52 (2-CH_3), 36.32 ($C(CH_3)_2$), 38.92 (CH_2 ring), 55.16 (NCH), 61.46 (OCH_2), 63.17 ($CHCO_2Et$), 167.22 (CO_2Et), 167.51 (NC=O), 205.87 (C=O) ppm. MS (CI): *m*/*z* (%) = 358 (16) $[M + C_2H_5]^+$, 330 (69) $[M + H]^+$, 284 (100) $[M – OC_2H_5]^+$. $C_{18}H_{19}NO_5$ (329.35).

Catalytic decomposition of diazoesters 1 and 8 in the presence of a dipolarophile. General procedure

To a refluxing mixture of $Rh_2(OAc)_4$ (13 mg, 0.03 mmol) and the appropiate dipolarophile (1.00 mmol) in dry benzene (20 mL) was added via a syringe pump a solution of the appropiate diazo compound **8** (1.00 mmol) in dry benzene (5 mL) during 1 h. After ca. 2 h the diazo stretching vibration had disappeared (IR control), and the solvent was evaporated. The green solid residue was dissolved in pentane–$CHCl_3$ (8:2) and passed through a syringe filter to remove the undissolved rhodium catalyst. However, as indicated by the greenish color, some of the catalyst in general remained in the solution.

Decomposition of 8a in the presence of *N*-phenylmaleimide. The crude product mixture consisted mostly of cycloadduct **12** (two diastereomers, **A**:**B** = 1.07), residual NPMI, and some impurities (^{1}H NMR). NPMI could be removed by sublimation (120 ºC, 0.03 mbar, 2 h). This treatment changed the diastereomeric ratio of **12** from 1.07 to 1.23 (^{1}H NMR integration). Cycloadduct **12** was purified, without separation of the diastereomers, by thick-layer chromatography (Macherey-Nagel, SIL G-200 UV_{254}, 2 mm, 20×20 cm, elution with ethyl acetate–cyclohexane (1:1)), followed by recrystallization from dichloromethane–pentane and drying (100 ºC/0.08 mbar). IR (KBr): ν = 3067 (w), 3033 (w), 2985 (w), 1719 (s), 1388 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$), major (**A**)/minor (**B**) diastereomer: δ = 1.43 (t, ^3J = 7.2 Hz, 3H, OCH_2CH_3), 1.73/1.80 (2 d, ^3J = 7.3/6.9 Hz, 3H total, CH_3CH), 3.83 and 4.06 (2 d, ^3J = 7.5 Hz, C*H*C*H*, **B**), 4.00 and 4.12 (2 d, ^3J = 7.6 Hz, C*H*C*H*, **A**), 4.20–4.65 (m, 2H, OCH_2, **A** and **B**), 4.69 (q, ^3J = 6.9 Hz, NC*H*CH_3, **B**), 4.80 (q, ^3J = 7.3Hz, NC*H*CH_3, **A**), 7.35–7.38 (m, 3H, H_{Ar}), 7.46–7.64 (m, 6H, H_{Ar}), 7.86–7.89 (m, 1H, H_{Ar}) ppm. ^{13}C NMR ($CDCl_3$), major (**A**)/minor (**B**) diastereomer: δ = 13.87 (OCH_2CH_3, **A**, **B**), 20.02/15.74 (CH_3CH); 50.88/50.86, 53.10/54.47, 55.67/56.99 (*C*H*C*H, CH_3CH); 62.94/62.92 (OCH_2), 88.82/89.62 (OC_q), 95.13/96.01 (OC_q); 123.66, 123.78, 123.82, 124.75, 126.03, 126.15, 128.99, 129.15, 129.29, 129.33, 129.38, 130.97, 131.00, 132.27, 131.44, 131.95, 132.65, 136.78, 137.13 (CH_{Pht}, C_{Pht}, CH_{Ph}, CPh); 161.76/161.79 (CO_2Et), 166.30/165.54 (NC=O), 170.78/170.67 (O=*C*NCO) 170.92/170.90 (OCN*C*=O), 195.52/195.71 (C=O) ppm. MS (CI): *m*/*z* (%) = 489 (8) $[M + C_2H_5]^+$, 461 (42) $[M + H]^+$. HRMS (ESI): *m*/*z* = 461.1339; calcd. for ($C_{25}H_{20}N_2O_7$ + H): 461.1343. Anal. calcd. for $C_{25}H_{20}N_2O_7$ (460.44): C 65.21, H 4.38, N 6.08; found: C 64.31, H 4.38, N 6.07. ($C_{25}H_{20}N_2O_7 \times 0.3\ H_2O$ requires: C 64.46, H 4.46, N 6.01.)

Decomposition of 8d in the presence of *N*-phenylmaleimide. A portion of the crude reaction product (243 mg) was dissolved in chloroform–pentane (1:1) (4 mL) followed by quick filtration to remove undissolved $Rh_2(OAc)_4$. From the filtered solution, a brown precipitate was formed overnight which was discarded. The solvent was evaporated and the solid residue was subjected to sublimation (120 ºC, 0.05 mbar, 1 h) in order to remove residual NPI. The remaining solid was worked up by thick-layer chromatography (Macherey-Nagel, SIL G-200 UV_{254}, 2 mm, 20×20 cm, elution with diethyl ether–petroleum ether (10:1)). The fraction containing cycloadduct **13** (R_f = 0.3) was collected, dried (100 ºC/0.02 mbar, 2 h), and recrystallized from dichloromethane–pentane to leave 45 mg of colorless **13** (two diastereomers, **A**:**B** = 2.66). IR (KBr): ν = 2960 (w), 2933 (w), 1718 (s), 1387 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$), major (**A**)/minor (**B**)

diastereomer: δ = 0.92/0.81 (2 t, ^3J = 7.2 Hz, 3H, butyl-CH_3), 1.24–1.44 and 1.54–1.70 (m, 4H, $H_3CC\mathit{H}_2C\mathit{H}_2$, **A** and **B**), 1.40 (t, ^3J = 7.2 Hz, 3H, $OCH_2C\mathit{H}_3$, **A** and **B**), 1.88–1.98 and 2.07–2.14 (2 m, $NCHC\mathit{H}_2$, **A**), 2.10–2.21 and 2.38–2.50 (2 m, $NCHC\mathit{H}_2$, **B**), 3.77 and 4.01 (2 d, ^3J = 7.6 Hz, 2H, C*H*C*H* bridgeheads, **B**), 4.02 and 4.13 (2 d, ^3J = 7.6 Hz, 2H, C*H*C*H* bridgeheads, **A**), 4.35–4.50 (m, 2H, OCH_2, **A** and **B**), 4.63–4.66 (m, NCH, **B**), 4.75 (dd, ^3J = 7.8 and 6.4 Hz, NCH, **A**), 7.23–7.35 (m, 3H, H_{Ph}), 7.41–7.62 (m, 5H, $3H_{Pht}$, $2H_{Ph}$), 7.83–7.87 (m, 1H, H_{Pht}) ppm. ^{13}C NMR ($CDCl_3$), major (**A**)/minor (**B**) diastereomer: δ = 13.77/13.61 (CH_3 butyl), 14.00 ($OCH_2\mathit{C}H_3$), 22.31/22.20 ($CH_2\mathit{C}H_2CH_3$), 28.21/26.67 ($\mathit{C}H_2CH_2CH_3$), 34.58/29.37 ($NCH\mathit{C}H_2$), 50.68/51.33 (*C*HCH), 53.03/54.99 (CH*C*H), 60.39/61.63 (NCH), 63.00/63.07 (OCH_2), 88.83/90.42 (C_q), 95.58/95.97 (C_q); 123.99–132.72 and 136.85/137.57 (C_{Pht}, CH_{Pht}, CH_{Ph}); 161.87/161.27 (*C*O_2Et), 166.82/165.50 (NC=O); 170.56, 170.70 and 170.78 (O=*C*N*C*=O); 194.25/196.10 (C=O) ppm. MS (CI): *m*/*z* (%) = 531 (2) $[M + C_2H_5]^+$, 503 (9) $[M + H]^+$. HRMS (ESI): *m*/*z* = 503.1813; calcd. for ($C_{28}H_{26}N_2O_7$ + H): 503.1813. Anal. calcd. for $C_{28}H_{26}N_2O_7$ (502.50): C 66.92, H 5.21, N 5.57; found: C 66.21, H 5.25, N 5.49. ($C_{28}H_{26}N_2O_7 \times 0.3\ H_2O$ requires: C 66.21, H 5.28, N 5.52.)

Decomposition of 8a in the presence of maleic anhydride. The crude product consisted of cycloadduct **14**, residual maleic anhydride and minor impurities (^{1}H NMR). Due to its lability toward chromatographic conditions, it was not possible to obtain **14** in pure form. Two diastereomers were present (molar ratio **A**:**B** = 0.90, ^{1}H NMR integration). IR (KBr): ν = 2989 (w), 1794 (s), 1718 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$), isomer **A** (minor)/isomer **B** (major): δ = 1.33–1.37 (m, 3H, $OCH_2C\mathit{H}_3$), 1.62/1.68 (d, ^3J = 7.2/6.9 Hz, 3H total, $C\mathit{H}_3CH$), 3.88 and 4.19 (d, ^3J = 8.0 Hz, C*H*C*H*, **B**), 4.01 and 4.24 (d, ^3J = 7.7 Hz, C*H*C*H*, **A**), 4.36–4.42 (m, 2H, OCH_2), 4.69/4.59 (q, ^3J = 6.9/7.2 Hz, 1H total, $CH_3C\mathit{H}$), 7.56–7.64 (m, 3H, CH_{Ar}), 7.77–7.85 (m, 1H, CH_{Ar}) ppm. ^{13}C NMR ($CDCl_3$), isomer **A** (minor)/isomer **B** (major): δ = 13.95 ($OCH_2\mathit{C}H_3$, **A** and **B**), 20.06/16.37 ($\mathit{C}H_3CH$); 52.09/52.06, 54.00/55.43, 55.76/57.14 (*C*H*C*H, $CH_3\mathit{C}H$, **A** and **B**); 63.55/63.60 (OCH_2); 89.47/90.51 (OC_q bridgehead), 95.50/96.31 (OC_q bridgehead); 123.79, 124.08, 124.19, 124.53, 131.84, 131.95, 132.06, 132.51, 132.65, 132.80, 136.42, 136.59 (CH_{Ar}, C_{Ar}, both isomers); 160.74, 160.80 (*C*O_2Et, **A** and **B**); 164.78, 165.65, 165.69, 165.74, 165.84, 166.30 (O=*C*O*C*=O and NC=O); 194.70/194.92 (C=O) ppm. HRMS (ESI): *m*/*z* = 386.0867; calcd. for ($C_{19}H_{15}NO_8$ + H): 386.0870.

Decomposition of 8a in the presence of DMAD. An excess of DMAD (2 mmol) was used. A small amount of diazo compound was still present after 2 h, therefore the reaction was continued for several hours. After cooling, the mixture was passed through a syringe filter in order to remove the suspended green catalyst. After evaporation of the solution a crude product was left, which consisted almost exclusively of cycloadduct **15** besides residual DMAD (^{1}H NMR). The latter could be removed by treating the crude product with diisopropyl ether/cyclohexane (1:5 *v*/*v*, 10 mL) in an ultrasonic bath for 1 h. The remaining white solid was washed with pentane and dried at 0.05 mbar/20 °C for 2 h to furnish 0.340 g (79%) of **15** as a 62.5:37.5 mixture of diastereomers, mp. 169–173 °C. Due to the lability toward chromatographic conditions, separation of the diastereomers by liquid chromatography was not possible. Partial crystallization

from CH_2Cl_2/*n*-pentane by the diffusion method afforded first some sticky crystals which were discarded. Slow evaporation of the mother liquor provided crystals of the major diastereomer (^{1}H NMR) which were suited for X-ray diffraction analysis (see Figure 4).

9-Ethyl-10,11-dimethyl (7*SR*, 9*RS*, 11a*SR*)-9,11a-epoxy-7-methyl-8-oxo-7,8,9,11a-tetrahydro-5*H*-azepino[2,1-*a*]isoindole-10,11-tricarboxylate (15). IR (KBr): ν = 2998, 2958, 2906 (all w), 1726 (s), 1373 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$), major (**A**)/minor (**B**) diastereomer: δ = 1.36/1.37 (2 t, ^3J = 7.1/7.1 Hz, 3H total, OCH_2CH_3), 1.66/1.96 (2 d, ^3J = 7.4/7.0 Hz, 3H, CH_3CH), 3.61/3.53 (2 s, OCH_3), 3.95/3.92 (2 s, OCH_3), 4.31–4.42 (m, 2H, OCH_2, **A** and **B**), 4.93/4.82 (2 q, ^3J = 7.4/7.0 Hz, 1H, CH_3CH), 7.61–7.70 (m, 3H, H_{Ar}), 7.84–7.88 (m, 1 H, H_{Ar}) ppm. ^{13}C NMR ($CDCl_3$), major (**A**)/minor (**B**) diastereomer: δ = 13.92 (OCH_2CH_3), 22.61/15.78 (CH_3CH), 52.84–53.40 (4 C, OCH_3, **A** and **B**), 58.08/58.96 (CH_3CHN), 63.32 (OCH_2, **A** and **B**), 92.24/92.75 (OC_q), 97.54/98.22 (OC_q, **A**); 123.96/123.64 or 123.44, 124.20/123.44 or 123.64, 131.45/131.32, 132.83/132.57, 135.79/136.20, 139.13/138.76, 143.75/143.39 (CH_{Ar}, C=C, signals of 2 C coincide); 159.59/159.57, 161.75/161.69, 162.24/162.00 (CO_2Me, CO_2Et), 166.24/164.90 (NC=O), 190.47/189.91 (C=O) ppm. HRMS (ESI): *m*/*z* = 452.1028; calcd. for ($C_{21}H_{19}NO_9$ + Na): 452.0958. Anal. calcd. for $C_{21}H_{19}NO_9$ (429.38): C 58.74, H 4.46, N 3.26; found: C 58.20, H 4.45, N 3.16. ($C_{21}H_{19}NO_9 \times 0.2\ H_2O$ requires: C 58.20, H 4.52, N 3.23.)

Decomposition of 8a in the presence of (3-cyclopropyl-1-phenylpropynylidene)-dimethylammonium triflate. The solid residue was triturated with several portions of dry ethyl acetate to leave cycloadduct **16** undissolved (0.42 g, 0.33 mmol, 67%), m.p. 223 °C (dec.). A 3.17:1 mixture of diastereomers was obtained. IR (KBr): ν = 3044, 2999, 2944 (all w), 1740 (s), 1718 (s), 1369 (s). ^{1}H NMR ($CDCl_3$) of major (**A**) and minor (**B**) diastereomer: δ = 0.93–1.10 (m, 2H, CH_{2cp}), 1.26–1.33 (m, 1H, CH_{2cp}), 1.36 (**A**)/1.37 (**B**) (2 t, ^3J = 7.2 Hz, 3H, OCH_2CH_3), 1.49–1.55 (m, 1H, CH_{2cp}), 1.67 (**A**)/1.76 (**B**) (d, ^3J = 7.2/7.0 Hz, 3H, CH_3CH), 2.34–2.41 (m, 1H, CH_{cp}), 3.73 (**B**)/3.74 (**A**) (2 s, 3H total, N^+CH_3), 4.14 (**B**)/4.18 (**A**) (2 s, 3H total, N^+CH_3), 4.33–4.44 (m, 2H, OCH_2), 4.50 (**B**)/4.72 (**A**) (q, 1H, ^3J = 7.0/7.2 Hz, CH_3CH), 6.70–6.77 (m, 2H, H_{Ph}), 7.17–7.22 (m, 2H, H_{Ph}), 7.42–7.48 (m, 2H, H_{Ph}, H_{Pht}), 7.57–7.62 (m, 1H, H_{Ar}), 7.68 (d, ^3J = 7.5 Hz, 1H, H_{Ar}), 7.76 (d, ^3J = 7.6 Hz, 1H, H_{Ar}), 7.88–7.95 (m, 1H, H_{Ar}) ppm. ^{13}C NMR ($CDCl_3$) of isomer **A**: δ = 8.00 (CH_{cp}), 10.59 (CH_{cp}), 12.44 (CH_{cp}), 14.04 (OCH_2CH_3), 20.42 (CH_3CH), 47.80 (N^+CH_3), 48.28 (N^+CH_3), 59.36 (CH_3CH), 63.84 (OCH_2), 94.22 (C_q), 98.20 (C_q), 123.79 (CH_{Ph}), 124.33 (CH_{Pht}), 127.33 (C_{Pht}), 128.21 (CH_{Ph}), 128.95 (CH_{Ph}), 131.89 (C_{Pht}), 132.28 (CH_{Pht}), 133.87 (*C*=C), 133.89 (CH_{Pht}), 135.19 (CH_{Pht}), 137.95 (C_{Pht}), 161.99 (CO_2Et), 162.62 (C=*C*), 166.94 (NC=O), 176.82 (C=N^+), 192.02 (C=O) ppm. Anal. calcd. for $C_{30}H_{29}F_3N_2O_8S$ (634.16): C 56.78, H 6.61, N 4.41; found: C 56.57, H 4.54, N 4.24.

Decomposition of 1 in the presence of *N*-phenylmaleimide. The crude product was dissolved in chloroform. After stirring for some minutes, a white precipitate started to form which was collected and dried at 25 °C/10^{-3} mbar. **Ethyl 4,12b-epoxy-3a,4,5,6,12b,12c-hexahydro-5,5-dihydroxy-1,3,8-trioxo-2-phenyl-1*H*-pyrrolo[3,4-*k*]5*H*-azepino[2,1-*a*]isoindole-4-carboxylate** (**17**) was obtained as a white powder (0.18 g, 0.39 mmol, 39%), m. p. 251–254 °C (dec.) (m. p. for the keto form **2**:[14b] 249–250 °C dec.). IR (KBr): ν = 3400–3140 (broad, m, OH),

1722 (vs), 1705 (s), 1386 (m), 1299 (m), 1276 (m), 1200 (m), 1137 (m), 1054 (s), 730 (m), 690 (m) cm^{-1}. ^1H NMR ([D_6]DMSO): δ = 1.19 (t, 3H, ^3J = 7.1 Hz, OCH_2CH_3), 3.37 (d, 1H, ^3J = 14.1 Hz, NCH^{endo}), 4.08–4.21 (m, 5H, C*H*C*H*, NCH^{exo}, OCH_2), 5.75 (s, 1H, OH), 6.90 (s, 1H, OH), 7.32–7.37 (m, 3H, H_{Ar}), 7.48–7.51 (m, 1H, H_{Ar}), 7.56–7.59 (m, 2H, H_{Ar}), 7.66–7.70 (m, 2H, H_{Ar}), 7.77–7.80 (m, 1H, H_{Ar}) ppm. ^1H NMR ([D_6]acetone): δ = 1.25 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3), 3.48 (d, ^3J = 14.2 Hz, 1H, NCH^{endo}), 4.09 (d, ^3J = 7.5 Hz, 1H, C*H*CH), 4.22–4.29 (m, 3H, NCH^{exo} and OCH_2), 4.41 (d, ^3J = 7.5 Hz, 1H, C*H*CH), 5.53 (s, 1H, OH), 6.30 (s, 1H, OH), 7.38–7.85 (m, 9H, H_{Ar}) ppm. ^{13}C NMR ([D_6]DMSO): δ = 13.63 (OCH_2CH_3), 45.32 and 49.29 (*CHC*H), 51.59 (NCH_2), 61.34 (OCH_2), 88.40 (*C*OC), 89.96 ($C(OH)_2$), 93.34 (CO*C*); 122.81, 125.11, 126.92, 128.80, 129.14, 130.88, 131.57 (2 C), 132.78, 137.03 (CH_{Pht}, C_{Pht}, CH_{Ph}, C_{Ph}); 162.84 (*C*O_2Et), 166.4 (NC=O), 172.38 and 173.48 (O=*C*N*C*=O) ppm. MS (CI): *m*/*z* (%) = 475 $[M + C_2H_5]^+$, 447 $[M + H]^+$. Anal. calcd. for $C_{24}H_{20}N_2O_8$ (464.44): C 62.07, H, 4.34, N, 6.03; found: C 61.95, H 4.35, N 6.02.

When gem-diol **17** was kept at 130 °C/0.08 mbar for 7 h, it was converted completely into ketone **2** ($C_{24}H_{18}N_2O_7$), which was identified by its spectroscopic data.[14b]

Crystal structure determination for compounds 10a and 15. Data collection for **10a** was performed with an image-plate diffraction system (IPDS, Stoe) using monochromated Mo-Kα radiation, that for **15** with a STADI VARI PILATUS (Stoe) using Cu-Ka radiation. The structures were solved with direct methods and refined by a full-matrix least-squares procedure using F^2 values. Software for structure solution and refinement: SHELX-97;[37] molecule plots: ORTEP-3.[38] CCDC-813221(**10a**) and -813222 (**15**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Data for **10a.** Crystal data: $C_{30}H_{26}N_2O_{10}$, M = 574.53, triclinic space group P -1, a = 10.0929(13), b = 10.1304(13), c = 14.0475(19) Å, α = 69.514(15), β = 76.960(16), γ = 87.645(16)°, V = 1309.6(3) $Å^3$, Z = 2, D_c = 1.457 g cm^{-3}, μ = 0.11 mm^{-1}. Data collection: crystal size 0.38×0.27×0.15 mm, T = 190 K, 12552 reflections in the range θ = 2.07–26.03°, 4766 unique reflections (R_{int} = 0.0405). Structure refinement results: Refinement of 383 parameters using all 4766 data gave final indices R_1 = 0.0716 and wR_2 = 0.0891 (0.0382 and 0.0811 for reflection data with $I > 2\sigma(I)$). The residual electron density was between 0.49 and -0.35 e $Å^{-3}$.

Data for **15.** Crystal data: $C_{21}H_{19}NO_9$, M = 429.37, triclinic space group P -1, a = 9.6943(5), b = 11.0681(6), c = 11.1106(6) Å, α = 65.539(4), β = 82.316(4), γ = 65.197(4)°, V = 983.89(9) $Å^3$, Z = 2, D_c = 1.449 g cm^{-1}, μ = 0.98 cm^{-1}. Data collection: crystal size 0.2×0.2×0.1 mm, T = 150 K, Cu-Ka radiation (λ = 1.54186 Å), 7349 reflections in the range θ = 4.39–75.97°, 3651 unique reflections (R_{int} = 0.0932). Structure refinement results: Refinement of 285 parameters using all 3651 data gave final indices R_1 = 0.1165 and wR_2 = 0.0963 (0.0447 and 0.0836 for reflection data with $I > 2\sigma(I)$). The residual electron density was between 0.30 and -0.25 e $Å^{-3}$.

Acknowledgements

We thank Jens Richter (Stoe & Cie GmbH, Darmstadt, Germany) for the data collection in the X-ray diffraction analysis of compound **15**.

References

1. Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley & Sons: New York, 1998.
2. Selected recent reviews: (a) Doyle, M. P.; Forbes, D. C. *Chem. Rev*. **1998**, *98*, 911. (b) Davies, H. M. L.; Beckwith, R. E. *Chem. Rev.* **2003**, *103*, 2861. (c) Wee, A. G. H. *Curr. Org. Synth.* **2006**, *3*, 499. (d) Ferreira, V. F. *Curr. Org. Chem.* **2007**, *11*, 177. (e) Zhang, T.; Wang, J. *Tetrahedron* **2008**, *64*, 6577.
3. (a) Podlech, J.; Seebach, D. *Liebigs Ann. Chem.* **1995**, 1217. (b) Seebach, D.; Ciceri, P. E.; Overhand, M.; Jaun, B.; Rigo, D.; Oberer, L.; Hommel, U.; Amstutz, R.; Widmer, H. *Helv. Chim. Acta* **1996**, *79*, 2043. (c) Marti, R. E.; Bleicher, K. H.; Bair, K. W. *Tetrahedron Lett.* **1997**, *38*, 6145. (e) Yang, H.; Foster, K.; Stephenson, C. R. J.; Brown, W.; Roberts, E. *Org. Lett.* **2000**, *2*, 2177 (photochemical reaction).
4. Podlech, J.; Linder, M. R. *J. Org. Chem.* **1997**, *62*, 5873.
5. Sengupta, S.; Das, D. *Synth. Commun.* **1998**, *28*, 403.
6. Podlech, J.; Seebach, D. *Helv. Chim. Acta* **1995**, 1238.
7. Hon, Y.-S.; Chang, R.-C. *Heterocycles* **1991**, *32*, 1089.
8. Hanessian, S.; Fu, J.-M. *Can. J. Chem.* **2001**, *79*, 1812.
9. Li, M.; Zhou, P.; Roth, H. F. *Synthesis* **2007**, 55.
10. Reviews: (a) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263. (b) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223.
11. Selected recent examples: (a) Padwa, A.; Hasegawa, T.; Liu, B.; Zhang, J. *J. Org. Chem.* **2000**, *65*, 7124. (b) Hodgson, D. M.; Stupple, P. A.; Pierard, F. Y. T. M.; Labande, A. H.; Johnstone, C. *Chem. Eur. J.* **2001**, *7*, 4465. (c) Zhou, C.-Y.; Chan, P. W. H.; Che, C.-M. *Synthesis* **2003**, 1403. (d) Molchanov, A. P.; Diev, V. V.; Kopf, J.; Kostikov, R. R. *Russ. J. Org. Chem.* **2005**, *41*, 194. (e) Tsutsui, H.; Shimada, N.; Abe, T.; Anada, M.; Nakajima, M.; Nakamura, S.; Nambu, H.; Hashimoto, S. *Adv. Synth. Catal.* **2007**, *349*, 521. (f) Oh, C. H.; Lee, J. H.; Lee, S. J.; Kim, J. I.; Hong, C. S. *Angew. Chem.* **2008**, *120*, 7615; *Angew. Chem. Int. Ed.* **2008**, 47, 7505. (g) Suga, H.; Ebiura, Y.; Fukushima, K.; Kakehi, A.; Baba, T. *J. Org. Chem.* **2005**, *70*, 10782. (h) Suga, H.; Higuchi, S.; Ohtsuka, M.; Ishimoto, D.; Arikawa, T.; Hashimoto, Y.; Misawa, S.; Tsuchida, T.; Kakehi, A.; Baba, T. *Tetrahedron* **2010**, *66*, 3070.
12. (a) McMills, M. C.; Wright, D. In *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*; Padwa, A.; Pearson, W. H. Eds.;

John Wiley & Sons: Hoboken, New Jersey, 2003; p 253. (b) France, S.; Phun, L. H. *Curr. Org. Synth*. **2010**, *7*, 332.
13. (a) Padwa, A.; Lynch, S. M.; Mejía-Oneto, J. M.; Zhang, H. *J. Org. Chem.* **2005**, *70*, 2206. (b) Mejía-Oneto, J. M.; Padwa, A. *Org. Lett.* **2006**, *8*, 3275. (c) Navickas, V.; Ushakov, D. B.; Maier, M. E.; Ströbele, M.; Meyer, H.-J. *Org. Lett.* **2010**, *12*, 3418. (d) Grillet, F.; Sabot, C.; Anderson, R.; Babjak, M.; Greene, A. E.; Kanazawa, A. *Tetrahedron* **2011**, *67*, 2579.
14. (a) Padwa, A.; Hertzog, D. L.; Chinn, R. L. *Tetrahedron Lett.* **1989**, *30*, 4077. (b) Padwa, A.; Dean, D. C.; Hertzog, D. L.; Nadler, W. R.; Zhi, L. *Tetrahedron* **1992**, *48*, 7565.
15. Nikolaev, V. V.; Krylov, I. S.; Schulze, B.; Rodina, L. L. *Russ. J. Org. Chem.* **2005**, *41*, 784.
16. The synthesis of **1** starting from *N*-phthaloylglycine is less proficient (28% yield); ref. 14.
17. (a) Bose, A. K.; Greer, F.; Price, C. C. *J. Org. Chem.* **1958**, *23*, 1335. (b) Bose, A. K. *Org. Synth. Coll. Vol. 5* **1973**, 973.
18. Griesbeck, A. G.; Mauder, H.; Müller, I. *Chem. Ber.* **1992**, *125*, 2467.
19. 19a. (a) Schuda, P. F.; Greenlee, W. J.; Chakravarty, P. K.; Eskola, P. *J. Org. Chem.* **1988**, *53*, 873. (b) For a mechanistic explanation, see: Mansour, T. S. *Synth. Commun.* **1989**, *19*, 659.
20. Goddard-Borger, E. D.; Stick, R. V. *Org. Lett.* **2007**, *9*, 3797.
21. Zimmerman, H. E.; Simkin, R. D. *Tetrahedron Lett.* **1964**, *28*, 1847.
22. Nilsen, B. J.; Undheim, K. *Acta Chem. Scand.* **1976**, *30*, 619.
23. (a) Ibata, T.; Toyoda, J.; Sawada, M.; Takai, Y.; Tanaka, T. *Tetrahedron Lett.* **1988**, *29*, 317. (b) Ueda, K.; Ibata, T.; Takebayashi, M. *Bull. Chem. Soc. Jpn*. **1972**, *45*, 2779.
24. (a) Toyoda, J.; Ibata, T.; Tamura, H.; Ogawa, K.; Nishino, T.; Takebayashi, M. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2212. (b) Ibata, T.; Toyoda, J. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2489.
25. Padwa, A.; Curtis, E. A. *Arkivoc* **2001**, (*ii*), 51.
26. (a) Maas, G.; Singer, B.; Wald, P.; Gimmy, M. *Chem. Ber.* **1988,** *121*, 1847. (b) Herz, H.-G.; Schatz, J.; Maas, G. *J. Org. Chem.* **2001**, *66*, 3176. (c) Nikolai, J.; Schlegel, J.; Regitz, M.; Maas, G. *Synthesis* **2002**, 497. (d) Gerster, H.; Espenlaub, S.; Maas, G. *Synthesis* **2006**, 2251. (e) Gerster, H.; Maas, G. *Z. Naturforsch.* **2008**, *63b*, 384.
27. Smith, M. B.; March, J. *March's Advanced Organic Chemistry*, 5th Ed.; John Wiley & Sons: New York, 2001; pp 1175.
28. See, for example: Thiakou, K. A.; Bekiari, V.; Raptopoulou, C. P.; Psycharis, V.; Lianos, P.; Perlepes, S. P. *Polyhedron* **2006**, *25*, 2869.
29. For an example – an α-chloropyruvamide – and some references, see: Majcen-Le Maréchal, A.; Le Grel, P.; Robert, A.; Pavc, J. *Tetrahedron* **1997**, *53*, 13739.
30. For a stable 2,3-diaza-7,7-dihydroxynorbornanone derivative, see: Marullo, N. P.; Alford, J. A. *J. Org. Chem*. **1968**, *33*, 2368.
31. Selected examples: (a) Serianni, A. S.; Clark, E. L.; Barker, R. *Carbohydrate Research* **1979**, *72*, 79. (b) McNally, D. J.; Schoenhofen, I. C.; Mulrooney, E. F.; Whitfield, D. M.; Vinogradov, E.; Lam, J. S.; Logan, S. M.; Brisson, J.-R. *ChemBioChem* **2006**, *7*, 1865.

32. See, for example: (a) Blanchard, J. S.; Brewer, C. F.; Englard, S.; Avigad, G. *Biochemistry* **1982**, *21*, 75. (b) Sheldrick, B.; Mackie, W.; Akrigg, D. *Acta Cryst.* **1983**, *C39*, 1259. (c) Sedmera, P.; Volc, J.; Havlíček, V.; Pakhomova, S.; Jegorov, A. *Carbohydrate Res.* **1997**, *297*, 375.
33. Solution and solid-state NMR studies on the hydration of the antibiotic trospectomycin sulfate: Likar, M. D.; Taylor, R. J.; Fagerness, P. E.; Hiyama, Y.; Robins, R. H. *Pharmaceut. Res.* **1993,** *10*, 75.
34. (a) MacConnell, J. G.; Arison, B. H.; Doss, G. A.; Monaghan, R. L. US 5,317,031 (May 31, 1994). (b) Treiber, L. R.; Doss, G. A.; Arison, B. H. US 5,322,855 (June 21, 1994).
35. Bregant, N.; Nuri, A.; Stromar, M. *Croat. Chem. Acta* **1975**, *47*, 595.
36. Adank, K.; Pfenninger, H. A.; Stoll, W. G.; Viscontini, M. *Helv.Chim. Acta* **1961**, *44*, 2131.
37. Sheldrick, G. M. SHELXS/L-97 – Program for the Solution and Refinement of Crystal Structures from Diffraction Data, University of Göttingen, Göttingen, 1997.
38. Farrugia, L. J. ORTEP-3 for Windows, University of Glasgow, Glasgow, 1998.

