Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron 63 (2007) 12172–12178
Tetrahedron

Ruthenium catalysts for carbenoid intramolecular C–H insertion of 2-diazoacetoacetamides and diazomalonic ester amides

Markus Grohmann and Gerhard Maas*

Institute for Organic Chemistry I, University of Ulm, Albert-Einstein-Allee 11, D-89081 Ulm, Germany

Received 20 August 2007; revised 20 September 2007; accepted 20 September 2007
Available online 26 September 2007

Abstract—The intramolecular carbenoid C–H insertion of 2-diazoacetoacetamides, leading to γ- and/or β-lactams, is catalyzed effectively by dinuclear Ru(I,I) complexes of the type $[Ru_2(\mu\text{-}L^1)_2(CO)_4L^2_2]$, where L^1 is a bidentate bridging acetate, calix[4]arenedicarboxylate, saccharinate or 6-chloropyridin-2-olate ligand. By comparison with rhodium catalysts, namely dirhodium tetraacetate and dirhodium calix[4]arenedicarboxylate complexes, product yields are similarly high and the regioselectivity of the insertion reaction is the same. Surprisingly, even the ruthenium(0) cluster $Ru_3(CO)_{12}$ was found to be an effective catalyst for carbenoid C–H insertion of 2-diazoacetoacetamides and also of some diazoacetamides. In terms of diastereoselectivity, trans-isomers of β- and γ-lactams are obtained. However, the β-lactam obtained from diazomalonic ester amide **2** yields the cis-isomer stereoselectively, which slowly rearranges to the trans-isomer.

1. Introduction

Transition-metal catalyzed intramolecular carbenoid C–H insertion of appropriate α-diazocarbonyl compounds is a modern tool for the convenient construction of carbo- and heterocyclic compounds. The versatility of this approach has been documented in several reviews.[1–5] Dinuclear Rh(II,II) complexes such as $Rh_2(OAc)_4$, other dirhodium tetracarboxylates and structurally similar dirhodium tetraamidates are the current catalysts of choice for these transformations. A notable application of the rhodium-mediated carbenoid intramolecular C–H insertion strategy is the conversion of a variety of α-diazoacetamides, 2-diazoacetoacetamides, diazomalonic ester amides, α-diazo-α-(phenylsulfonyl)acetamides, and α-diazo-α-(dialkoxyphosphoryl)acetamides into β- and γ-lactams.[6] The influence of different factors, such as electronic properties of the catalyst, constitution of the diazo compound, and substitution pattern at the amide nitrogen atom, on the regio- and stereoselectivity of lactam formation has been reviewed.[7,8]

Recently, several types of ruthenium complexes are emerging as potential alternatives to the established rhodium catalysts for carbenoid transformations of diazo compounds. While most attention has been paid so far to ruthenium-catalyzed olefin cyclopropanation reactions,[9,10] some reports have indicated lately that certain ruthenium complexes effectively catalyze intramolecular carbenoid C–H insertion reactions as well. Thus, Che et al. have identified ruthenium porphyrins as effective catalysts for this reaction type, including the formation of β-lactams from the anion of 2-(tosylhydrazono)acetoacetamides.[11] Furthermore, they have reported that $[RuCl_2(p\text{-cymene})]_2$ effectively catalyzes the formation of lactams from diazomalonic ester amides and 2-diazo-3-oxocarboxamides.[12]

We have found that dinuclear Ru(I,I) complexes of the type $[Ru_2(\mu\text{-}L^1)_2(CO)_4L^2_2]$, where L^1 is a bidentate bridging carboxylate or amidate ligand and L^2 represents a weakly coordinating neutral axial ligand, catalyze effectively the conversion of α-diazoacetamides into γ- and/or β-lactams by carbenoid C–H insertion.[13] In particular, complexes with bridging 6-chloropyridin-2-olate or saccharinate ligands emerged as interesting alternatives to $Rh_2(OAc)_4$ and related rhodium catalysts. We have now turned our attention to ruthenium-catalyzed carbenoid reactions of 2-diazoacetoacetamides and diazomalonic ester amides. Due to the presence of a second electron-withdrawing substituent at the diazo function, the diazo carbon atom is less nucleophilic than in α-diazoacetamides, and we wondered whether our Ru(I,I) complexes, which appear to be somewhat less electrophilic than dirhodium tetraacetate, would be able to induce effectively the elimination of dinitrogen en route to the reactive ruthenium carbene intermediates. We report now that dinuclear Ru(I,I) carboxylate and amidate complexes catalyze very effectively the conversion of the mentioned 3-oxo-2-diazoacetamides into lactams; moreover, we show for the first time that the trinuclear ruthenium cluster $Ru_3(CO)_{12}$ catalyzes intramolecular carbenoid C–H

Keywords: C–H insertion; Diazo compounds; Diazoacetoacetamides; Lactams; Ruthenium.
* Corresponding author. Tel.: +49 (0)731 5022790; fax: +49 (0)731 5022803; e-mail: gerhard.maas@uni-ulm.de

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.09.053

insertion of diazoacetamides, 2-diazoacetoacetamides, and diazomalonic ester amides.

2. Results and discussion

2-Diazoacetoacetamides **1a–d** were prepared, with some modifications, along known procedures[14,15] by reaction of a *sec*-amine with diketene followed by a diazo transfer reaction using tosyl azide.[16] Diazomalonic ester amide **2** was also obtained by diazo group transfer (Fig. 1).

The catalysts used in this work are shown in Figure 2. We have reported before that dinuclear Ru(I,I) complexes **4** (existing as a coordination polymer in the solid state) and **6–8** are suitable catalysts for the conversion of α-diazoacetamides into lactams by intramolecular C–H insertion.[13] The Ru(II)-*p*-cymene complex **9** is less suited for this particular transformation, but was included here because it converts, e.g., the ethylester analog of **2** into a β-lactam in excellent yield.[12] The results obtained with the ruthenium catalysts were compared with those obtained with the benchmark catalyst $Rh_2(OAc)_4$ (**3**). In addition, dirhodium bis(calix[4]-arenedicarboxylate) **5** was included for comparison with the diruthenium calix[4]arenecarboxylate complex **6**; in both cases, it was interesting to learn whether the calixarene ligands would exert a steric influence on the regioselectivity of the intramolecular carbenoid C–H insertion.

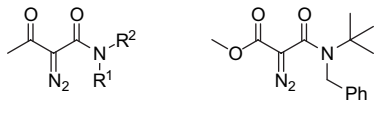


Figure 1.

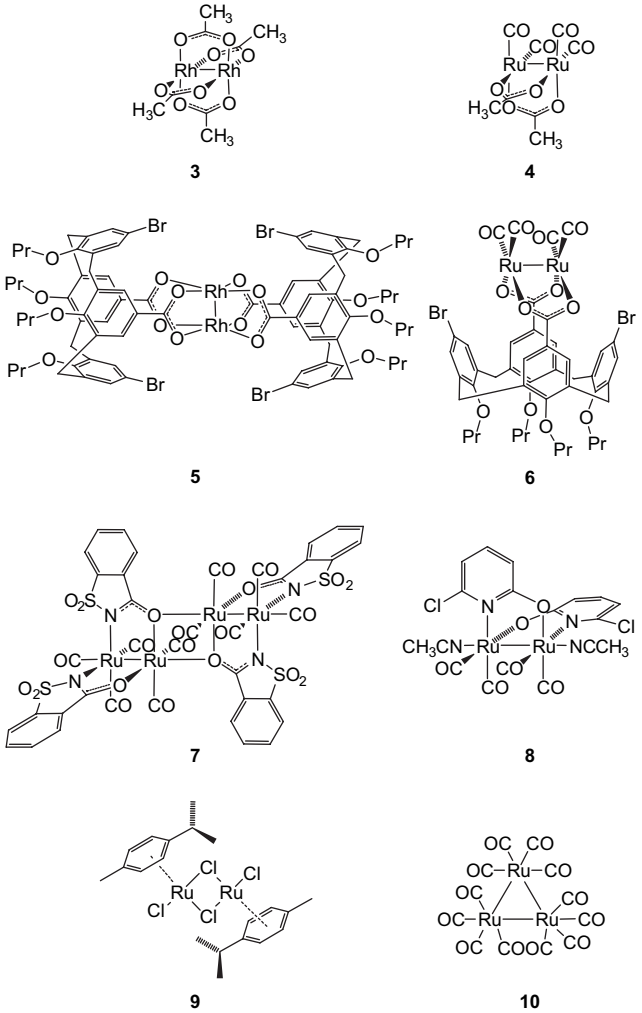
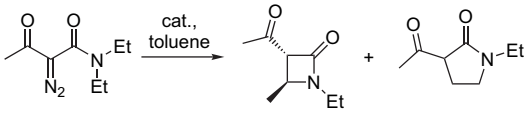


Figure 2. Catalysts used in this study.

The results of the catalytic decomposition of diazoamides **1a–d** and **2** are presented in Tables 1–5. In each case, the reaction with at least one of the catalysts was worked up, and the products were fully characterized. In all other cases, the yields were determined after complete conversion of the diazo compound by ^{1}H NMR analysis of the crude reaction mixture using naphthalene as an internal reference.

The following general observations were made: (a) the dinuclear Ru(I,I) carboxylate and amidate complexes **4** and **6–8** are excellent catalysts for the conversion of diazoacetoacetamides into γ- and/or β-lactams by carbenoid C–H insertion. In many cases, yields above 90% are achieved, which are practically the same as with the two rhodium catalysts **3** and **5**. Only in the case of diethylamide **1a**, the rhodium catalysts are the better choice, because they catalyze the carbenoid insertion into the non-activated methyl C–H bond, leading to γ-lactam **12a**, more effectively than the ruthenium catalysts. Nevertheless, it should be noted that the ruthenium catalysts convert **1a** into lactams **11a** and **12a** in a much higher combined yield (65–87%) than in the case of *N*,*N*-diethyl-2-diazoacetamide, where the γ-lactam was obtained in 5–28% yield and no β-lactam was formed.[13] (b) The reactions were fast and high-yielding under the chosen standard conditions (toluene, 70 °C, 3 mol % of catalyst). When the reactions with **1b** were run in dichloromethane at 40 °C,

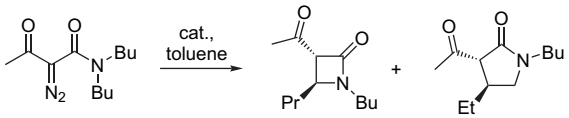
Table 1. Catalytic decomposition of *N*,*N*-diethyl-2-diazoacetoacetamide (**1a**) in toluene at 70 °C



Catalyst[a]	Time [h]	Yield[b] [%]		Ratio of **12a/11a**	Total yield of lactams [%]
		11a	**12a**		
3	1	17 (11[c])	77 (68[c])	4.5	94 (79[c])
4	12	18	48	2.7	66
5	1	13	77	5.9	90
6	12	20	48	2.4	68
7	12	15	50	3.3	65
8	5	17	70	4.1	87
9	12	9	19	2.1	28

[a] Catalyst loading was 3 mol % (1 mol % for **11**).
[b] Yields were determined by ^{1}H NMR analysis of the reaction mixture.
[c] Isolated yield after purification by column chromatography over basic alumina.

Table 2. Catalytic decomposition of *N*,*N*-dibutyl-2-diazoacetoacetamide (**1b**)



1b **11b** **12b**

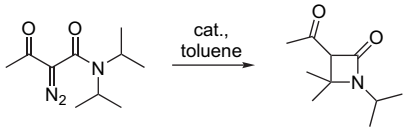
Catalyst	Catalyst loading [mol %]	Solvent	*T* [°C]	Time [h]	Yield[a] [%]		Ratio of **12b/11b**	Total yield of lactams [%]
					11b	**12b**		
3	3	Toluene	70	1	3	91	30.3	94
	3	CH_2Cl_2	40	1	2	90	45.0	92
4	3	Toluene	70	12	5	83	16.6	88
	3	CH_2Cl_2	40	72	3	92	30.7	95
5	1	Toluene	70	1	12 (7[b])	81(70[b])	6.8	93 (77[b])
	1	CH_2Cl_2	40	1	4	75	18.8	79
6	3	Toluene	70	1	4	80	20.0	84
	3	CH_2Cl_2	40	1	2	94	47.0	96
7	3	Toluene	70	1	2	89	44.5	91
	3	CH_2Cl_2	40	1	2	83	41.5	85
8	3	Toluene	70	1	1	98	98.0	99
	3	CH_2Cl_2	40	1	1	98	98.0	99
9	3	Toluene	70	8	4	44	11.0	48
	3	CH_2Cl_2	40	144	2	53	26.5	55

[a] Yields were determined by ^{1}H NMR analysis of the reaction mixture.
[b] Isolated yield after purification by column chromatography over basic alumina.

however, almost the same reaction time and yields were generally observed (Table 2). Furthermore, the use of only 1 mol % of catalyst somewhat enhances the reaction time, but does not affect the yields significantly (Table 5). (c) By comparison with catalysts **4** and **6–8**, $[RuCl_2(p\text{-cymene})]_2$ (**9**) is much less suited to catalyze carbenoid C–H insertion of *N*,*N*-dialkyl-diazoacetoacetamides **1a–c**; high catalytic effectiveness is only observed when β-lactam formation by insertion into the activated *N*-benzyl C–H bond can occur (**1d**, **2**), in agreement with reported examples.[12]

In terms of regioselectivity (formation of β- vs γ-lactam), the ruthenium catalysts studied here show the same general trends as the two rhodium carboxylate catalysts (for a discussion of results obtained with $Rh_2(OAc)_4$ as catalyst, see Refs. 7,14,15,17), but in the case of diethylamide **1a**, a lower preference for the γ-lactam in the ruthenium-catalyzed reactions can be noted. Whether this is related to electronic[17] or steric properties of the metal fragment in the intermediate metal–carbene complexes is not clear. It was also interesting to see whether rhodium complex **5**, bearing two dibromocalix[4]arenedicarboxylate ligands, would give rise to a particular regioselectivity. As Tables 1 and 2 show, the effect appears to be contradictory, giving the highest γ/β ratio in the case of **1a**, but the lowest one in the case of **1b** (reaction in toluene). However, considering the absolute

Table 3. Catalytic decomposition of *N*,*N*-diisopropyl-2-diazoacetoacetamide (**1c**) in toluene at 70 °C

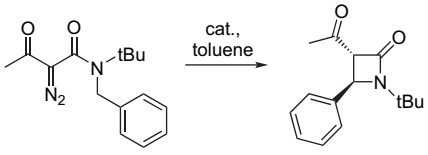


1c **11c**

Catalyst[a]	Time [h]	Yield[b] of **11c** [%]
3	1	96 (91[c,d])
4	5	87
5	1	96
6	1	90
7	5	84
8	1	78
9	8	46

[a] Catalyst loading was 3 mol % (1 mol % for **5**).
[b] Yields were determined by ^{1}H NMR analysis of the reaction mixture.
[c] Isolated yield after purification by column chromatography over basic alumina.
[d] A yield of 89% has been reported (benzene, rt, 1 mol % of $Rh_2(OAc)_4$).[14]

Table 4. Catalytic decomposition of *N*-benzyl-*N*-*tert*-butyl-2-diazoacetoacetamide (**1d**) in toluene at 70 °C

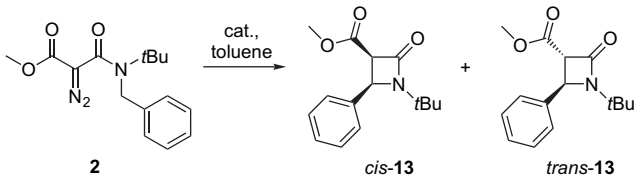


1d **11d**

Catalyst[a]	Time [h]	Yield[b] of **11d** [%]
3	1	93 (93[c,d])
4	1	81
5	1	99
6	1	90
7	1	93[e]
8	1	90[e]
9	1	91

[a] Catalyst loading was 3 mol % (1 mol % for **5**).
[b] Yields were determined by ^{1}H NMR analysis of the reaction mixture.
[c] Isolated yield after purification by column chromatography over basic alumina.
[d] A 98% yield has been reported (benzene, 80 °C, 1 mol % of $Rh_2(OAc)_4$).[14]
[e] Cis/trans mixture, see text.

Table 5. Catalytic decomposition of *N*-benzyl-*N*-*tert*-butyl-2-methoxycarbonyl-2-diazoacetamide (**2**) in toluene at 70 °C



2 *cis*-**13** *trans*-**13**

Catalyst	Catalyst loading [mol %]	Time [h]	Yield[a] [%]		Ratio of cis/trans	Total yield [%]
			cis-**13**	*trans*-**13**		
3	3	1	86	11	7.8	97 (96[b])
	1	2	86	12	7.2	98
4	3	8	78	14	5.6	92
	1	14	22	70	0.3	92
5	1	1	58	39	1.5	97
6	3	1	72	27	2.7	99
	1	1.5	84	13	6.5	97
7	3	1	86	8	10.8	94
	1	1.5	61	30	2.0	91
	0.1	168	42	35	1.2	77
8	3	1	78	18	4.3	96
	1	1.5	77	19	4.8	96
9	3	1	93	4	23.2	97
	1	1	95	4	23.8	99

[a] Yields were determined by ^{1}H NMR analysis of the reaction mixture.
[b] Isolated yield after purification by column chromatography over basic alumina.

yields of the two lactams in both cases, the deviations from reactions using the other catalysts are not large.

β-Lactams **11a**,**b**,**d** were obtained with complete trans-selectivity (^{1}H NMR: $^3J_{H,H}$=2.0–2.3 Hz for ring protons) in most cases, which confirms results already reported.[14,17] However, we observed that treatment of **1d** with the ruthenium saccharinate complex **7** produced a cis/trans mixture of **11d**, the ratio of which varied in different runs. Control experiments showed an approximate 1:1 ratio immediately after complete conversion of the diazo compound (ca. 1 h), whereas an almost complete cis→*trans* isomerization had taken place after the reaction mixture had been kept at 70 °C for 12 h. Similar observations were made when catalyst **8** was used. It has been reported that related β-lactams bearing phosphoryl groups[6k] undergo this epimerization in the presence of basic alumina, and for 3-methoxycarbonyl-azetidinones, epimerization 'under the reaction conditions' has been suggested.[18]

In contrast to the acetyl-substituted diazocarboxamides **1**, the methoxycarbonyl-substituted analog **2** yields cis/trans-mixtures of β-lactam **13** in ratios which are strongly catalyst-dependent (Table 5). With catalyst **9**, the cis-isomer is formed almost exclusively, similar to the corresponding ethoxycarbonyl analog.[12] With all other catalysts, the amount of *trans*-**13** increases markedly under identical reaction conditions, the highest yield being 39 and 27% for the two calixarenedicarboxylate complexes **5** and **6**, respectively. An unusual dependence of the cis/trans ratio on the catalyst concentration was observed for some of the ruthenium catalysts: a reduction of the catalyst concentration from 3 to 1 (and eventually 0.1) mol % caused a strong decrease of the cis/trans ratio for the ruthenium acetate (**4**) and saccharinate (**7**) catalysts, but an increase of that ratio for ruthenium-calixarenedicarboxylate catalyst **6**. The observed diastereoselectivities are likely to represent the original results of the respective reaction, because control experiments showed that the cis/trans ratio was not a function of the reaction time (which was longer with lower catalyst concentrations), in contrast to the decomposition of **11d** by ruthenium saccharinate **7**, as described above. The reason for this correlation between catalyst concentration and diastereoselectivity is not known so far.

The readily available[19] complex $Ru_3(CO)_{12}$ has largely been neglected as a catalyst for diazo decomposition reactions so far. Doyle et al.[20] have reported that this complex catalyzes two carbenoid reactions of ethyl diazoacetate, namely cyclopropanation of the electron-rich double bond of butyl vinyl ether in 65% yield, and *S*-ylide chemistry with allyl methyl sulfide in 96% yield. We were pleased to find that $Ru_3(CO)_{12}$ also catalyzes the lactam formation from 2-diazo-3-oxocarboxamides **1a–d** and **2** (Table 6). Although the reactions proceed significantly slower in most cases, yields are similar or not much lower than with the other ruthenium carbonyl catalysts used in this study. The regio- and stereoselectivity of the carbenoid cyclization reaction places this catalyst in the neighborhood of **4** and **7**.

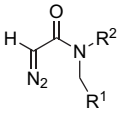
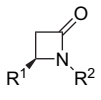
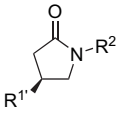
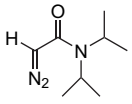
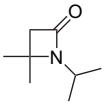
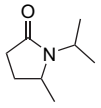
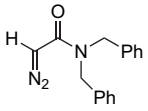
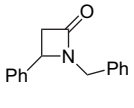
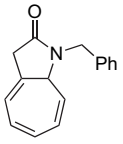
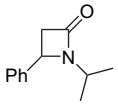
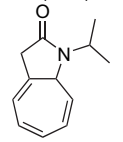
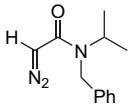
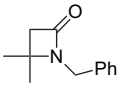
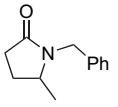
Encouraged by these results, we investigated also the $Ru_3(CO)_{12}$-catalyzed decomposition of 2-diazoacetamides **14a–e** (Table 7). Again, the reactions proceeded more slowly than with the other ruthenium carbonyl catalysts. The product distribution is similar to that obtained with catalysts **4**, **6**, **8**, and **9**,[13] but the total yields of lactams are generally lower.

Table 6. Decomposition of 2-diazo-3-oxocarboxamides **1a–d** and **2** with $Ru_3(CO)_{12}$ (**10**)

Diazoamide	Catalyst loading [mol %]	Solvent	*T* [°C]	Time [h]	Products (yield,[a] %)	
					β-Lactam	γ-Lactam
1a	3	Toluene	70	12	**11a** (16)	**12a** (58)
1b	3	Toluene	70	12	**11b** (4)	**12b** (73)
	3	CH_2Cl_2	40	30	**11b** (2)	**12b** (93)
1c	3	Toluene	70	5	**11c** (75)	
1d	3	Toluene	70	1	**11d** (84)	
2	3	Toluene	70	4	*cis*-**13** (77), *trans*-**13** (9)	
	1	Toluene	70	6	*cis*-**13** (80), *trans*-**13** (7)	

[a] Yields were determined by ^{1}H NMR analysis of the reaction mixture.

Table 7. $Ru_3(CO)_{12}$-catalyzed decomposition of 2-diazoacetamides **14a–e**[a]

Diazoacetamide	Products (yield,[b] %)	
		
14a: R^1 = Me, R^2 = Et **14b**: R^1 = Pr, R^2 = Bu	**15a** (0%) **15b** (0%)	**16a** (24%) ($R^{1'}$ = H) **16b** (63%) ($R^{1'}$ = Et)
		
14c	**15c** (49%)	**16c** (22%)
		
14d	**15d** (2%)	**17** (45%)
		
	15e (1%)	**18** (45%)
		
14e	**15f** (9%)	**16e** (17%)

[a] Conditions: dichloromethane, 40 °C, 12 h (**14a**: 24 h), 3 mol % of catalyst; the reactions were carried out by analogy to the procedure given in Section 4.4.

[b] Yields were determined by ^{1}H NMR analysis of the reaction mixture; see Ref. 13 for characterization of the products.

3. Conclusion

We have found that diruthenium(I,I)-tetracarbonyl complexes bearing chelating carboxylate, saccharinate, and 6-chloropyridin-2-olate ligands are excellent catalysts for the carbenoid C–H insertion by which *N*,*N*-disubstituted 2-diazoacetoacetamides and malonic ester amides are converted into γ- and/or β-lactams. With respect to yields and regioselectivity, large differences between the various catalysts were not observed. For the first time, the trinuclear ruthenium(0) cluster $Ru_3(CO)_{12}$, which is a practical synthetic precursor for complexes **4** and **6–8**, was identified as a catalyst for intramolecular carbenoid C–H insertion; although it reacts more sluggishly than the latter catalysts, the lactam yields are (almost) the same and regio- and stereoselectivity are similar. Considering the much higher prize of rhodium compared to ruthenium, some of the ruthenium catalysts are in general attractive alternatives to the established rhodium catalysts for the carbenoid transformations described in this study.

4. Experimental

4.1. General methods

Column chromatography was performed on silica gel 60 (0.063–0.2 mm, Merck) or alumina (aluminum oxide 90 basic, activity I, 0.063–0.2 mm, Merck) with distilled cyclohexane and ethyl acetate as eluents. NMR spectra were recorded at 400.1 MHz (^{1}H) or 100.6 MHz (^{13}C) in $CDCl_3$ solution with tetramethylsilane (TMS) as the internal standard (m_c=centered multiplet). Infrared spectra were recorded on a Bruker Vector 22 spectrometer. Mass spectra were obtained on a Finnigan MAT SSQ 7000 spectrometer in the CI mode. Elemental analyses were carried out with an Elementar Vario EL elemental analyzer.

4.2. Materials

Diazo compounds **1a**,[21] **1c**,[14] and **1d**[14] have been prepared before, but details of the synthesis and/or spectroscopic data have not been communicated. The catalysts $[Ru_2(\mu\text{-}OAc)_2(CO)_4]_n$ (**4**),[22] **5**,[23] **6**,[24] **7**,[25] and **8**[26] were prepared as described in the literature. The activity of catalyst **8** decreases on storing; therefore, it was re-activated prior to use by dissolution in dry acetonitrile, warming at 60 °C for 10 min, and evaporation of the solvent in a flow of argon.

4.3. Synthesis of diazoacetoacetamides 1; general procedure

2,2,6-Trimethyl-1,3-dioxen-4-one (50 mmol) and a *sec*-amine (50 mmol) were dissolved in *m*-xylene (10 mL). The mixture was heated at 120 °C. After the elimination of acetone had ceased, the mixture was kept at 150 °C for 30 min. Then, *m*-xylene was evaporated at 120 °C/80 mbar. The remaining crude acetoacetamide was used for the following diazo transfer reaction. Per 10 mmol of acetoacetamide, 20 mL of acetonitrile was added, followed by triethylamine (2 equiv) and *p*-toluenesulfonyl azide (1.1 equiv). The reaction mixture was stirred for 12 h before the solvent was evaporated. The crude product was dissolved in dichloromethane and pentane was added to precipitate most of the by-product (*p*-tosylamide). The solution was concentrated and the residue was subjected to column chromatography on silica gel.

4.3.1. *N*,*N*-Diethyl-2-diazo-3-oxobutanamide (1a). After column chromatography (chloroform as eluent), a yellow oil was obtained; yield: 74%. ^{1}H NMR: δ 1.21 (t, 6H, ^3J=7.1 Hz, CH_3), 2.34 (s, 2H, $COCH_3$), 3.38 (q, 4H, ^3J= 7.2 Hz, CH_2). ^{13}C NMR: δ 13.1 (CH_3), 27.3 ($COCH_3$), 41.9 (CH_2) 72.4 (CN_2), 160.4 (CO-amide), 190.1 (CH_3CO). IR (neat): ν 2104 (s), 1653 (s), 1457 (m), 1361 (m) cm^{-1}. MS (100 eV): *m*/*z* (%) 184 (21), 156 (100). Anal. Calcd for $C_8H_{13}N_3O_2$ (183.21): C 52.45, H 7.15, N 22.94. Found: C 52.26, H 7.21, N 23.01.

4.3.2. *N*,*N*-Dibutyl-2-diazo-3-oxobutanamide (1b). Column chromatography with cyclohexane/ethyl acetate (2:1) as eluent afforded a yellow oil; yield: 81%. ^{1}H NMR: δ 0.94 (t, 6H, ^3J=7.3 Hz, CH_3), 1.33 (m, 4H, CH_3CH_2), 1.57 (m, 4H, NCH_2CH_2), 2.33 (s, 3H, $COCH_3$), 3.32 (q, 4H, ^3J=7.6 Hz, CH_2). ^{13}C NMR: δ 13.6 (CH_3), 19.9 (CH_3CH_2), 27.1 ($COCH_3$), 29.8 (NCH_2CH_2), 47.2 (NCH_2), 72.3 (CN_2), 160.6 (CO-amide), 189.9 (CH_3CO). IR (neat): ν 2099 (s), 1635 (s), 1457 (m), 1422 (m), 1361 (m) cm^{-1}. MS (100 eV): *m*/*z* (%) 240 (37), 212 (100). Anal. Calcd for $C_{12}H_{21}N_3O_2$ (239.16): C 60.23, H 8.84, N 17.56. Found: C 60.22, H 8.77, N 17.24.

4.3.3. *N*,*N*-Diisopropyl-2-diazo-3-oxobutanamide (1c). Column chromatography with cyclohexane/ethyl acetate (2:1) as eluent afforded a yellow oil; yield: 62%. ^{1}H NMR: δ 1.35 (d, 12H, ^3J=6.6 Hz, CH_3), 2.31 (s, 3H, $COCH_3$), 3.68 (sept, 2H, ^3J=6.6 Hz, CH). ^{13}C NMR: δ 20.7 (CH_3), 27.0 ($CO\mathit{C}H_3$), 49.2 (CH), 72.8 (CN_2), 159.2 (CO-amide), 189.9 ($CH_3\mathit{C}O$). IR (neat): ν 2098 (s), 1639 (s), 1434 (m), 1362 (m), 1331 (m) cm^{-1}. MS (100 eV): *m*/*z* (%) 212 (66), 184 (34). Anal. Calcd for $C_{10}H_{17}N_3O_2$ (211.13): C 56.85, H 8.11, N 19.89. Found: C 56.69, H 8.02, N 19.78.

4.3.4. *N*-Benzyl-*N*-*tert*-butyl-2-diazo-3-oxobutanamide (1d). Column chromatography with cyclohexane/ethyl acetate (2:1) as eluent gave a yellow oil; yield: 91%. ^{1}H NMR: δ 1.43 (s, 9H, CH_3) 2.23 (s, 3H, $COCH_3$), 4.59 (s, 2H, CH_2), 7.18–7.32 (m, 10H, H_{Ph}). ^{13}C NMR: δ 27.0 ($CO\mathit{C}H_3$), 28.6 (CH_3), 51.0 (CH_2), 58.9 (C_q), 75.8 (CN_2), 126.2, 127.5, 128.8, 138.9 (all C_{Ph}), 163.2 (CO-amide), 189.5 ($CH_3\mathit{C}O$). IR (neat): 2102 (s), 1652 (s), 1453 (m), 1385 (m), 1362 (s) cm^{-1}. MS (100 eV): *m*/*z* (%) 274 (22), 246 (9), 218 (100). Anal. Calcd for $C_{15}H_{19}N_3O_2$ (273.15): C 65.91, H 7.01, N 15.37. Found: C 65.90, H 7.02, N 15.30.

4.3.5. *N*-Benzyl-*N*-*tert*-butyl-2-methoxycarbonyl-2-diazoacetamide (2). A solution of *N*-benzyl-*N*-*tert*-butylamine (10.7 mL, 59 mmol) in dichloromethane was added to a solution of malonic acid methylester chloride (6 mL, 56.2 mmol) in dichloromethane (30 mL). After 10 min 2 N aq NaOH (6 mL) was added and the solution was stirred for 4 h. The reaction mixture was extracted four times with a satd aq NH_4Cl solution. After drying (Na_2SO_4) and evaporation of the solvent, the crude malonic ester amide was used without further purification. The amide (9.07 g, 34.4 mmol) was dissolved in acetonitrile (90 mL), triethylamine (9.6 mL, 68.9 mmol) and *p*-toluenesulfonyl azide (7.46 g, 37.8 mmol) were added, and the mixture was stirred for 36 h at 20 °C. The solvent was evaporated, the crude product was dissolved in dichloromethane, and pentane was added in order to precipitate most of the by-product (tosylamide). After column chromatography over silica gel (220 g) with petroleum ether/ethyl acetate (9:1) as eluent, a yellow solid was obtained; yield: 4.46 g (45%), mp: 80.2–81.9 °C. ^{1}H NMR: δ 1.39 (s, 9H, $C(CH_3)_3$), 3.77 (s, 3H, OCH_3), 4.62 (s, 2H, CH_2), 7.19–7.34 (m, 5H, H_{Ph}). ^{13}C NMR: δ 28.7 (CH_3), 51.4 (CH_2), 52.1 (OCH_3), 58.9 (C_q), 68.0 (br, C=N_2), 126.7, 127.3, 128.6, 139.5 (C_{Ph}), 162.9 (CO), 163.1 (CO). IR (neat): ν 2128 (s), 1714 (s), 1612 (s), 1435 (br, m), 1363 (m) cm^{-1}. MS (100 eV): *m*/*z* (%) 290 (100), 262 (18), 234 (93). Anal. Calcd for $C_{15}H_{19}N_3O_3$ (289.33): C 62.27, H 6.62, N 14.52. Found: C 62.20, H 6.59, N 14.46.

4.4. Catalytic decomposition of diazocarboxamides 1a–d and 2; general procedure

The catalyst (1 or 3 mol %) was added to dry toluene (25 mL). At 70 °C a solution of diazocarboxamides **1a–d** or **2** (2–6 mmol) in dry toluene (4 mL) was added via a syringe pump during a period of 1 h. After complete addition, the mixture was kept stirring at 70 °C until the diazo compound had been consumed (IR control, see Tables 1–6 for details). The solvent was evaporated, and the residue was separated by column chromatography over basic alumina (85–110 g). Elution with cyclohexane/ethyl acetate mixtures furnished the β-lactam. When γ-lactam was also formed, it was isolated by subsequent elution with methanol and isolated either by a second column chromatography (cyclohexane/ethyl acetate, 3:1) or by vacuum distillation in a Kugelrohr apparatus.

For experiments without product isolation, the solvent was evaporated at 60 °C/60 mbar, and the crude product mixture was analyzed by ^{1}H NMR spectroscopy, whereby the product yields were determined by integration using naphthalene as an internal standard.

4.4.1. *trans*-3-Acetyl-1-ethyl-4-methylazetidin-2-one (11a). Colorless oil, bp 110 °C/0.06 mbar (Kugelrohr). ^{1}H NMR: δ 1.17 (t, 3H, ^3J=7.3 Hz, CH_3), 1.37 (d, 3H, ^3J=6.3 Hz, 4-CH_3), 2.30 (s, 3H, $COCH_3$), 3.07 (m_c, 1H, ^3J=7.1 Hz, NCH), 3.36 (m_c, 1H, ^3J=7.2 Hz, NCH), 3.72 (d, 1H, ^3J=2.0 Hz, 3-H), 4.07 (dq, 1H, ^3J=2.1 and 6.2 Hz, 4-H). ^{13}C NMR: δ 13.1 (CH_3 (Et)), 17.6 (4-CH_3) 29.7 ($CO\mathit{C}H_3$), 35.1 (NCH_2), 48.4 (C-4), 69.3 (C-3), 162.2 (CO-ring), 200.5 (CO). IR (neat): ν 1752 (s), 1711 (s), 1448 (m), 1382 (m) cm^{-1}. MS (100 eV): *m*/*z* (%) 156 (9). Anal. Calcd for $C_8H_{13}NO_2$ (155.19): C 61.91, H 8.44, N 9.03. Found C 61.90, H 8.48, N 9.14. This compound was prepared before by irradiation of **1a**.[21]

4.4.2. 3-Acetyl-1-ethylpyrrolidin-2-one (12a). Colorless oil, bp 140 °C/0.11 mbar (Kugelrohr). ^{1}H NMR: δ 1.11 (t, 3H, ^3J=7.2 Hz, $CH_2C\mathit{H}_3$), 1.99–2.08 (m, 1H, 4-H), 2.42 (s, 3H, CH_3), 2.49–2.58 (m, 1H, 4-H_2), 3.32 (q, 2H, ^3J=7.3 Hz, $C\mathit{H}_2CH_3$), 3.32 (m_c, 1H, 5-H), 3.42 (dt, 1H, ^3J=9.1 and 5.6 Hz, 5-H) 3.58 (dd, 1H, ^3J=9.3 and 6.1 Hz, 3-H). ^{13}C NMR: δ 12.3 ($CH_2\mathit{C}H_3$), 19.5 (C-4), 29.9 ($CO\mathit{C}H_3$), 37.5 (NCH_2), 44.7 (C-5), 55.9 (C-3), 169.2 (CO-ring), 203.8 (CO). IR (neat): ν 1717 (s), 1683 (s), 1459 (m), 1380 (m) cm^{-1}. MS (100 eV): *m*/*z* (%) 156 (100). Anal. Calcd for $C_8H_{13}NO_2$ (155.19): C 61.91, H 8.44, N 9.03. Found: C 61.86, H 8.44, N 9.02.

4.4.3. *trans*-3-Acetyl-1-butyl-4-propylazetidin-2-one (11b). Colorless oil, bp 110 °C/0.09 mbar (Kugelrohr). ^{1}H NMR: δ 0.92 (t, 3H, ^3J=7.3 Hz, CH_3), 0.96 (t, 3H, ^3J=7.2 Hz, CH_3), 1.26–1.56 (m, 7H, CH_2), 1.75–1.85 (m, 1H, CH_2), 2.30 (s, 3H, $COCH_3$), 2.99 (m_c, 1H, NCH), 3.34 (m_c, NCH), 3.74 (d, 1H, ^3J=2.0 Hz, 3-H), 3.92–3.96 (m, 1H, 4-H). ^{13}C NMR: δ 13.5 (CH_3), 13.9 (CH_3), 18.9 (CH_2), 20.1 (CH_2), 29.7 ($CO\mathit{C}H_3$), 30.0 (CH_2), 34.0 (4-CH_2), 40.4 (NCH_2), 53.0 (C-4), 67.8 (C-3), 162.8 (CO-ring), 200.7 (CO). IR (neat): ν 1753 (s), 1712 (s), 1409 (m), 1360 (m) cm^{-1}. MS (100 eV): *m*/*z* (%) 212 (5), 113 (100). Anal. Calcd for $C_{12}H_{21}NO_2$ (211.16): C 68.21, H 10.02, N 6.63. Found C 68.36, H 10.01, N 6.60.

4.4.4. *trans*-3-Acetyl-1-butyl-4-ethylpyrrolidin-2-one (12b). Colorless oil, bp 155 °C/0.17 mbar (Kugelrohr). ^{1}H NMR: δ 0.90 (t, 3H, ^3J=7.6 Hz, $CH_2C\mathit{H}_3$), 0.92 (t, 3H, ^3J=7.6 Hz, $(CH_2)_3C\mathit{H}_3$), 1.25–1.34 (m, 2H, CH_2), 1.40–1.52 (m, 4H, 2 CH_2), 2.41 (s, 3H, $COCH_3$), 2.69–2.78 (m_c, 1H, 4-H), 2.95 (dd, 1H, $|^2J|$=9.6 Hz, ^3J=6.1 Hz, 5-H^A), 3.25 (t, 2H, ^3J=7.2 Hz, NCH_2), 3.26 (d, 1H, ^3J=7.1 Hz,

3-H), 3.50 (dd, 1H, $|^2J|$=9.6 Hz, ^3J=8.3 Hz, 5-H^B). ^{13}C NMR: δ 11.4 (CH_3), 13.6 (CH_3), 19.8 (CH_2), 27.0 (4-CH_2), 29.1 (CH_2), 30.2 (COCH_3), 34.7 (C-4), 42.5 (NCH_2), 50.8 (C-5), 62.1 (C-3), 169.3 (CO-ring), 203.9 (CO). IR (neat): ν 1717 (s), 1685 (s), 1459 (m), 1356 (m) cm^{-1}. MS (100 eV): *m/z* (%) 212 (100). Anal. Calcd for $C_{12}H_{21}NO_2$ (211.16): C 68.21, H 10.02, N 6.63. Found: C 67.91, H 9.98, N 6.77.

4.4.5. 3-Acetyl-1-isopropyl-4,4-dimethylazetidin-2-one (11c). Colorless oil, bp 120 °C/0.09 mbar (Kugelrohr). ^{1}H NMR: δ 1.33 (d, 6H, ^3J=6.8 Hz, CH_3), 1.39 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 2.29 (s, 3H, $COCH_3$), 3.52 (sept, 1H, ^3J=6.8 Hz, NCH), 3.65 (s, 1H, 3-H). ^{13}C NMR: δ 21.7 and 21.8 (CH(CH_3)$_2$), 22.8 (4-CH_3), 27.3 (4-CH_3), 30.9 (COCH_3), 44.4 (NCH), 59.9 (C-4), 69.8 (C-3), 162.3 (CO-ring), 202.1 (CO). IR (neat): ν 1746 (s), 1711 (s), 1412 (m), 1373 (m) cm^{-1}. MS (100 eV): *m/z* (%) 184 (17). Anal. Calcd for $C_{10}H_{17}NO_2$ (183.25): C 65.54, H 9.35, N 7.64. Found: C 65.29, H 9.49, N 7.63.

4.4.6. 3-Acetyl-1-*tert*-butyl-4-phenylazetidin-2-one (11d); *trans*-11d. White solid, mp 84.9–89.7 °C. NMR (^{1}H, ^{13}C) and IR data agree with reported[14] values. Anal. Calcd for $C_{15}H_{19}NO_2$ (245.32): C 73.44, H 7.81, N 5.71. Found: C 73.31, H 7.82, N 5.71. *cis*-**11d** (in admixture with trans-isomer): δ_H 4.18 and 4.86 (AB system, ^3J=6.0 Hz).

4.4.7. *cis*- and *trans*-*N*-*tert*-Butyl-3-methoxycarbonyl-4-phenylazetidin-2-one (13). White solid, obtained as a diastereomeric mixture. ^{1}H NMR, *cis*-**13**: δ 1.31 (s, 9H, C(CH_3)$_3$), 3.72 (s, 3H, OCH_3), 4.23 (d, 1H, ^3J=6.3 Hz, 4-H), 4.91 (d, 1H, ^3J=6.3 Hz, 3-H), 7.29–7.39 (m, 5H, H_{Ph}); *trans*-**13**: δ 1.27 (s, 9H, C(CH_3)$_3$), 3.71 (d, 1H, ^3J=2.3 Hz, 4-H), 3.78 (s, 3H, OCH_3), 4.86 (d, 1H, ^3J=2.3 Hz, 3-H), 7.29–7.39 (m, 5H, H_{Ph}). ^{13}C NMR, *cis*-**13**: δ 28.0 (C(CH_3)$_3$), 51.8 (OCH_3), 55.2 (C(CH_3)$_3$), 56.6 (C-3), 59.9 (C-4), 127.0, 128.4, 128.7, 136.6 (all C_{Ph}), 162.8 (CO), 166.4 (CO); *trans*-**13**: δ 28.0 (C(CH_3)$_3$), 52.6 (OCH_3), 55.2 (C(CH_3)$_3$) 56.5 (C-3), 62.3 (C-4), 126.6, 128.4, 128.9, 139.1 (all C_{Ph}), 162.0 (CO), 166.4 (CO). IR (neat): ν 1762 (s), 1735 (s) cm^{-1}. MS (100 eV): *m/z* (%) 262 (31), 163 (100). Anal. Calcd for $C_8H_{15}NO$ (261.32): C 68.94, H 7.33, N 5.36. Found: C 68.87, H 7.38, N 5.32.

Acknowledgements

The support and sponsorship contributed by COST Action D24 'Sustainable Chemical Processes: Stereoselective Transition-Metal Catalyzed Reactions' is kindly acknowledged.

References and notes

1. Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley and Sons: New York, NY, 1998.
2. Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911–935.
3. Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385–5453.
4. Pfaltz, A. *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, NY, 1999; Vol. 2, pp 513–538.
5. Davies, H. M. L.; Beckwith, R. E. *Chem. Rev.* **2003**, *103*, 2861–2903.
6. Recent publications on rhodium-catalyzed carbenoid syntheses of β- and γ-lactams: (a) Candeias, N. R.; Gois, P. M. P.; Afonso, C. A. M. *J. Org. Chem.* **2006**, *71*, 5489–5497; (b) Wee, A. G. H.; Duncan, S. C.; Fan, G. *Tetrahedron: Asymmetry* **2006**, *17*, 297–307; (c) Chen, Z.; Chen, Z.; Jiang, Y.; Hu, W. *Tetrahedron* **2005**, *61*, 1579–1586; (d) Liu, W.-J.; Chen, Z.-L.; Chen, Z.-Y.; Hu, W.-H. *Tetrahedron: Asymmetry* **2005**, *16*, 1693–1698; (e) Gois, P. M. P.; Candeias, N. R.; Afonso, C. A. M. *J. Mol. Catal. A* **2005**, *227*, 17–24; (f) Muroni, D.; Saba, A. *ARKIVOC* **2005**, *xiii*, 1–7; (g) Flanigan, D. L.; Yoon, C. H.; Jung, K. W. *Tetrahedron Lett.* **2005**, *46*, 143–146; (h) Chen, Z.-L.; Chen, Z.-Y.; Jiang, Y.-H.; Hu, W. *Synthesis* **2004**, 1763–1764; (i) Doyle, M. P.; Hu, W.; Wee, A. G. H.; Wang, Z.; Duncan, S. C. *Org. Lett.* **2003**, *5*, 407–410; (j) Yoon, C. H.; Niagle, A.; Chen, C.; Gandhi, D.; Jung, K. W. *Org. Lett.* **2003**, *5*, 2259–2262; (k) Gois, P. M. P.; Afonso, C. A. M. *Eur. J. Org. Chem.* **2003**, 3798–3810.
7. Gois, P. M. P.; Afonso, C. A. M. *Eur. J. Org. Chem.* **2004**, 3773–3788.
8. Merlic, C. A.; Zechman, A. L. *Synthesis* **2003**, 1137–1156.
9. Maas, G. *Chem. Soc. Rev.* **2004**, *33*, 183–190.
10. Nishiyama, H. *Ruthenium in Organic Synthesis*; Murahashi, S.-I., Ed.; Wiley-VCH: Weinheim, 2004; Chapter 7.
11. (a) Zheng, S.-L.; Yu, W.-Y.; Che, C.-M. *Org. Lett.* **2002**, *4*, 889–892; (b) Cheung, W.-H.; Zheng, S.-L.; Yu, W.-Y.; Zhou, G.-C.; Che, C.-M. *Org. Lett.* **2003**, *5*, 2535–2538.
12. Choi, M. K.-W.; Yu, W. Y.; Che, C.-M. *Org. Lett.* **2005**, *7*, 1081–1084.
13. Grohmann, M.; Buck, S.; Schäffler, L.; Maas, G. *Adv. Synth. Catal.* **2006**, *348*, 2203–2211.
14. Doyle, M. P.; Shanklin, M. S.; Oon, S.-M.; Pho, H. Q.; van der Heide, F. *J. Org. Chem.* **1988**, *53*, 3384–3386.
15. Doyle, M. P.; Pieters, R. J.; Taunton, J.; Pho, H. Y.; Padwa, A.; Hertzog, D. L.; Precedo, L. *J. Org. Chem.* **1991**, *56*, 820–829.
16. Regitz, M.; Hocker, J.; Liedhegener, A. *Org. Prep. Proced.* **1969**, *1*, 99–104.
17. Padwa, A.; Austin, D. J.; Price, A. T.; Semones, M. A.; Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Tran, A. *J. Am. Chem. Soc.* **1993**, *115*, 8669–8680.
18. Wee, A. G. H.; Duncan, S. C. *Tetrahedron Lett.* **2002**, *43*, 6173–6176.
19. (a) Mantovani, A.; Cenini, S. *Inorg. Synth.* **1976**, *16*, 47–48; (b) Eady, C. R.; Jackson, P. F.; Johnson, B. F. G.; Lewis, J.; Malatesta, M. C.; McPartlin, M.; Nelson, W. J. H. *J. Chem. Soc., Dalton Trans.* **1980**, 383–392.
20. Tamblyn, W. H.; Hoffmann, S. R.; Doyle, M. P. *J. Organomet. Chem.* **1981**, *216*, C64–C68.
21. Tomioka, H.; Kondo, M.; Izawa, Y. *J. Org. Chem.* **1981**, *46*, 1090–1094.
22. Maas, G.; Werle, T.; Alt, M.; Mayer, D. *Tetrahedron* **1993**, *49*, 881–888.
23. Maas, G.; Seitz, J. *Chem. Commun.* **2002**, 338–339.
24. Seitz, J. Doctoral Thesis. University of Ulm, Ulm, Germany, 2002.
25. Buck, S.; Maas, G. *J. Organomet. Chem.* **2006**, *691*, 2774–2784.
26. Schäffler, L.; Müller, B.; Maas, G. *Inorg. Chim. Acta* **2006**, *359*, 970–977.