Rhodium(II) Acetate Catalyzed Synthesis of Cyclic Enamides and Enamines via β-Hydride Elimination

Sengodagounder Muthusamy,* Chidambaram Gunanathan, Srinivasaarao Arulananda Babu
Silicates and Catalysis Discipline, Central Salt and Marine Chemicals Research Institute, Bhavnagar 364 002, India
Fax +91(278)567562; E-mail: salt@csir.res.in
Received 24 October 2001; revised 21 January 2002

Abstract: A series of cyclic diazoamides and diazoamines were synthesized. Treatment of these cyclic diazoamides and diazoamines with a catalytic amount of rhodium(II) acetate furnished the corresponding cyclic enamides and enamines, respectively. Interestingly, cyclic diazoamines produced stereoselectively Z-enamines.

Key words: diazoamides, diazoamines, enamides, enamines, rhodium(II) acetate

The utility of α-diazo carbonyl compounds in modern organic synthesis and their participation in a variety of transformations like cyclopropanation, insertion reaction and ylide formation is well documented. The tandem processes involving rhodium carbenoids generated from diazo carbonyl compounds with a catalytic amount of rhodium(II) acetate have been used to construct various complex polycyclic systems. The rhodium(II)-catalyzed reactions of cyclic and acyclic diazo ketoamides were skillfully applied to generate ylides followed by trapping with dipolarophiles to synthesize various alkaloids and to expose the novel utilities of these diazoamides and diazoamines. In continuation of our interest on the reactions of diazo carbonyl compounds and to expose the novel utilities of these diazo compounds, we herein wish to report the results of β-hydride elimination reactions of cyclic diazoamides and diazoamines in the presence of rhodium(II) acetate as a catalyst.

For this purpose, α-diazo carbonyl compounds 4a–f having β-hydrogen atoms were chosen for this study. The required cyclic diazoamides 4a–c can be easily prepared from the corresponding cyclic amides 1a–c as described below. The Michael addition reaction9 of cyclic amides 1a–c and ethyl acrylate afforded the corresponding cyclic amides 2a–c in quantitative yields. To generate a diazo group adjacent to ester functionality, the formylation10 reaction of cyclic amides 2a–c using sodium hydride/ethyl formate was carried out. The formylation took place smoothly only α to the ester functional group and provided compounds 3. Without the isolation of formyl compounds 3, the diazo transfer reaction was performed using mesyl azide to afford the cyclic diazoamides 4a–c in good yields (Scheme 1).

We initially investigated the performance of diazoamide 4a using rhodium(II) acetate as a catalyst in the absence of any dipolarophile. Diazoamide 4a was dissolved in anhydrous benzene and refluxed with 0.3 mol% of rhodium(II) acetate for 25 h. The reaction was followed by TLC until the disappearance of diazoamide 4a. The chromatographic purification of the crude reaction mixture afforded two products which were characterized as cyclic enamides of type 5a (40%) and 6a (31%) with Z and E geometry, respectively (Scheme 1, Table).

IR spectrum of compound 5a showed a band at 1632 cm⁻¹ indicating the presence of a olefin functional group. The 1H NMR spectrum of 5a displayed characteristic two doublets at δ = 5.14 and 7.10 with a coupling constant of 𝐽 = 10.6 Hz confirming the Z geometry. The 13C NMR and DEPT-135 spectra of 5a disclosed the presence of one CH₃, four CH₂, two CH and two quaternary carbons, which clearly confirmed the structure of compound 5a as an Z enamide.

IR spectrum of compound 6a had absorption band at 1629 cm⁻¹ for the presence of olefin moiety. The 1H NMR spectrum of 6a showed two characteristic doublets at δ =5.21 and 8.09 with a coupling constant of 𝐽 = 14.2 Hz indicating the E geometry. The 13C NMR and DEPT-135 spectra of 6a revealed the presence of one CH₃, four CH₂, two CH and two quaternary carbons, which confirmed the structure of compound 6a as an E enamide.

Scheme 1

[Diagram of the reaction scheme]

ISSN 0039-7881
Diazoamides 4b,c were also studied under similar reaction conditions to afford the corresponding cyclic enamides 5/6b and 5/6c in good yields, respectively. The rhodium(II) acetate catalyzed reaction of 4c was followed by IR until the disappearance of the characteristic diazo peak at 2108 cm⁻¹ since the Rv values of 4c and 6c in TLC are identical.

After studying various cyclic diazoamides, we extended the study to the rhodium(II)-catalyzed behavior of cyclic diazoamines 4d–f. Thus, we synthesized the diazoamines 4d–f from the corresponding cyclic amines 1d–f by following the similar procedure described for compounds 4a–c. Subsequently, the rhodium(II) catalyzed reaction of compound 4d was carried out followed by alumina column chromatographic purification of the residue to afford only one product 5d in moderate yield. Based on its interrelated spectral data, compound 5d was characterized as an Z-enamine. Surprisingly this reaction afforded stereoselectively Z-isomer 5d and no E-isomer could be observed. The similar reaction was carried out with diazoamines 4e,f which also afforded exclusively the corresponding enamines 5e,f with Z geometry. The formation of products 5 and 6 may be explained by a β-hydride elimination of diazo compounds 4a–f in the presence of rhodium(II) acetate catalyst. Interestingly, a complete stereoselectivity was observed in cyclic amines 4d–f but not in the case of cyclic amines 4a–c. This may be rationalized where the intermediate rhodium carbenoids formed from cyclic amines 4a–c may exist in two conformations 7a and 7b (Scheme 2) which lead to a mixture of stereoisomers 5 and 6. Interestingly, the rhodium carbenoids formed from cyclic amines 4d–f exist only in the conformation 6 7a (X = H₂) to afford product 5 with Z stereochemistry. The additional carbonyl group adjacent to nitrogen atom in compounds 4a–c assists partially to the presence of conformer 7b, which resulted in the E-isomer 6.

<table>
<thead>
<tr>
<th>Entry</th>
<th>X</th>
<th>Y</th>
<th>n</th>
<th>Yield of 4 (%)</th>
<th>Yield of 5 and 6 (%)</th>
<th>% of Z/E-Isomers</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>O</td>
<td>CH₂</td>
<td>0</td>
<td>95</td>
<td>71</td>
<td>57          43</td>
</tr>
<tr>
<td>b</td>
<td>O</td>
<td>CH₂</td>
<td>1</td>
<td>98</td>
<td>76</td>
<td>30          70</td>
</tr>
<tr>
<td>c</td>
<td>O</td>
<td>CH₂</td>
<td>2</td>
<td>97</td>
<td>65</td>
<td>40          60</td>
</tr>
<tr>
<td>d</td>
<td>H₂</td>
<td>CH₂</td>
<td>0</td>
<td>60</td>
<td>45</td>
<td>100          0</td>
</tr>
<tr>
<td>e</td>
<td>H₂</td>
<td>CH₂</td>
<td>1</td>
<td>65</td>
<td>47</td>
<td>100          0</td>
</tr>
<tr>
<td>f</td>
<td>H₂</td>
<td>O</td>
<td>1</td>
<td>68</td>
<td>48</td>
<td>100          0</td>
</tr>
</tbody>
</table>

* Yields refer to isolated pure diazo compounds 4 from 2.

Scheme 2

The β-hydride elimination is generally considered as a relatively low-energy pathway for metal carbene decomposition reactions. But the literature precedents show that this elimination is competitive with the other reaction pathways like C–H insertion, O–H insertion, intramolecular cyclopropanation, dimerization and Wolff rearrangement. We could not observe any other product produced by possible competition reactions like C–H insertion or ylide formation in the above substrates 4.

In conclusion, we have studied the β-hydride elimination reactions of cyclic diazoamides which afforded both Z- and E-enamides without any selectivity in the presence of rhodium(II) acetate as a catalyst, whereas the cyclic diazoamines stereoselectively produced only the Z-enamine under the similar experimental conditions.

Mps are uncorrected. IR spectra were recorded on a Perkin-Elmer Spectrum GX FT-IR spectrophotometer. 1H NMR and 13C NMR spectra were recorded on a Bruker DPX 200 (200 MHz and 50.3 MHz respectively) spectrometer and referenced to internal standard TMS using CDCl₃ as solvent. Carbon types were determined from DEPT 13C NMR experiments. Mass analyses were obtained using either a Finnigan MAT 8230 (with an ionizing voltage of 70eV) or Jeol M Station 700 (FD⁺ method in absolute CH₂Cl₂) mass spectrometer. Elemental analyses were performed on a Perkin-Elmer Model 2400 analyzer.
Ethyl (2Z)-3-(2-Oxopyrrolidin-1-yl)prop-2-enoate (5a) and Ethyl (2E)-3-(2-Oxopyrrolidin-1-yl)prop-2-enoate (6a); Reactions of Diazoo Compound 4 with Rhodium(II) Acetate Catalyst; Typical Procedure

To a stirred solution of the diazo compound 4a (0.30 g, 1.4 mmol) in anhyd benzene (15 mL) was added a 0.3 mol% of Rh₂(OAc)₄ under an argon atmosphere. The reaction mixture was refluxed for 25 h by following the reaction with TLC until the disappearance of the diazo compound 4a. Then the solvent was removed under reduced pressure and the residue was purified using alumina column chromatography (EtOAc–hexane, 1:2) to afford the enamides 5a (0.125 g, 40%) and 6a (0.095 g, 31%) as colorless solids.

**Ethyl (2Z)-3-(2-Oxopyrrolidin-1-yl)prop-2-enoate (5a)**

Yield: 104 mg (40%); colorless solid; mp 35–37 °C (hexanes–EtOAc).

IR (CHCl₃): 2956, 1709, 1623 (C=C), 1475, 1409, 1262, 1161, 1095, 830, 738 cm⁻¹.

Anal. Calcd for C₁₀H₁₅NO₃: C, 60.97; H, 7.65; N, 7.13. Found: C, 60.97; H, 7.12; N, 7.67.

**Ethyl (2E)-3-(2-Oxopyrrolidin-1-yl)prop-2-enoate (6a)**

Yield: 116 mg (45%); colorless liquid.

IR (CHCl₃): 2949, 1667, 1621 (C=C), 1451, 1411, 1292, 1259, 1167, 1097, 1024 cm⁻¹.

**Ethyl (2E)-3-(2-Oxopyrroolidin-1-yl)prop-2-enoate (6b)**

Yield: 139 mg (53%); colorless liquid.

IR (CHCl₃): 2949, 1667, 1621 (C=C), 1451, 1411, 1292, 1259, 1167, 1097, 1024 cm⁻¹.

FD-MS: m/z = 197 (M⁺).

Analysis. Found: C, 60.84; H, 7.66; N, 7.08.

Ethyl (2Z)-3-(2-Oxooazepan-1-yl)prop-2-enoate (5c)

Yield: 80 mg (31%); colorless solid; mp 57–58 °C (hexanes–EtOAc).

IR (CHCl₃): 2921, 1718, 1632 (C=C), 1517, 1458, 1356, 1162, 1042, 805 cm⁻¹.

**Ethyl (2Z)-3-(2-Oxooazepan-1-yl)prop-2-enoate (5d)**

Yield: 104 mg (40%); colorless liquid.

IR (CHCl₃): 2949, 1667, 1621 (C=C), 1451, 1411, 1292, 1259, 1167, 1097, 1024 cm⁻¹.

FD-MS: m/z = 197 (M⁺).

Analysis. Found: C, 60.84; H, 7.66; N, 7.08.
Anal. Calcd for C₉H₁₅NO₂: C, 63.88; H, 9.35; N, 8.28. Found: C, 63.84; H, 8.92; N, 8.29.

Ethyl (2Z)-3-(Piperidin-1-yl)prop-2-enolate (5e)
Yield: 122 mg (47%); colorless liquid.
IR (CHCl₃): 2929, 1731, 1682 (C=C), 1613, 1446, 1372, 1261, (CH), 151.7 (NCH), 170.3 (quat-C, CO₂Et).

1H NMR: J = 13.2 Hz, CH), 7.36 (d, 1 H, J = 7.1 Hz, CH₃), 7.29 (d, 1 H, J = 13.2 Hz, CH₃, 3.20 (complex, 4 H), 4.13 (q, 2 H, J = 7.1 Hz, OCH₂), 4.62 (d, 1 H, J = 13.1 Hz, CH), 7.30 (d, 1 H, J = 13.1 Hz, CH).

13C NMR: δ = 14.6 (CH₂), 24.1 (CH₂), 25.4 (CH₂), 55.8 (OCH₂), 83.8 (CH), 152.0 (NCH), 170.1 (quat-C, CO₂Et).

FD-MS: m/z = 183 (M+).
Anal. Calcd for C₉H₁₅NO₂: C, 63.88; H, 8.92; N, 8.29.

Ethyl (2Z)-3-(Morpholin-4-yl)acrylate (5f)
Yield: 125 mg (48%); colorless liquid.
IR (CHCl₃): 2929, 1731, 1682 (C=C), 1613, 1446, 1372, 1261, 1166, 909, 733 cm⁻¹.
1H NMR: δ = 1.26 (t, 3 H, J = 7.1 Hz, CH₃), 3.20 (complex, 4 H), 4.13 (q, 2 H, J = 7.1 Hz, OCH₂), 4.62 (d, 1 H, J = 13.2 Hz, CH), 7.36 (d, 1 H, J = 13.2 Hz, CH).

13C NMR: δ = 14.2 (CH₂), 48.6 (CH₂), 59.1 (CH₂), 66.2 (CH₂), 86.3 (CH), 151.7 (NCH), 170.3 (quat-C, CO₂Et).
EIMS: m/z (%) = 185 (M⁺, 62), 156 (96), 140 (100), 112 (55), 82 (62), 45 (29), 79 (79).
Anal. Calcd for C₉H₁₅NO₂: C, 58.36; H, 8.16; N, 7.56. Found: C, 58.41; H, 8.13; N, 7.54.

Acknowledgments
This research was supported by Young Scientist Scheme, CSIR, New Delhi. We thank Dr. P. K. Ghosh, Director and Dr. R. V. Jasra, Head of the division, for their encouragement shown in this work. C. G. and S. A. B. thank CSIR, New Delhi for a Fellowship.

References


(11) 1H NMR spectra showed no trace of the E-isomer in the crude reaction mixtures of 4d–f even before chromatography.


