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Cycloadditions of 1,3-Oxazolium-4-olates (Isomünchnones) by Rhodium(II)-Induced Decomposition of α-Diazocarbonyl Derivatives of (5*R*)- and (5*S*)-Phenyloxazin-3-one as a Chiral Template.

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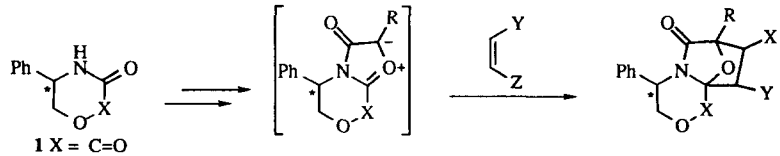
Abstract: Cycloadducts (**6-9**) were synthesised from isomünchnone derivatives of (5*R*)- and (5*S*)-phenyloxazin-3-one by rhodium(II)-catalysed decomposition of α-diazocompounds (**3a-c**). Additions to various carbon-carbon dipolarophiles proceeded with high *endo*/*exo*-selectivities and moderate diastereofacial selectivities. © 1997 Elsevier Science Ltd.

We have previously described the use of (5*R*)- and (5*S*)-phenyloxazin-2,3-dione **1** in a novel chirally templated isomünchnone cycloaddition (**Scheme 1**).[1] The observed moderate diastereocontrol up to 4.5 : 1 by the phenyl substituent on the stereogenic centre of the 1,3-dipole derived from the corresponding oxazindione encouraged us to study other potential chiral auxiliaries especially since no report of chirally templated isomünchnone additions existed at the outset of this work. Desiring a template that could be easily prepared from an inexpensive starting material, we selected (5*R*)- and (5*S*)-phenyloxazin-3-one **2** since we expected a higher diastereocontrol by the less flattened oxazinone ring in contrast to the dione analogue **1** (**Scheme 1**). Furthermore oxazinone **2** can be prepared in one step from phenylglycinol following the methodology of Clark (**Scheme 2**).[2]

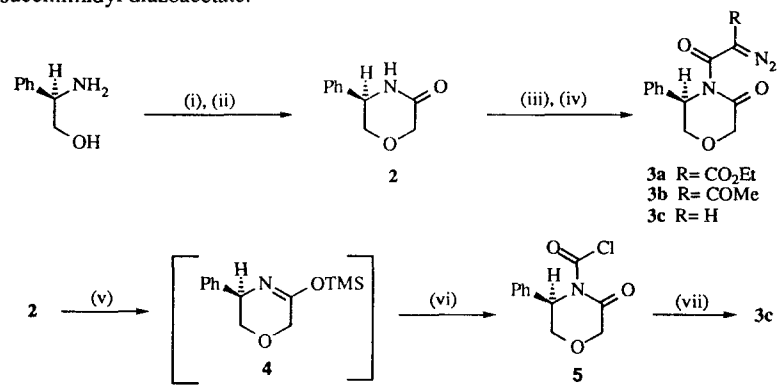


1 X = C=O
2 X = CH_2

Scheme 1

As shown in Scheme 2 the template allowed access to 3 different types of diazocompounds that would be expected to show differing behaviour in the cycloadditions. Diazoimides **3a-c** were prepared in analogy to literature procedures.[3-5] The monostabilized diazocompound **3c** could be synthesised *via* the iminoether **4** and

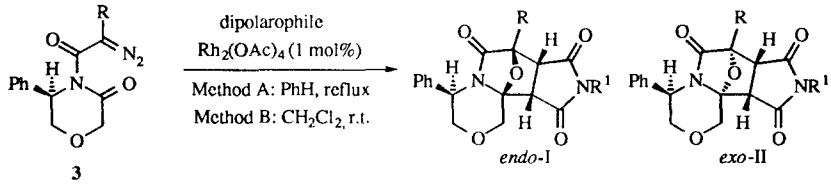
treatment with triphosgene to furnish the acid chloride **5**. Alternatively it could be obtained in a "one-pot" procedure using succinimidyl diazoacetate.[6]



(i) 1.0 eq. NaH, THF, 0°C (ii) 1.5 eq. $ClCH_2CO_2Et$, 51 % 3a: (iii) *n*-BuLi, THF, -78°C (iv) ethyl diazomalonyl chloride,[3] 60 % **3b:** (iii) 2,2,6- trimethyl-4*H*-1,3-dioxane-4-one,[4] xylene, reflux, 44 % (iv) $MesN_3$,[5] NEt_3, CH_3CN, r.t., 76 % **3c:** (iii) 3.0 eq. NaH, THF, r.t. (iv) succinimidyl diazoacetate, [6] 30 % (v) TMSCl, NEt_3, dioxane, 0°C (vi) triphosgene, THF, 0°C, 69 % (vii) CH_2N_2, THF, 0°C, 60 %.

Scheme 2

For the transformation of the α-diazocarbonyl compounds into isomünchnones the starting material was treated with rhodium(II) acetate (1 mol %) in the presence of a dipolarophile.[7] Best results (**Scheme 3**) were obtained in each case with *N*-phenyl- and *N*-methylmaleimide; whilst slightly lower yields were observed in additions to acetylenic compounds such as dimethyl acetylenedicarboxylate and methylpropiolate.[8]

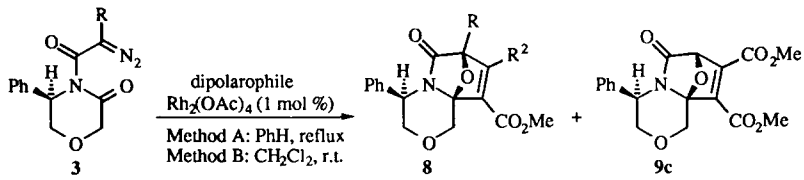


	dipolarophile	6	7
a R= CO_2Et	Ph	54 %	20 %
b R= C(O)Me		59 %	21 %
c R= H		37 %	25 %
d R= CO_2Et	Me	65 %	15 %
e R= C(O)Me		70 %	19 %
f R= H		52 %	8 %

Scheme 3

Analysis of the data disclosed that in case of the additions to maleimide derivates the dominant pathway was the approach of the dipolarophile from the less hindered α-face of the template in an *endo*-fashion. In accordance with the previously published results of additions to chiral oxazindione derivatives,[1] also an approach from the β-face occured with total *exo*-selectivity. The formation of the *endo*-adduct can be explained

as a consequence of electronic factors imposed on the transition state by the isomünchnone and the dipolarophile; whereas we reason that the steric hindrance of the C-5 phenyl substituent leads to the addition in *exo*-fashion for the minor isomer. For additions to acetylenic compounds the isomünchnones derived from disubstituted diazocompounds **3a** and **3b** led exclusively to the adducts formed by approach of the dipolarophile from the less hindered side. In contrast, the monosubstituted derivative **3c** gave a mixture of two isomers (**8c/9c**) in a ratio of 3:2 as observed for corresponding additions to the oxazindione derivatives.[1]



	dipolarophile	8	9
a R= CO_2Et	$MeO_2C{-}{\equiv}{-}CO_2Me$	65 %	—
b R= C(O)Me		46 %	—
c R= H		65 %* 8c/9c = 3:2	
d R= CO_2Et	$MeO_2C{-}{\equiv}{-}H$	65 %	—
e R= C(O)Me		70 %	—

*isolated yield of inseparable mixture

Scheme 4

The stereochemistry of the cycloadducts was assigned by evaluation of ^{1}H-NMR data and NOE results. In conclusion it has been demonstrated that (5*R*)- or (5*S*)-phenyloxazin-3-one is a superior template to the previously introduced oxazindione derivative. Oxazinone **2** can be prepared in one step from phenylglycinol and modified to generate diazocompounds **3a-c.** Rhodium-(II)-catalysed decomposition permits formation of isomünchnones that undergo cycloaddition in moderate to high diastereoselectivity and high *endo*/*exo*-control following the previously reported pattern.

General procedure for dipolar isomünchnone cycloadditions

Method A : A mixture of diazoimide, dipolarophile and catalytic amount of rhodium(II) acetate (1 mol %) was heated under reflux in benzene until t.l.c. analysis revealed the absence of starting material. The solvent was removed under reduced pressure, the residue redissolved in dichloromethane and the mixture filtered through a pad of Celite® to remove any rhodium residues. Gradient column chromatography permitted isolation of the product(s).

Method B: The starting materials were stirred at r.t. in dichloromethane in the presence of $Rh_2(OAc)_4$. Work-up follows that of Method A.

Acknowledgements

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References and Notes

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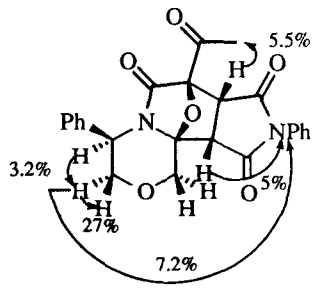
8. All novel compounds described had structures in accordance with their spectroscopic data. Selected spectroscopic data, **7d**: m.p. 166°C; $C_{20}H_{20}N_2O_7$ requires C, 60.00; H, 5.08; N, 7.00; found C, 59.97; H, 4.78; N, 6.73; ν_{max} (KBr disc) 2925, 1761, 1765, 1707, 1338, 1139, and 669 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.67-7.31 (5H, m, Ph), 5.01 (1H, d, *J* 3.9 Hz, 13-Hb), 4.80 (1H, d, *J* 12.3 Hz, 10-Ha or 10-Hb), 4.48 (2H, m, $C\underline{H}_2CH_3$), 4.00 (1H, dd, *J* 4.2, *J* 12.3 Hz, 12-Hb), 3.97 (1H, d, *J* 12.0 Hz, 12-Ha), 3.26 (1H, d, *J* 6.8 Hz, 4-Hb), 3.07 (1H, d, *J* 6.8 Hz, 8-Hb), 2.92 (3H, s, Me), 1.43 (3H, t, *J* 7.2 Hz, $CH_2C\underline{H}_3$); δ_C (125.5 MHz, $CDCl_3$) 172.12, 171.50, 165.92, 162.03, 137.25, 129.16, 128.77, 128.13, 89.10, 86.31, 68.97, 65.14, 63.07, 52.36, 52.21, 47.87, 25.47, 15.27, 14.14; $^m/_z$ CI(NH_3) 401 (100%, MH^+), 289; $[\alpha]_D^{26}$ -50.88 (c 1.02, acetone). **7e**: m.p. 125-127°C; $C_{20}H_{21}N_2O_7$ requires 401.134862; found MH^+, 401.134536; ν_{max} (KBr disc) 2925, 1752, 1750, 1707, 1308, 1134, 705 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.39-7.19 (5H, m, Ph), 4.68 (1H, d, *J* 11.7 Hz, 10-Ha or 10-Hb), 4.50-4.33 (3H, m, $C\underline{H}_2CH_3$ and 13-Hb), 4.04 (1H, dd, *J* 4.6, *J* 12.1 Hz, 12-Hb), 3.98 (1H, d, *J* 11.8 Hz, 10-Ha or 10-Hb), 3.74 (1H, d, *J* 6.9Hz, 4-Hb), 3.51 (1H, t, *J* 12.1 Hz, 12-Ha), 3.02 (3H, s, Me), 1.38 (3H, t, *J* 7.2 Hz, $CH_2C\underline{H}_3$); δ_C (125.5 MHz, $CDCl_3$) 172.16, 171.64, 166.33, 161.90, 133.15, 128.84, 127.33, 126.84, 90.88, 86.91, 73.31, 65.43, 63.03, 57.97, 55.14, 50.60, 48.06, 25.69, 13.99; $^m/_z$ CI(NH_3) 401 (100%, MH^+), 289; $[\alpha]_D^{26}$ -90.2 (c 0.45, acetone).**7f**: m.p. 235-237°C; $C_{17}H_{16}N_2O_5$ requires 328.1059; found M^+, 328.1065; ν_{max} (KBr disk) 2 986-2 886, 1 703, 1 781, 1 103, 928, 898, 784, 741, and 705 cm^{-1}; d_H (500 MHz, $CDCl_3$) 7.65-7.31 (5H, m, Ph), 5.03 (1H, d, *J* 3.9 Hz, 13-Ha), 4.90 (1H, s, 3-H), 4.79 (1H, d, *J* 12.0 Hz, 10-Ha or 10-Hb), 4.55 (1H, d, *J* 12.0 Hz, 12-Hb), 3.97 (1H, dd, *J* 4.25, *J'* 12.3 Hz, 12-Ha), 2.98 (1H, d, *J* 6.8 Hz, 4-Hb or 8-Hb), 2.97 (1H, d, *J* 6.8 Hz, 4-Hb or 8-Hb), 2.93 (3H, s, N<u>Me</u>); d_C (125.5 MHz, $CDCl_3$) 173.76, 173.00, 170.00, 137.64, 129.03, 128.56, 127.99, 90.97, 79.77, 69.00, 65.38, 51.82, 50.99, 45.86, and 25.27; $[a]_D^{24}$ -248.5 (c 0.2, $CHCl_3$).
9. Illustrative NOE results for cycloadduct **6b**.



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