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Novel chemoselective 1,3-dipolar cycloaddition of rhodium generated carbonyl ylides with arylidenetetralones

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Abstract

Treatment of various α-diazo ketones **1** and arylidenetetralones **2** in the presence of rhodium(II) acetate dimer leads to spiro-dioxa ring systems **3** as the only C=O addition products with high regio- and chemoselectivity. © 2000 Published by Elsevier Science Ltd.

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The tandem cyclization-1,3-dipolar cycloaddition chemistry of rhodium carbenoids has been developed as a general approach[1] to oxa-bridged ring systems. 1,3-Dipolar cycloaddition offers a versatile route[2] for the construction of a variety of complex five-membered heterocycles that are synthetically useful compounds. The 1,3-dipolar cycloaddition reaction has been applied to the synthesis of various natural products such as illudin[3] (sesquiterpenes), phorbol esters[4] (diterpenes), vindoline[5] (alkaloids) and brevicomin[6] (pheromones). Conceptually, the 1,3-dipolar cycloaddition of carbonyl ylides with π-bonds represents an attractive strategy for tetrahydrofuran formation.[2] The reaction of carbonyl ylides with α,β-unsaturated ketones and esters was studied[7] and found to provide cycloadducts without any regio- or chemoselectivity. Cyclic α,β-unsaturated ketones have also been used as dipolarophiles in the synthesis of the illudin[3] family of sesquiterpenes where only C=C addition products were observed.

To the best of our knowledge, the reaction of carbonyl ylides with α,β-unsaturated carbonyl compounds provides only the C=C addition products[3,7] **A**, **B** without much regioselectivity and no formation of the C=O addition product **C**. The general synthetic approach is outlined in Scheme 1. As a part of our ongoing research program into the construction of oxa-polycyclic systems[8] using rhodium carbenoids, we herein report that the novel cycloaddition of carbonyl ylides with arylidenetetralones leads only to C=O addition products **C** with high regio- and chemoselectivity.

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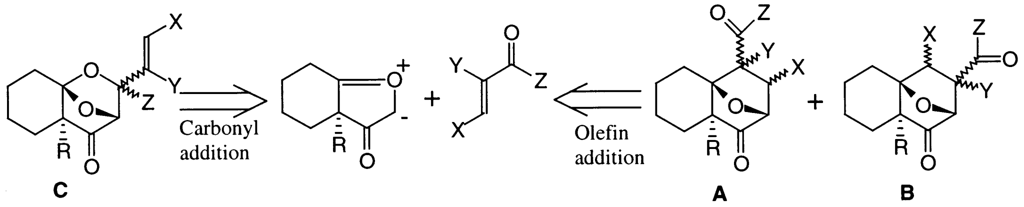
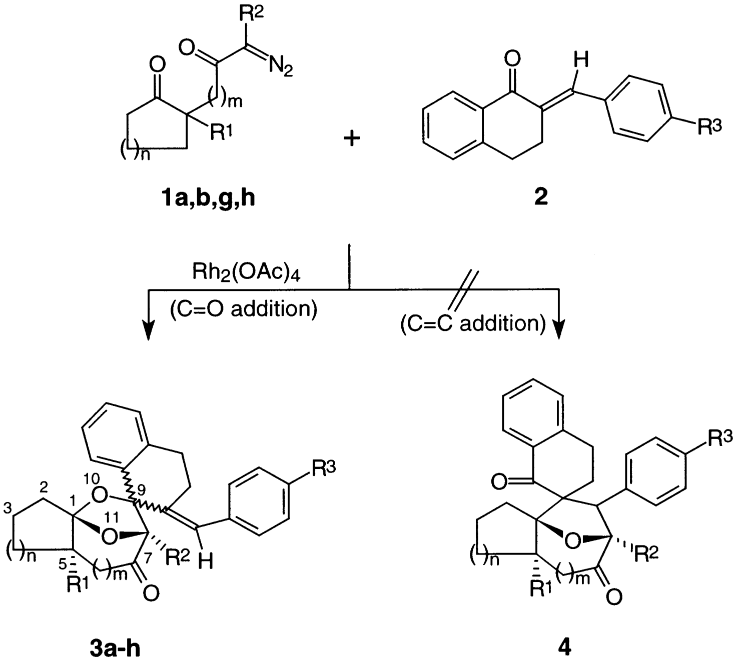


Scheme 1.

To evaluate the effect of the 1,3-dipolar cycloaddition reaction with α,β-unsaturated carbonyl compounds, the α-diazo ketones **1** and dipolarophiles **2** were prepared from commercially available materials. The α-diazo ketones **1a**,**b**,**g**,**h** were prepared according to our earlier work[8] from the corresponding carbethoxy cycloalkanones. The required α,β-unsaturated carbonyl compounds **2** were prepared by the base catalyzed condensation[9] of 1-tetralone with aromatic aldehydes. The above-prepared arylidenetetralones **2** were assigned the *E*-configuration based on the relative chemical shift value of olefinic protons at about δ 7.8, in accordance with ^{1}H NMR literature[10] data.

We investigated the rhodium(II) catalyzed behavior of the above α-diazo ketones **1** with arylidenetetralones **2**. An equimolar amount of **1a** and 2-benzylidene-1-tetralone (**2a**) with 1 mol% rhodium acetate dimer catalyst in dry dichloromethane was stirred at room temperature under an argon atmosphere for 7 h and the residue was chromatographically purified using a silica gel column. Product **3a** was obtained as a mixture of diastereomers in 43% yield (Scheme 2). The yield of this reaction was quantitative, based on the recovery of the starting 2-benzylidene-1-tetralone (**2a**) and the product **3a** obtained as a diastereomeric mixture (**3a$_1$** and **3a$_2$**) in



Scheme 2.

a ratio of 2:3. Repetitive silica gel column chromatography of the above diastereomeric mixture furnished the pure products **3a$_1$** and **3a$_2$**. The presence of a singlet at δ 4.57 and 6.93 for the bridgehead H-7 proton and olefin proton, respectively, in the ^{1}H NMR spectrum, the presence of nine CH signals in the dept-90 spectrum including a CH signal at δ 89.0, a quaternary carbon at δ 87.5 and the absence of a carbonyl group of tetralone ring in the ^{13}C NMR spectrum clearly established the formation of the spiro-dioxatricyclic ring system of **3a$_1$**. The presence of an olefin moiety indicates the novel selective cycloaddition to the C=O bond. The structure of the product **3a$_2$** was deduced as the diastereomer of **3a$_1$** from their interrelated spectral data.[11]

The Rh(II) catalyzed behavior of α-diazo compounds **1a**,**b**,**g** was also studied for five-membered cyclic carbonyl ylides, which further undergo 1,3-dipolar cycloaddition in the presence of various arylidenetetralones **2** to furnish the spiro-dioxatricyclic compounds **3b**–**g** in moderate yields (Table 1) as separable diastereomers. The α-diazo ketone **1h** was found to form a six-membered cyclic carbonyl ylide, which afforded the respective cycloadduct **3h** in 51% yield. The quantity of the catalyst was maintained at 1 mol% for all experiments and the products **3** were obtained as diastereomers in the ratio of 2:3. In all the reactions the yield was quantitative, based on the recovery of the starting tetralone derivative **2**.

Table 1
Spiro-dioxatricyclic ring systems **3a**–**h** produced via Scheme 2

Substrate **1**	*n*	*m*	R^1	R^2	R^3	Product **3**	Yield%[a]
a	1	0	CH_3	H	H	**a**	43
b	2	0	CH_3	H	H	**b**	54
b	2	0	CH_3	H	F	**c**	47
b	2	0	CH_3	H	Cl	**d**	44
b	2	0	CH_3	H	CH_3	**e**	49
b	2	0	CH_3	H	OCH_3	**f**	48
g[b]	2	0	CH_3	COOEt	H	**g**	49
h	2	1	H	H	H	**h**	51

[a] Yields (unoptimized) refer to an isolated diastereomeric mixture **3** and quantitative yields were obtained based on the recovery of starting material **2**.

[b] Dry benzene has been used as a solvent and the reaction mixture was refluxed for 6 h.

Carbonyl ylides are known[7] to provide only C=O addition products with benzaldehyde and other aldehydes having no alkene unit. It is also very interesting to note that 2-arylidene-1-tetralones are known[12] to undergo regioselective 1,3-dipolar cycloaddition with diphenylnitrilimine (DPNI) to afford only C=C cycloadducts. Moreover, we have not isolated any 2:1 cycloadducts as described in the literature[7] for rhodium-catalyzed cycloaddition reactions with an excess of diazo ketone **1**. Pirrung has very recently reported[13] that the reactions of carbonyl ylides with *p*-quinones afford both C=O and C=C addition products.

In the present work, we observed only both diastereomers of the C=O addition products and no detectable amount of either the C=C addition product or other possible regio-isomers. There is no significant difference in the formation of the C=O cycloadduct, even in the presence of electron withdrawing (**2c**,**d**) or electron donating (**2e**,**f**) substituents (R^3) on the aromatic ring of compounds **2**. The very facile formation of the spiro-dioxatricyclic ring system by the reaction of the α-diazo ketones and arylidenetetralones is worth noting. Currently, we are investigating further applications of this chemoselective reaction.

Acknowledgements

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References

1. Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223–269.
2. (a) In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A. Ed.; Wiley-Interscience: New York, 1984; Vols. 1 and 2. (b) Padwa, A. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I. Eds.; Pergamon: Oxford, 1991, Vol. 4, p. 1069.
3. (a) Padwa, A.; Curtis, E. A.; Sandanayaka, V. P. *J. Org. Chem.* **1997**, *62*, 1317–1325. (b) McMorris, T. C.; Hu, Y.; Yu, J.; Kelner, M. J. *J. Chem. Soc., Chem. Commun.* **1997**, 315–316. (c) Kinder Jr., F. R.; Bair, K. W. *J. Org. Chem.* **1994**, *59*, 6965–6967.
4. (a) McMills, M. C.; Zhuang, L.; Wright, D. L.; Watt, W. *Tetrahedron Lett.* **1994**, *35*, 8311–8314. (b) Dauben, W. G.; Dinges, J.; Smith, T. C. *J. Org. Chem.* **1993**, *58*, 7635–7637.
5. Padwa, A.; Price, A. T. *J. Org. Chem.* **1995**, *60*, 6258–6259.
6. Padwa, A.; Chinn, R. L.; Zhi, L. *Tetrahedron Lett.* **1989**, *30*, 1491–1494.
7. Padwa, A.; Fryxell, G. E.; Zhi, L. *J. Am. Chem. Soc.* **1990**, *112*, 3100–3109.
8. Muthusamy, S.; Babu, S. A.; Gunanathan, C.; Suresh, E.; Dastidar, P.; Jasra, R. V. *Tetrahedron* **2000**, *56*, 6307–6318.
9. Mitsui, S.; Senda, Y.; Saito, H. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 694–697.
10. Kevill, D. N.; Weiler, D.; Cromwell, N. H. *J. Org. Chem.* **1964**, *29*, 1276–1278.
11. All the new compounds exhibited spectral data consistent with their structures. Selected spectral data, $\mathbf{3a_1}$: mp 148–150°C; IR (KBr): ν_{max} 2965, 1763, 1457, 1346, 1301, 1265, 1143, 1061, 1001, 977 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 7.58–7.53 (1H, m), 7.36–7.20 (7H, m), 7.09–7.05 (1H, m), 6.93 (1H, s, C=C*H*), 4.57 (1H, s, H-7), 3.08–2.94 (3H, m), 2.80–2.60 (1H, m), 2.58–2.32 (2H, m), 2.15–1.93 (3H, m), 1.65–1.55 (1H, m), 1.26 (3H, s, CH$_3$); ^{13}C NMR (50 MHz, CDCl$_3$): δ 210.8 (C=O), 140.6 (*quat-C*), 137.2 (*quat-C*), 136.8 (*quat-C*), 135.8 (*quat-C*), 129.3, 128.6, 128.5, 128.4, 127.2, 126.4, 126.1, 125.4, 123.7 (*quat-C*), 89.0 (C-7), 87.5 (C-1), 59.2 (C-5), 34.0 (CH$_2$), 29.6 (CH$_2$), 26.0 (CH$_2$), 24.4 (CH$_2$), 20.4 (CH$_2$), 16.9 (CH$_3$); Mass m/z (%): 372 (M$^+$, 27), 275 (92), 259 (38), 247 (70), 235 (42), 202 (20), 171 (38), 109 (100), 91 (94); Anal. calcd for C$_{25}$H$_{24}$O$_3$: C, 80.61; H, 6.49; found: C, 80.68; H, 6.54%. $\mathbf{3a_2}$: mp 193–195°C; IR (KBr): ν_{max} 2940, 1767, 1652, 1456, 1347, 1136, 1053, 1002, 755 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 7.55–7.63 (1H, m), 7.35–7.10 (8H, m), 6.78 (1H, s, C=C*H*), 4.77 (1H, s, H-7), 3.06–2.91 (3H, m), 2.85–2.68 (1H, m), 2.48–2.30 (2H, m), 2.18–1.92 (3H, m), 1.65–1.53 (1H, m), 1.31 (3H, s, CH$_3$); ^{13}C NMR (50 MHz, CDCl$_3$): δ 210.6 (C=O), 140.0 (*quat-C*), 137.8 (*quat-C*), 137.5 (*quat-C*), 136.0 (*quat-C*), 129.4, 128.5, 128.1, 127.0, 126.7, 125.8, 124.4, 122.9 (*quat-C*), 88.1 (C-1), 84.9 (C-7), 59.6 (C-5), 34.3 (CH$_2$), 28.1 (CH$_2$), 25.91 (CH$_2$), 25.86 (CH$_2$), 20.3 (CH$_2$), 16.5 (CH$_3$); Mass m/z (%): 372 (M$^+$, 2), 274 (83), 247 (35), 235 (28), 202 (27), 109 (100), 91 (94); Anal. calcd for C$_{25}$H$_{24}$O$_3$: C, 80.61; H, 6.49; found: C, 80.55; H, 6.53%.
12. Shanmugasundaram, M.; Babu, S. A.; Ragunathan, R.; Malar, E. J. P. *Heteroatom. Chem.* **1999**, *10*, 331–336.
13. Pirrung, M. C.; Kaliappan, K. P. *Org. Lett.* **2000**, *2*, 353–355.