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Efficient synthesis of oxindoles by thermal and rhodium(II)-catalyzed Wolff rearrangement

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Abstract

An efficient synthesis of oxindoles is achieved from a thermal and rhodium(II)-catalyzed Wolff rearrangement of diazoquinolinediones in moderate yields.

Oxindoles and their derivatives are very important compounds as synthetic intermediates of natural products and pharmaceutical reagents.[1] Numerous methods for the synthesis of oxindoles have been carried out by Friedel–Crafts reaction,[2] Gassman reaction,[3] metal-catalyzed reactions,[4] photoinduced cyclization,[5] and radical cyclizations.[6] Although a number of methods for the synthesizing of oxindoles have been reported, simple and efficient approaches still remain scarce.

The thermal, photochemical, and metal-mediated Wolff rearrangement is a well-known and useful reaction in organic synthesis.[7] We have been interested in the synthesis of oxindoles. Our strategy for the synthesis of oxindoles begins with a ring contraction of diazodicarbonyl compounds **1** and **3** utilizing Wolff rearrangement. The Wolff rearrangement of diazocarbonyl compounds has been widely investigated by many groups.[8] However, no study has been made of a thermal and rhodium(II)-catalyzed Wolff rearrangement of diazoquinolinediones. We describe here a novel route to the synthesis of biologically interesting oxindoles and their derivatives by using thermal and rhodium(II)-catalyzed Wolff rearrangements.

Diazoquinolinediones **1** and **3** were prepared by the diazotransfer reaction of the corresponding 4-hydroxy-2-quinolones with mesyl azide according to Taber's method.[9] In order to check the reactivity of *N*-methyl diazoquinolinedione **1** for a Wolff rearrangement, thermal reactions in several solvents were first investigated (Scheme 1). When acetonitrile, fluorobenzene, or toluene as undried solvents (containing a little amount of water) was heated at reflux for 24 h in the absence of a metal catalyst, only starting material was recovered. However, when xylene was used at reflux for 6 h, *N*-methyloxindole **2** was obtained in a 55% yield. Support for the structural assignment of **2** comes from their spectroscopic

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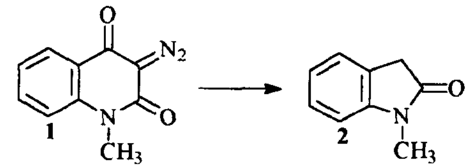
analysis[10] and data in the literature.[11] Similarly, with phenylacetonitrile as another polar solvent at 140°C for 3 h, **2** is also produced in a 41% yield. Although yields of **2** are low, no by-products were observed, and no starting material was recovered in these reactions.

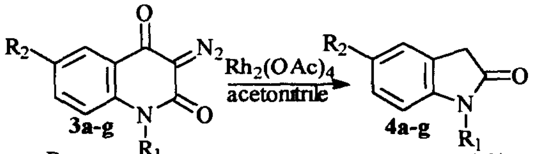


solvent	metal salt	temp	time(h)	yield(%)
acetonitrile	none	reflux	24	0
fluorobenzene	none	reflux	24	0
toluene	none	reflux	24	0
xylene	none	reflux	6	55
phenylacetonitrile	none	140	3	41
acetonitrile	Ag_2O	reflux	48	0
acetonitrile	$Cu(acac)_2$	reflux	48	0
acetonitrile	$Pd(OAc)_2$	reflux	48	26
acetonitrile	$Rh_2(OAc)_4$	reflux	10	58

Scheme 1.

Next, reaction of **1** in refluxing acetonitrile was attempted by using 2 mol% of several metal catalysts. Both Ag_2O and $Cu(acac)_2$ gave no reaction, whereas $Pd(OAc)_2$ and $Rh_2(OAc)_4$ provided the desired *N*-methyloxindole **2** in 26 and 58% yields, respectively. Surprisingly, in these reactions, no cycloaddition products to the acetonitrile by metal carbenoid reactions were detected. Also, we found $Rh_2(OAc)_4$ was more efficient than $Pd(OAc)_2$ for the production of oxindole derivatives. In an effort to optimize reaction conditions, we surveyed other nonpolar solvents. However, when fluorobenzene and toluene were used, the yields were somewhat decreased in comparison with acetonitrile.

Finally, rhodium(II)-catalyzed reactions of several diazoquinolinediones **3a–g** in refluxing acetonitrile were carried out to give a variety of oxindole derivatives **4a–g** (Scheme 2). In all cases, only a single product was seen. In particular, the reaction of diazoquinolinediones **3a** and **3b** afforded oxindole **4a** and its derivative **4b** in 40 and 87% yields, respectively.[12]



	R_1	R_2	yield(%)	mp(°C)
a	H	H	40	126-128
b	CH_3	OCH_3	87	87-88
c	CH_2CH_3	H	51	84-85
d	$CH_2CH_2CH_3$	H	55	61-63
e	$CH_2CH{=}CH_2$	H	74	41-42
f	CH_2Ph	H	70	80-81
g	CH_2Ph-4-OCH_3	H	63	103-104

Scheme 2.

In conclusion, thermal and rhodium(II)-catalyzed Wolff rearrangements of diazoquinolinediones are described. This method provides a novel entry into biologically interesting oxindoles. Further mechanistic studies and applications of these reactions are in progress in our laboratory.

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10. Spectral data for **2**: mp 85°C, lit.[11] mp 86.5–87°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (1H, t, J=7.57 Hz), 7.22 (1H, d, J=7.76 Hz), 7.02 (1H, t, J=7.57 Hz), 6.79 (1H, d, J=7.76 Hz), 3.50 (s, 2H), 3.19 (s, 3H); IR (KBr) 3061, 1701, 1615, 1495, 1466, 1370, 1350, 1265, 1213, 1192, 1127, 1094, 1020, 949, 914, 754 cm^{-1}.
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12. Spectral data for **4b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.87 (1H, d, J=2,38 Hz), 6.78 (1H, dd, J=8.48, 2.38 Hz), 6.69 (1H, d, J=8.48 Hz), 3.76 (3H, s), 3.48 (2H, s), 3.16 (3H, s); IR (KBr) 2943, 1697, 1602, 1541, 1496, 1394, 1359, 1292, 1240, 1151, 1028, 945, 952 cm^{-1}.