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Efficient synthesis of phenalenone derivatives by rhodium(II)-catalyzed reactions

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Abstract

An efficient synthesis of phenalenone derivatives is achieved by rhodium(II)-catalyzed reactions of 2-diazo-1*H*-1,3-phenalenedione with a variety of substrates in moderate yields. This method also provides a rapid route to biologically interesting polycycles and heterocycles. © 2000 Elsevier Science Ltd. All rights reserved.

Phenalenone derivatives are widely distributed in nature.[1] They are produced de novo by some plant organs when provoked by biotic, physical, and chemical agents.[2] They are also reported to have various important biological activities such as antibiotic, antimicrobial, and phytoalexin.[3] This wide range of biological properties has stimulated the development of new methods for the synthesis of phenalenone derivatives. The strategy for the synthesis of phenalenone derivatives begins with the reaction of 2-diazo-1*H*-1,3-phenalenedione (**2**) with a number of substrates under the rhodium catalysis.

The rhodium-catalyzed decomposition of diazocarbonyl compounds has become an important method in organic synthesis.[4] However, the rhodium-catalyzed reaction of 2-diazo-1*H*-1,3-phenalenedione to substrates has not been investigated. Recently, we have been interested in rhodium(II)-catalyzed reactions of diazodicarbonyl compounds to a number of substrates.[5] We report here an efficient synthesis of phenalenone derivatives utilizing the rhodium(II)-catalyzed reaction of 2-diazo-1*H*-1,3-phenalenedione with several unsaturated substrates.

Diazodicarbonyl compound **2** was readily prepared by the diazotransfer reaction of 3-hydroxy-1*H*-phenalen-1-one (**1**) with mesyl azide according to Taber's method in 82% yield (Eq. (1)).[6] It is

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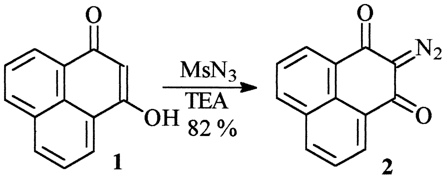
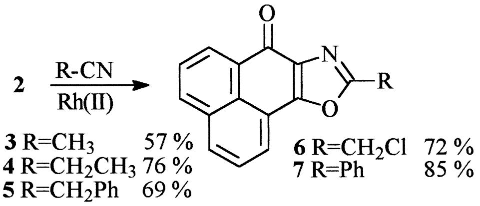
stable at room temperature and it can be stored in the refrigerator for a long time without any decomposition.



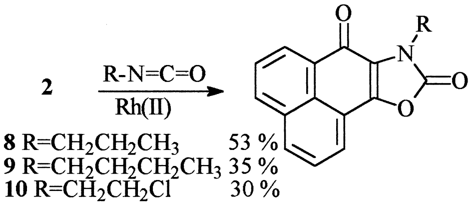
(1)

Reactions of **2** with several types of substrates containing heteroatoms such as nitriles, isocyanates, and ketones were first examined to synthesize phenalenone derivatives with five-membered heterocycles. When acetonitrile was used at 60°C for 5 h as a solvent and a reactant in the presence of 2 mol% $Rh_2(OAc)_4$, oxazole **3** was obtained in 57% yield (Eq. (2)). The structure of oxazole **3** is easily established spectroscopically. Similarly, with other nitriles containing electron-donating and -withdrawing groups, the expected oxazoles **4**–**7** were also produced in 57–85% yields.



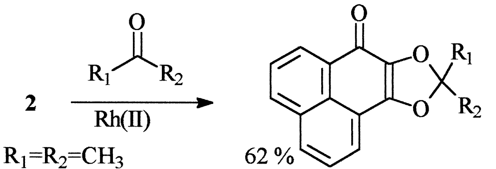
(2)

Next, when propyl isocyanate was used at 60°C for 5 h, oxazolone **8** was obtained in 53% yield (Eq. (3)). The structure of oxazolone **8** is easily identified by observation of IR absorption at ~1776 cm^{-1} associated with a carbonyl group of the oxazolone ring. In this case, only a single product was seen and no regioisomers were found. Similarly, under the same conditions, other oxazolones **9** and **10** were also obtained in 35 and 30% yields, respectively.



(3)

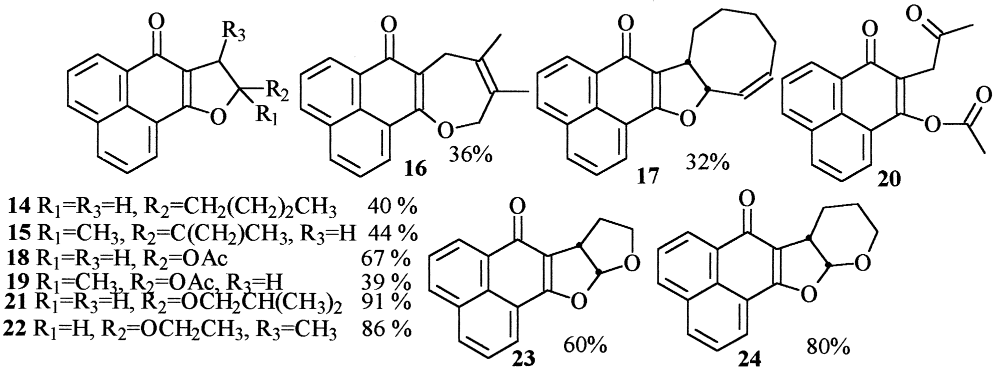
Rhodium-catalyzed reactions of diazocarbonyl compounds to ketones have not been studied. In related work, Alonso has demonstrated that copper(II)-mediated cycloaddition of methyl 2-diazo-3-oxobutyrate to ketones delivers the 1,3-dioxazole in moderate yield.[7] Treatment of **2** with acetone at reflux for 3 h gave the 1,3-dioxole **11** in 62% yield (Eq. (4)). The formation of **11** is supported by the observation of a peak in the IR spectum at ~1631 cm^{-1} (enone C=O) and a singlet in the ^1H NMR spectrum at δ 1.81 (geminal dimethyl groups). Reactions of **2** with 3-methyl-2-butanone and cyclohexanone also gave 1,3-dioxole **12** and **13** in 65 and 42% yields, respectively.



11 $R_1=R_2=CH_3$ 62 %
12 $R_1=CH_3$, $R_2=CH(CH_3)_2$ 65 %
13 $R_1=R_2=CH_2(CH_2)_3CH_2$ 42 %

(4)

To synthesize a variety of phenalenone derivatives, additional reactions with olefins were examined (Fig. 1). Reaction with 1-hexene as a reactant and a solvent (reflux, 5 h, 2 mol% $Rh_2(OA)_4$) gave dihydrofuran **14** in 40% yield. The dihydrofuran **14** is confirmed by analysis of the expected chemical shifts of methine and methylene protons associated with the dihydrofuran ring. The formation of **14** is very surprising in comparison to the reported results by Shechter that the rhodium(II)-catalyzed reaction of 2-diazo-1,3-indandione with 1-octene gave exclusively a cyclopropanation product.[8]


16 36%
17 32%
20
23 60%
24 80%

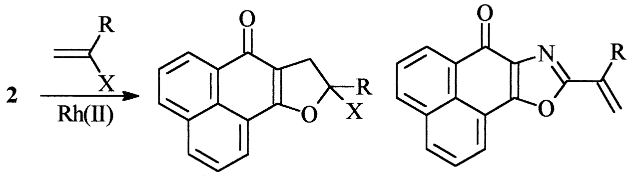
14 $R_1=R_3=H$, $R_2=CH_2(CH_2)_2CH_3$ 40 %
15 $R_1=CH_3$, $R_2=C(CH_2)CH_3$, $R_3=H$ 44 %
18 $R_1=R_3=H$, $R_2=OAc$ 67 %
19 $R_1=CH_3$, $R_2=OAc$, $R_3=H$ 39 %
21 $R_1=R_3=H$, $R_2=OCH_2CH(CH_3)_2$ 91 %
22 $R_1=H$, $R_2=OCH_2CH_3$, $R_3=CH_3$ 86 %

Figure 1.

Reaction of **2** with 2,3-dimethyl-1,3-butadiene at 60°C for 5 h gave dihydrofuran **15** and dihydrooxepine **16** as a separable mixture in 44 and 36% yields, respectively. The formation of dihydrofuran **15** is defined by the chemical shifts and geminal coupling constants associated with the methylene group of the dihydrofuran ring, whereas the dihydrooxepine **16** is identified by two methylene peaks of the seven-membered ring. However, reaction with *cis,cis*-1,3-cyclooctadiene as a cyclic 1,3-butadiene afforded cycloadduct **17** (32%) as a single compound.

As electron-rich olefins, reaction with an excess amount of vinyl acetate at 60°C for 5 h afforded the dihydrofuran **18** in 67% yield. Under the same conditions, reaction with isopropenyl acetate gave the dihydrofuran **19** (39%) and unexpected rearranged product **20** (30%) as a mixture of isomers. The methylene protons of **20** are observed at δ 3.67 as a singlet, and two methyl signals of the ester and the ketone are shown at δ 2.46 and δ 2.21, also as singlets. Further support for the structural assignment of **20** is also accomplished from its IR spectrum, which clearly shows the expected three C=O absorptions at 1763, 1713, and 1640 cm^{-1} due to one ester and two ketones. With isobutyl vinyl ether and ethyl 1-propenyl ether, dihydrofuran **21** and **22** were produced in 91 and 86% yields, respectively. The dihydrofuran **22** was isolated as a *cis*-compound despite the use of a 3:1 mixture of *cis*- and *trans*-isomers. Other electron-rich olefins, such as dihydrofuran and dihydropyran, gave the fused acetals **23** and **24** in 60 and 80% yields, respectively. The structures of **23** and **24** are also clearly assigned as *cis*-compounds by analysis of the vicinal coupling constant of the two methine protons and by the analogy of the earlier reported data.[9] The methine proton of **23** appeared as a doublet (J = 5.8 Hz) at δ 6.56 and that of **24** as a doublet (J = 7.6 Hz) at δ 6.23.

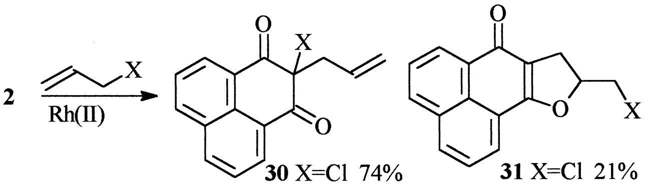
Extension of the rhodium(II)-catalyzed reaction of other electron-deficient olefins was also successful (Eq. (5)). Treatment with an excess of ethyl acrylate as a solvent and a reactant in the presence of 2 mol% $Rh_2(OAc)_4$ at 60°C for 5 h gave dihydrofuran **25** in 26% yield. Similarly, reaction with methyl methacrylate gave the expected dihydrofuran **26** in 30% yield. As another electron-deficient olefin, reaction with acrylonitrile at 60°C for 5 h gave oxazole **27** (57%) as a single compound without any trace of the expected dihydrofuran adduct. However, on heating of **2** with methacrylonitrile, oxazole **28** and dihydrofuran **29** were obtained in 31 and 38% yield as an inseparable mixture. The ratio of yield is calculated from the data of ^1H NMR spectrum. In view of our results, it may be expected that the formation of phenalenone derivatives is facilitated by both electron-rich and -deficient olefins. However, reactions with electron-rich olefins proceed in higher yields than electron-deficient olefins.



25 R=H, X=$CO_2CH_2CH_3$ 26 % **27** R=H 57%
26 R=CH_3, X=CO_2CH_3 30 % **28** R=CH_3 31%
29 R=CH_3, X=CN 38 %

(5)

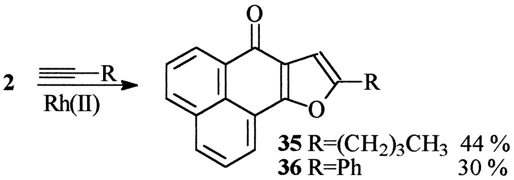
As other electron-deficient olefins, several allylic halides were next investigated (Eq. (6)). The metal-catalyzed reactions of acyclic diazo compounds with allyl halides have been shown by Doyle.[10] Reaction of **2** with allyl chloride at room temperature for 5 h gave the [2,3]-sigmatropic rearrangement product **30** (74%) as a major component in competition with the dihydrofuran product **31** (21%). Similarly, reactions with allyl bromide also afforded the [2,3]-sigmatropic rearrangement product **32** (60%) and cycloaddition product **33** (26%). However, reaction with allyl iodide gave the cycloaddition product **34** as a single compound in an 81% yield without any trace of the expected rearrangement product. These results are in clear contrast to those of Doyle, who reported that the rhodium(II)-catalyzed reactions of ethyl diazoacetate with allyl iodide afforded the [2,3]-rearranged product as a single compound, whereas the cyclopropanation adduct occurred almost exclusively with allyl chloride and bromide.



30 X=Cl 74% **31** X=Cl 21%
32 X=Br 60% **33** X=Br 26%
34 X=I 81%

(6)

In order to extend the utility of these reactions as the synthesis of phenalenone derivatives, two types of alkynes were finally examined (Eq. (7)). Reaction with 1-hexyne at 60°C for 5 h resulted in furan **35** (44%) as a single compound. In the ^{1}H NMR spectrum of **35**, the vinyl proton of furan ring was found at δ 6.64. Similarly, reaction with phenyl acetylene gave the expected furan **36** in 30% yield.



35 R=$(CH_2)_3CH_3$ 44 %
36 R=Ph 30 %

(7)

In conclusion, rhodium(II)-catalyzed reactions of **2** with several unsaturated substrates are described. These reactions provide a rapid entry to the synthesis of phenalenone derivatives found in nature. Further mechanistic studies and applications of these rhodium(II)-catalyzed reactions are in progress in our laboratory.

Acknowledgements

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