Pergamon

Tetrahedron Letters 42 (2001) 6561–6563

TETRAHEDRON
LETTERS

Novel method for the synthesis of β-substituted α-haloenones by rhodium(II)-catalyzed reactions of diazodicarbonyl compounds with benzyl halides

Yong Rok Lee* and Dae Hwan Kim

School of Chemical Engineering and Technology, Yeungnam University, Kyongsan 712-749, South Korea

Received 23 April 2001; revised 16 July 2001; accepted 19 July 2001

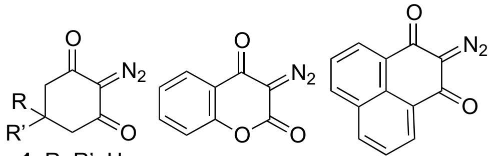
Abstract—The rhodium(II)-catalyzed reactions of diazodicarbonyl compounds with benzyl halides give β-substituted α-haloenones in good yields. © 2001 Elsevier Science Ltd. All rights reserved.

α-Haloenones have widely been used as valuable and versatile intermediates in the synthesis of α-carbon substituted enones[1] and biologically active natural products.[2] α-Haloenones are typically prepared by a halogenation–dehydrohalogenation reaction,[3] an addition–elimination reaction,[4] and a halohydrin–dehydration reaction.[5] Although many methods for the preparation of these compounds have been developed, their synthetic exploitation has been limited due to the difficulty in controlling their regioselectivity, the strong acidic conditions, and the side reactions involving polyhalogenation.[6] The necessity for overcoming these serious problems has prompted a research for new methods for the preparation of α-haloenones.

We have been interested in developing a new method for the preparation of α-haloenones utilizing halonium ylides. The metal-catalyzed reaction of diazocarbonyl compounds with allyl halides has been shown by other groups.[7] We have recently reported a new preparation of β-substituted α-chloroenones starting from diazodicarbonyl compounds with acid chlorides.[8] We also found that these reactions sometimes afforded α-chloroenones in low yields. Following our studies on new and improved procedures based on diazodicarbonyl compounds, we examined the reactions of several diazodicarbonyl compounds with benzyl halides. We report here a new and more efficient synthesis of β-substituted α-haloenones utilizing rhodium(II)-catalyzed reactions of cyclic diazodicarbonyl compounds with a variety of benzyl halides.

Diazodicarbonyl compounds **1**–**5** were prepared by the diazotransfer reaction of the corresponding 1,3-dicarbonyl compounds with mesyl azide according to Taber's method (Fig. 1).[9] These compounds are fairly stable and can be stored in a refrigerator for a long time without any decomposition.

Reactions with benzyl halides (10-fold excess), which serve as a solvent and a reactant, in the presence of 1 mol% of $Rh_2(OAc)_4$, were first examined. Treatment of 2-diazo-1,3-cyclohexanedione (**1**) with benzyl chloride at room temperature for 12 h gave 3-benzyloxy-2-chloro-cyclohex-2-enone (**6**) in an 80% yield (Scheme 1).[10] Support for the structural assignment comes from

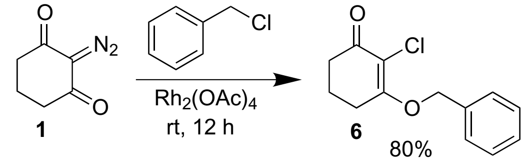


1 R=R'=H
2 R=R'=CH_3
3 R=H, R'=$CH(CH_3)_2$

4

5

Figure 1.



1

6

80%

Scheme 1.

---

* Corresponding author.

PII: S0040-4039(01)01345-4

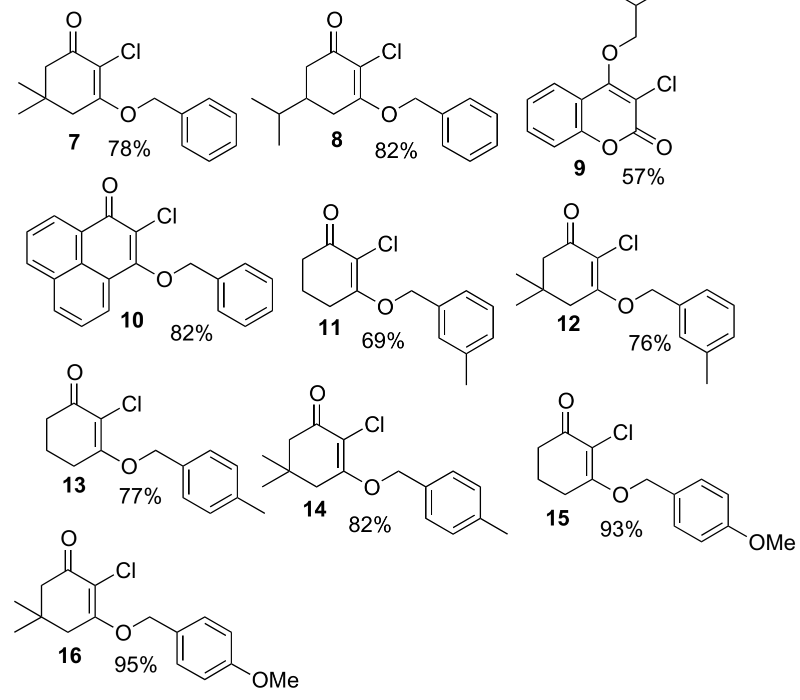
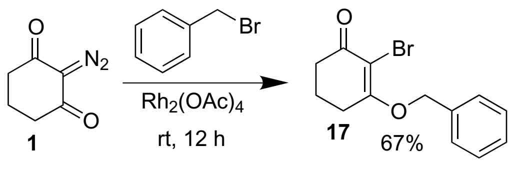


Figure 2.

its spectroscopic analyses. The α-chloroenone **6** is identified by its IR carbonyl absorption of the enone at 1657 cm^{-1} and its ^1H NMR peak of the methylene protons of benzyl group as a singlet at δ 5.24.[11] Similarly, reactions of diazodicarbonyl compounds **2**–**5** with benzyl chloride afforded α-chloroenones **7**–**10** in 57–82 yields. With 3- and 4-methylbenzyl chloride, α-chloroenones **11**–**14** were obtained in 69–82% yields. In particular, reactions of diazodicarbonyl compounds, **1** and **2**, with 4-methoxybenzyl chloride also afforded α-chloroenone **14** (93%) and **15** (95%) in high yields, respectively. The results are collected in Fig. 2.

In order to extend the utility of this methodology, reactions of diazodicarbonyl compounds with several benzyl bromides were next examined. Treatment of **1** with benzyl bromide at room temperature for 12 h in the presence of 1 mol% of $Rh_2(OAc)_4$ afforded 3-benzyloxy-2-bromo-cyclohex-2-enone (**17**) in 67% yield (Scheme 2).[12] With 2- and 3-methylbenzyl bromide, the expected α-bromoenones **18**–**22** were also produced in 50–70% yields. The results are also summarized in Fig. 3.



Scheme 2.

Although the exact mechanism of the reaction is still not clear, it is best described as shown in Scheme 3. The diazodicarbonyl compound **1** first gives a carbenoid **23** (or a carbene) by displacement of nitrogen by $Rh_2(OAc)_4$. Intermediate **23** is attacked by chloride of benzyl chloride to give an ylide **24**, which subsequently undergoes intramolecular substitution to give product **6**.

In conclusion, rhodium-catalyzed reaction of cyclic diazodicarbonyl compounds with a variety of benzyl halides offers a simple and efficient method for the preparation of α-halo-α,β-unsaturated enones. Further application of this reaction will be investigated, and is now in progress in our laboratory.

Acknowledgements

This work was supported by grant (2000-1-12300-001-3) from the Basic Research Program of the Korea Science and Engineering Foundation. Dr. Ronald Tepper in discussion of this work is greatly appreciated.

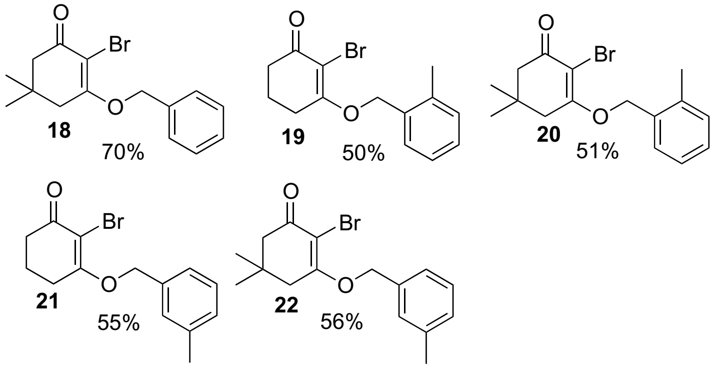
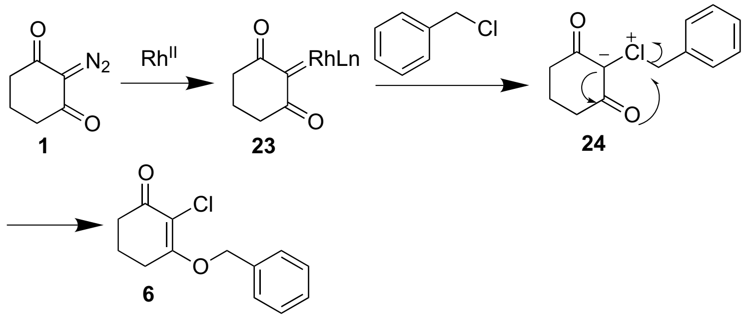


Figure 3.



Scheme 3.

References

1. (a) Kamikubo, T.; Ogasawara, K. *Chem. Commun.* **1996**, 1679; (b) Atsuta, H.; Fujiwara, K.; Murai, A. *Synlett* **1997**, 307; (c) Liebeskind, L. S.; Wang, J. *Tetrahedron Lett.* **1990**, *31*, 4293; (d) Negishi, E.-I.; Owczarczyk, Z. R.; Swanson, D. R. *Tetrahedron Lett.* **1991**, *32*, 4453; (e) Kabat, M.; Kiegiel, J.; Cohen, N.; Toth, K.; Wovkulich, P. M.; Uskokovic, M. R. *Tetrahedron Lett.* **1991**, *32*, 2343; (f) Johnson, C. R.; Adams, J. P.; Braun, M. P.; Senanayake, C. B. W. *Tetrahedron Lett.* **1992**, *33*, 919.
2. (a) Johnson, C. R.; Braun, M. P. *J. Am. Chem. Soc.* **1993**, *115*, 11014; (b) Johnson, C. R.; Harikrishnan, L. S.; Golebiowski, A. *Tetrahedron Lett.* **1994**, *35*, 7735; (c) Johnson, C. R.; Adams, J. P.; Collins, M. A. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1.
3. (a) Bordwell, F. G.; Wellman, K. M. *J. Org. Chem.* **1963**, *28*, 2544; (b) Kowalski, C. J.; Weber, A. E.; Fields, K. W. *J. Org. Chem.* **1982**, *47*, 5088; (c) Dunn, G. L.; Dipasquo, V. J.; Hoover, J. R. E. *J. Org. Chem.* **1968**, *33*, 1454.
4. (a) Kamigata, N.; Satoh, T.; Yoshida, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 449; (b) Ley, S. V.; Whittle, A. J. *Tetrahedron Lett.* **1981**, *22*, 3301.
5. Righi, G.; Bovicelli, P.; Sperandio, A. *Tetrahedron Lett.* **1999**, *40*, 5889.
6. (a) Bovonsombat, P.; Angara, G. J.; Mc Nelis, E. *Tetrahedron Lett.* **1994**, *35*, 6787; (b) Johnson, C. R.; Adams, J. P.; Braun, M. P.; Senanayake, C. B. W.; Wovkulich, P. M.; Uskokovic, M. R. *Tetrahedron Lett.* **1992**, *33*, 917; (c) Sha, C.-K.; Huang, S.-J. *Tetrahedron Lett.* **1995**, *36*, 6927; (d) Whang, J. P.; Yang, S. G.; Kim, Y. H. *J. Chem. Soc., Chem. Commun.* **1997**, 1355; (e) Matsuo, K.; Ishida, S.; Takuno, Y. *Chem. Pharm. Bull.* **1994**, *42*, 1149.
7. (a) Ando, W.; Kondo, S.; Nakayama, K.; Ichibori, K.; Kohoda, H.; Yamato, H.; Imai, I.; Nakaido, S.; Migita, T. *J. Am. Chem. Soc.* **1972**, *94*, 3870; (b) Doyle, M. P.; Tamblyn, W. H.; Bagheri, V. *J. Org. Chem.* **1981**, *46*, 5094.
8. Lee, Y. R.; Suk, J. Y. *Chem. Commun.* **1998**, 2621.
9. Taber, D. F.; Ruckle, Jr., R. E.; Hennessy, M. *J. Org. Chem.* **1986**, *51*, 4077.
10. Typical procedure: To a solution of **1** (138 mg, 1.0 mmol) and benzyl chloride (1.26 g, 10.0 mmol) was added rhodium(II) acetate (4.4 mg, 1 mol%) at room temperature under a N_2 atmosphere. The reaction mixture was stirred at room temperature for 12 h. The mixture was purified by flash column chromatography on silica gel resulting in product formation.
11. Spectral data for **6**: mp 98–99°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41–7.33 (5H, m), 5.24 (2H, s), 2.67 (2H, dd, $J=6.2$, 6.1 Hz), 2.48 (2H, dd, $J=7.0$, 6.2 Hz), 1.98 (2H, m); IR (KBr) 2945, 2889, 1657, 1589, 1458, 1368, 1294, 1262, 1192, 1154, 1080, 1026, 1007, 922, 905, 817 cm^{-1}.
12. Spectral data for **17**: mp 104–105°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.33 (5H, m), 5.25 (2H, s), 2.66 (2H, dd, $J=6.3$, 6.1 Hz), 2.51 (2H, dd, $J=6.8$, 6.3 Hz), 1.99 (2H, m); IR (KBr) 2949, 2888, 1655, 1586, 1368, 1287, 1259, 1192, 1154, 1080, 1026, 988, 920, 804 cm^{-1}.