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Intermolecular Rhodium(II)-Catalyzed Reactions with Silicon-Substituted Carbonyl Ylides

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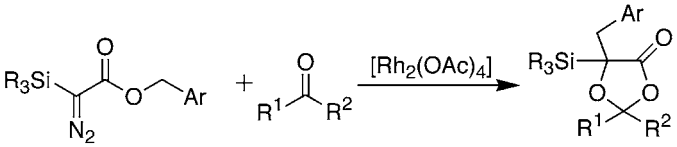
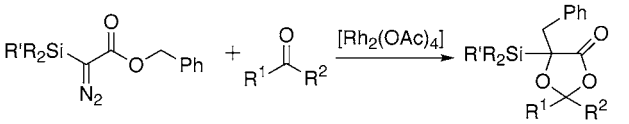
ABSTRACT



The Rh(II)-catalyzed reaction of benzyl 2-trialkylsilyl-2-diazoacetates with various acyclic and cyclic ketones affords novel dioxolanones via silicon-substituted carbonyl ylides in up to 98% yield.

The catalytic generation of carbonyl ylides from diazo compounds continues to be a subject of intensive investigation.[1] One particular area of interest lies in the use of tandem cyclization−cycloaddition reactions of rhodium carbenoids as a key strategic element in natural product synthesis.[2] Furthermore, 1,3-dipolar cycloadditions between a suitable dipolarophile, such as an alkene or alkyne, and a carbonyl ylide have become a powerful method for constructing highly substituted heterocycles.[3] *Inter*molecular reactions of carbonyl ylides with aldehydes or ketones have been less commonly used in the past, and are just recently receiving more attention.[4] For example, Jiang et al. reported the formation of 1,3-dioxolanes bearing a C-4 trifluoromethyl group with remarkable diastereoselectivity, as a result of the Rh(II)-catalyzed reaction of methyl diazo(trifluoromethyl) acetate with aryl aldehydes.[5] Moreover, Hodgson and coworkers developed the first examples of enantioselective carbonyl ylide cycloaddition using unsaturated α-diazo-*β*-keto esters, achieving 53% ee.[6] Our interest in this field is focused on intermolecular Rh(II)-catalyzed reactions of benzyl 2-trialkylsilyl-2-diazoacetates with various acyclic and cyclic ketones (Scheme 1).

Scheme 1



1a: R = R' = Et
1b: R = Me, R' = *t*-Bu
1c: R = R' = Me

2

3

These diazo compounds have already been used as precursors in the generation of α-silyl-substituted keto esters, α-hydroxyacetic acids, and α-amino acids, as well as in peptide synthesis.[7] We now find that decomposition of **1** with $[Rh_2(OAc)_4]$ in the presence of excess ketones **2** affords dioxolanones **3** in up to 98% yield (Table 1).[8]

We were pleased to find that this reaction proceeds well with simple acyclic ketones as well as various cyclic ketones.

(1) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263.
(2) (a) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223. (b) Padwa, A.; Brodney, M. A.; Marino, J. P., Jr.; Sheehan, S. M. *J. Org. Chem.* **1997**, *62*, 78. (c) Padwa, A.; Price, A. T. *J. Org. Chem.* **1998**, *63*, 556.
(3) (a) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919. (b) Padwa, A. *Acc. Chem. Res.* **1991**, *24*, 22. (c) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911. (d) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley & Sons: New York, 1998. (e) Kitagaki, S.; Yasugahira, M.; Anada, M.; Nakajima, M.; Hashimoto, S. *Tetrahedron Lett.* **2000**, *41*, 5931. (f) Johnson, T.; Cheshire, D. R.; Stocks, M. J.; Thurston, V. T. *Synlett* **2001**, 646. (g) Hodgson, D. M.; Stupple, P. A.; Pierard, F. Y. T. M.; Labande, A. H.; Johnstone, C. *Chem. Eur. J.* **2001**, *7*, 4465. (h) Savinov, S. N.; Austin, D. J. *Org. Lett.* **2002**, *4*, 1415. (i) Skaggs, A. J.; Lin, E. Y.; Jamison, T. F. *Org. Lett.* **2002**, *4*, 2277.

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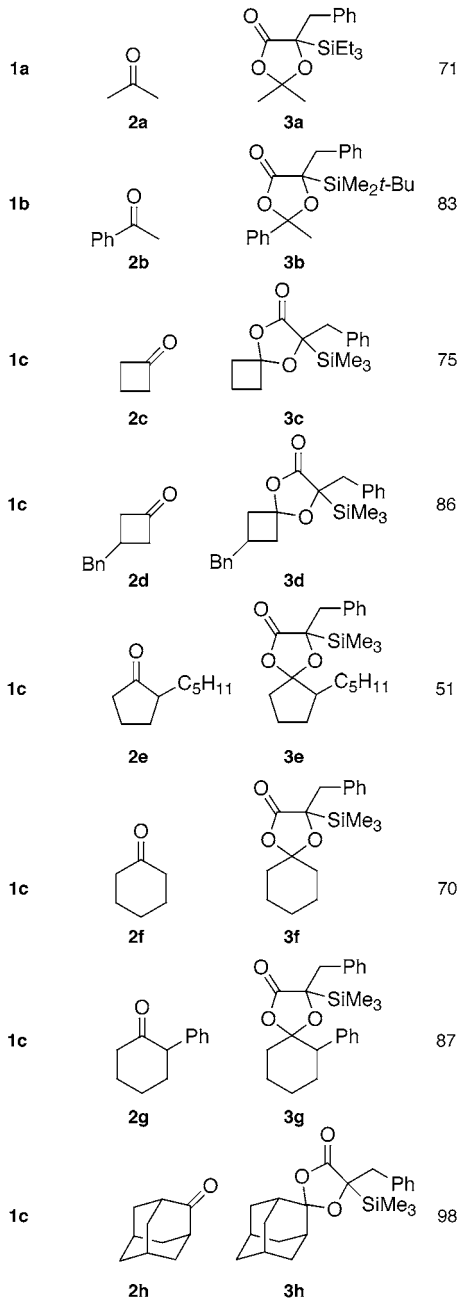
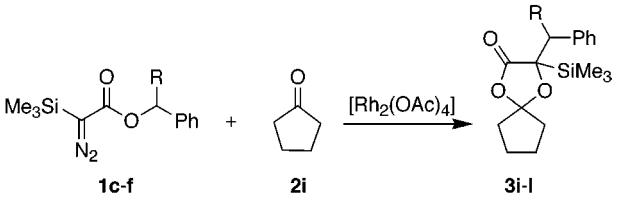
Table 1. Formation of α-Trialkylsilanyldioxolanones



Large groups in the α-position to the carbonyl group as in **2e** and **2g** only mildly hindered the cyclization process in the case of **2e**, and the desired dioxolanone **3e** was formed in a lower yield. The best result was achieved in the case of the polycyclic adduct adamantanone **2h**, which reacted smoothly with benzyl trimethylsilyldiazoacetate to give **3h** in 98% yield. Interestingly, Maas and Alt have reported the formation of dioxolanones in the dirhodium perflourobutyrate-catalyzed reactions of allylic diazoacetates with various aldehydes, including acetaldehyde, crotonaldehyde and aromatic aldehydes.[9] Analogous to the reactions with aldehydes, they also observed the formation of the corresponding dioxolanone in the reaction with acetone. It occurred to us that the ester functionality could have a profound impact on the course of this reaction. Hence, the benzylic position was substituted α to the phenyl ring with methyl, ethyl, and phenyl groups as shown in Table 2.

Table 2. Effect of the Ester Functionality



diazo ester	R	product	yield (%)
1c	H	**3i**	84
1d	Me	**3j**	78
1e	Et	**3k**	81
1f	Ph	**3l**	92

These substituents at the α-position did not alter the outcome of the reaction, and dioxolanones in up to 92% yield were isolated. (*R*)-(+)-1-Phenylethanol was used for the synthesis of **1d**, and the dioxolanone cycloadduct **3j** was obtained in a diastereoselectivity of 3.5:1 due to the effect of the chirality of the ester functionality.

Moreover, we investigated the influence of various substituents on the benzene ring as shown in Table 3. In the case of the electron-donating methoxy group in the para position as in **1g**, dioxolanone **3m** was formed exclusively. However, contrary to our expectation, enolether **4a** was isolated in 73% yield when the methoxy group was replaced by a nitro group. Interestingly, in the case of triflouromethyl in the para position, a mixture of products **3n** and **4b** in a ratio of 1:5 was obtained. Maas and Alt have observed the formation of an enolether as the product of the Rh(II)-catalyzed reaction involving trimethylsilyldiazoacetate, dim-

(4) (a) Kharasch, M. S.; Rudy, T.; Nudenberg, W.; Büchi, G. *J. Org. Chem.* **1953**, *18*, 1030. (b) Huisgen, R.; de March, P. *J. Am. Chem. Soc.* **1982**, *104*, 4953. (c) Alonso, M. E.; Garcia, M.-C.; Chitty, A. W. *J. Org. Chem.* **1985**, *50*, 3445. (d) L'Esperance, R. P.; Ford, T. M.; Jones, M., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 209. (e) Lottes, A. C.; Landgrebe, J. A.; Larsen, K. *Tetrahedron Lett.* **1989**, *30*, 4093. (f) Doyle, M. P.; Forbes, D. C.; Protopopova, M. N.; Stanley, S. A.; Vasbinder, M. M.; Xavier, K. R. *J. Org. Chem.* **1997**, *62*, 7210. (g) Hamaguchi, M.; Matsubara, H.; Nagai, T. *J. Org. Chem.* **2001**, *66*, 5395. (h) Nakamura, Y.; Ukita, T. *Org. Lett.* **2002**, *4*, 2317.

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(8) **Standard protocol for the catalysis**: The corresponding trialkylsilyldiazo benzyl ester (1 mmol) was added dropwise under an argon atmosphere to a stirring degassed solution of $[Rh_2(OAc)_4]$ (8.8 mg, 0.02 mmol, 2 mol %) and the corresponding ketone (2 mmol) in dry toluene (8 mL) at room temperature. The reaction mixture was heated to 40 °C and was left stirring at this temperature for 16 h. After the reaction mixture was cooled to ambient temperature, the solvent was removed in vacuo, and the crude product was purified by flash chromatography on silica gel or Florisil (petroleum ether/*tert*-butyl methyl ether, various gradients).

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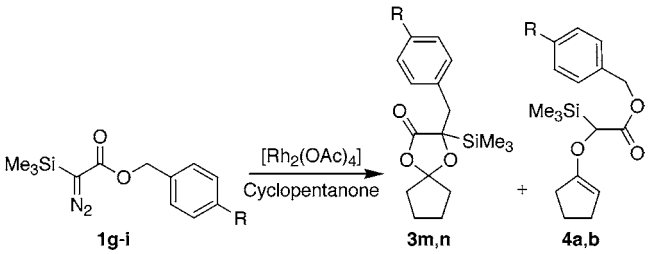
Table 3. Effect of Substituents on the Benzene Ring



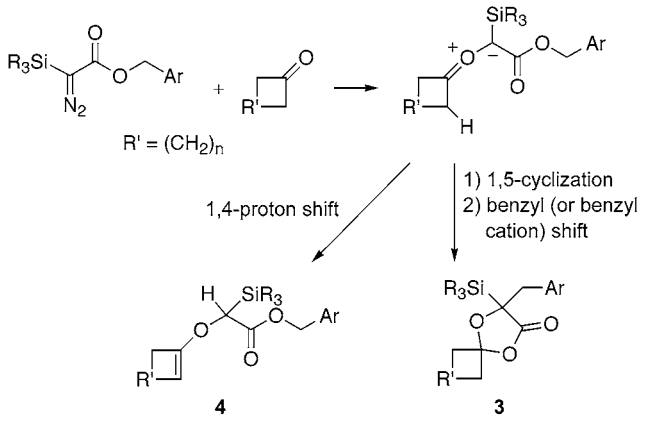
		product ratio	
diazo ester	R	dioxolanone	enol ether
1g	OMe	**3m**	
1h	NO_2		**4a**
1i	CF_3	**3n**	**4b**

ethylfumarate, and cyclohexanone.[10] In addition, Corey and co-workers reported the Rh(II)-catalyzed reaction of diazoacetic esters with various carbonyl compounds as a method for synthesizing acetic ester ethers of the corresponding enol forms.[11]

Although the mechanism of this reaction is unclear, we propose that it proceeds via an initially generated silicon-substituted carbonyl ylide. This can either undergo a 1,4-proton shift to give enol ether **4** or cyclize involving a benzyl shift to yield **3**. The latter process could also proceed via benzyl cations, which would be recaptured (Scheme 2). Details of this mechanism will be studied in due course.

In summary, we found that the Rh(II)-catalyzed reaction between various α-trialkylsilyldiazo precursors with cyclic and acyclic ketones affords dioxolanones in up to 98% yield. Further studies with respect to substituent effects on this reaction are in progress, which should also shed light on the mechanism.

Scheme 2



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Supporting Information Available: Experimental procedures and full characterization (^{1}H and ^{13}C NMR data, MS, IR, and CHN analyses) for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL026987M

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