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A Conformationally Controlled Regioselective Rearrangement of 2-Substituted 1-Alkynylcyclopropanols to 2-Cyclopenten-1-ones via Hexacarbonyldicobalt Complex

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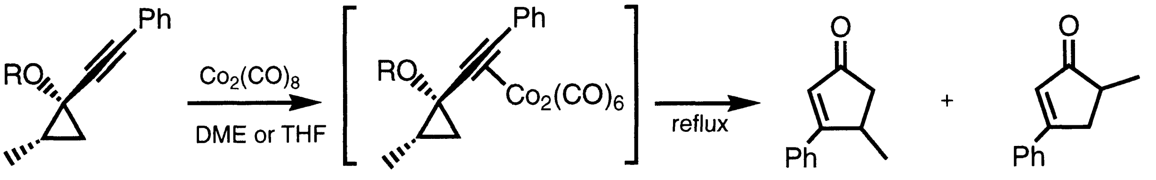
The rearrangement of hexacarbonyldicobalt-complexed 2-substituted 1-alkynylcyclopropanol derivatives is conformationally controlled to give 4- or 5-substituted 2-cyclopentenones regioselectively. In the cases of the reactions of 2-monosubstituted 1-alkynylcyclopropanol derivatives, either regioisomer can be selectively obtained by the appropriate choice of the substrates.

In the previous paper, we reported that a novel rearrangement reaction of hexacarbonyldicobalt-complexed 1-(1-alkynyl)cyclopropanols proceeds to give 2-cyclopenten-1-ones in good yields.[1] Our next concern is the regioselectivity of the reaction when 2-substituted 1-(1-alkynyl)cyclopropanols are employed as the substrates. In this case, two regioisomers, that is, 4-substituted and 5-substituted cyclopentenones, could be formed depending on which bond of cyclopropane will be cleaved. In this paper is described a regioselective rearrangement of 2-mono- or 2,2-di-substituted 1-(1-alkynyl)cyclopropanol derivatives to cyclopentenones via their hexacarbonyldicobalt complexes.

In the first place, the reaction of (1R*, 2S*)-2-methyl-1-phenylethynylcyclopropanol (**1a**) was examined according to the original procedure.[1,2] Thus, **1a** was treated with 1.1-1.2 equiv. of octacarbonyldicobalt in



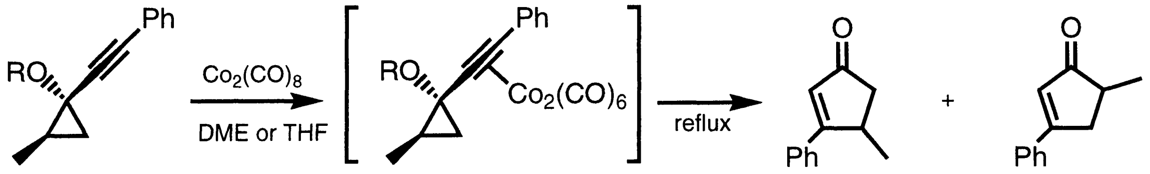
1 **2** **3** **4**

Table 1. The Reaction of (1R*, 2S*)-2-Methyl-1-phenylethynylcyclopropanol and its Silyl Ethers

R in **1**	Solvent	Reaction time/h	Yield/%	**3 : 4**
H(**1a**)	DME	1.5	75	50 : 50
$SiMe_3$	DME	1.5	73	70 : 30
$SiBu^tMe_2$	DME	1.25	83	91 : 9
$SiBu^tMe_2$	THF	5	77	94 : 6
$SiPr^i_3$	DME	1.5	72	93 : 7
$SiPr^i_3$	THF	3	70	94 : 6

dimethoxyethane (DME) at room temperature, and after complete formation of hexacarbonyldicobalt complex **2a** was observed by thin layer chromatography (about 30 min), the mixture was refluxed for 1.5 h under an atmospheric pressure of argon. Purification of the crude product by preparative thin layer chromatography (silica gel) revealed that almost equal amounts of 4-methyl-3-phenyl-2-cyclopenten-1-one (**3**) and 5-methyl-3-phenyl-2-cyclopenten-1-one (**4**) were produced in the total yield of 75%.3) As no regioselectivity of the rearrangement was observed in this reaction, the reactions of various silyl ethers of **1a** were examined and the results are summarized in Table 1. As clearly shown in this Table, the bulkiness of the silyl group greatly influences the regioselectivity of the rearrangement, and by using the *t*-butyldimethylsilyl or triisopropylsilyl ether of **1**, the 4-methyl isomer **3** was obtained in high selectivity (**3** : **4** = 94 : 6) in good yield.4)

Next, the reactions of (1R*, 2R*)-2-methyl-1-phenylethynylcyclopropanol (**5a**), the diastereomer of **1a**, and its silyl ethers were examined. As shown in Table 2, **4** was obtained exclusively when **5a** itself was employed as a substrate, and the regioselectivity slightly lowered as the bulkiness of the silyl group increased.4)

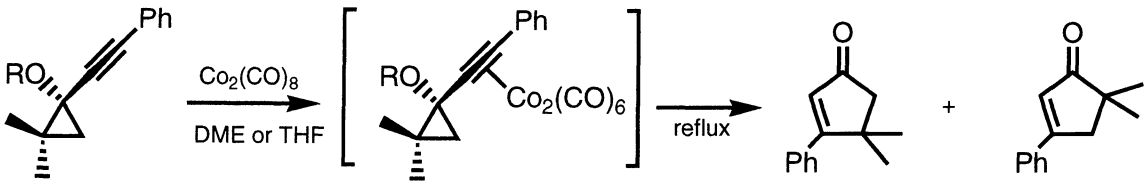


5 **6** **3** **4**

Table 2. The Reaction of (1R*,2R*)-2-Methyl-1-phenylethynylcyclopropanol and its Silyl Ethers

R in **5**	Solvent	Reaction time/h	Yield/%	**3** : **4**
H(**5a**)	DME	1.5	86	<1 : >99
$\mathrm{SiBu^{t}Me_2}$	DME	1.25	88	1 : 99
$\mathrm{SiPr^{i}_3}$	DME	5	47	2 : 98

In order to make clear the controlling factor for the determination of the regioselectivity, the reactions of 2,2-dimethyl-1-phenylethynylcyclopropanol (**7a**) and its silyl ether were examined next. And it was found that in this case, 5,5-dimethyl-3-phenyl-2-cyclopenten-1-one (**10**) was obtained as a single regioisomer when



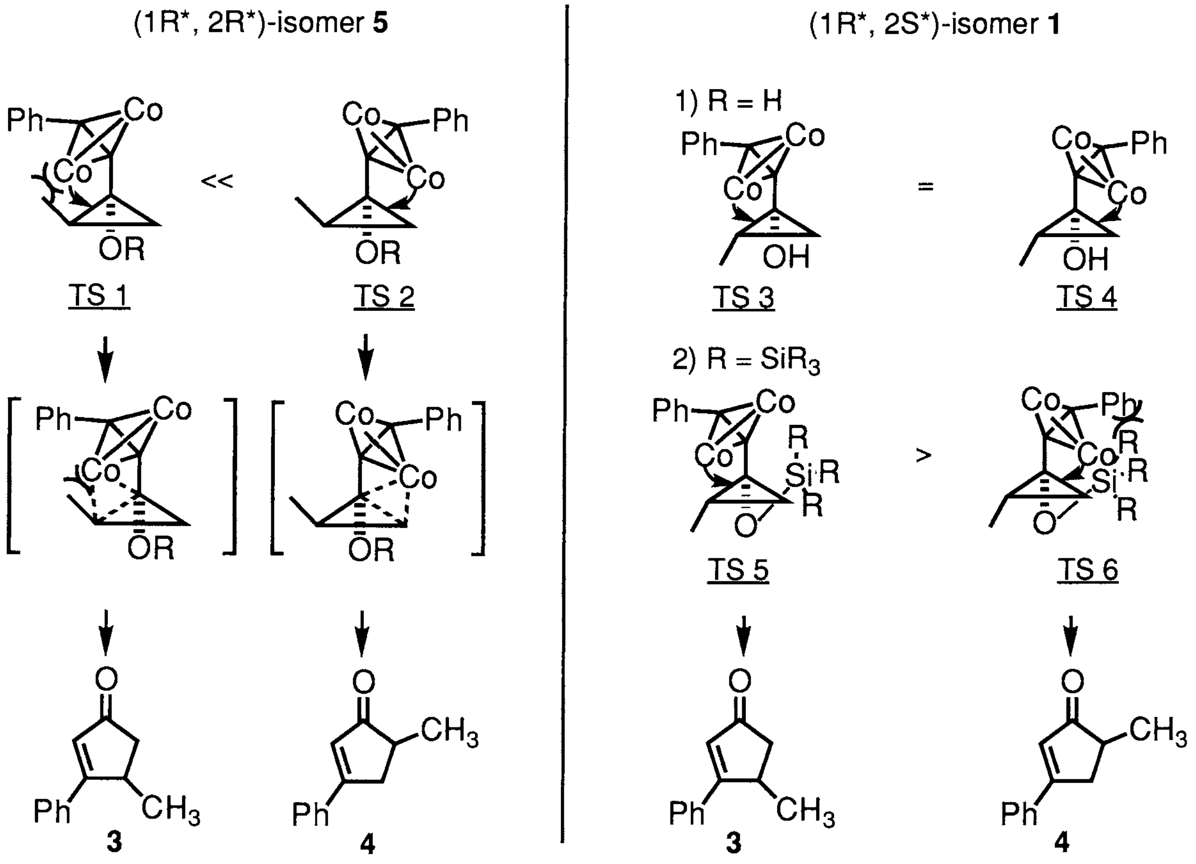
7 **8** **9** **10**

Table 3. The Reaction of 2,2-Dimethyl-1-phenylethynylcyclopropanol and its Silyl Ether

R in **7**	Solvent	Reaction time/h	Yield/%	**9** : **10**
H(**7a**)	DME	1	80	<1 : >99
$\mathrm{SiBu^{t}Me_2}$	DME	1.5	88	3 : 97

2,2-dimethyl-1-phenylethynylcyclopropanol (**7a**) itself was employed as a substrate. The use of the *t*-butyldimethylsilyl ether of **7a** also gave the same regioisomer as the major product with a small amount of the other regioisomer **9**.[3] This result indicates that the substituent cis to the alkynyl group plays a dominant role in determining the regioselectivity of the reaction.

Although the exact mechanism of the reaction has not yet been made clear, it is supposed that the reaction would proceed by the oxidative addition of cobalt species to the cyclopropane ring to make metallacyclic intermediate.[5] So the regioselectivity of this reaction is controlled by the feasibility of the two carbon-carbon bonds for the insertion of the cobalt species. With the assumptions described above, the regioselectivity of the reaction can be explained by considering the conformation of the molecules (Scheme 1). Thus, in the case of the reaction of (1R*, 2R*)-isomer **5**, 5-methyl-3-phenyl-2-cyclopentenone (**4**) could be produced via TS2 without any serious steric repulsion, while 4-methyl isomer **3** must be produced via TS1 in which severe steric repulsion between methyl group and cobalt moiety exists. In the case of the reaction of (1R*, 2S*)- isomer **1**, unprotected derivative **1a** gave equal amount of **3** and **4**, because the reaction can proceed via either TS3 or TS4 with the same efficiency. When silyl derivatives of **1** were employed, the silyl groups would take a position to minimize the repulsion with methyl group as shown in TS5 and TS6. Between these two conformations, TS5 is thought to be favored because there is no steric repulsion between phenyl group on alkyne and silyl group. Thus, as bulkier the silyl group became, the higher the selectivity became in favor of the formation of **3**.



Carbonyl ligands are omitted from the figure for the sake of simplicity.

Scheme 1.

Finally, the generality of the regioselectivities of these reactions was examined employing several mono- or di- substituted 1-(1-alkynyl)cyclopropanols. As shown in Table 4, in the cases of the reactions of mono-substituted 1-(1-alkynyl)cyclopropanols, 5-substituted cyclopentenones were obtained with complete selectivity, when (1R*, 2R*)-isomers were used as substrates. On the contrary, 4-substituted cyclopentenones were obtained in good to high regioselectivity by employing *t*-butyldimethylsilyl ethers of (1R*, 2S*)-isomers as substrates.[3] Furthermore, various 5,5-disubstituted cyclopentenones including a spirocyclic derivative were obtained selectively starting from 2,2-disubstituted 1-(1-alkynyl)cyclopropanols.

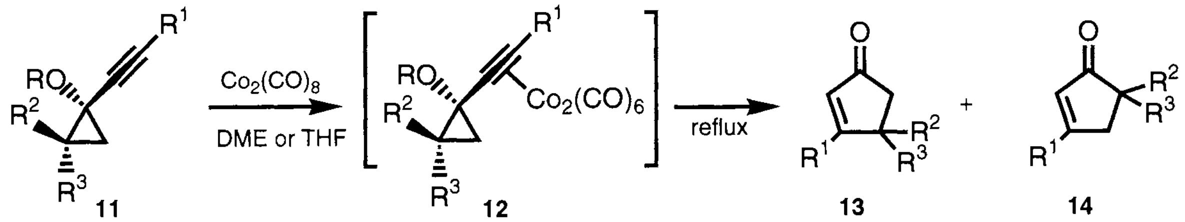


Table 4. The Reaction of Various 2-Substituted 1-(1-Alkynyl)cyclopropanols

R^1	R^2	R^3	R	Solvent	Reaction time/h	Yield/%	**13** : **14**
Ph	Pr^i	H	H	DME	2.5	86	<1 : >99
Ph	H	Pr^i	$SiBu^tMe_2$	THF	7	75	96 : 4
Hex^n	Me	H	H	DME	2.5	83	<1 : >99
Hex^n	H	Me	$SiBu^tMe_2$	THF	14	71	77 : 23
Hex^n	Pr^i	H	H	DME	2	88	<1 : >99
Hex^n	H	Pr^i	$SiBu^tMe_2$	THF	32	85	85 : 15
Ph	Me	Me	H	DME	1	80	<1 : >99
Ph	$-(CH_2)_5-$		H	DME	1	83	<1 : >99
Hex^n	Me	Me	H	DME	1.5	81	<1 : >99

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References

1) N. Iwasawa, Chem. Lett., **1992**, 473.

2) The starting materials were prepared by the Simmons-Smith cyclopropanation of the silyl enol ethers derived from the corresponding ketones. Either diastereomer can be obtained as a major product depending on the reaction conditions of the enolization. See; R. E. Ireland, R. H. Muller, and A. K. Willard, J. Am. Chem. Soc., **98**, 2868 (1976).

3) The isomer ratio was determined by the 500 MHz ^1H NMR spectra.

4) When the reaction of *t*-butyldimethylsilylether of **1a** was tried using 10 mol% amount of $Co_2(CO)_8$ and 20 mol% amount of $P(OPh)_3$, the rearranged product was obtained in low yield (about 10% yield). On the other hand, the reaction of **5a** under the similar catalytic conditions gave the rearranged product **4** in about 85% yield regioselectively. For the catalytic reactions, see; N. Iwasawa and T. Matsuo, Chem. Lett., **1993**, 997.

5) The supposed mechanism of this reaction will be discussed in a full account in due course.

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