Tetrahedron Letters,Vol.30,No.44,pp 6039-6040,1989
Printed in Great Britain

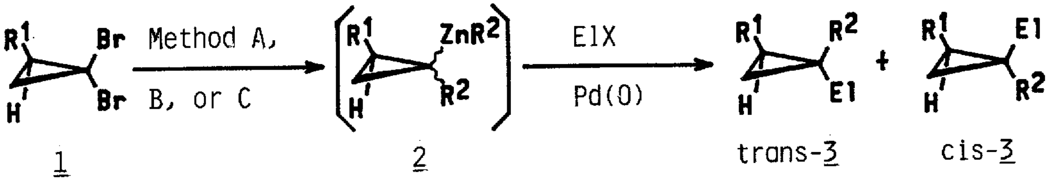
0040-4039/89 $3.00 + .00
Pergamon Press plc

# STEREOSELECTIVE SYNTHESIS OF gem-DISUBSTITUTED CYCLOPROPANES FROM gem-DIBROMOCYCLOPROPANES

Toshiro Harada, Takeshi Katsuhira, Kazuhiro Hattori, and Akira Oku*
Department of Chemistry, Kyoto Institute of Technology,
Matsugasaki, Sakyo-ku, Kyoto 606, Japan

Summary: The title reaction is realized by utilizing an intramolecular alkylation reaction of zincate carbenoids followed by a Pd(0)-catalyzed coupling reaction with acyl, aryl, and alkenyl halides.

gem-Dihalocyclopropanes which can be readily prepared by the addition reaction of dihalocarbenes with olefins are one of the most versatile starting materials for the synthesis of substituted cyclopropanes.[1] Previously, Nozaki and coworkers reported an efficient one-pot dialkylation of gem-dihalocyclopropanes where two halogen atoms are displaced successively with $R^1$ and $R^2$ by the reaction with dialkylcuprate ($(R^1)_2CuLi$) and iodoalkane ($R^2I$).[2] However, the stereoselectivity of this reaction was not always satisfactory and limitation existed in the form of $R^2$ groups to be introduced. We wish to report here a one-pot procedure for the stereoselective synthesis of gem-disubstituted cyclopropanes from gem-dibromocyclopropanes by utilizing a Pd(0)-catalyzed coupling reaction of organozinc intermediates[3] with acyl, aryl, and alkenyl halides.



(1)

Method A; $(R^2)_3ZnLi$ (1.3 equiv), 0 °C. Method B; 1) n-BuLi (1 equiv), -85 °C, 2) $ZnCl_2$ (1 equiv), $R^2Li$ (1 equiv), -85 °C - r.t.. Method C; 1) n-BuLi (1 equiv), freon-113 (1 equiv), -85 °C, 2) $(R^2)_3ZnLi$ (1.3 equiv), -85 °C- r.t..

As shown in eq 1, treatment of cyclopropylzinc 2 generated from dibromocyclopropane 1 under the reaction conditions of Method A, B, or C[4] with acetyl chloride (4 equiv) in the presence of $Pd(PPh_3)_2$ (10 mol%)[5] at a room temperature for 16 - 24 h gave cyclopropyl ketone 3 (El = $CH_3CO$). Under the similar conditions, cyclopropylzinc 2 underwent Pd(0)-catalyzed coupling reaction not only with acyl halides but also with aryl and alkenyl halides to afford the corresponding 1,1-disubstituted cyclopropanes (Table I)[6].

Although stereoselectivities were low when Method A was employed, either trans-3 or cis-3 was selectively obtained in the reaction of Method B or C, respectively. These results demonstrate clearly that Pd(0)-catalyzed coupling reaction of tert-cyclopropylzinc **2** proceeded stereospecifically with retention of the configuration. As shown in entries 4 and 5 sterically hindered ketones can be prepared without appreciable loss of stereoselectivities and efficiencies by the present reactions.[7]

Table I Stereoselective Synthesis of gem-Disubstituted Cyclopropanes

| Entry | Dibromocyclo-propane | R$^2$ | Electro-phile(ElX) | Method | Isolated Yield of 3 | trans:cis[a] |
|---|---|---|---|---|---|---|
| 1 | **1a**; R$^1$ = Ph | n-Bu | AcCl | A | 76% | 1:1.9 |
| 2 | | | | B | 74% | 16:1 |
| 3 | | | | C | 50% | 1:7.0 |
| 4 | **1a** | t-Bu | | B | 50% | 6.7:1 |
| 5 | | | | C | 50% | 1:14 |
| 6 | **1a** | s-Bu | | B | 74% | –[b] |
| 7 | **1a** | n-Bu | EtOCOCl | B | 58% | 60:1 |
| 8 | | | | C | 45% | 1:28 |
| 9 | **1a** | n-Bu | PhBr | B | 60% | 9.1:1 |
| 10 | | | | C | 68% | 1:16 |
| 11 | **1a** | n-Bu | CH$_2$=C(Me)Br | B | 76% | 8.5:1 |
| 12 | | | | C | 45% | 1:9.2 |
| 13 | **1b**; R$^1$ = CH$_2$OBn | n-Bu | AcCl | A | 96% | 2.4:1 |
| 14 | | | | B | 65% | 5.7:1 |
| 15 | | | | C | 52% | 1:21 |
| 16 | **1c**; R$^1$ = n-Hex | n-Bu | AcCl | B | 75% | 11:1 |
| 17 | | | | C | 66% | 1:32 |

[a] Determined by capillary GLC analysis. [b] The ratio was not determined.

**References and Notes**

(1) Review; P. Weyerstahl, "The Chemistry of Functional Groups", Supplement D, S. Patai and Z. Rappoport, Eds., John Wiley & Sons, New York (1983), Chapter 27.

(2) K. Kitatani, T. Hiyama, and H. Nozaki, *J. Am. Chem. Soc.*, **98**, 2362 (1976). *idem.*, *Bull. Chem. Soc. Jpn.*, **50**, 1600 (1977).

(3) (a) T. Sato, K, Naruse, M. Enokiya, and T. Fujisawa, *Chem. Lett.*, 1135 (1981). E. Negishi, V. Bagheri, S. Chatterjee, F.-T. Luo, J. A. Miller, and A. T. Stoll, *Tetrahedron Lett.*, **24**, 5181 (1983). (c) T. Hayashi, M. Konishi, Y. Kobori, M. Kumada, T. Higuchi, and K. Hirotsu, *J. Am. Chem. Soc.*, **106**, 158 (1984) and references cited therein.

(4) See for details, T. Harada, K. Hattori, T. Katsuhira, and A. Oku, preceding report of this issue.

(5) Prepared in situ from Cl$_2$Pd(PPh$_3$)$_2$ and (iso-Bu)$_2$AlH (2 equiv).[3b]

(6) A coupling reaction of R$^2$ group with ElX also proceeded to give R$^2$El as a by-product. Disubstituted cyclopropane **3** was readily isolated by Kugel rohr distillation and/or silica gel column chromatography.

(7) Acknowledgment: This work was supported by Grant-in-Aid for Special Project Research (No. 62215019) from Japan Ministry of Education, Science, and Culture.

(Received in Japan 15 June 1989)