## Communications to the Editor

Chem. Pharm. Bull.
36( 4 )1601—1603(1988)

# ONE-POT UNSYMMETRICAL DOUBLE SUBSTITUTION OF 8,8-DIBROMOBICYCLO[5.1.0]OCTANE AND ITS STEREOCHEMISTRY

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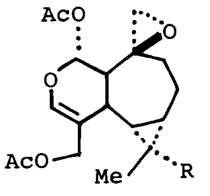
A differential substitution reaction of trans-dibromide (9) in one pot using higher order organocuprate-carbon dioxide or -allyl bromide gave compound 12 or 13 in moderate yield as shown in Table I. Its stereochemistry was deduced by the reaction mechanism and by chemical means.

KEYWORDS —— differential substitution; one-pot; higher order organocuprate; stereochemistry; mechanism; secoaromadendrane sesquiterpene

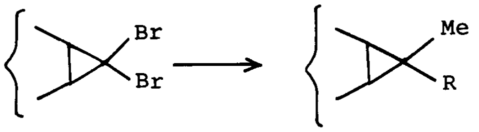
In connection with synthesis studies on sesquiterpenes having 8,8-dimethylbicyclo[5.1.0]octane skeleton such as plagiochiline A (1),[1) we have recently reported an efficient method for preparing dimethylcyclopropanes (B) from dibromides (A) using higher order organocuprate-MeI.[2,3) Subsequently, in relation to synthesis studies on plagiochiline B (2),[4) we planned to develop a method of synthesizing compounds C by replacing each bromine atom of dibromides (A) successively with two different groups. Recently, we reported that treating cis-dibromide (3) with $Me_2Cu(SCN)Li_2$-MeI gave tricyclic ketone (4) via the intermediate (D), together with 5.[2) Therefore, it was expected that the reaction of 6 with higher order organocuprate might produce the corresponding type (C) compound by an acetyl group migration via the metalated intermediate. Treatment of 6 under the same reaction conditions, however, did not produce the expected product, instead it produced the dimethylated products (7) and (8) in 57.6% and 20.1% yields, respectively.[6) Then, a differential substitution reaction of trans-dibromide (9)[2) in one-pot was examined. Compound 9 was treated successively with 8 eq of higher order organocuprate in ether for 1-2 h at -45° C and $CO_2$ gas or allyl bromide in situ to yield the desired products in moderate yields as shown in Table I. The reaction with benzyl bromide, butyl bromide, methyl chloroformate, and methyl cyanoformate in place of allyl bromide afforded no expected products.[7)

Hiyama et al. reported an excellent method for a selective dialkylation of gem-dihalocyclopropane with $Bu_2CuLi-R^2Y$, in which the $R^2$ group was selectively introduced from a more hindered side to afford a cis (or endo) product as shown in Chart 1.[8) They also reported that the reactivity of $Me_2CuLi$ is clearly different from that of $Bu_2CuLi$.[8) In order to determine the stereochemistry of 12 and 13, compound 9 was treated with Hiyama's procedure ($Bu_2CuLi$-MeI) and ours [$Bu_2Cu(SCN)Li$-MeI] to yield the same product 14 in 85.7% and 75.6% yields,



(1) R=Me

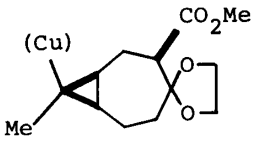
(2) $R=CH_2OAc$



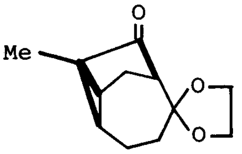
(A)

(B) R=Me

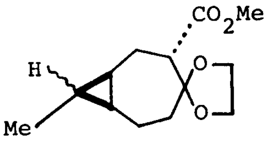
(C) R$\neq$Me



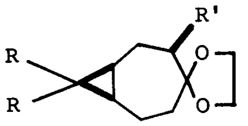
(D)



(4)



(10)



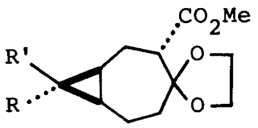
(3) R=Br, $R'=CO_2Me$

(5) R=Me, $R'=CO_2Me$

(6) R=Br, $R'=CH_2OAc$

(7) R=Me, $R'=CH_2OAc$

(8) R=Me, $R'=CH_2OH$



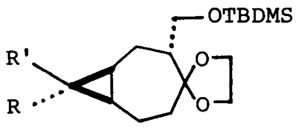
(9) R=R'=Br

(11) R=R'=Me

(12) R=Me, $R'=CO_2Me$

(13) R=Me, $R'=CH_2CH=CH_2$

(14) R=Bu, R'=Me



(15) R=Me, $R'=CH_2CH=CH_2$

(16) R=Me, $R'=(CH_2)_3OH$

(17) R=Me, $R'=(CH_2)_2CHO$

(18) R=Me, R'=Bu

(19) R=Bu, R'=Me

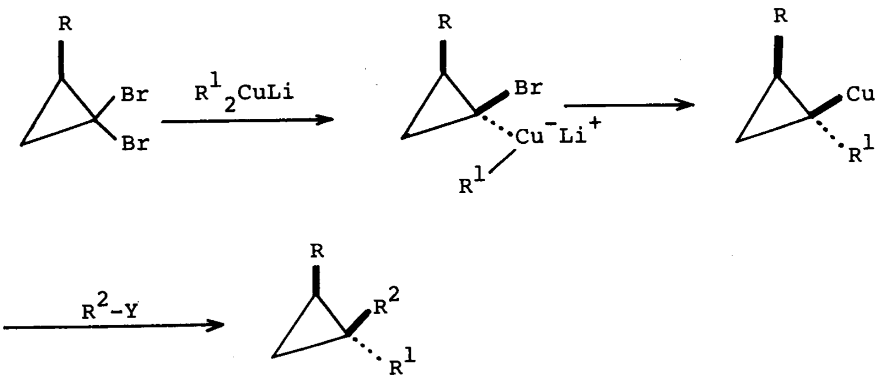


Chart 1

respectively. So compound 14 can be represented by formula 14 in consideration of the mechanism mentioned above, and compounds 12 and 13 can be represented by formulas 12 and 13, respectively. This assumption was supported by the following results: successive treatment of 13 with $LiAlH_4$ and t-$BuMe_2SiCl$ afforded 15 in 81.1% yield. Hydroboration of 15 with disiamylborane, followed by oxidation with $H_2O_2$-$OH^-$ gave alcohol 16, which was converted to aldehyde (17) by oxidation with PDC$^{9)}$ in 41.2% yield from 15. The Wittig reaction of 17 with $(C_6H_5)_3P=CH_2$ and substituent catalytic hydrogenation over $PtO_2$ gave compound 18 in 26.4% yield. On the other hand, reduction of 14 with $LiAlH_4$, followed by silylation with t-$BuMe_2SiCl$ gave compound 19 in 81.1% yield, which proved to be a diastereomer of 18. In conclusion, reaction of 9 with higher order organocuprate-electrophile proceeds via a similar mechanism to Hiyama's reaction to yield compound 12 or 13, which has a suitable stereochemistry for synthesis of 2. However, since the present method has some limitations of generality and selectivity, we are now investigating how to overcome these disadvantages.

Table I. Results of a Differential Substitution of 9

| Reaction conditions | Products (%) | | |
|---|---|---|---|
| | (10) | (11) | (12) |
| $Me_2Cu(SCN)Li_2$-$CO_2$, $CH_2N_2$ | 13 | 29 | 25 |
| | (11) | (13) | |
| $Me_2Cu(SCN)Li_2$-allyl bromide | 43.4 | 47.1 | |
| $Me_2Cu(CN)Li_2$-allyl bromide | 36.2 | 56.5 | |

REFERENCES AND NOTES

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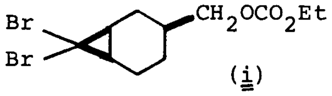
5) Compound 6 was prepared quantitatively from the corresponding alcohol$^{2)}$ by acetylation.

6) In this connection, compound i$^{3)}$ gave no acyl migrating product but a dimethylated product instead.



(i)

7) The reaction of 9 with $Me_2Cu(SCN)Li_2$-crotyl bromide proceeded smoothly but gave a mixture of α- and γ-substituted products together with 11.
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(Received February 5, 1988)