

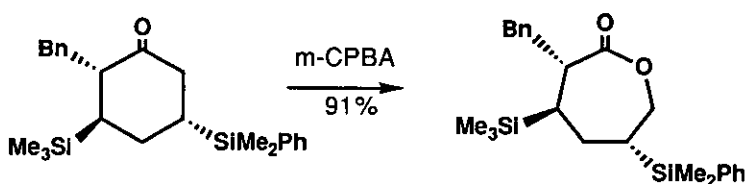
ON THE REGIOSELECTIVITY IN THE SILYL GROUP DIRECTED BAEYER-VILLIGER REACTION

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Abstract - In the Baeyer-Villiger reaction of 3,5-bis-silylated cyclohexanones, preferential migration of the less substituted α -carbon was observed.

The trimethylsilyl group directed Baeyer-Villiger reaction of β -trimethylsilyl ketones was reported by P. F. Hudrlik *et al.*¹ in 1980. In connection with our work, the silyl group directed diastereoselective synthesis, we have been utilizing the above reaction,² and recently, we had a chance to study the Baeyer-Villiger reaction of 2-benzyl-5-dimethylphenylsilyl-3-trimethylsilylcyclohexanone. Surprisingly, high yield product was formed *via* an exclusive migration of the less substituted carbon (Scheme 1).



Scheme 1.

As the directing effect of the trimethylsilyl (TMS) and dimethylphenylsilyl (DMPS) groups is expected to be almost the same, it seems reasonable that the migrating carbon center in the present reaction is more substituted one since in the Baeyer-Villiger reaction, the general trend of the migratory aptitude of groups follows the order: Tertiary>secondary—phenyl>primary alkyl. The above unexpected results prompted us to study the trend of regioselectivity in such a system.

The Baeyer-Villiger reaction of some trimethylsilyl group substituted cyclohexanones³ was carried out, and the results are shown in Table 1.⁶ The following features are apparent from this study: (1) The strong directing effect of the silyl group¹ is confirmed (Entries 1, 2 and 8). (2) There is no remarkable difference of directing efficiency between TMS and DMPS (Entry 3). (3) The directing effect of the silyl group is so strong that α -methylation of the carbonyl group does not effect the regioselectivity (Entry 4). (4) When the substituent R³ becomes large, rearrangement of the less substituted carbon becomes predominant (Entries 5 and 6). (5) In the case of trisubstituted derivatives, there is slight difference between TMS and DMPS (Entries 5 and 7). (6) When DMPS in Entry 5 is replaced with the tert-butyl group, TMS directed product is obtained exclusively (Entry 8).

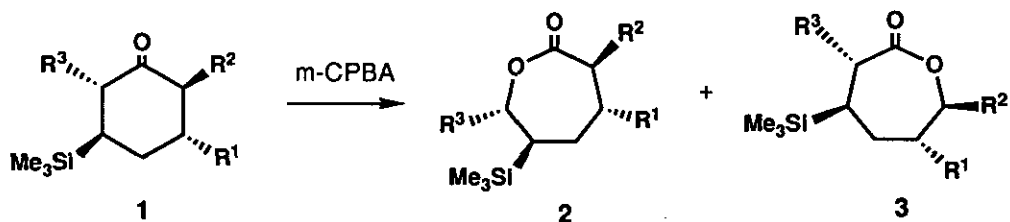


Table 1. The Baeyer-Villiger Reaction of 1

Entry	1	R ¹	R ²	R ³	Yield(2+3, %)	Ratio ^a 2 : 3
1	1a	Me	H	H	88	100 : 0
2	1b	Ph	H	H	95	100 : 0
3	1c	Me ₂ PhSi	H	H	94	50 : 50 ^b
4	1d	Me ₂ PhSi	H	Me	70	50 : 50 ^b
5	1e	Me ₂ PhSi	H	Pr	76	21 : 79
6	1f	Me ₂ PhSi	H	Bn	91	0 : 100
7	1g	Me ₂ PhSi	Pr	H	78	88 : 12
8	1h	t-Bu	H	Pr	60 ^c	100 : 0

a) Ratio of isolated products. b) Determined by ¹H nmr. c) Ketone (1) (40%) was recovered.

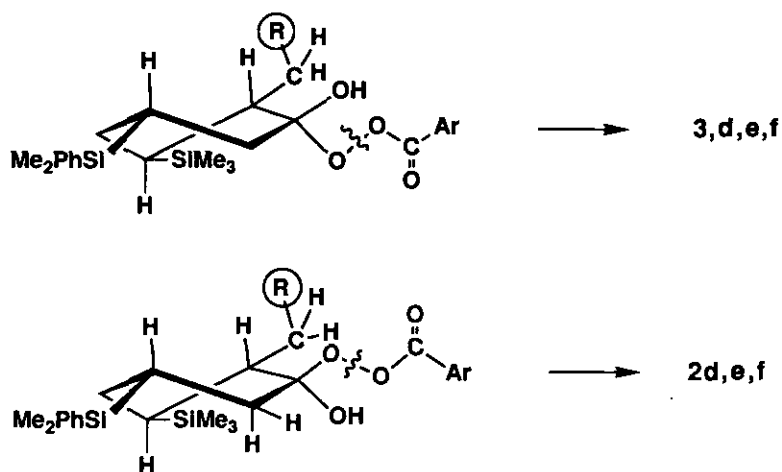


Figure 1.

In the usual Baeyer-Villiger reaction, though the carbonium ion rearrangement does not occur during migration, in general, groups able to tolerate positive charge migrate most readily. In the system examined, the efficiency of the β -silyl group participation would determine the regioselectivity, i.e., antiperiplanar arrangement of the contiguous 5 bonds from Si-C to cleaving O-O bond of the "twist boat" intermediates (Figure 1), which should be the most stable form for such cyclohexanes bearing bulky 1,3-*trans* substituents, would be the most important factor, and the silyl group syn to the perbenzoate moiety satisfies the above array. Consequently, the face selectivity of peracid addition to the carbonyl group would determine the regioselectivity.

According to the above assumption, our result indicates preferential introduction of perbenzoate moiety occurred from the same side of α -substituents and the syn silyl group participates effectively to direct the migration of the less substituted carbon center. Though the mechanism of the facial selectivity in *m*-CPBA addition controlled by α -substituent is still obscure, it is apparent that the R group in Figure 1 plays an important role since R=H did not cause any selectivity.

In conclusion, in this paper we have provided the evidence that in the silyl group directed Baeyer-Villiger reaction, suitable conformational arrangement of the silyl group for optimal participation is an important factor for the regioselectivity.

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3. Starting enones (**1**) in Entries 3 to 7 were prepared by the 1,4-addition of $\text{Me}_2\text{PhSiCuLiX}^4$ to corresponding 5-trimethylsilyl-2-cyclohexenones prepared by the reported method.⁵
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6. The ^1H nmr spectral data of lactones (**2**) and (**3**) in CDCl_3 are shown below. **2a**: δ 0.0 (9H, s), 0.95 (3H, d, $J=6$ Hz), 0.8-2.4 (4H, m), 2.4-2.8 (2H, m), 4.0-4.3 (2H, m). **2b**: δ 0.13 (9H, s), 0.9-1.6 (1H, m), 1.7-2.4 (2H, m), 2.5-3.4 (3H, m), 4.1-4.7 (2H, m), 7.07 (5H, s). A mixture of **2c** and **3c**: δ -0.05 (4.5H, s) and -0.01 (4.5H, s), 0.31 (3H, s) and 0.36 (3H, s), 0.6-2.0 (4H, m), 2.4-2.65 (2H, m), 4.20 (2H, broad d, $J=5$ Hz), 7.25 (broad s, 5H). A mixture of **2d** and **3d**: δ -0.06 (4.5H, s) and -0.03 (4.5H, s), 0.32 (6H, s), 0.95 (1.5H, broad s) and 1.21 (1.5H, d, $J=7$ Hz), 0.6-2.0 (4H, m), 2.07-2.35 (1H, m) and 2.55-3.10 (0.5H, m), 3.75-4.05 (0.5H, m) and 4.28 (1H, broad d, $J=5$ Hz), 7.33 (5H, broad s). **2e**: δ 0.02 (9H, s), 0.32 (6H, s), 1.55-2.0 (11H, m), 2.0-2.6 (2H, m), 3.9-4.6 (1H, m), 7.28 (5H, broad s). **3e**: δ 0.05 (9H, s), 0.35 (6H, s), 0.6-2.1 (11H, m), 2.6-3.1 (1H, m), 4.15-4.5 (2H, m), 7.33 (5H, broad s). **3f**: δ 0.05 (9H, s), 0.34 (6H, s), 0.5-2.0 (4H, m), 2.35-3.4 (3H, m), 4.13 (1H, broad d, $J=5.5$ Hz), 7.08 (5H, s), 7.28 (5H, broad s). **2g**: δ -0.07 (9H, s), 0.38 (6H, s), 0.5-2.0 (11H, m), 2.3-3.2 (1H, m), 4.0-4.5 (2H, m), 7.33 (5H, broad s). **3g**: δ -0.15 (9H, s), 0.33 (6H, s), 0.5-2.0 (11H, m), 2.16-2.6 (2H, m), 3.8-4.5 (1H, m), 7.25 (5H, broad s). **2h**: δ 0.13 (9H, s), 0.93 (9H, s), 0.6-2.0 (11H, m), 2.5-2.85 (2H, m), 4.0-4.6 (1H, m).

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