SYNTHESIS OF OXASTEROIDAL SKELETONS BY (4+2) TYPE CYCLOADDITION OF COUMARIN AND 6-METHYL-2-PYRONE WITH SILOXYDIENES MEDIATED BY t-BUTYLDIMETHYLSILYL TRIFLATE

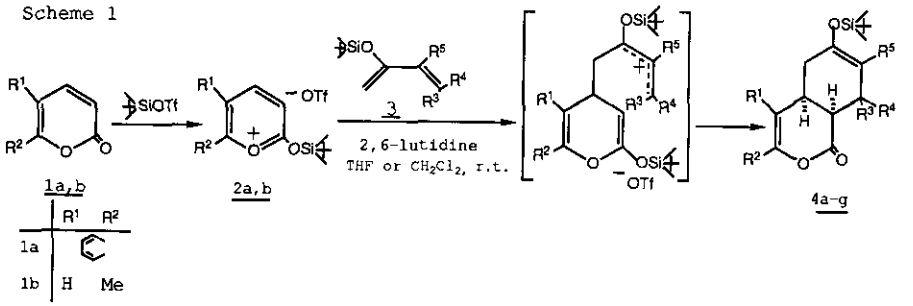
Yong-gyun Lee, Yukinori Utsumi, Katsuo Ohkata, and Kin-ya Akiba*

Department of Chemistry, Faculty of Science, Hiroshima University
Higashisenda-machi, Naka-ku, Hiroshima 730, Japan

Abstract — A new simple methodology is described for the preparation of oxasteroidal skeletons containing a lactone ring via cycloaddition of 2-t-butyldimethylsiloxypyrylium triflate (2a,b) with siloxydienes (3).

The preparation of heterocyclic steroids is one of the current interests in synthetic organic chemistry for several reasons. Particularly, their preparation is a stimulating challenge to the organic chemists and their derivatives play an important role for the study of naturally occurring substances.[1] Recently, we have described an effective approach to xanthone derivatives based upon (4+2) type cycloaddition of 4-t-butyldimethylsiloxy-1-benzopyrylium triflate with α,β-unsaturated ketones.[2] In relation to this subject, we here describe (4+2) type cycloaddition of coumarin and 6-methyl-2-pyrone with siloxydienes (3) mediated by t-butyldimethylsilyl triflate, whose reaction proceeds through 2-t-butyldimethylsiloxypyrylium triflate (2a,b) (Scheme 1). This simple method is quite effective for the preparation of oxasteroidal skeletons containing a lactone ring, which is very difficult to prepare until now.

Scheme 1



Reaction of 2-t-butyldimethylsiloxy-1-benzopyrylium salt (2a), which was prepared from coumarin and t-butyldimethylsilyl triflate (160 °C, 15 h, without solvent), with siloxydienes (3) in the presence of 1 equiv. of 2,6-lutidine in CH_2Cl_2 at room temperature for 30 min proceeded to give the cycloadducts 4a-4g in moderate yield. Almost the same results were obtained in the reaction of coumarin (1a) with siloxydienes (3) in the presence of 1 equiv. of t-butyldimethylsilyl triflate and 1 equiv. of 2,6-lutidine in THF at room temperature for 3-5 hours. In contrast to the similar reaction of xanthone, this reaction did not proceed with α,β-unsaturated ketones but only with siloxydienes.[2] The results by this process are summarized in Table 1. It is assumed that the cycloaddition between coumarin and siloxydienes proceeded via the in situ formation of 2-t-butyldimethylsiloxy-1-benzopyrylium salt (2a), which was in equilibrium with coumarin.

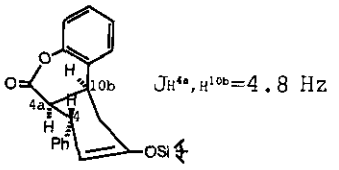
Table 1. (4+2) Type Cycloaddition of 2-Siloxypyrylium Salts (2a, b) to Siloxydienes (3)

Entry	R^1	R^2	R^3	R^4	R^5	product	yield (%)
1			H	Ph	H	4a	48
2		〃	Me	Me	H	4b	47
3		〃	H	$-(CH_2)_3-$		4c	52
4		〃	H	$-(CH_2)_4-$		4d	68
5	H	Me	H	$-(CH_2)_3-$		4e	35
6	H	Me	H	$-(CH_2)_4-$		4f	60
7	H	Me	H	Ph	H	4g	30

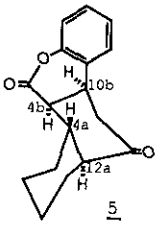
Under the latter reaction conditions, 6-methyl-2-pyrone (1b) reacted with siloxydienes (3) to give cycloadducts in fair yields except 4f. These lower yields were probably due to the decomposition of the cycloadducts by atmospheric moisture or on silica gel during separation.

The structure of the cycloadducts was confirmed by spectral and elemental analyses along with chemical behaviors. The relative stereochemistry of the cycloadducts was assigned by ^1H nmr. In the case of 4a, the stereochemistry between H_{4a} and H_{10b} was assigned cis geometry due to the small coupling constant ($J_{H4a-H10b}$=4.8 Hz)(Figure. 1).

As all the other adducts also showed a small coupling constant (4-5 Hz) between the two methine protons, the ring fusion is considered to be the same cis geometry as that of 4a.



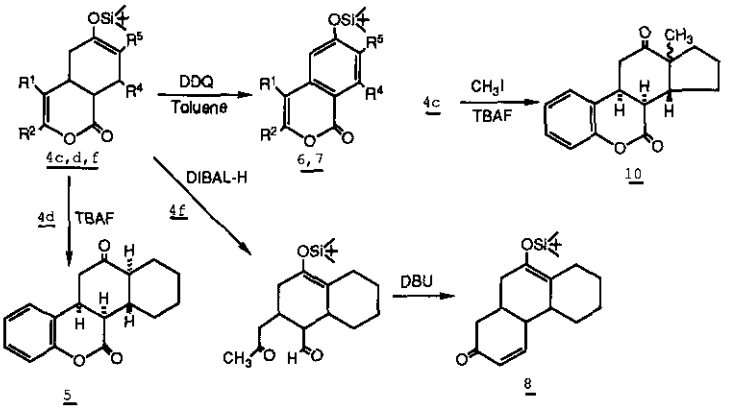
4a Figure 1



5 Figure 2

Desilylation of 4d with TBAF gave a 32% yield of ketone (5, mp; 138-140 °C). According to ^{1}H nmr spectral analysis of 5, the stereochemistry between the C and D rings was assigned to be trans geometry ($J_{H4a-H12a}$=11.5 Hz) as shown in Figure 2. Among the cycloadducts, 4c-d can be regarded as precursor for oxasteroidal compounds.[3] For example, reaction of 4c with MeI in the presence of TBAF afforded the corresponding ketone (10) in 30% yield. Dehydrogenation of 4d,4f with DDQ afforded 6 (80%, mp:158-160 C) and 7 (40%, mp:141-142 C), respectively. Compound 6 may be a useful synthon for other aglycon derivatives and 7 may be an effective precursor for Xanthomegnine.[4,5] Reduction of 4f with DIBAL-H followed by cyclization with DBU gave perhydrophenanthrene derivative (8) in 25% yield (Scheme 2).

Scheme 2



ACKNOWLEDGEMENT

This research was partially supported by a Grant-in Aid for Scientific Research on Priority Areas, "Advanced Molecular Conversion (No. 63607522)" and No. 01540427 administered by the Ministry of Education, Science, and Culture of the Japanese Government.

REFERENCES AND NOTES

1) H. O. Huisman, Angew. Chem. Int. Ed. Eng, 1971, 10 , 450.

2) a) Y. G. Lee, H. Iwasaki, Y. Yamamoto, K. Ohkata, and K-y. Akiba, Heterocycles, 1989, 29, 35. b) H. Iwasaki, T. Kume, Y. Yamamoto, and K-y. Akiba, Tetrahedron Lett., 1987, 28, 6355.

3) E. Mincione, P. Bovicelli, and M. L. Forcellese, Heterocycles, 1988, 27, 889.

4) F. M. Hauser and D. W. Combs, J. Org. Chem., 1980, 45, 4071.

5) T, J. Simpson, J. Chem. Soc., Perkin Trans. I, 1977, 592.

6) 4a: semi-oil; ^{1}H nmr (δ, $CDCl_3$) 0.12 (s, 3H), 0.14 (s, 3H), 0.90 (s, 9H), 2.40-2.58 (m, 2H), 3.20-3.45 (m, 1H), 3.50 (dd, J=4.8, 5.8Hz, 1H), 4.01 (dd, J=3.1, 5.8 Hz, 1H), 5.15 (d, J=3.1 Hz, 1H), 7.02-7.30 (m, 9H); ms m/z 406 (M^+). 4b: oil; ^{1}H nmr (δ, $CDCl_3$) 0.13 (s, 3H), 0.15 (s, 3H), 0.90 (s, 9H), 1.08 (s, 3H), 1.18 (s, 3H), 2.23-2.35 (m, 2H), 2.65 (d, J=4.8 Hz, 1H), 3.40-3.58 (m, 1H), 4.60 (s, 1H), 6.90-7.10 (m, 4H); ir (neat) 2950, 1762, 1480, 1050 cm^{-1}; ms m/z 358 (M^+). 4d: colorless crystals, mp; 107-109 °C; ^{1}H nmr(δ, $CDCl_3$) 0.15 (s, 3H), 0.17 (s, 3H), 0.97(s, 9H),1.10-2.60 (m, 10H), 2.78-2.82 (m, 2H), 3.10-3.25 (m, 1H), 7.00-7.40 (m, 4H); ir (KBr)2960, 1760, 1480, 1070 cm^{-1}; ms m/z 384 (M^+). Anal. Calcd for $C_{23}H_{32}O_3Si$: C, 71.80; H, 8.38. Found: C, 71.58; H, 8.65. 4f: oil; ^{1}H nmr (δ, $CDCl_3$) 0.13 (s, 6H), 0.95 (s, 9H), 1.84 (s, 3H), 2.02-2.90 (m, 13H), 5.03 (d, J=4.7Hz, 1H); ir (neat, cm^{-1}) 2960, 1770, 1180, 1070; ms m/z 348(M^+).

7) 5: colorless crystals, mp; 138-140 °C; ^{1}H nmr (δ, $CDCl_3$) 1.02-2.30 (m, 9H), 2.08 (ddd, J=11.5, 8.5, 2.9 Hz, 1H), 2.78 (dd, J=15.0, 4.8 Hz, 1H), 3.05 (dd, J=11.0, 4.7 Hz, 1H), 3.12 (dd, J=15.0, 3.5 Hz, 1H), 3.89-4.92 (m, 1H), 7.00-7.40 (m, 4H); ms m/z 270(M^+). Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.50; H, 6.71. Found: C, 75.32; H, 6.91. 6: colorless crystals, mp; 158-160 °C ; ^{1}H nmr (δ, $CDCl_3$) 0.40 (s, 6H), 1.20 (s, 9H), 7.23-7.60 (m, 5H), 7.80 (dd, J=1.8, 7.4 Hz, 1H), 8.02 (d, J=8.0 Hz, 1H), 8.31 (dd, J=1.8, 8.0 Hz, 1H), 9.70 (d, J=7.4 Hz, 1H); ms m/z 377 (M^+). Anal. Calcd for $C_{23}H_{24}O_3Si$: C, 73.30; H, 6.42. Found: C, 73.06; H, 6.48. 8: oil; ^{1}H nmr (δ, $CDCl_3$) 0.18 (s, 6H), 0.95 (s, 9H), 1.10-1.29 (m, 15H), 6.00 (dd, J=10.1, 3.8 Hz, 1H), 6.95 (d, J=10.0 Hz, 1H); ms m/z 332 (M^+). 10: oil; ^{1}H nmr (δ, $CDCl_3$) 1.20-2.03 (m, 7H), 1.75 (s, 3H), 2.50 (dd, J=5.0, 8.7 Hz, 1H), 2.85-3.23 (m, 2H), 3.58 (ddd, J=3.2, 5.0, 6.5 Hz, 1H), 7.02-7.45 (m, 4H); ms m/z 270 (M^+).

Received, 19th October, 1989