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(4+2)TYPE CYCLOADDITION OF CHROMONES WITH α,β-UNSATURATED KETONES MEDIATED BY t-BUTYLDIMETHYLSILYL TRIFLATE: ONE-POT PREPARATION OF XANTHONE DERIVATIVES

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Abstract —— 4-t-Butyldimethylsiloxy-1-benzopyrylium salt (2a,b) reacted with various α,β-unsaturated ketones (3a-g) in the presence of t-BuMe$_2$SiOTf and 2,6-lutidine to afford the corresponding (4+2)type cycloadducts (4a-i) in high yield. The ring fusion of the adduct was determined to be cis geometry on the basis of the ^{1}H nmr spectral features.

In a preceding communication,[1] we reported introduction of an oxoalkyl group into chromone (1a) using enol silyl ether or active methylene compounds via 4-siloxybenzopyrylium salt. Although chromones contain α,β-unsaturated ketone part, their use as 2π component in (4+2)type cycloaddition is rare. Very recently, Wallace et al. showed the cycloaddition of activated benzopyran-4-ones (chromones) to 2,3-dimethyl-1,3-butadiene by using catalytic amount of titanium(IV) chloride and to Danishefsky's electron rich dienes in the absence of any Lewis acid catalysts.[2] We now describe that (4+2)type cycloaddition of chromones (1a,b) with α,β-unsaturated ketones could be mediated with t-butyldimethylsilyl triflate to afford the corresponding adducts in high yield in one pot process. 4-t-Butyldimethylsiloxy-1-benzopyrylium triflate (2a,b) was prepared by heating the corresponding chromone and t-butyldimethylsilyl triflate (2 eq) as reported already.[1] Reaction of 2 with α,β-unsaturated ketones (3a-g) in the presence of 2 equiv. of 2,6-lutidine in CH$_2$Cl$_2$ solution proceeded smoothly to give the cycloadducts (4a-i) in high yield.[3,4] The results are summarized in scheme 1 and Table 1.

Scheme 1

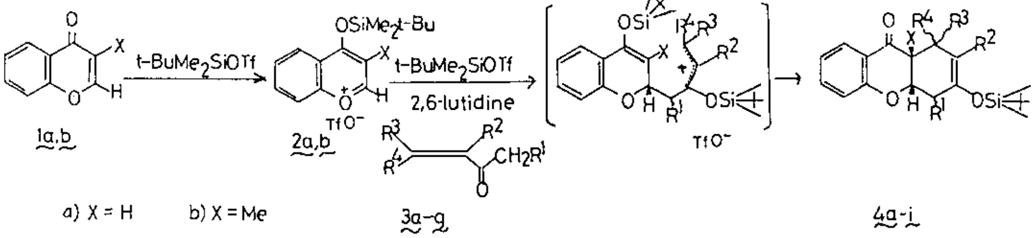
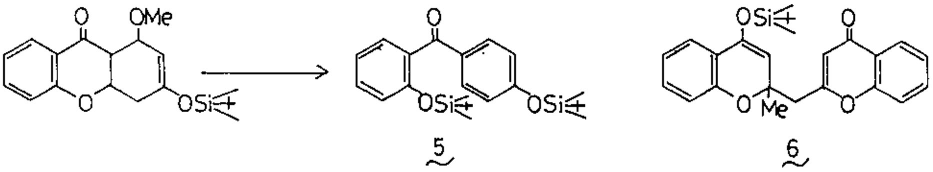


Table 1. (4+2)Type Cycloaddition of Chromones (1a,b) to Various α,β-Unsaturated Ketones (3a-g)

entry	X	R^1	R^2	R^3	R^4	product	yield (%)
1	H	H	H	H	H	4a	94
2	H	H	H	Me	Me	4b	92
3	H	H	H	Ph	H	4c	96
4	H	H	$-(CH_2)_3-$		H	4d	92
5	H	H	$-(CH_2)_4-$		H	4e	92
6	H	Me	$-(CH_2)_4-$		H	4f	85
7	H	Et	$-(CH_2)_4-$		H	4g	77
8	Me	H	H	Ph	H	4h	87
9	Me	Me	$-(CH_2)_4-$		H	4i	97

Under the same reaction conditions, chromone (1a) reacted with 4-methoxy-3-buten-2-one to give 2,4'-disiloxybenzophenone (5) in fair yield (24%).[5] Although the corresponding pyrylium salt of 2-methylchromone was prepared, the salt did not undergo such a (4+2)type cycloaddition with any α,β-unsaturated ketones in the presence of 1 equiv. of 2,6-lutidine but dimerized to give 6 almost quantitatively (scheme 2).[5]

Scheme 2



A typical experimental procedure was as follows: a mixture of chromone (1a, 450.8 mg, 3.09 mmol) and t-butyldimethylsilyl triflate (1.42 ml, 2 eq) was heated to 80 °C with stirring for 1 h. After the mixture was cooled to room temperature 2,6-lutidine (0.67 ml, 2 eq) in 5 ml of CH_2Cl_2 was added, followed by the addition of benzalacetone (3c, 550 mg, 1.7 eq) in 2 ml of CH_2Cl_2 the mixture was refluxed for 3 h under nitrogen atmosphere. After cooling, the mixture was poured into saturated aqueous sodium bicarbonate (50 ml). The product was extracted into CH_2Cl_2 (30 ml x 3) and the solvent was evaporated in vacuo after being dried over anhydrous magnesium sulfate. The crude product was purified by flash column chromatography (SiO_2) with hexane and ethyl acetate (10 : 1) as eluent to afford 4c (866 mg, 96%) as a yellow oil.

In the presence of 1 equiv. of t-butyldimethylsilyl triflate and 2,6-lutidine, reaction of 1a with enol t-butyldimethylsilyl ether of 3c also afforded 4c in 95% yield.

Structural assignment is based on ^1H nmr spectral data and chemical behaviors. In ^1H nmr spectrum of 4c, the vinyl proton appears at δ 5.13 as a doublet (J = 5.0 Hz) and the signals due to H-4a and H-9a are seen at δ 4.80 (dd, J = 3.1 and 6.4 Hz) and δ 2.99 (dd, J = 3.1 and 8.7 Hz), respectively. The small coupling constant (J = 3.1 Hz) between H-4a and H-9a indicates that the relative stereochemistry of the two methine protons is equatorial-axial. The H-9a hydrogen is consistent with 1,2-diaxial relationship with the adjacent methine hydrogen H-1 as judged from the larger coupling constant (J = 8.7 Hz). On the basis of these spectral features, the phenyl group is oriented at the equatorial position in half-chair conformer of cyclohexenyl ring in 4c as indicated in [4c].

Scheme 3

[4c]

[4f.g.i]

As all the other adducts also show a small coupling constant (J = 2-5 Hz) between H-4a and H-9a, the ring fusion at C-4a and C-9a is considered to be the same cis geometry as that of 4c. However, the relative stereochemistry of alkyl group at

C-4 in **4f**,**g** and **4i** remains obscure because of the medium size of vicinal coupling constant (J = 5-6 Hz).

ACKNOWLEDGEMENT

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2. P. J. Cremins, S. T. Saengchantara, and T. W. Wallace, *Tetrahedron*, 1987, **43**, 3075.
3. Acetylcyclopentene (**3d**) and acetylcyclohexene (**3e**) were prepared according to the literature: L. Rand and R. J. Dolinski, *J. Org. Chem.*, 1966, **31**, 3063, 4061; A. L. Henne and J. M. Tedder, *J. Chem. Soc.*, 1953, 3628.
4. **4a**: oil; ^{1}H nmr (δ, $CDCl_3$) 0.20 (s, 6H), 0.96 (s, 9H), 2.46 (m, 2H), 2.57 (m, 1H), 2.63 (dd, J = 6.9, 2.4 Hz, 1H), 2.76 (dd, J = 6.9, 2.6 Hz, 1H), 4.82 (ddd, J = 2.6, 2.4, 1.7 Hz, 1H), 4.95 (ddd, J = 6.4, 2.9, 1.1 Hz, 1H), 6.9-7.93 (m, 4H). **4c**: oil; ^{1}H nmr (δ, $CDCl_3$) 0.16 (s, 6H), 0.98 (s, 9H), 2.66 (dd, J = 6.4, 1.0 Hz, 1H), 2.68 (dd, J = 1.0, 0.1 Hz, 1H), 2.99 (dd, J = 8.7, 3.1 Hz, 1H), 4.00 (dd, J = 8.7, 5.0 Hz, 1H), 4.80 (dd, J = 6.4, 3.1 Hz, 1H), 5.13 (dd, J = 0.1, 5.0 Hz, 1H), 6.53-7.52 (m, 9H). **4e**: colorless crystal, mp 110-113 °C; ^{1}H nmr (δ, $CDCl_3$) 0.18 (s, 6H), 0.98 (s, 9H) 1.05-1.79 (m, 8H), 2.54 (bs, 2H), 2.75 (dd, J = 8.2, 2.9 Hz, 1H), 2.90 (dd, J = 11.9, 1.3 Hz, 1H), 4.72 (ddd, J = 2.9, 2.2, 1.3 Hz, 1H), 6.90-7.96 (m, 4H); ir 2950, 1720, 1600, 1450 cm^{-1}; ms *m/z* 384 (M$^+$). Anal. Calcd for $C_{23}H_{32}O_3Si$: C, 71.83; H, 8.39. Found: C, 71.59; H, 8.01.
5. **5**: oil; ^{1}H nmr (δ, $CDCl_3$) 0.00 (s, 6H), 0.15 (s, 6H), 0.63 (s, 9H), 0.93 (s, 9H), 6.80 (d, J = 9.0 Hz, 2H), 6.80-7.10 (m, 2H), 7.24-7.40 (m, 1H), 7.80 (d, J = 9.0 Hz, 2H), 7.80-7.92 (m, 1H); ms *m/z* 442 (m$^+$). **6**: oil. ^{1}H nmr (δ, $CDCl_3$) 0.04 (s, 6H), 0.98 (s, 9H), 1.56 (s, 3H), 2.95 (s, 2H), 4.83 (s, 1H), 6.22 (s, 1H), 6.75-7.71 (m, 7H), 8.17 (dd, J = 6.4, 2.0 Hz, 1H); ir 2900, 1640, 1600, 1570, 1460, 1380 cm^{-1}; ms *m/z* 434 (M$^+$).

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