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Pyrylium Salt Promoted Substitution Reactions of Acetals with Various Silylated Nucleophiles

Masaki Kamata,*[a] Satoshi Nagai,[a] Mitsuaki Kato,[a] and Eietsu Hasegawa*[b]

[a]Department of Chemistry, Faculty of Education and [b]Department of Chemistry, Faculty of Science,
Niigata University, Ikarashi, Niigata 950-21, Japan

Abstract: Catalytic amounts of triarylpyrylium salts photochemically and thermally promoted the substitution reactions of dimethyl acetals with silylated nucleophiles.

Extensive efforts have been devoted to the carbon-carbon bond formation of acetals with silylated nucleophiles promoted by various reagents.[1] Although various Lewis acids have been already employed for such reactions, the development of new types of effective reagents is still synthetically attractive.[2] Recently Masaki *et al.* reported that tetracyanoethylene (TCNE) thermally promoted the Mukaiyama reaction of acetals with silylated nucleophiles through a single electron transfer (SET) mechanism.[3] We have recently reported that a catalytic amount of tris(*p*-bromophenyl)aminium hexachloroantimonate was effective for the Mukaiyama reaction of acetals with silylated nucleophiles through the SET mechanism.[4] The photoinduced electron transfer (PET) process is among the most useful methods to generate ion radical species which undergo a variety of reactions;[5] however, we noticed that the PET process has not been previously applied to the Mukaiyama reaction. In connection with our studies regarding the reactions of thioacetal cation radicals initiated by the PET process using pyrylium salts,[6] we became interested in determining the applicability of this PET method to the reactions of acetals with various silylated nucleophiles. Herein we report that catalytic amounts of 2,4,6-triarylpyrylium perchlorates (TArPClO$_4$) photochemically and thermally promoted the substitution reactions of acetals with various silyl compounds (eq. 1).

$$R^1R^2C(OMe)_2 \ + \ R_3Si\text{-}Nu \ \xrightarrow[\text{MeCN}]{h\nu\ (\text{or}\ \Delta)\ /\ \text{TArPClO}_4\ /\ N_2} \ R^1R^2(MeO)C\text{-}Nu' \qquad (\text{eq. } 1)$$

As shown in Figure 1 and Table 1, the pyrylium salt sensitized photoreactions of substrates **1** with silyl compounds **2**-**4** produced the substituted compounds **5**-**7**.[7] The reaction was first carried out using acetals **1** and allyltrimethylsilane **2** with 2,4,6-triphenylpyrylium perchlorate (TPPClO$_4$).[8] When an acetonitrile solution of acetal **1a**, **2** and a catalytic amount of TPPClO$_4$ (3 mol%) was irradiated (λ>360 nm), the reaction smoothly proceeded and 90% of allylsubstituted product **5a** was isolated (entry 1 in Table 1). Similarly, allylated products **5b**-**g** were isolated in moderate to excellent yields for the reactions of acetals **1b**-**g** (entries 2-7). Next, we conducted the reactions of acetals **1** with 1-(trimethylsilyloxy)cyclohexene **3** to find that β-methoxyketones **6a**-**g** were isolated in 62-99% yields as diastereomeric mixtures (entries 8-14).[9] Interestingly, the photoreactions of acetals **1** with a poor electron donor, triethylsilane **4**, also afforded reduced products **7a**-**g** in good yields except for **7e** (entries 15-21). Detailed mechanistic studies further provided the following results. Both the presence of TPPClO$_4$ and irradiation were essential for the promotion of these reactions. Addition of 1,2,4,5-tetramethoxybenzene (TMB, 1 equiv. to **1a**, $E_{1/2}^{ox}$ = 0.74 V vs. SCE), which is known as an effective quencher for the SET processes,[10] suppressed the reactions of **1a** with **2**-**4**. The fluorescence of TPPClO$_4$ (E^*_{red} ≈ 2.5 V) was efficiently quenched by **2** and **3**.[11] Another interesting

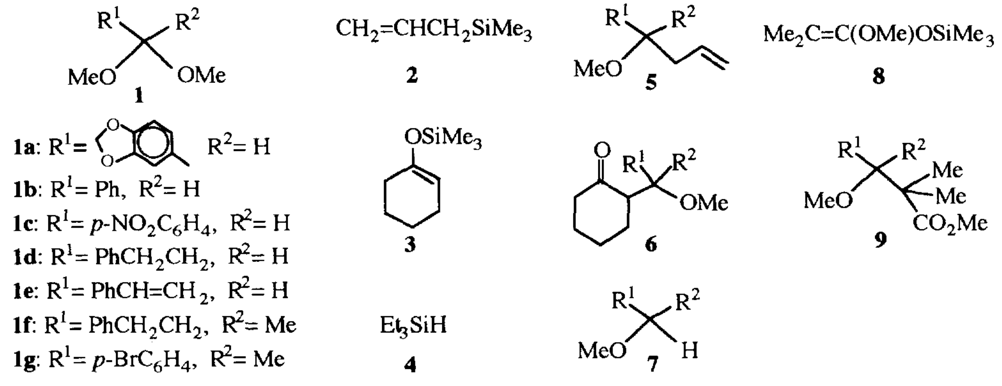

Fig. 1

observation was that 2,4,6-triphenylpyrylium tetrafluoroborate ($TPPBF_4$) was less effective than perchlorate salt ($TPPClO_4$) for the reactions of **1a** with **2**-**4**.[12] It was also found that typical PET sensitizers such as 9,10-dicyanoanthracene and anthraquinone were not effective at all for the reactions of **1a** with **2**-**4**. These results indicate that the reactions proceed through a PET mechanism and the perchlorate anion plays a key role in promoting the reactions.

Unexpectedly, the above substitution reactions were found to proceed upon heating at reflux in CH_3CN. Especially, 2,4,6-tris(p-chlorophenyl)pyrylium perchlorate ($TCPPClO_4$) was found to be a more effective promoter. The results are summarized in Table 1 (entries 22-42). In addition, the substitution reactions of **1** with dimethylketene methyltrimethylsilylacetal **8** in the presence of $TCPPClO_4$ smoothly proceeded at room temperature to afford esters **9a-g** in excellent yields (within 60 minutes, 94-99%). In contrast to the photoreactions, addition of TMB did not suppress the thermal reactions.

Based on the above results and the literature observations,[14] a plausible mechanism is proposed in Scheme 1. In the photoreactions, initial SET occurs between the singlet excited $TPPClO_4$ and silyl compounds rather than acetals since most of the acetals used would not be easily oxidized except for **1a** and **1e**.[15] If the silyl compounds are first oxidized, fragmentation of their cation radicals give carbon radicals and silyl cations.[14] The generated silyl cations couple with perchlorate anions and attack acetal oxygens followed by the reaction with silyl compounds, which are well known thermal processes.[1] On the other hand, in the thermal reactions, a Lewis acid mechanism shown in Scheme 2[16] could be preferable to the SET mechanism since the SET between $TCPPClO_4$ and the silyl compounds is highly endothermic.

As described above, we have first discovered that acetals reacted with various silylated nucleophiles under the pyrylium salts catalyzed conditions. PET-induced fragmentations of silyl compounds are not rare;[14] however, application of the PET methodology to the substitution reactions described here is unprecedented. Therefore, combination of the photoexcited pyrylium perchlorate and silyl compounds must provide a new route to generate silyl perchlorate[17] which is expected to promote various cationic reactions. Moreover, we have first found that the pyrylium perchlorate operated as a non-photochemical catalyst. Thus, triarylpyrylium salts should be recognized as synthetically convenient agents since they can be easily prepared, handled, and used under mild conditions. We are conducting further studies to elucidate the more detailed mechanism for this catalytic reaction and to apply this methodology to other synthetically useful reactions.

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Table 1. Substitution Reactions of Acetals with Silyl Compounds Promoted by Triarylpyrylium Perchlorate.[a]

Photoreactions promoted by $TPPClO_4$[b]					Thermal reactions promoted by $TCPPClO_4$[c]				
entry	TMSNu	acetal	time/min	product[d] (yield/%)	entry	TMSNu	acetal	time/min	product[d] (yield/%)
1	**2**	**1a**	5	**5a** (90)	22	**2**	**1a**	120	**5a** (78)
2	**2**	**1b**	10	**5b** (80)	23	**2**	**1b**	300	**5b** (74)
3	**2**	**1c**	10	**5c** (99)	24	**2**	**1c**	300	**5c** (99)
4	**2**	**1d**	60	**5d** (78)	25	**2**	**1d**	600	**5d** (93)
5	**2**	**1e**	60	**5e** (51)	26	**2**	**1e**	600	**5e** (64)
6	**2**	**1f**	20	**5f** (83)	27	**2**	**1f**	300	**5f** (24)
7	**2**	**1g**	20	**5g** (65)	28	**2**	**1g**	600	**5g** (25)
8	**3**	**1a**	5	**6a** (92)[e]	29	**3**	**1a**	10	**6a** (99)[e]
9	**3**	**1b**	10	**6b** (94)[e]	30	**3**	**1b**	10	**6b** (99)[e]
10	**3**	**1c**	10	**6c** (99)[e]	31	**3**	**1c**	60	**6c** (91)[e]
11	**3**	**1d**	80	**6d** (88)[e]	32	**3**	**1d**	30	**6d** (91)[e]
12	**3**	**1e**	5	**6e** (94)[e]	33	**3**	**1e**	10	**6e** (82)[e]
13	**3**	**1f**	20	**6f** (78)[e]	34	**3**	**1f**	10	**6f** (80)[e]
14	**3**	**1g**	30	**6g** (62)[e]	35	**3**	**1g**	30	**6g** (78)[e]
15	**4**	**1a**	10	**7a** (86)	36	**4**	**1a**	120	**7a** (78)
16	**4**	**1b**	10	**7b** (80)	37	**4**	**1b**	300	**7b** (70)
17	**4**	**1c**	120	**7c** (61)[f]	38	**4**	**1c**	300	**7c** (95)
18	**4**	**1d**	80	**7d** (83)	39	**4**	**1d**	600	**7d** (79)
19	**4**	**1e**	60	**7e** (39)	40	**4**	**1e**	600	**7e** (73)
20	**4**	**1f**	20	**7f** (95)	41	**4**	**1f**	600	**7f** (76)
21	**4**	**1g**	30	**7g** (86)	42	**4**	**1g**	600	**7g** (66)

[a, b] See reference 8. [c] Heated at reflux with $TCPPClO_4$ (1~5 mol%) in the dark. [d] Isolated yields.

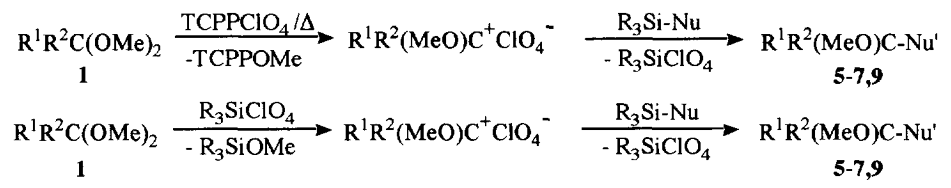
[e] Compounds **6** were obtained as diastereomeric mixtures. The diastereomeric ratios in the photoreactions were as follows: **6a** (76/24), **6b** (syn/anti = 66/34), **6c** (57/43), **6d** (57/43), **6e** (70/30), **6f** (50/50), **6g** (40/60). Those in the thermal reactions were as follows: **6a** (62/38), **6b** (syn/anti = 60/40), **6c** (55/45), **6d** (62/38), **6e** (61/39), **6f** (46/54), **6g** (39/61). The relative configurations were not assigned except for **6b**. [f] **1c** (37 %) was recovered.

$$TPPClO_4 \xrightarrow{h\nu} TPPClO_4{}^{*1} \xrightarrow{R_3Si\text{-}Nu} TPPClO_4{}^{-\bullet} + R_3Si\text{-}Nu^{+\bullet}$$

$$\longrightarrow TPP^{\bullet} + Nu'^{\bullet} + R_3SiClO_4$$

$$\underset{\mathbf{1}}{R^1R^2C(OMe)_2} \xrightarrow[-\,R_3SiOMe]{R_3SiClO_4} R^1R^2(MeO)C^+ClO_4{}^- \xrightarrow[-\,R_3SiClO_4]{R_3Si\text{-}Nu} \underset{\mathbf{5\text{-}7}}{R^1R^2(MeO)C\text{-}Nu'}$$

Scheme 1



Scheme 2

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7. All products were isolated by silica gel TLC and characterized by their spectroscopic data.
8. A typical procedure for the reactions of acetals with silylated nucleophiles: Piperonal dimethyacetal **1a** (196.2 mg, 1.00 mmol), allyltrimethylsilane **2** (120.0 mg, 1.05 mmol), and $TPPClO_4$ (12.3 mg, 0.03 mmol) were dissolved in nitrogen purged dry MeCN (10 cm^3). The solution was irradiated in a Pyrex tube with a stopcock immersed in a water bath with a 2 kW xenon lamp through a Toshiba glass cut filter (λ>360 nm). After 5 minutes' irradiation, [2.2.2]diazabicyclooctane (DABCO, 16.8 mg, 0.15 mmol) was added to quench the reaction. Concentration of the photolysate followed by silica gel TLC (ether-*n*-hexane, 1:2) afforded 1-methoxy-1-piperonyl-3-butene **5a** (184.7 mg, 90%) as a colorless oil.
9. The configurations of diastereomeric mixture **6b** were determined by comparison of their nmr data with those of literature.[2a]
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11. The fluorescence quenching experiments for **1**-**4** were conducted in CH_3CN ($k_q\tau$ M^{-1}) : **1a** (82.4), **1b** (3.0), **1c** (2.2), **1d** (65.9), **1e** (71.0), **1f** (61.9), **1g** (48.2), **2** (97.1), **3** (126.8), **4** (0.7).
12. One plausible explanation for this observation is that decomposition of the formed silyl tetrafluoroborate gives silyl fluoride and boron trifluoride which would not be effective promoters for the reaction.[13]
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15. The oxidation peak potentials (E_p^{ox} vs. SCE) of acetals **1** and the silyl compounds were measured by cyclic voltammetry at v = 100 mV/sec in acetonitrile containing 0.1 M Et_4NClO_4: **1a** (1.84 V), **1b** (>3.00 V), **1c** (>3.00 V), **1d** (2.45 V), **1e** (2.25 V), **1f** (2.30 V), **1g** (2.75), **2** (2.24 V), **3** (1.15 V), **4** (> 3.00 V), **8** (1.05 V).
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