Quaternary Ammonium Dendrimers as Lewis Base Catalysts for Mukaiyama–Aldol Reaction

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Surface-alkylated poly(propylene imine) dendrimer was treated with methyl iodide to afford quaternarized ammonium iodide dendrimer. The quaternarized dendrimer catalyzed the Mukaiyama–Aldol reaction of trimethylsilyl acetal with various aldehydes as a Lewis base in apolar toluene solvent.

Dendrimers are highly branched macromolecules with highly congested peripheral end groups and hollow interiors.[1] Various organic molecules,[2] metal complexes,[3] and metal nanoparticles[4] can be encapsulated within voids in the dendrimers to construct nanoreactors, which have received considerable attention because of their unique catalyses.[5]

The Mukaiyama–Aldol reaction of silyl enolates with aldehydes is a powerful tool for selective carbon–carbon bond formations and is classically promoted by Lewis acids through activation of the aldehyde.[6] Concerning dendrimer catalysts, Reetz et al. have reported that Sc-containing dendrimer acted as efficient heterogeneous catalysts for the aldol reaction.[7] Recently, several methods activating silyl enolate by Lewis bases such as phosphoramide,[8] $CaCl_2$,[9] and lithium amides[10] were reported. Also, quaternary ammonium fluorides[11] and phosphines[12] are known to accelerate the aldol reaction in polar solvents by nucleophilic cleavage of the O–Si bonds of silyl enolates.[13] Herein, we describe that an alkylated dendrimer having quaternary ammonium iodides can catalyze the Mukaiyama–Aldol reaction of silyl enolates with aldehydes in nonpolar solvents such as toluene.

Poly(propylene imine) (PPI) dendrimer was selected because of the high density of tertiary amino groups within the dendrimer. Primary amino groups on the periphery of the PPI dendrimer were modified with decanoyl chloride (C_{10}) or palmitoyl chloride (C_{16}) to give the corresponding alkylated dendrimers.[14] Figure 1 shows a typical procedure for synthesis of the quaternarized ammonium iodide dendrimer as follows: the third generation alkylated dendrimer (G$_3$-C$_{10}$ 1 g, 3.37 mmol of tertiary
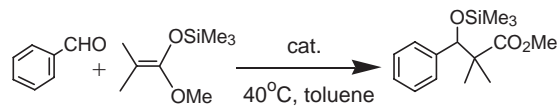
amino groups) was dissolved in 10 mL of DMF and then CH$_3$I (33.7 mmol, 10 equiv. to tertiary amino group) was added and stirred at 50 °C for 15 h under Ar.

After evaporation of DMF and excess CH$_3$I, the residue was washed with ether and dried in vacuo at 50 °C to yield the corresponding quaternary ammonium iodide dendrimer (Q-G$_3$-C$_{10}$(I$^-$)) as shown in Figure 1.[15] ^{1}H NMR (CDCl$_3$, 400 MHz, 50 °C): $\delta = 0.880$ (t, $J = 6.79$ Hz, –CH$_2$CH_3), 1.26 (br, –(CH_2)–), 1.60 (br –CH_2CH$_3$), 2.0–2.8 (br, –N$^+$CH_3), 3.2–4.2 (br, –N$^+$(CH_2)$_3$–). Anal. Calcd for C$_{262}$H$_{538}$N$_{30}$O$_{16}$I$_{14}$: C, 51.23; H, 8.83; N, 6.84. Found: C, 50.73; H, 9.13; N, 6.54. Q-G$_3$-C$_{16}$(I$^-$) was also prepared according to the above procedure.[16]

The catalytic performance of the quaternarized dendrimers was examined in the Mukaiyama–Aldol reaction of 1-methoxy-2-methyl-1-(trimethylsilyloxy)propene with benzaldehyde at 40 °C in toluene. As shown in Table 1, an aldol product was obtained in 98% yield within 12 h using Q-G$_3$-C$_{10}$(I$^-$) (Entry 1). The dendrimer modified with palmitoyl chloride (Q-G$_3$-C$_{16}$(I$^-$)) showed a low catalytic activity (Entry 2). The Q-G$_3$-C$_{10}$(I$^-$) dendrimer exhibited higher catalytic activity than common quaternary ammonium iodides such as tetrabutylammonium iodide (TBAI) and tetraheptylammonium iodide (THAI) (Entries 5 and 6). As a Lewis base catalyst, the iodide anion was superior to BF$_4^-$ or PF$_6^-$ (Entries 3 and 4). No reaction occurred using the non-quaternarized G$_3$-C$_{10}$ (Entry 7). These results show that encapsulation of quaternary ammonium iodides within alkylated PPI dendrimers efficiently promotes the aldol reaction.

Table 2 shows typical examples of the Mukaiyama–Aldol

Table 1. Mukaiyama–Aldol reaction catalyzed by various dendrimers[a]

Entry	Catalyst	Conv./%[b]	Yield/%[b]
1	Q-G$_3$-C$_{10}$(I$^-$)	98	98
2	Q-G$_3$-C$_{16}$(I$^-$)	32	32
3	Q-G$_3$-C$_{10}$(PF$_6^-$)	9	9
4	Q-G$_3$-C$_{10}$(BF$_4^-$)	6	6
5[c]	N(n-Hep)$_4$I	11	10
6[c]	N(n-Bu)$_4$I	2	2
7	G$_3$-G$_{10}$	no reaction	—
8	none	no reaction	—

[a]Reaction conditions: dendrimer 0.0036 mmol (0.05 mmol of I$^-$), benzaldehyde 0.5 mmol, silyl enolate 0.7 mmol, toluene 2 mL, 12 h, Ar atmosphere. [b]Based on benzaldehyde. [c]Tetraalkylammonium salts 0.05 mmol.
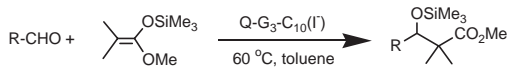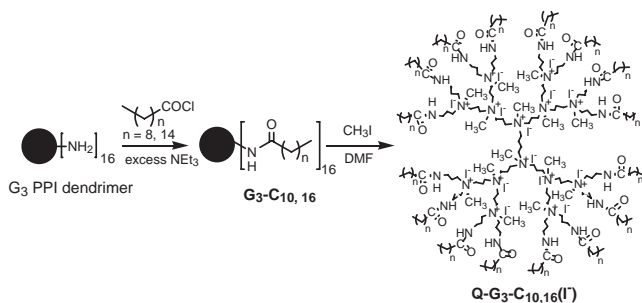

Figure 1. Preparation of quaternary ammonium iodide dendrimer.

Table 2. Mukaiyama–Aldol reaction of trimethylsilyl enolate with various aldehydes catalyzed by Q-G$_3$C$_{10}$(I$^-$)[a]

Entry	Aldehyde	Time /h	Conv. /%[b]	Yield /%[b]
1	◇–CHO	8	98	98
2	Cl–◇–CHO	3	>99	99
3	O$_2$N–◇–CHO	8	88	88
4	MeO–◇–CHO	8	98	98
5	Me–◇–CHO	8	>99	98
6	(thiophene)–CHO	8	96	94
7	(naphthalene)–CHO	8	98	98
8	⋀$_5$–CHO	9	>99	96
9	Ph⋀–CHO	4	>99	98
10	Ph⋀–CHO	3	>99	96[c]

[a]Reaction conditions: aldehyde 0.5 mmol, silyl enolate 0.7 mmol, Q-G$_3$-C$_{10}$(I$^-$) 0.0036 mmol (0.05 mmol of I$^-$), toluene 2 mL, Ar atmosphere. [b]Determined by GC based on aldehyde. [c]1,4-addition product was obtained (1,2-/1,4- = 1.9).

reaction of the trimethylsilyl enolate with various aldehydes catalyzed by Q-G$_3$-C$_{10}$(I$^-$) at 60 °C. Aromatic aldehydes functioned succesfully as acceptors (Entries 1–5). The heteroaromatic aldehyde of 2-thiophencalbaldehyde, known to deactivate Lewis acid catalysts,[10] also afforded the corresponding aldol product (Entry 6). Compared with the aromatic aldehydes, the aliphatic aldehyde of *n*-octanal required longer reaction time (Entry 8), which was similar to that for other Lewis base catalysts.[6,10] In the case of α,β-unsaturated carbonyl compound, cinnamaldehyde gave a mixtures of 1,2- and 1,4-addition of the silyl acetal (Entry 10).

The interaction between Q-G$_3$-C$_{10}$(I$^-$) and 1-methoxy-2-methyl-1-(trimethylsilyloxy)propene was examined by ^{13}C NMR spectroscopy. Figure 2 shows the chemical shifts of the α and β carbons of the silyl acetal at 149.2 and 90.6 ppm, respectively. These signals shifted to 177.2 and 77.2 ppm, respectively, in the presence of Q-G$_3$-C$_{10}$(I$^-$).[17] In contrast, treatment of Q-G$_3$-C$_{10}$(I$^-$) with benzaldehyde did not cause any change in the chemical shift of the carbonyl carbon of benzaldehyde, which indicates that benzaldehyde was not activated by Q-G$_3$-C$_{10}$(I$^-$). Presumably, the quaternary ammonium iodide dendrimer acts not as a Lewis acid but as a Lewis base catalyst to afford the aldol products. In contrast to TBAI and THAI, the high activity of the quaternarized dendrimers would be due to the high polarity within the dendrimers, which might accelerate severance of the oxygen–silicon bond even in toluene solvent.[13]

In summary, we report the quaternary ammonium iodide
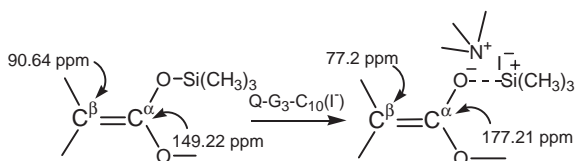
Figure 2. ^{13}C NMR shifts of the silyl acetal with quaternarized dendrimer Q-G$_3$-C$_{10}$(I$^-$).

dendrimer acts as a nanoreactor encapsulating a Lewis base catalyst for the Mukaiyama–Aldol reaction of the trimethylsilyl enolate with aldehydes. The high catalytic activity for the Mukaiyama–Aldol reaction in toluene is ascribed to the highly dense quaternary ammonium iodide within the dendrimer.

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16 BF$_4$$^-$ and PF$_6$$^-$ dendrimers were prepared by anion exchange of Q-G$_3$-C$_{10}$(I$^-$) using AgBF$_4$ and AgPF$_6$ in DMF. Q-G$_3$-C$_{16}$(I$^-$); Anal. Calcd for C$_{358}$H$_{730}$N$_{30}$O$_{16}$I$_{14}$: C, 57.42; H, 9.83; N, 5.61. Found: C, 58.12; H, 9.13; N, 5.14%. Q-G$_3$-C$_{10}$(BF$_4$$^-$); Anal. Calcd for C$_{262}H_{538}N_{30}O_{16}$ B$_{14}$F$_{64}$: C, 54.89; H, 9.46; N, 7.33. Found: C, 54.21; H, 9.85; N, 6.86%. Q-G$_3$-C$_{10}$(PF$_6$$^-$); Anal. Calcd for C$_{262}H_{538}N_{30}O_{16}P_{14}F_{84}$: C, 49.21; H, 8.48; N, 6.57. Found: C, 48.73; H, 9.02; N, 6.12%.
17 In ^{13}C NMR spectrum, the chemical shifts of the α and β carbons of the silyl enolate did not change with the parent dendrimer G$_3$-C$_{10}$.