A Novel Concept of Acid Proliferation. Autocatalytic Fragmentation of an Acetoacetate Derivative as an Acid Amplifier[1]

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(Received April 10, 1995)

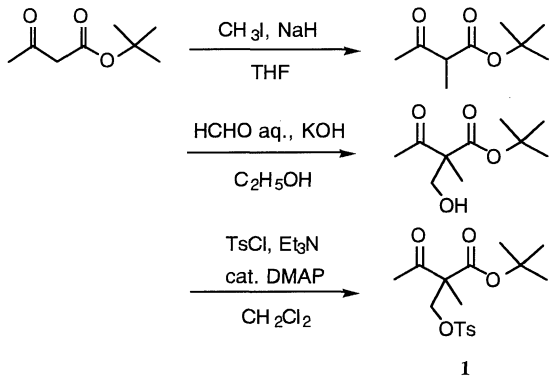
tert-Butyl 2-methyl-2-(p-toluenesulfonyloxymethyl)acetoacetate was designed to be subjected to the acid-catalyzed fragmentation to liberate p-toluenesulfonic acid which can act as the autocatalyst to lead to the increment of the acid concentration in geometric progression.

A catalyst is defined as a chemical species which initiates and/or accelerates a thermodynamically favorable reaction without any change of its concentration during the chemical transformation. One of important catalysts is unequivocally acidic substances. If an acid catalyst can be produced by an autocatalytic transformation of a substrate and increases in geometric progression, a catalyzed reaction rate should be enhanced explosively. This means that a tiny amount of an acidic species like a photogenerated strong acid can be breeded to result in a drastic and non-linear enhancement of a subsequent acidolytic reaction by the autocatalytic decomposition of an acid precursor which is called an acid amplifier.

Aiming at the improvement of photosensitivity of photoimaging materials triggered by photogenerated acids,[2] our efforts have been focused on development of acid amplifiers which should fulfill the following requirements. First, an acid amplifier should be readily subjected to the acid-catalyzed decomposition to liberate a strong acid which catalyzes the transformation of itself. Second, an acid amplifier should be thermally stable in the absence of an acid at least under reaction conditions to proceed the autocatalytic decomposition and a subsequent acid-catalyzed reaction. Thirdly, a liberated acid should be so strong to catalyze subsequent chemical reaction(s) to display a non-linear process. The major concern of this letter is to present an acetoacetate derivative substituted with a p-toluenesulfonyloxy (TsO) residue which is subjected to the fragmentation reaction catalyzed by p-toluenesulfonic acid (TsOH) to release a new molecule of the same acid.

We designed tert-butyl 2-methyl-2-(p-toluenesulfonyloxymethyl)acetoacetate (**1**)[3] as an acid amplifier. This was synthesized in a 10% overall yield by monomethylation of tert-butyl acetoacetate, hydroxymethylation with formalin under an alkaline condition,[4] followed by tosylation with p-toluenesulfonyl chloride in the presence of triethylamine (Et_3N) and 4-dimethylaminopyridine (DMAP) (Scheme 1). The carbon atom at the β-position of TsO group is methylated to inhibit the β-elimination of TsOH. The tert-butyl ester of the acetoacetate is deprotected by the action of an acid to give an acetoacetic acid (**2**) which is readily decarboxylated to yield a β-tosyloxyketone (**3**) (Scheme 2). Owing to the presence of the electron-withdrawing carbonyl group, the elimination of TsOH takes place readily to produce 2-methyl-1-buten-3-one (**4**).

The thermal behavior of **1** was studied by NMR spectroscopy. A solution of **1** (70 mmol/dm^3) in a 3:1 mixture of diphenyl ether and toluene-d_8 was heated at 100°C. No change in the NMR spectrum was observed in the absence of



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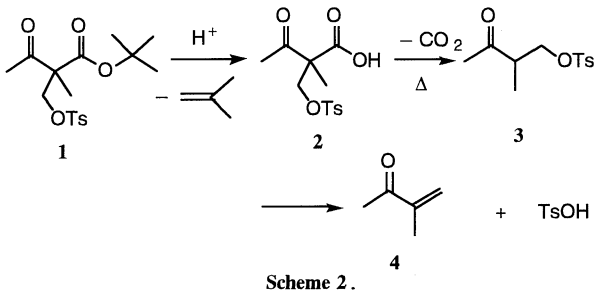
Scheme 1.



1 2 3 4

Scheme 2.

TsOH. The decomposition of **1** was induced by the presence of 9.1 mmol/dm^3 of TsOH at the same temperature. The fragmentation reaction of **1** was followed by monitoring the decrease of the proton signals due to tert-butyl and β-methyl groups while the formation of the unsaturated ketone (**4**) was checked by the proton signal due to a methyl group adjacent to an olefinic carbon with the use of 2-methoxynaphthalene as an internal standard. Figure 1 shows that both the consumption of the acetoacetate and the formation of the unsaturated ketone take place abruptly to display a sigmoidal time course, indicating that the fragmentation proceeds autocatalytically to lead to the proliferation of the acid. The reduction of the yield of **4** may be ascribable to its volatility leading to a partial loss during the reaction at an elevated temperature. A quantitative formation of TsOH was confirmed by the titration of a reaction mixture in a THF solution. These facts support that the acetoacetate (**1**) fulfills the two requirements stated above.

In order to confirm the third requirement for an acid amplifier, the acetoacetate (**1**) was coupled with poly[p-(tert-butoxycarbonyloxy)styrene](PBOCST) (**5**) as an acid-labile polymer.[5] A thin film of PBOCST containing 10 wt% of **1** was spin-coated on a silicon wafer and heated at 100°C for 1 hr. No change in IR spectra of the film was observed, showing again that the acetoacetate is thermally stable in the polymeric matrix.

The acid proliferation as a result of the acid-catalyzed

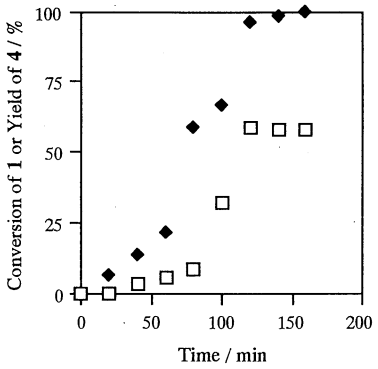


Figure 1. Time courses of (◆) the decomposition of **1** and (□) the formation of **4** in diphenyl ether/toluene-d8 = 3/1 at 100°C in the presence of TsOH. The initial concentrations were 70 mmol/dm^3 for **1** and 9.1 mmol/dm^3 for TsOH, respectively.

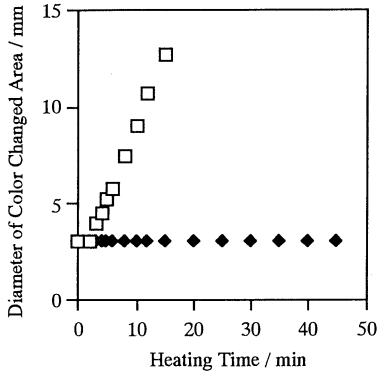
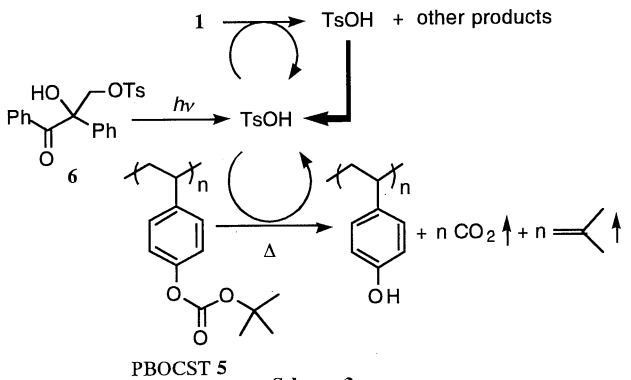


Figure 2. Time courses of the diameter of an interference-color changed area of a PBOCST film containing 3.6 wt% of **6** in the presence of (□) 30 wt% of **1** and (◆) 29 wt% of tert-butyl 2-(benzoyloxymethyl)-2-methylacetoacetate.

fragmentation of **1** in a polymeric thin film was determined by the use of a film of PBOCST doped with 30 wt% of **1** in the presence of 3.6 wt% of a tosylated benzoin derivative (**6**) which generates TsOH upon UV-irradiation.[6] A thin film of PBOCST containing the photoacid generator (**6**) and the acid-amplifier (**1**) was made by spin-coating on a silicon wafer to put on color due to the interference of light. Therefore, the progress of the acid-catalyzed polymeric reaction was monitored in real time simply by observing the interference color change because the film thickness is markedly reduced owing to the elimination of isobutene and carbon dioxide (Scheme 3). When a film was heated on a hot plate at 100°C after UV-irradiation through a circular window of 3 mm diameter, the color change took place exclusively at an irradiated circle within a few minutes. Surprisingly, prolonged heating of the film gave birth to gradual enlargement of the circle as a result of the lateral expansion of the color change to unexposed areas. Figure 2 shows the expansion of the bleached circle as a function of heating time. This phenomenon was not observed in the absence of **1** nor in a system containing a related compound, tert-butyl 2-methyl-2-(benzoyloxymethyl)acetoacetate, which liberates benzoic acid with much weaker acidity and hence cannot act as an acid-amplifier at all. Moreover, the color change did not occur in the absence of **6**. These mean clearly that the area expansion of the polymer decomposition reflects



Scheme 3.

the proliferation of **6**-derived TsOH by the decomposition of **1** in the polymer matrix.

The sudden acceleration of the alkaline hydrolysis of a carboxylic acid ester has been reported to take place autocatalytically in a micellar system.[7] To our knowledge, the reaction of **1** is the first example of a simple organic compound demonstrating the molecular proliferation. The concept of the acid proliferation is of practical significance to improve photosensitivity of polymeric materials for image formation when coupled with acid-catalyzed or acid-initiated transformation of versatile substances. Some of the typical applications will be shown elsewhere.

References and Notes

1 Acid proliferation reactions and their applications. Part I.

2 E. Reichmanis in *Polymers for Electronic and Photonic Applications*, ed by C. P. Wong, Academic Press, San Diego (1993) pp. 67-117 .

3 Colorless crystals of mp=52~53°C. ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.38 (s, 3H, -COC(CH_3)COO-), 1.40 (s, 9H, -C(CH_3)$_3$), 2.15 (s, 3H, CH_3CO), 2.47 (s, 3H, Ar-CH_3), 4.28 (ABq, J=10Hz, 2H, -CH_2OSO_2-), 7.38 (d, J=7.7Hz, 2H, Ar-H), 7.77 (d, J=7.7Hz, 2H, Ar-H). IR (cm^{-1}): 3000, 1738 (>C=O of ester), 1719 (>C=O). Found: C; 57.18, H; 6.90, S; 8.84%. Calcd. for $C_{17}H_{24}O_6S$: C; 57.29, H; 6.79, S; 9.00%.

4 tert-Butyl 2-(hydroxymethyl)-2-methylacetoacetate: an oily substance. ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.37 (s, 3H, -COC(CH_3)COO), 1.50 (s, 9H, -C(CH_3)$_3$), 2.24 (s, 3H, CH_3CO-), 2.89 (broad t, J=6Hz, 1H, -OH), 3.82 (broad d, J=6Hz, 2H, -CH_2-O-). IR (cm^{-1}): 3502 (OH), 1725 (>C=O of ester), 1711 (>C=O of ketone). Found: C; 58.92, H; 9.23%. Calcd. for $C_{10}H_{18}O_4$: C; 59.39, H; 8.97%.

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7 P. A. Bachmann, P. L. Luisi, and J. Lang, *Nature*, **357**, 57 (1992).