



Diphenylammonium triflate (DPAT): efficient catalyst for esterification of carboxylic acids and for transesterification of carboxylic esters with nearly equimolar amounts of alcohols

Kazunori Wakasugi, Tomonori Misaki, Kayo Yamada and Yoo Tanabe*

School of Science, Kwansei Gakuin University, 1-1-155 Uegahara, Nishinomiya, Hyogo 662-8501, Japan

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Abstract

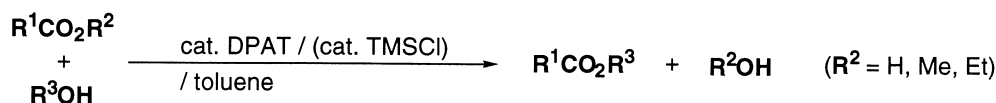
Diphenylammonium triflate (DPAT) efficiently catalyzed esterification between equimolar amounts of carboxylic acids and alcohols in good to excellent yields under mild reaction conditions. Transesterification of carboxylic esters with a slight excess of alcohols also proceeded using DPAT as catalyst with TMSCl as a co-catalyst. © 2000 Elsevier Science Ltd. All rights reserved.

Esterification (and transesterification) of carboxylic acids (and carboxylic esters) with alcohols have been recognized as one of the most important unit reactions in organic synthesis.¹ Of a number of well known methods applicable to both reactions, those using catalytic amounts of promoter and/or dehydrating reagents under mild liquid-phase conditions are quite limited; representatively, Otera and co-workers found an efficient method using distannoxanes such as $[(\text{SCN})\text{Bu}_2\text{SnOSnBu}_2(\text{OH})]$.²

From a recent atom-economical standpoint, the uses of nearly equimolar amounts of carboxylic acids (or carboxylic esters) and alcohols are strongly required. Mukaiyama and Shiina reported such direct esterifications mediated by $\text{TiCl}_2(\text{ClO}_4)_2$ and $\text{TiCl}(\text{OTf})_3$ reagents;³ however, they necessitated more than equimolar amounts of anhydride and silyl dehydrating additives, respectively. We introduce here diphenylammonium triflate (DPAT),⁴ which worked as an efficient catalyst (1–10 mol%) for the esterification between equimolar amounts of carboxylic acids and alcohols under mild conditions. In addition, the transesterification catalyzed by DPAT (10–20 mol%) was performed between carboxylic esters and slightly excess alcohols, wherein TMSCl (10 mol%) was found to be an efficient co-catalyst (Scheme 1).

PPTS (pyridinium *p*-toluenesulfonate) is widely used as a mild and efficient catalyst in acetalization and its related reactions.⁵ To extend this methodology toward the carboxylic ester syntheses, we

* Corresponding author.

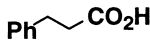
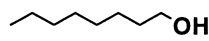
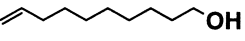
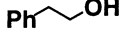
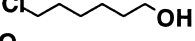
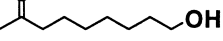
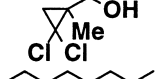
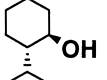
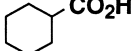
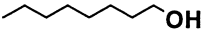
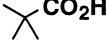
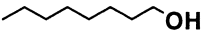
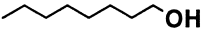


Scheme 1.

examined several ammonium triflates (1.0 mol%) guided by a direct esterification using 3-phenylpropionic acid (1.0 mmol) and 1-octanol (1.0 mmol) at 110°C in toluene (2.0 ml). These results are as follows: pyridinium triflate (53%, 24 h), $\text{Bu}_3\text{NH}^+\cdot\text{OTf}^-$ (16%, 24 h), and $\text{Me}_2\text{PhNH}^+\cdot\text{OTf}^-$ (64%, 24 h).⁶ Compared with these, DPAT showed a remarkable effect, namely, 94% within 1 h, whose result encouraged us to investigate the reactivity of DPAT.⁷

Table 1 lists those results.⁸ Only 1 mol% of DPAT was sufficient for primary alcohols (entries 1–5, 9 and 10). Relatively sterically crowded secondary alcohols and/or benzoic acid required 5–10 mol% of DPAT with a little prolonged time (entries 6–8 and 11). Several functionalities such as a double bond, a halogen, a ketone, and a cyclopropane are tolerated. This method did not necessitate special use of the dehydrating reagent and/or the technique of azeotropic removal of water.

Table 1
Esterification between equimolar amounts of carboxylic acids and alcohols using DPAT catalyst^{a)}

Entry	R ¹ CO ₂ H	R ³ OH	DPAT / mol%	Time / h	Yield / %
1			1	4	93
2			1	8	96
3			1	8	92
4			1	8	90
5			1	8	89
6			5	24	92
7			5	24	90
8			10	48	92 ^{b)}
9			1	8	90
10			5	24	78
11			1	24	92
12			5	48	94

a) In toluene at 80 °C. Molar ratio / R¹CO₂H : R³OH = 1 : 1. b) [α]_D²³ -59.5° (c 1.47, CHCl₃).

The transesterification⁹ was also performed using DPAT as catalyst (10 mol%), although the rate of conversion was somewhat slower than that of esterification mentioned above: A mixture of methyl 3-phenylpropionate (164 mg, 1.0 mmol), 1-octanol (195 mg, 1.5 mmol), and DPAT (32 mg, 0.1 mmol) were heated (80°C, 24 h) in toluene to give desired 1-octyl ester (197 mg, 75%). When 10 mol% TMSCl (11 mg, 0.1 mmol) was employed as co-catalyst, the yield was improved (83%, 80°C, 24 h; 90%, 80°C, 20 h and 110°C, 4 h).

Table 2 lists the results of the transesterification. DPAT and TMSCl system could catalyze the transesterification of primary alcohols efficiently (entries 1–3 and 5). Unfortunately, 2-octanol, *tert*-Bu ester, and α -branched esters resisted the esterification (entries 4, 7 and 8). It should be noted a β -keto ester, which is prone to decarboxylation, was employable (entry 9).

Table 2
Transesterification between nearly equimolar amounts of carboxylic esters and alcohols using DPAT catalyst and TMSCl co-catalyst^{a)}

Entry	R ¹ CO ₂ R ²	R ³ OH	Yield / %
1			90 (80) ^{b)}
2			97
3			94
4			30
5			94
6			2 ^{c)}
7			90 ^{c)}
8			33
9			79 ^{d)}

a) In toluene at 80 °C for 20 h and 110 °C for 4 h. Molar ratio / R¹CO₂R² : R³OH : DPAT : TMSCl = 1 : 1.5 : 0.1 : 0.1. b) Parenthesis indicates the data in the case using 1.0 equiv of 1-octanol. c) DPAT (0.2 equiv) was used. d) TMSCl (1.0 equiv) was used.

In conclusion, we achieved both the efficient esterification and transesterification catalyzed by DPAT whose reactivities are comparable to the methods using organotin^{2,9} and organotitanium³ catalysts. The use of DPAT includes a lot of merits from the viewpoint of green chemistry, for example DPAT is air-stable, cheap, low toxic, and easy to handle. The operation is quite simple, because the dehydrating system such as a Dean–Stark apparatus is not necessary.

Acknowledgements

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2. Otera, J.; Dan-oh, N.; Nozaki, H. *J. Org. Chem.* **1991**, 56, 5307.
3. (a) Shiina, I.; Mukaiyama, T.; Miyoshi, S.; Miyashita, M. *Chem. Lett.* **1994**, 515. (b) Mukaiyama, T.; Shiina, I. *Chem. Lett.* **1995**, 141.
4. DPAT was very easily prepared in a high yield as follows: $\text{CF}_3\text{SO}_3\text{H}$ (0.75 g, 5.0 mmol) was added to a solution of Ph_2NH (0.85 g, 5.0 mmol) in toluene (10.0 ml) at 20–25°C, and the mixture was stirred for 15 min. Evaporation of the solvent gave the crude product, which was washed with hexane (ca. 50 ml) to give a pure DPAT (1.55 g, 97%) as colorless crystals (mp 172–173°C).
5. Miyashita, M.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, 42, 3772.
6. $\text{Et}_3\text{NH}^+\cdot\text{OTf}^-$ and $\text{Ph}_3\text{NH}^+\cdot\text{OTf}^-$ did not crystallize, so they were excluded from this investigation.
7. With decreasing the basicity of the counter amine part, the ability of the esterification seem to be higher. Solvent effect (DPAT, 1 mol%, 80°C, 15 h): toluene (93%), 1,2-dichloroethane (90%), 1,4-dioxane (54%), CH_3CN (46%), DME (27%), DMF (trace).
8. Typical procedure: 3-Phenylpropionic acid (150 mg, 1.0 mmol), 1-octanol (130 mg, 1.0 mmol), and DPAT (3.2 mg, 0.01 mmol) were heated (80°C) in toluene for 4 h. Evaporation of toluene (ca. 40°C) under reduced pressure gave the crude material, which was purified by column chromatography (hexane:ether=10:1) to give the desired carboxylic ester (244 mg, 93%). For recent representative works, see: (a) Masaki, Y.; Tanaka, N.; Miura, T. *Chem. Lett.* **1997**, 55. (b) Ponde, D. E.; Deshpande, V. H.; Bulbule, V. J.; Sudalai, A.; Gajare, A. S. *J. Org. Chem.* **1998**, 63, 1058. (c) Furlan, R. L. E.; Mata, E. G.; Mascaretti, O. A. *Tetrahedron Lett.* **1998**, 39, 2257. (d) Krasik, P. *Tetrahedron Lett.* **1998**, 39, 4223.
9. In the case of an organotin-catalyzed method,² the transesterification is smoother than the esterification. In contrast, the present method shows a reverse relationship.