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A Convenient One-Pot Synthesis of Carboxylic Acid Anhydrides Using 1,1'-Oxalyldiimidazole¹⁾

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Aliphatic, aromatic, and heteroaromatic carboxylic acids (**5a—i**) react with 1,1'-oxalyldiimidazole (**6**) in acetonitrile under reflux in the presence of methanesulfonic acid (**12**) to give the corresponding carboxylic acid anhydrides (**9a—i**) in 30—98% yields.

Keywords—dehydration; carboxylic acid anhydride; *N*-acylimidazole; 1,1'-carbonyldiimidazole; 1,1'-oxalyldiimidazole

It is well known that 1,1'-carbonyldiimidazole (**1**)²⁾ is a useful dehydrating reagent. For example, the reaction between maleic acid (**2**) and **1** in tetrahydrofuran has been shown to afford maleic acid anhydride (**3**) in 88% yield.³⁾ More recently, Iizuka and co-workers have also reported that carboxamides (**4**) react with **1** in the presence of allyl bromide to give the corresponding nitriles (**5**) in good yield.⁴⁾ Compound **1**, though commercially available, is too expensive to utilize on a large scale. Furthermore, the toxicity of phosgene, used for the preparation of **1**, means that preparation of **1** in the laboratory is quite troublesome. On account of these shortcomings, we were prompted to examine the possibility that 1,1'-oxalyldiimidazole (**6**)⁵⁾ in place of **1** may be generally effective as a dehydration reagent. As a result of our study on the reactivity of **6**, we have reported recently that **6** can be conveniently

Chart 1

Chart 2

used for the dehydration of aldehyde oximes (7) to the corresponding nitriles (5) under mild and neutral conditions.⁶⁾ As a continuation of our work on the utility of 6, we sought a convenient synthesis of carboxylic acid anhydrides (9).

In this short communication we would like to report another successful application of a readily available dehydration reagent, 6, for the transformation of carboxylic acids (8) into 9. Thus, the reaction of benzoic acid (5b) (1 eq) with 6 (1 eq) in acetonitrile was carried out at 40 °C for 2 h, with liberation of carbon dioxide and carbon monoxide, to provide the corresponding *N*-acylimidazole intermediate (11), which subsequently reacted with a second molecule of the acid 8 (1 eq) under refluxing conditions for 3 h in the presence of methanesulfonic acid (12) to afford benzoic anhydride (9b) in 98% yield. Similarly, heteroaromatic compounds, 2-furoic and 2-thenoic acids (8d and 8e) were converted to the desired carboxylic acid anhydrides (9d and 9e) in 66% and 71% yields, respectively. A dicarboxylic acid, phthalic acid (8h) was intramolecularly dehydrated with 6 to give phthalic anhydride (9h) in 84% yield. An advantage of 6 as a dehydrating reagent is that 9 can be isolated very easily; the removal of the by-products, imidazole, methanesulfonic acid, and/or imidazolium methanesulfonate is achieved simply by washing the reaction mixture with water. Representative results are summarized in Table I.

As shown in Chart 3, the reaction probably proceeds *via* the formation of a mixed acid anhydride intermediate (10) from the reaction of the carboxylic acid 8 with 6 at 40 °C, and subsequently concerted eliminations of CO₂, CO, and imidazole occur to afford the corresponding *N*-acylimidazole 11 through step 2. At step 3, 11 reacts with a second molecule

TABLE I. Preparation of Carboxylic Acid Anhydrides ((RCO)₂O; 9)
Using 1,1'-Oxalyldiimidazole (ODI; 6)

Compd. No. 9a—i	R	Reaction time (h)		Yield ^{a)} (%)	mp (°C) ^{b)}		IR $\nu_{\text{max}}^{\text{KBr}}$ cm ⁻¹ C=O	
		Steps 1 and 2, at 40 °C	Step 3 under reflux		Found	Reported		
a	CH ₃ (CH ₂) ₁₄ —	1	3	94	61—63 ^{c)}	62.5—63.5 ⁸⁾	1803	1740
b		2	3	98	41—42 ^{d)}	41—42 ⁹⁾	1788	1725
c		1	2	56	188—190 ^{f)}	189—190 ⁹⁾	1797	1728
d		1	2	66	71—72 ^{f)}	71—73 ¹⁰⁾	1791	1734
e		1	2	71	59—61 ^{f)}	60.5—61.5 ¹¹⁾	1761	1701
f	—CH ₂ ·CH ₂ —	1	3	39	119—120 ^{g)}	118—119 ¹²⁾	1866	1782
g	—CH ₂ ·CH ₂ ·CH ₂ —	1	2	30	55—56 ^{h)}	52—55 ¹³⁾	1806	1755
h		2	2	84	132—133 ^{e)}	133 ^{10a)}	1854	1764
i		3	2	42	218—220 ^{e)}	217 ¹⁴⁾	1764	1734

a) Yield of the products (9a—i) after purification. Compounds (9a—i) were characterized by comparison of their melting point and IR data with those of authentic samples. b) All melting points are uncorrected. c) Recrystallized from *n*-hexane. d) Recrystallized from benzene-pet. ether. e) Recrystallized from benzene. f) Recrystallized from benzene-cyclohexane. g) Recrystallized from ethyl acetate. h) Recrystallized from ether.

of **8** in refluxing acetonitrile in the presence of **12** to provide the corresponding carboxylic acid anhydride (**9**) as the final product.

Thin layer chromatography (TLC) monitoring showed that there was no detectable benzoic anhydride **9b** when the reaction of benzoic acid (**8b**) with **6** was performed under the above-mentioned reaction conditions without **12** at step 3. This finding suggests that the formation of *N*-acylimidazolium methanesulfonate from the reaction of **11** with **12** as shown in Chart 4 is essential to enhance the leaving ability of the imidazole ring from **11**, so that concerted nucleophilic attack of **8** on the carbon atom of the acyl group of **11** can take place smoothly to form the corresponding **9**.

Thus, in conclusion 1,1'-oxalyldiimidazole (**6**) can be conveniently used for the direct conversion of carboxylic acids **8** to the corresponding carboxylic acid anhydrides **9** under mild reaction conditions.

Experimental⁷⁾

Carboxylic Acid Anhydrides (9a–e) from Monocarboxylic Acids (8a–e)—General Procedure: Compound **6** (5 mmol) was added to a solution of a carboxylic acid **8** (5 mmol) in acetonitrile (30 ml). The mixture was stirred at 40 °C for the time listed in Table I (steps 1 and 2). After cooling to room temperature, the same carboxylic acid **8** (5 mmol) was further added in one portion, and a solution of **12** (10 mmol) in acetonitrile (10 ml) was added dropwise at room temperature. The resultant mixture was stirred under reflux for the time listed in Table I (step 3). On cooling to room temperature again, the mixture afforded a white precipitate. This was filtered off, and the filtrate was evaporated *in vacuo*. The residue thus obtained was poured into ice water and extracted with two 50 ml portions of ethyl acetate. The extract was washed with water, and dried over anhydrous sodium sulfate, then the organic solvent was removed *in vacuo* to give the crude product (**9**), which was further purified by recrystallization (see Table I).

Cyclic Carboxylic Acid Anhydrides (9f–i) from Dicarboxylic Acids (8f–i)—General Procedure: Compound **6** (2 mmol) was added to a solution of a dicarboxylic acid (**8**) (4 mmol) in acetonitrile (30 ml). The resultant mixture was stirred at 40 °C for the time listed in Table I (steps 1 and 2), then allowed to cool to room temperature. A solution of **12** (10 mmol) in acetonitrile (10 ml) was added dropwise at room temperature. The reaction mixture was stirred under reflux for the time listed in Table I (step 3). The white precipitate was filtered off, and the filtrate was worked up as described for **9a–e** to give the crude cyclic product (**9**), which was further purified by recrystallization (see Table I).

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References and Notes

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