Esterification of Aromatic Carboxylic Acids with Alcohols Using 2-Chloro-3,5-dinitropyridine as a Condensing Agent

Seiji TAKIMOTO,* Naomi ABE, Yasushi KODERA, and Hiroshi OHTA

Department of Chemistry, Faculty of Science, Fukuoka University, 8-19-1 Nanakuma, Johnan-ku, Fukuoka 841-01

(Received May 26, 1982)

Synopsis. The reaction of 2-chloro-3,5-dinitropyridine (CDNP) with carboxylic acids and alcohols was examined, and it was found that CDNP was a useful condensing agent. Various esters were prepared in good yields.

It has been reported[1,2] that polynitrohalobenzenes are useful condensing agents for the ester synthesis. In continuation of our studies on the development of new condensing agents, we tried to use 2-chloro-3-nitropyridine, 2-chloro-5-nitropyridine, and 2-chloro-3,5-dinitropyridine (CDNP) and found that CDNP was a useful condensing agent for the preparation of esters.

In the first place, we searched for effective bases for the condensation of benzoic acid and 1-propanol using CDNP.

Pyridine and 4-dimethylaminopyridine (DMAP)[3] proved to give good results (94 and 93% yields, respectively).

Other bases such as triethylamine or 1,8-diazabicyclo-[5.4.0]undec-7-ene did not give good yields (56 and 17% yields, respectively).

In the next experiment, the reaction of benzoic acid with 1-propanol using CDNP was carried out in the presence of Lewis acid with the consideration that the coordination of Lewis acid to CDNP would form reactive species. Lewis acids such as $BF_3 \cdot OEt_2$, $TiCl_4$, $AgBF_4$, and AgCN, which are often used as efficient catalysts, gave only small amounts of the ester.

A significant solvent effect was observed in the condensation of 2,4,6-trimethylbenzoic acid and 1-propanol using CDNP in the presence of DMAP, the ester being obtained in 81% yield in acetonitrile, and 62% yield in dichloromethane as solvents.

Examples of esterification are shown in Table 1.

Benzoic acid was smoothly esterified in pyridine by the procedure in the experimental part. The esterification of sterically hindered 2,4,6-trimethylbenzoic acid with alcohols in pyridine was slow at room temperature. Consequently, the reactions were run by refluxing to give the desired esters in good yields (entries 6, 8, 9, and 11). It has been reported[2] that the esterification of 2,3,6-trimethylbenzoic acid with secondary or tertiary alcohols using 2-chloro-1,3,5-trinitrobenzene is difficult. In contrast, it was found that 2,4,6-trimethylbenzoic acid was esterified with tertiary alcohols such as 2-methyl-2-propanol or 3-ethyl-3-pentanol using CDNP (entries 13 and 15).

The esterification in acetonitrile using a limited amount of DMAP (2 mol equiv. per 1 mol of CDNP) did not give good results (entries 10, 12, 14, and 16) except for entry 7.

When 4-nitro- or 3,5-dinitrobenzoic acid was esterified, yields of the esters were satisfactory (entries 17—26).

On the other hand, when CDNP, benzoic acid, and pyridine were mixed in a 1 : 1 : 2 molar ratio under the absence of alcohol, benzoic anhydride was formed in 79% yield.

Although clear conclusions regarding the esterification reaction mechanism await further study, the main esterification reaction seems to proceed through the acid anhydrides presumably formed from the dinitropyridyl esters by the attack of carboxylate anions remaining in the mixture. However, the direct attack of alcohols on dinitropyridyl esters are considered to participate to varied extents.

TABLE 1. ESTERIFICATION OF CARBOXYLIC ACIDS

	Acid (1 mmol)	Alcohol (1.2 mmol)	Reaction conditions[a] base; temp/°C	Yield of ester/%
1	$C_6H_5CO_2H$	1-Propanol	Pyridine; r.t.	94[b]
2	$C_6H_5CO_2H$	Benzyl alcohol	Pyridine; r.t.	86[b]
3	$C_6H_5CO_2H$	2-Propanol	Pyridine; r.t.	89[b]
4	$C_6H_5CO_2H$	Cyclohexanol	Pyridine; r.t.	74[b]
5	$C_6H_5CO_2H$	2-Methyl-2-propanol	Pyridine; r.t.	70[b]
6	$2,4,6\text{-}(CH_3)_3C_6H_2CO_2H$	1-Propanol	Pyridine; 115	96[c]
7	$2,4,6\text{-}(CH_3)_3C_6H_2CO_2H$	1-Propanol	DMAP; r.t.	81[c]
8	$2,4,6\text{-}(CH_3)_3C_6H_2CO_2H$	Benzyl alcohol	Pyridine; 115	98[c]
9	$2,4,6\text{-}(CH_3)_3C_6H_2CO_2H$	2-Propanol	Pyridine; 115	90[c]
10	$2,4,6\text{-}(CH_3)_3C_6H_2CO_2H$	2-Propanol	DMAP; 82	53[c]
11	$2,4,6\text{-}(CH_3)_3C_6H_2CO_2H$	Cyclohexanol	Pyridine; 115	94[c]
12	$2,4,6\text{-}(CH_3)_3C_6H_2CO_2H$	Cyclohexanol	DMAP; 82	37[c]
13	$2,4,6\text{-}(CH_3)_3C_6H_2CO_2H$	2-Methyl-2-propanol	Pyridine; 115	91[c]
14	$2,4,6\text{-}(CH_3)_3C_6H_2CO_2H$	2-Methyl-2-propanol	DMAP; 82	30[c]
15	$2,4,6\text{-}(CH_3)_3C_6H_2CO_2H$	3-Ethyl-3-pentanol	Pyridine; 115	84[c,d]
16	$2,4,6\text{-}(CH_3)_3C_6H_2CO_2H$	3-Ethyl-3-pentanol	DMAP; 82	12[c]
17	$4\text{-}NO_2C_6H_4CO_2H$	1-Propanol	Pyridine; r.t.	88[e]
18	$4\text{-}NO_2C_6H_4CO_2H$	Benzyl alcohol	Pyridine; r.t.	76[e]
19	$4\text{-}NO_2C_6H_4CO_2H$	2-Propanol	Pyridine; r.t.	79[e]
20	$4\text{-}NO_2C_6H_4CO_2H$	Cyclohexanol	Pyridine; r.t.	82[e]
21	$4\text{-}NO_2C_6H_4CO_2H$	2-Methyl-2-propanol	Pyridine; 115	68[e]
22	$3,5\text{-}(NO_2)_2C_6H_3CO_2H$	1-Propanol	Pyridine; r.t.	73[e]
23	$3,5\text{-}(NO_2)_2C_6H_3CO_2H$	Benzyl alcohol	Pyridine; r.t.	92[e]
24	$3,5\text{-}(NO_2)_2C_6H_3CO_2H$	2-Propanol	Pyridine; r.t.	80[e]
25	$3,5\text{-}(NO_2)_2C_6H_3CO_2H$	Cyclohexanol	Pyridine; r.t.	88[e]
26	$3,5\text{-}(NO_2)_2C_6H_3CO_2H$	2-Methyl-2-propanol	Pyridine; 115	58[e]

a) All reactions were carried out for 30 min. b) Isolated yield of once distilled product. c) Isolated yield of purified product by filtration through a short column of silica gel employing chloroform as an eluant. d) Spectral data (NMR, IR) were consistent with the indicated structure. e) Yield of crude ester. All these crude crystalline esters gave the previously determined mp without further purification.

Experimental

All reagents employed were dried by appropriate methods Commercial 2-chloro-3,5-dinitropyridine (CDNP) was used without further purification.

Ester of Carboxylic Acids. The preparations of *t*-butyl 2,4,6-trimethylbenzoate and *t*-butyl 4-nitrobenzoate are described here as typical examples. To a mixture of 2,4,6-trimethylbenzoic acid (1 mmol, 164 mg) and 2-methyl-2-propanol (1.2 mmol, 114 μl) in pyridine (1 ml) under nitrogen atmosphere was added CDNP (1 mmol, 204 mg) with stirring at 115 °C. After stirring for 30 min, an 8% aqueous sodium hydrogencarbonate solution (20 ml), water (10 ml), and petroleum benzine (40 ml) were added to the reaction mixture, and the whole mixture was well stirred. The mixture was transferred into a separatory funnel and the petroleum benzine layer was separated. The aqueous phase was again extracted with petroleum benzine (20 ml). The combined petroleum benzine extracts were washed with water (10 ml) several times until the yellow color of the solution was removed. The

petroleum benzine layer was then washed twice with 2% hydrochloric acid (20 ml) and twice with water (10 ml), and dried over anhydrous sodium sulfate. The organic layer was concentrated, and the residue was purified by filtration through a short column of silica gel employing chloroform as an eluant. The desired ester (200 mg, 91%) was the only compound observed on solvent removal.

NMR ($CDCl_3$) $\delta=1.58$ (s, 9H), 2.26 (s, 3H), 2.30 (s, 6H), 6.81 (s, 2H).

t-Butyl 4-nitrobenzoate is a solid, which was obtained directly after the reaction mixture was treated with an aqueous sodium hydrogencarbonate solution and washed with water.

The ester (152 mg, 68%) melted at 115—116 °C, pure enough before recrystallization. (lit,[4] mp 115.5 °C)

References

1) K. Inomata, H. Kinoshita, H. Fukuda, K. Tanabe, and H. Kotake, *Bull. Chem. Soc. Jpn.*, **51**, 1866 (1978).

2) S. Takimoto, J. Inanaga, T. Katsuki, and M. Yamaguchi, *Bull. Chem. Soc. Jpn.*, **54**, 1470 (1981).

3) G. Höfle, W. Steglich, and H. Vorbüggen, *Angew. Chem., Int. Ed. Engl.*, **17**, 569 (1978).

4) R. Adams, E. K. Rideal, W. B. Burnett, R. L. Jenkins, and E. E. Dreger, *J. Am. Chem. Soc.*, **48**, 1758 (1926).