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THE REACTION OF POLYNITROHALOBENZENES WITH CARBOXYLIC ACIDS. USE OF 2-FLUORO-1,3,5-TRINITROBENZENE (FTNB) AS A NEW CONDENSING REAGENT

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The reaction of polynitrohalobenzenes with carboxylic acids in the presence of a base was examined, and it was found that 2-fluoro-1,3,5-trinitrobenzene (FTNB) was the most reactive polynitrohalobenzene. Various carboxanilides were prepared under mild conditions in excellent yields using FTNB as a new condensing reagent.

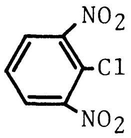
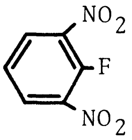
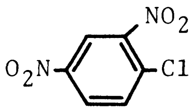
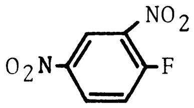
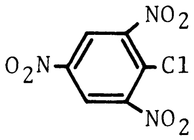
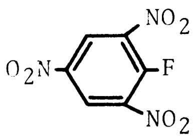
Esters were generally synthesized from carboxylic acids and alcohols using condensing reagents such as dicyclohexylcarbodiimide (DCC). In the present study, we first undertook to synthesize polynitrophenyl esters by the nucleophilic reaction of carboxylic acid with polynitrohalobenzene in the presence of a base in order to find a more convenient method for the preparation of amides or esters.

Various polynitrohalobenzenes (Ia-f) were allowed to react with an equimolar amount of phenylacetic acid and triethylamine at an appropriate temperature in acetonitrile to give the expected esters, which were further treated with twice molar quantity of aniline at room temperature for 30 min to afford phenylacetanilide (II). It was found that 2-fluoro-1,3,5-trinitrobenzene (FTNB, If) was the most reactive polynitrohalobenzene as shown in Table 1.

Next, the utility of FTNB as a new condensing reagent was examined for various carboxylic acids. The following procedure is representative for the preparation of carboxanilides from the corresponding carboxylic acids and aniline with FTNB. To a mixed solution of FTNB (116 mg, 0.5 mmol) and cinnamic acid (74 mg, 0.5 mmol) in acetonitrile (3 ml) was added an acetonitrile solution (1 ml) of triethylamine (55 mg, 0.55 mmol) at room temperature under a nitrogen atmosphere. After 1 hr, a solution of aniline (93 mg, 1 mmol) in acetonitrile (1 ml) was added to the solution

Table 1. The Reaction of Polynitrohalobenzenes with Phenylacetic Acid

$$\underset{\text{Ia-f}}{\text{ArX}} + PhCH_2CO_2H + Et_3N \xrightarrow[\text{in } CH_3CN]{\text{(A)}} \xrightarrow[\text{r.t.,30 min}]{2\ PhNH_2} \underset{\text{II}}{PhCH_2CONHPh} + \underset{\text{IIIa-f}}{\text{ArNHPh}}$$

ArX	Conditions (A)	Isolated yield,[a] %	
		II	III
Ia, 	reflux, 2 hr	—	7[b]
Ib, 	reflux, 2 hr	58	9
Ic, 	reflux, 2 hr	12	58
Id, 	reflux, 2 hr	75	12
Ie, 	r.t., 3 hr	48[c]	52
"	reflux, 2 hr	44[c]	40
If, 	r.t., 2 hr	89	4

a) All compounds exhibited ir and pmr spectral data in accordance with assigned structure.

b) 70% of Ia was recovered.

c) See ref. 6 for details of the reaction.

and the reaction mixture was stirred for an additional 1 hr at room temperature. The solution was evaporated under reduced pressure, and the residue was partitioned between ethyl acetate and saturated solution of $NaHCO_3$. The organic layer was further washed with 1 M HCl and saturated solution of NaCl, dried over Na_2SO_4, filtered, and evaporated to dryness under reduced pressure. The desired product, cinnamanilide, was separated from the residue by preparative tlc in a nearly quantitative yield (112 mg, mp 151-2°C).

In a similar manner, various carboxanilides were prepared in excellent yields from the corresponding carboxylic acids and aniline with FTNB as listed in Table 2.

Cinnamoyl fluoride (VI)[1] was isolated from the reaction mixture of FTNB with cinnamic acid and triethylamine by sublimation in 68 % yield. From the fact, it was inferred that the active intermediate for the formation of cinnamanilide was not 2,4,6-trinitrophenyl cinnamate, but cinnamoyl fluoride as shown in the following scheme. In contrast, it was found that the reaction of 1-fluoro-2,4-dinitrobenzene (FDNB, Id) with phenylacetic acid and triethylamine gave 2,4-dinitrophenyl phenylacetate (VIII)[2] in 71 % yield by refluxing for 2 hr in acetonitrile.[3,4] The difference between the results may be attributed to the anion stability ($1,3,5\text{-}(O_2N)_3C_6H_2O^{\ominus} > F^{\ominus} > 2,4\text{-}(O_2N)_2C_6H_3O^{\ominus}$)[5] of leaving group from anionic sigma complex (V or VII) formed *via* an aro-

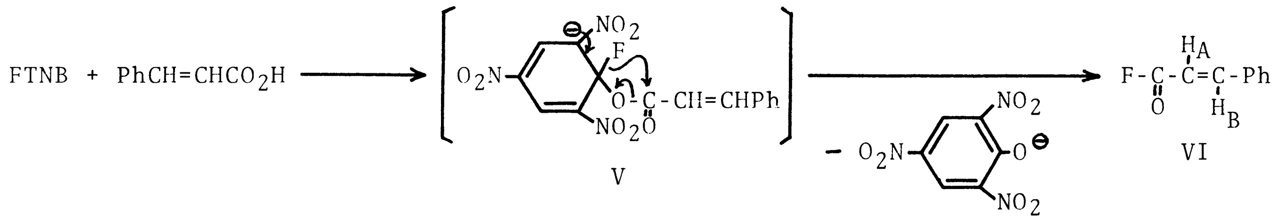
Table 2. Preparation of Carboxanilides from Carboxylic Acids and Aniline with FTNB

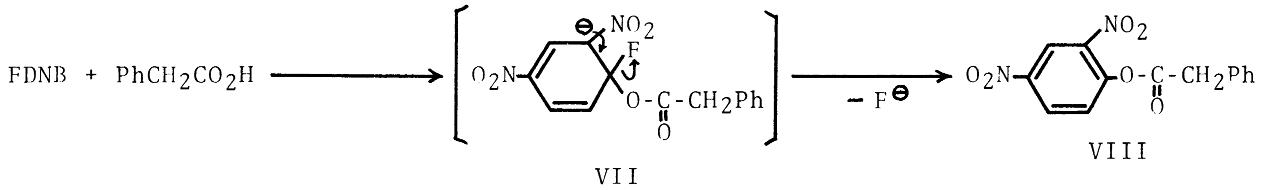
$$\text{FTNB} + \text{RCO}_2\text{H} + \text{Et}_3\text{N} \xrightarrow[\text{in CH}_3\text{CN}]{\text{r.t., 1 hr}} \xrightarrow[\text{r.t., (B)}]{2\ \text{PhNH}_2} \underset{\text{IV}}{\text{RCONHPh}}$$

RCO_2H	Time (B)	Isolated yield, % IV	Mp[a] °C
$PhCH{=}CHCO_2H$	1 hr	quant.	151-2
$PhCO_2H$	"	93	161-2
$PhCH_2CO_2H$	"	88	116-7
Z-Gly-OH	"	87	143-4
CH_3CO_2H	1.5 hr	82	111-3
$(CH_3)_2CHCO_2H$	2.5 hr	96	103-5
$(CH_3)_3CCO_2H$	2 days	93	128-31

a) Mp of crude samples. They were in accordance with the values cited in the literatures.

matic nucleophilic addition mechanism.





REFERENCES AND NOTES

1) VI: mp 30°C (lit.[7] 31-31.5°C), ir 1782, 1615, 1182, 1092 cm^{-1}; pmr ($CDCl_3$) δ 6.32 (H_A, d·d, J_{HH}=16.2 Hz, J_{HF}=7.2 Hz), 7.44 (Ph, m), 7.82 (H_B, d, J_{HH}=16.2 Hz).

2) VIII: yellow oil, ir 1775, 1600, 1530, 1342, 1205, 1085 cm^{-1}. The structure was further confirmed by direct comparison with an authentic sample prepared from phenylacetic acid and 2,4-dinitrophenol using DCC.

3) Wittmann reported that the reaction of phosphoric acid monoester with FDNB gave monofluorophosphoric acid monoester; see Chem. Ber., 96, 771 (1963).

4) This result is different from the observation reported by other group. They noted that acyl fluorides were detected by the ir spectroscopic measurement in the same reaction mixture as present one; see T. Mukaiyama and T. Tanaka, Chem. Lett., 1976, 303.

5) The value of pKa at 25°C is as follows: 2,4,6-trinitrophenol 0.708, HF 3.173, 2,4-dinitrophenol 4.110.

6) Acid anhydride was detected by the ir spectroscopic measurement (1812, 1740 cm^{-1}, and a very strong, broad band at near 1040 cm^{-1} characteristic of phenylacetic anhydride) in the reaction mixture of phenylacetic acid with 2-chloro-1,3,5-trinitrobenzene (Ie) in the presence of triethylamine.

7) F. Seel and J. Langer, Chem. Ber., 91, 2553 (1958); Chem. Abstr., 53, 7976b (1959).

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