

This article was downloaded by:

On: 27 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



## Organic Preparations and Procedures International

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t902189982>

### SYNTHESES OF 2-CHLORO-4,5-DIFLUOROBENZOIC ACID

Zhibin Li<sup>a</sup>; Naihua Huang<sup>a</sup>

<sup>a</sup> Department 1XV, an Modern Chemistry Research Institute, Shaanxi, PR CHINA

**To cite this Article** Li, Zhibin and Huang, Naihua(1996) 'SYNTHESES OF 2-CHLORO-4,5-DIFLUOROBENZOIC ACID', *Organic Preparations and Procedures International*, 28: 2, 245 – 246

**To link to this Article:** DOI: 10.1080/00304949609356532

**URL:** <http://dx.doi.org/10.1080/00304949609356532>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

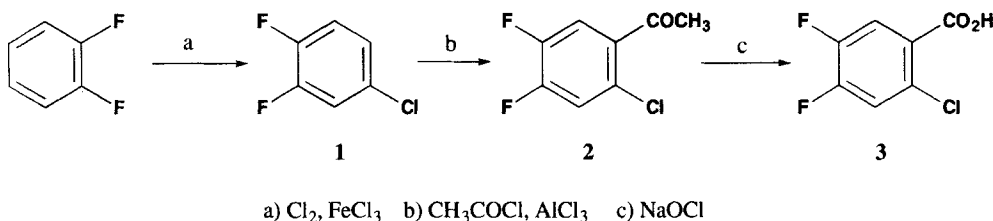
## SYNTHESES OF 2-CHLORO-4,5-DIFLUOROBENZOIC ACID

Submitted by Zhibin Li \* and Naihua Huang  
(09/22/95)

Department 1  
Xi'an Modern Chemistry Research Institute  
Xi'an, Shaanxi 710061, P. R. CHINA

2-Chloro-4,5-difluorobenzoic acid (**3**) is an important intermediate of medicinal products and pesticides. It can be synthesized from dichlorophthalic anhydride,<sup>1</sup> 1,4-dichloro-2-nitrobenzene,<sup>2</sup> dichlorofluorobenzonitrile,<sup>3</sup> 4,5-difluorophthalic acid<sup>4</sup> and 2,4-dichlorofluorobenzene.<sup>5</sup> However, all these methods are either laborious or use expensive reagents. We now report an efficient synthesis of **3** from *o*-difluorobenzene, which is commercially available or which may be easily synthesized from 2-nitrochlorobenzene by halogen-fluorine exchange<sup>6</sup> and by the Balz-Schiemann reaction<sup>7</sup> to introduce the fluorine atoms.

Chlorination of *o*-difluorobenzene in the presence of FeCl<sub>3</sub> and Cl<sub>2</sub> provided 3,4-difluorochlorobenzene (**1**) in 90% yield. Friedel-Crafts acylation of **1** with acetyl chloride in the presence of aluminum chloride provided the compound **2** (75%), which upon oxidation with NaOCl provided 2-chloro-4,5-difluorobenzoic acid (**3**) in 80% yield.



## EXPERIMENTAL SECTION

Mps reported are uncorrected. <sup>1</sup>H NMR spectra were recorded in CDCl<sub>3</sub> containing TMS as internal reference (chemical shifts in δ, ppm). Microanalyses were performed by our Analytical Department.

**3,4-Difluorochlorobenzene (1).**- Through a mixture of *o*-difluorobenzene (114g, 1.0 mol) and FeCl<sub>3</sub> (2.0g, 12 mmol) was bubbled chlorine gas (56.8g, 0.8 mol) at 50° over 3 hrs; the mixture was washed with water (3 x 200 mL) and dried over MgSO<sub>4</sub>, and then distilled through a 15 cm column of glass beads to give 134g (90%) of a colorless oil, bp. 118-120°, lit.<sup>2</sup> bp. 118-120°. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.14 (m, 1H), 7.07 (m, 2H).

**2-Chloro-4,5-difluoroacetophenone (2).**- 3,4-Difluorochlorobenzene (149g, 1.0 mol) and aluminum chloride (267g, 2.0 mol) and acetyl chloride (109g, 1.4mol) were mixed and heated to 60° for 9 hrs. The reaction mixture was cooled and quenched with 800g ice and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 200 mL). The combined organic layers were steam-distilled to give an oily product, which was distilled

through a 15 cm column of glass beads to give 143.2g (75%) of a colorless oil, bp. 65-67°/5mmHg, lit.<sup>5</sup> bp. 65-67°/4-5mmHg. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.74 (m, 1H), 7.02 (m, 1H), 2.61 (d, 3H).

**2-Chloro-4,5-difluorobenzoic Acid (3).**- 2-Chloro-4,5-difluoroacetophenone (95.9g, 0.5mol) and 3.5 L of 5% NaOCl were heated to reflux for 6 hrs. The mixture was cooled and its pH was adjusted to 1 with conc. HCl, and then extracted with 800 mL of CH<sub>2</sub>Cl<sub>2</sub> and the extract was dried over MgSO<sub>4</sub>. Evaporation of the solvent provided 89.7g (93%) of a crude product, which was recrystallized from cyclohexane-water (1:1 v:v) to give 77.2g (80%) of a white solid, mp. 86-88°, lit.<sup>8</sup> mp. 87-89°. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.87 (m, 1H), 7.01 (m, 1H).

*Anal.* Calcd for C<sub>7</sub>H<sub>3</sub>F<sub>2</sub>ClO<sub>2</sub>: C, 43.64; H, 1.56; Cl, 18.44; F, 19.74

Found: C, 43.54; H, 1.54; Cl, 18.56; F, 19.70

### REFERENCES

1. M. J. FifoIt and A. M. Foster, *US Patent* 4,374,266; *Chem. Abs.*, **97**, 197986h (1982).
2. T. F. Braish and D. E. Fox, *Org. Prep. Proced. Int.*, **23**, 655 (1991).
3. W. Didier, *Eur. Pat. Appl.*, 433,124 (1991); *Chem. Abs.*, **115**, 11417a (1991).
4. L. B. Fertel, *US Patent* 5,003,103; *Chem Abs.*, **115**, 71134 (1991).
5. K. Seisaku, *Eur. Pat. Appl.*, 431,373 (1991); *Chem. Abs.*, **115**, 207663g (1991).
6. Dainippon Ink, *Japan Kokai* 57 197,226; *Chem. Abs.*, **98**, 160397m (1983).
7. Ostuka Pharmaceutical Co. Ltd., *Japan Kokai* 59 67232; *Chem. Abs.*, **101**, 54688c (1986).
8. K. Seisaku, *Eur. Pat. Appl.*, 303,291 (1989); *Chem. Abs.*, **111**, 77647j (1989).