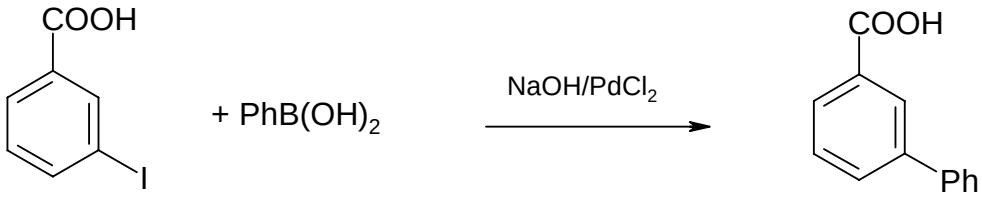
3018 Synthesis of 3-phenylbenzoic acid from 3-iodobenzoic acid



$C_7H_5IO_2$	$C_6H_7BO_2$	NaOH	$PdCl_2$	$C_{13}H_{10}O_2$
(248.0)	(121.9)	(40.0)	(177.3)	(198.2)

Literature

N. A. Bumagin, V. Bykov, *Tetrahedron* **1997**, *53*, 14437-14450.

Classification

Reaction types and substance classes

Suzuki reaction

arylboronic acid, iodoaromatics, aromatics, transition metal catalyst

Work methods

working with protective gas, stirring with magnetic stir bar, shaking out, extracting, filtering, evaporating with rotary evaporator

Instruction (batch scale 2 mmol)

Equipment

50 mL two-neck flask, protective gas supply, adapter (with ground glass joint, ground-in stopcock and hose coupling), bubble counter, separating funnel, glass frit (porosity 2), suction flask, rotary evaporator, magnetic stirrer, magnetic stir bar

Substances

3-iodobenzoic acid (mp 186-188 °C)	496 mg (2.00 mmol)
benzeneboronic acid (mp 217-220 °C)	268 mg (2.20 mmol)
NaOH	320 mg (8.00 mmol)
palladium(II) chloride	3.55 mg (0.020 mmol)
water	108 mL
hydrochloric acid (conc.)	some drops
tert-butyl methyl ether (bp 55 °C)	30 mL
silica gel 60 (0.063-0.200 mm)	
sodium sulfate for drying	

Reaction

The reaction apparatus consists of a 50 mL two-neck flask with a magnetic stir bar, a bubble counter, and an adapter with ground glass joint, ground-in stopcock and hose coupling connected to a nitrogen piping. The reaction flask is filled with a solution of 320 mg (8.00 mmol) sodium hydroxide in 8 mL water. Under stirring at room temperature and under nitrogen atmosphere 496 mg (2.00 mmol) 3-iodobenzoic acid are added and then to this solution 268 mg (2.20 mmol) benzeneboronic acid and 3.54 mg (0.020 mmol) palladium(II) chloride. The mixture is stirred for further ten minutes.

Work up

The reaction mixture is filtered over a glass frit or a folded filter. The filtrate is diluted with 100 mL water and acidified with some drops of conc. hydrochloric acid. The precipitating solid is filtered and dissolved in about 30 mL *tert*-butyl methyl ether. The ether solution is filtered over silica gel, washed with water in a separating funnel and dried over sodium sulfate. After filtering of the drying agent the solvent is evaporated at a rotary evaporator. The crystalline product remains as residue.

Yield: 353 mg (1.78 mmol, 89%); colourless residue, mp 166 °C (purity see analytics)

Waste management

Recycling

The evaporated *tert*-butyl methyl ether is collected and redistilled.

Waste disposal

Waste	Disposal
aqueous phases	neutralizing, then: solvent water mixtures, containing halogen, containing heavy metals
sodium sulfate	solid waste, free from mercury
silica gel	solid waste, free from mercury

Time

1 hour

Break

After precipitating of 3-phenylbenzoic acid

Degree od difficulty

Easy

Instruction (batch scale 10 mmol)

Equipment

100 mL two-neck flask, protective gas supply, adapter (with ground glass joint, ground-in stopcock and hose coupling), bubble counter, separating funnel, glass frit (porosity 2), suction flask, rotary evaporator, magnetic stirrer, magnetic stir bar

Substances

3-iodobenzoic acid (mp 186-188 °C)	2.48 g (10.0 mmol)
benzeneboronic acid (mp 217-220 °C)	1.34 g (11.0 mmol)
NaOH	1.60 g (40.0 mmol)
palladium(II) chloride	17.7 mg (0.100 mmol)
water	290 mL
hydrochloric acid (conc.)	some drops
tert-butyl methyl ether (bp 55 °C)	100 mL
silica gel 60 (0.063-0.200 mm)	
sodium sulfate for drying	

Reaction

The reaction apparatus consists of a 100 mL two-neck flask with a magnetic stir bar, a bubble counter and an adapter with ground glass joint, ground-in stopcock and hose coupling connected to a nitrogen piping. The reaction flask is filled with a solution of 1.60 g (40.0 mmol) sodium hydroxide in 40 mL water. Under stirring at room temperature and under nitrogen atmosphere 2.48 g (10.0 mmol) 3-iodobenzoic acid are added and to this solution 1.34 g (11.0 mmol) benzeneboronic acid and 17.7 mg (0.100 mmol) palladium chloride. The mixture is stirred for further 10 minutes.

Work up

The reaction mixture is filtered over a glass frit or a folded filter. The filtrate is diluted with 250 mL water and acidified with conc. hydrochloric acid. The precipitating solid is filtered and dissolved in about 100 mL *tert*-butyl methyl ether. The ether solution is filtered over silica gel, washed with water in a separating funnel and dried over sodium sulfate. After filtering of the drying agent the solvent is evaporated at a rotary evaporater. The crystalline product remains as residue.
Yield: 1.73 g (8.72 mmol, 87%); colourless solid, mp 166 °C (purity see analytics)

Waste management

Recycling

The evaporated *tert*-butyl methyl ether is collected and redistilled.

Waste disposal

Waste	Disposal
aqueous phases	neutralizing, then: solvent water mixtures, containing halogen, containing heavy metals
sodium sulfate	solid waste, free from mercury
silica gel	solid waste, free from mercury

Time
1 hour

Break
After precipitating of 3-phenylbenzoic acid

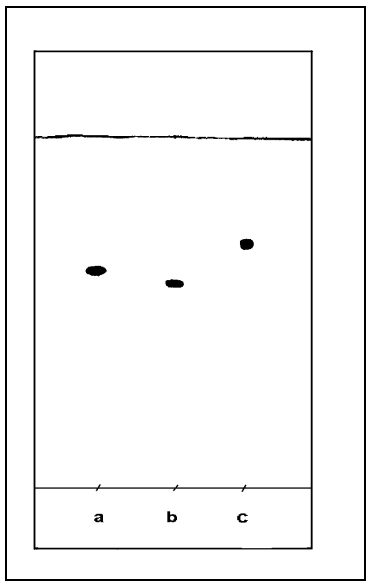
Degree od difficulty
Easy

Analytics

TLC

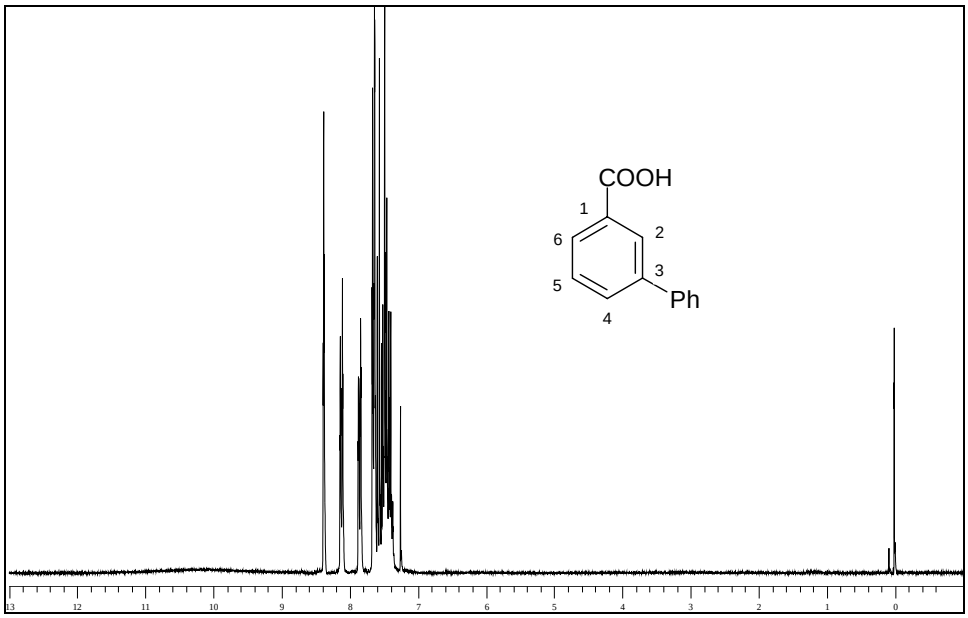
TLC- conditions:
adsorbant: Merck silica gel 60 F_{254}, 5 x 10 cm
eluent: ethanol

R_f (3-phenylbenzoic acid) 0.61
R_f (3-iodobenzoic acid) 0.58
R_f (benzeneboronic acid) 0.69



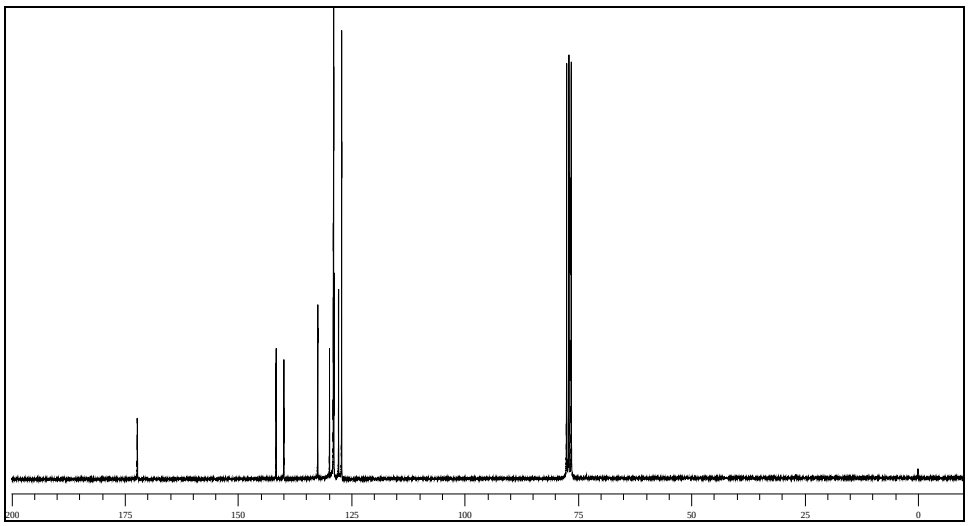
a) 3-phenylbenzoic acid (product)
b) 3-iodobenzoic acid (educt)
c) benzeneboronic acid (educt)

^{1}H NMR spectrum of the product (250 MHz, $CDCl_3$)



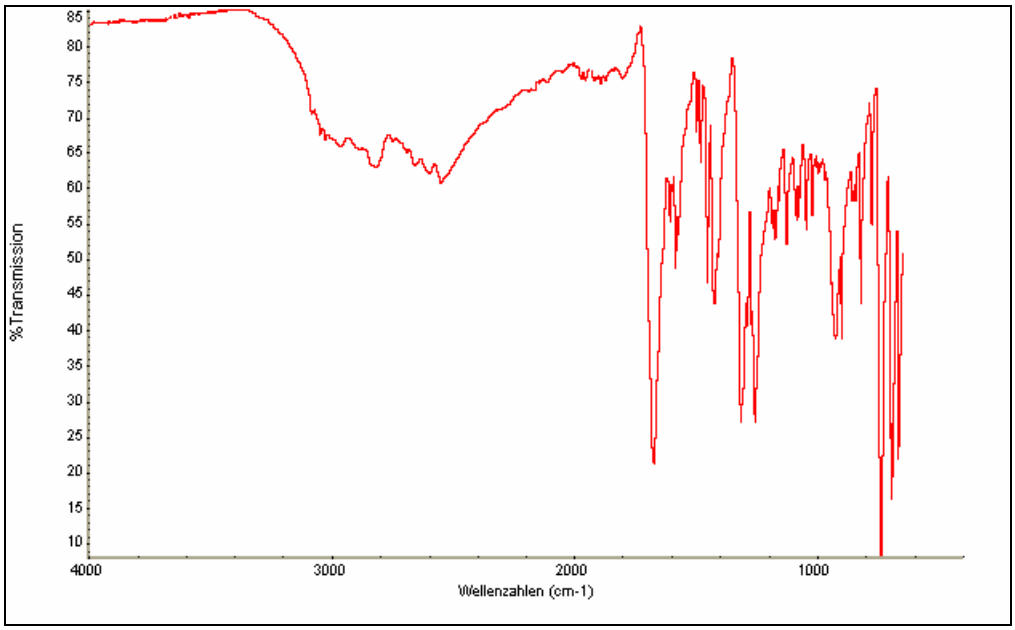
δ (ppm)	Multiplicity	Number of H	Assignment
7.34-7.69	m	6	phenyl-H + 5-H
7.86	m (d)	1	4-H
8.12	m (d)	1	6-H
8.38	m (s)	1	2-H
10.20	bs	1	COOH
7.26			solvent

^{13}C NMR spectrum of the product (62.5 MHz, $CDCl_3$)



δ = 127.16, 127.83, 128.85, 128.92, 128.95, 128.98, 129.82, 132.42, 139.91, 141.62, 172.22 (COOH), 76.5-77.5 (solvent)

IR spectrum of the product (ATR)



(cm^{-1})	**Assignment**
2500-3300	O-H-valence, carboxylic acid, superimposed by C-H-valence
1675	C=O-valence, carboxylic acid
1584	C=C-valence, arene