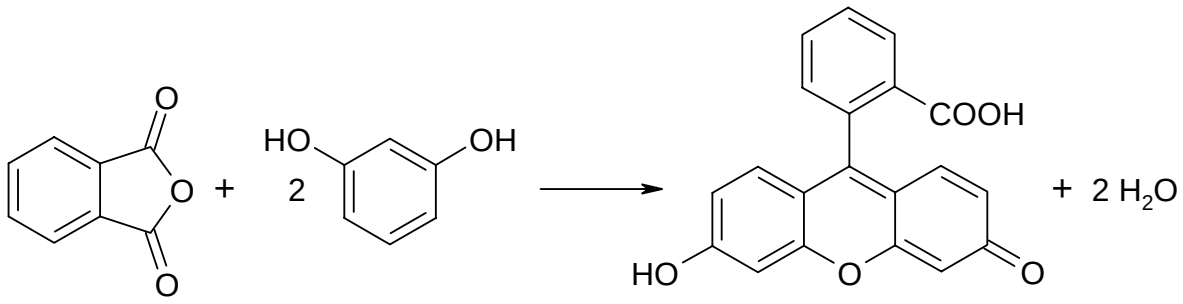
5007 Reaction of phthalic anhydride with resorcin to fluorescein



$C_8H_4O_3$ (148.1) $C_6H_6O_2$ (110.1) $C_{20}H_{12}O_5$ (332.3)

Classification

Reaction types and substance classes

reaction of the carbonyl group in carboxylic acid derivatives, electrophilic substitution of aromatics, Friedel-Crafts acylation, ring closure reaction
carboxylic acid anhydride, phenol, dye

Work methods

microwave-assisted reaction, stirring with magnetic stir bar, heating under reflux, adding dropwise with an addition funnel, filtering, extracting

Instruction (batch scale 50 mmol)

Equipment

Microwave system ETHOS 1600, 100 mL two-neck flask, magnetic stirrer, magnetic stir bar, glass tube (40 cm, NS 29), 1 L beaker, addition funnel, suction flask, Buechner funnel (diameter 8-10 cm), 250 mL two-neck flask, reflux condenser, desiccator

Substances

phthalic anhydride (mp 129-132 °C)	7.77 g (52.5 mmol)
resorcin (mp 109-111 °C)	11.0 g (100 mmol)
conc. hydrochloric acid	50 mL
sodium hydroxide	8.00 g (200 mmol)
phosphorus(V)-oxide for drying	5 g

Reaction

7.77 g (52.5 mmol) phthalic anhydride and 11.0 g (100 mmol) resorcin are filled in a 100 mL two-neck flask with magnetic stir bar and six drops water are added. The reaction flask is equipped with an electronic temperature control and installed by means of the glass tube in the microwave (see "Technical instructions: Standard refluxing-apparatus for microwave

systems "). The mixture is treated whilst stirring for 40 minutes with 900 W at a target temperature of 220 °C. First the reaction mixture is viscous, at the end of the reaction time completely solid.

Work up

Initially, the crude product solidified in the reaction flask is purified by transferring it with an aqueous sodium hydroxide solution into the water-soluble disodium salt and afterwards precipitating the product with hydrochloric acid.

For this procedure a sodium hydroxide solution is prepared by dissolving 8.00 g (200 mmol) sodium hydroxide in 80 mL of water. 40 mL conc. hydrochloric acid are filled in a 1 L beaker with magnetic stir bar, containing 200 mL water. An addition funnel is installed over the beaker.

Now, 20 mL from the sodium hydroxide solution are filled in the reaction flask with the solidified crude product and stirred for 10 minutes (if the magnetic stir bar is stucked in the melt, a second one is put into the flask). Then 30 mL water is added in the reaction flask and stirred for further 5 minutes. The resulting deep-red solution is decanted from the still existing solid into the addition funnel and added dropwise slowly (1 to 2 drops per second) to the strongly stirred hydrchloric acid in the beaker. The product precipitates as an orange-red solid.

During the addition time, one adds a further portion of 20 mL sodium hydroxide solution in the reaction flask with the remaining crude product, stirs it like before for 10 minutes, adds 30 mL water, stirs it for further 5 minutes, then decants the red solution into the addition funnel and adds these dropwise in the beaker with the hydrochloric acid like previously done. This procedure is repeated twice until the entire sodium hydroxide solution is used up.

The content of the beaker is cooled down to room temperature and the precipitation is sucked off over a Buechner funnel. (If the filter paper is blocked through the fine crystals, one can filter through a folded filter).

For further purification, the still humid product is filled together with 100 mL of water and 10 mL of conc. hydrochloric acid in a 250 mL two-neck flask, which is equipped with magnetic stir bar, electronic temperature control, glass tube and reflux condenser and is installed as before in the microwave system. The mixture is heated under reflux for 10 minutes in the microwave with 800 W and at a target temperature of 103 °C. After cooling down to room temperature, it is sucked off again over a Buechner funnel. The product is washed on the Buechner funnel with several portions of water (total volume 300 mL), dry-sucked and dried in the desiccator over phosphorus(V)-oxid at reduced pressure until mass constancy.

Yield: 16.2 g, 48.8 mmol, 98 %); mp 320-325 °C, literature: 316-320 °C. the colour of the product is according to grain size of the crystals russet-red (coarse crystals) or orange-red (fine crystals).

Comments

The water added at the beginning facilitates the launching of microwave energy in the reaction mixture until melting. Rubbing in of the educts before the reaction is not necessary since they melted completely in the microwave within one minute under stirring.

The purification process with hot diluted hydrochloric acid serves to separate water-soluble impurities, for example not reacted educts, from the sparingly water soluble product. Through the previous dissolving and precipitating of the crude product with base and acid, one receives a very fine-grained substance, better suitable for the subsequent extracting than the crude product only shreded in the mortar.

The reaction can be easily carried out with batch scales up to 1 mol.

Waste management

Waste Disposal

Waste	Disposal
aqueous filtrates	neutralize, then: solvent water mixtures, containing halogen

Time

About 4 hours (without the time for drying)

Break

Before work up

Before extraction in the microwave

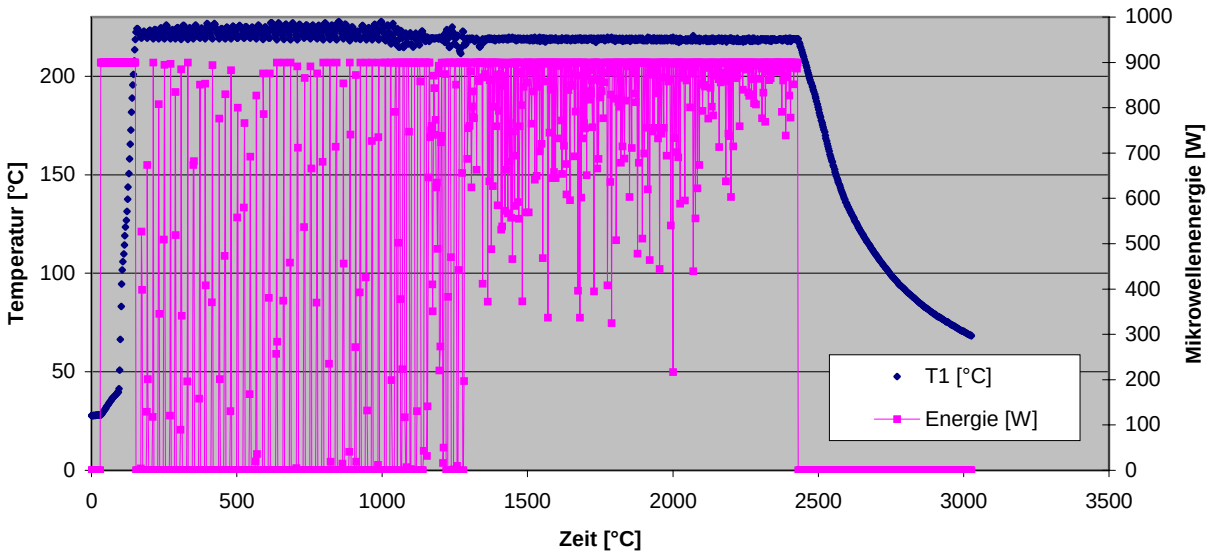
Degree of difficulty

Easy

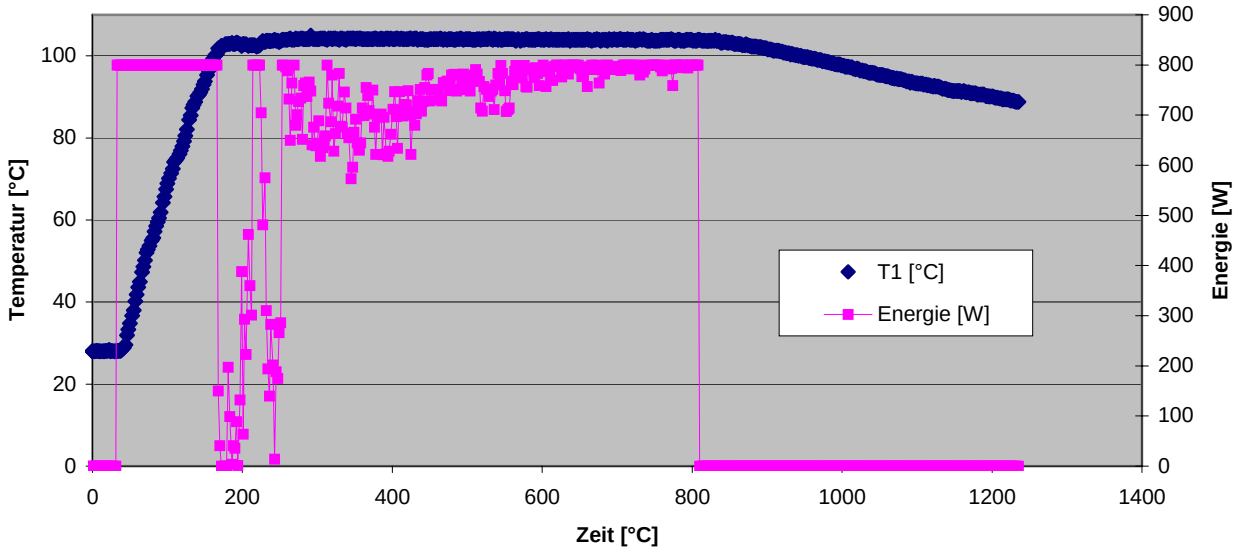
Analytics

Temperature-time-dependence of the reaction steps in the microwave

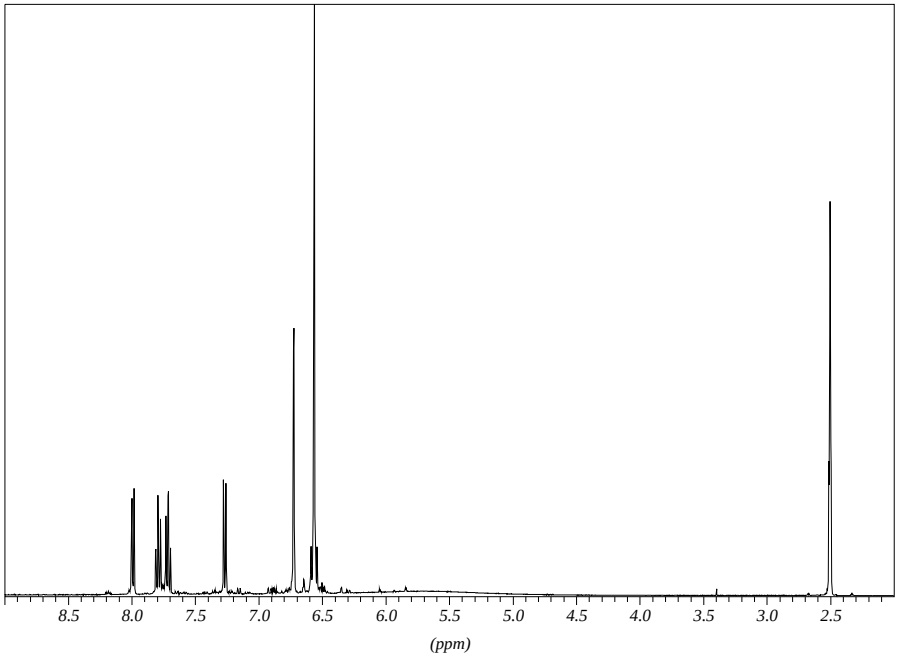
Reaction of phthalic anhydride with resorcin to fluorescein

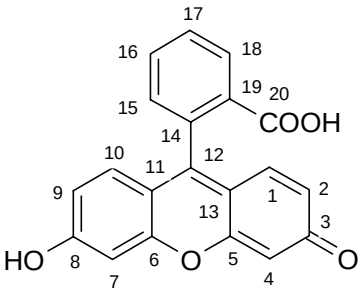


Extraction of the crude product



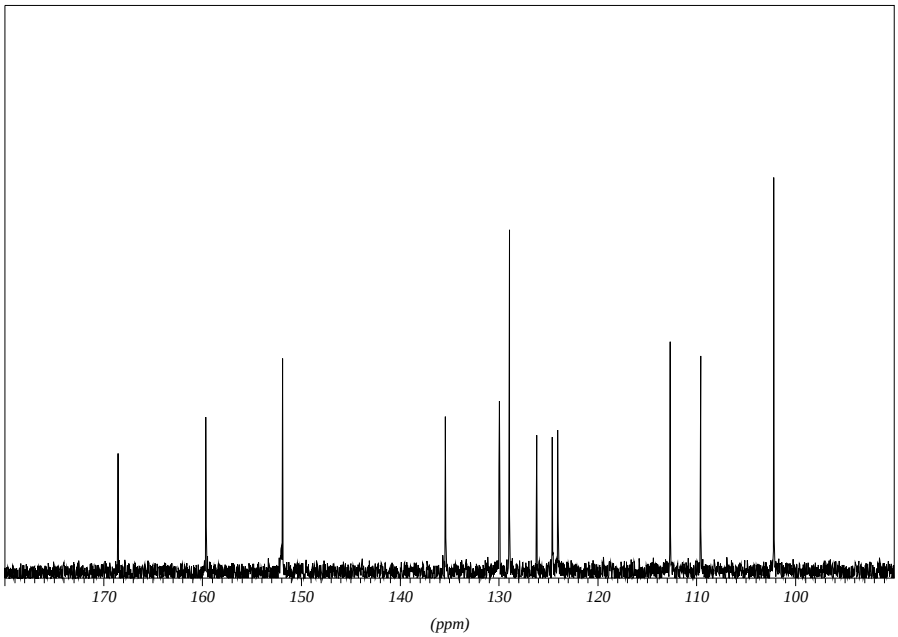
^{1}H NMR spectrum of the product fluorescein (400 MHz, DMSO-D_6)



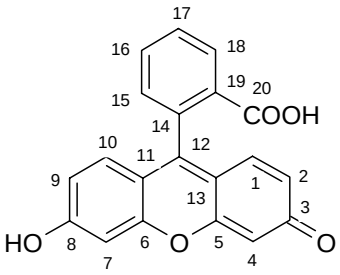


δ (ppm)	Multiplicity	Number of H	Assignment
7.99	d	1	18-H
7.79	dt	1	16-H
7.71	dt	1	17-H
7.26	d	1	15-H
6,72	m	2	4-H, 7-H
6.57	m	4	1-H, 2-H, 9-H, 10-H
2.53			solvent

^{13}C NMR spectrum of the product fluorescein (400 MHz, DMSO- D_6)



δ (ppm)	Assignment
168.52	C-20
159.62	C-3, C-8
151.85	C-5, C-6, C-14
135.38	C-16
129.93	C-17
128.91	C-1, C-10
126.14	C-19
124.56	C-18
124.00	C-15
112.65	C-2, C-9
109.56	C-11, C-13
103.15	C-4, C-7
39.5	solvent



IR spectrum of the product fluorescein (KBr)