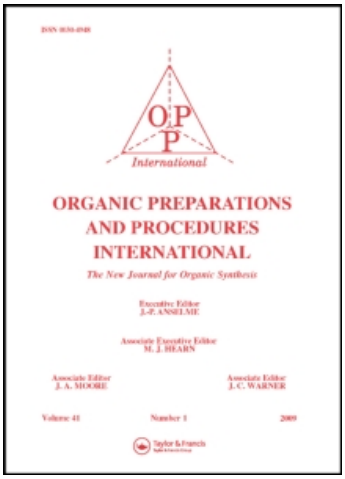

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ESTERIFICATION BY MICROWAVE IRRADIATION ON ACTIVATED CARBON

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5. B. Illesca, N. Martin, C. Seoane, P. Cruz, F. Langa, F. Wudl, *ibid.*, **36**, 8307 (1995).

6. D. Bogdal, J. Pielichowski and K. Jaskot, *Syth. Commun.*, **27**, 1553 (1997).

7. R. A. Abramovitch, Q. Shi and D. Bogdal, *Syth. Commun.*, **25**, 1 (1995).

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ESTERIFICATION BY MICROWAVE IRRADIATION ON ACTIVATED CARBON

Submitted by (06/24/99)

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The most common method for the preparation of esters is the esterification of carboxylic acids generally catalyzed by acids, the equilibrium being shifted to products by azeotropic removal of water. Some of the acids such as H_2SO_4 or *p*-toluenesulfonic acid are strong corrosives, and large amounts of organic solvents and long reaction time must be used. This method also leads to environment problems. Although solid acid catalysts constitute an improvement, their use also requires several hours to complete the reaction.[1]

The application of microwave in organic synthesis has been sparked by the pioneering work of Gedye and Majetich and their co-workers in 1986.[2] Recent reports have demonstrated that organic reactions may be conducted safely in microwave ovens with remarkable rate enhancements and dramatic reductions of reaction times compared to conventional heating.[3] Among these studies, solvent-free conditions have been receiving increasing interest as they have the advantage of avoiding the use of solvent and being more benign to the environment.[4]

The influence of microwave irradiation on the rate of esterification under solvent-free condition has also been studied.[5] Good results were obtained in the esterification of carboxylic acids or of carboxylate ions with halohydrocarbons with the use of montmorillonite catalysts.[6] But in the esterification of carboxylic acids with alcohols which is generally used in industry, the use of inorganic solid supports such as silica gel (SiO_2), alumina (Al_2O_3), montmorillonite under solvent-free reactions proved to have low efficiency of transforming electromagnetic energy into thermal energy,[7] and gave lower yields. Loupy and co-workers have stated that the solid acids lose their efficiency when impregnated on solid supports.[8]

We now report that the use of activated carbon which has better ability of absorbing the energy from microwave irradiation as support for the esterification of carboxylic acids with alcohol or anhydride led to complete reactions rapidly under solvent-free conditions and in high yields. It is possible that the reactive polar molecules absorb microwaves selectively enhancing the reaction rapidly. In the conventional method, the whole reaction system has to be heated before the reaction may take place. By comparison of the temperature variation of the different supported type catalysts, activated carbon supported catalyst was found to be the fastest, reaching high temperatures in the shortest time. Using activated carbon as support, the ideal reaction temperature can be reached in few seconds and can initiate the reaction rapidly, similar to "hot spots" in sono-chemistry. In other words, under microwave irradiation activated carbon as *p*-toluenesulfonic carrier can generate more "hot spots" than other inorganic carriers and the efficiency of solid acids catalyst was greatly improved.

EXPERIMENTAL SECTION

IR spectra were measured for KBr discs using an Nicolet FT-IR spectrophotometer. The element analysis was determined by Carlo-Erba 1106 element analyzer. Microwave irradiation is carried out with a commercial microwave oven Galanz WP750B at 2450MHz. An approximate temperature measurement was performed by introducing a digtal thermometer to the sample at the end of each irradiation. Gas chromatographic analysis were performed on SC-7 capillary apparatus fitted with a capillary FFAP (16m) column under a pressure of 0.5 Bar using nitrogen as carrier gas.

Catalyst Preparation.- Activated carbon (10 g) was dried at 110° for 3 hours. After cooling, 5 g of the activated carbon was stirred in a 20 mL 25% PTSA aqueous solution for 30 hours at room temperature. This solid was then collected by suction and dried at 120° for 5 hours. This type of catalyst may be stored in desiccator at room temperature for at least one week without loss of activity. Activity may be regenerated by heating at 120° for 5 hours if the catalyst loses its activity. The activity of the catalyst could be determined by the yield of the same esterification reaction.

Table 1. Esterification under Microwave Irradiation

R	R'	Acid/alcohol (mmol/mmol)	Power (Time)	Yield (%)	Element Anal. Cald.(Found) C	H
Methyl	$PhCH_2$	2.5/5.0	675w(12sec.)	83	71.98(71.95)	6.71(6.70)
Ethyl	$PhCH_2$	2.5/5.0	675w(25sec.)	87	73.15(73.15)	7.37(7.39)
n-Propyl	$PhCH_2$	2.5/5.0	675w(20sec.)	92	74.13(74.16)	7.92(7.89)
n- Butyl	$PhCH_2$	2.5/5.0	675w(28sec.)	96	74.97(74.95)	8.39(8.41)
n-Pentyl	$PhCH_2$	2.5/5.0	675w(28sec.)	92	75.69(75.71)	8.79(8.76)
n-Heptyl	$PhCH_2$	2.5/5.0	675w(28sec.)	90	76.88(76.91)	9.46(9.47)
Ph	$PhCH_2$	2.5/5.0	675w(35sec.)	89	79.23(79.20)	5.70(5.67)
Ph	*n*-Butyl	1.0/3.0	600w(35sec.)	92	74.13(74.11)	7.92(7.95)
Ph	*n*-Pentyl	1.0/3.0	600w(35sec.)	94	74.97(75.00)	8.39(8.37)
Ph	*n*-Hexyl	1.0/3.0	600w(35sec.)	95	75.69(75.71)	8.79(8.80)

Table 1. Continued...

R	R'	Acid/alcohol (mmol/mmol)	Power (Time)	Yield (%)	Element Anal. Cald.(Found) C	H
PTH[a]	$PhCH_2$	1.0/4.0	525w(55sec.)	80	76.29(76.27)	5.24(5.22)
PTH	*n*-Butyl	1.0/4.0	525w(55sec.)	75	69.04(69.01)	7.97(8.01)
PTH	*n*-Pentyl	1.0/4.0	525w(55sec.)	74	70.56(70.56)	8.55(8.54)
PTH	*n*-Hexyl	1.0/4.0	525w(55sec.)	71	71.82(71.85)	9.04(9.00)
PTH	*n*-Octyl	1.0/4.0	525w(55sec.)	89	73.81(73.79)	9.81(9.84)
PTH	*i*-Octyl	1.0/4.0	525w(55sec.)	92	73.81(73.85)	9.81(9.78)
PTH	*n*-Decyl	1.0/4.0	525w(55sec.)	90	74.61(74.58)	10.67(10.64)
$(CH_2)_4CO_2H$	*n*-Pentyl	1.0/5.0	525w(55sec.)	93[b]	67.10(67.08)	10.56(10.53)
$(CH_2)_4CO_2H$	*n*-Hexyl	1.0/5.0	600w(40sec.)	92[b]	68.75(68.71)	10.90(10.87)
$(CH_2)_4CO_2H$	*n*-Octyl	1.0/5.0	600w(40sec.)	90[b]	71.31(71.26)	11.42(11.46)
$(CH_2)_4CO_2H$	*i*-Octyl	1.0/5.0	600w(40sec.)	91[b]	71.31(71.28)	11.42(11.47)

a) PTH= phthalic anhydride, the product is diester. b) The product is diester.

Esterification. General Procedure.- The catalyst (0.5 g) was mixed together with carboxylic acid and alcohol in the proportions indicated in the Table 1 and irradiated in a domestic microwave oven. The reaction mixture was extracted thoroughly with ether and filtered. The filtrate was washed with 5% $NaHCO_3$ (aq) and then with water, the organic layer was dried over anhydrous Na_2SO_4. The organic solvent was distilled off under vacuum. The remainder was passed through a silica gel column (15cm × 2.0cm o.d.) eluted with benzene (for entry 1~10) or benzene/dichloromethane (6/1) (for entry 11~22). The solvent was removed under vacuum and the residue was distilled. The products were identified by IR and gas chromatography comparison with standard samples.

REFERENCES

1. J. I. Yoshida, J. Hashimoto and N. Kawabata, *Bull. Chem. Soc. Jpn.*, **54**, 309 (1981); A. R. Banks, R. F. Fibiger and T. Jones, *J. Org. Chem.*, **42**, 65 (1977).

2. R. N. Gedye, F. E. Smith, K. C. Westaway, H. Ali, L. Baldisera, L. Laberge and J. Rousell, *Tetrahedron Lett.*, **27**, 279 (1986); R. J. Giguere, T. L. Bray, S. M. Duncan and G. Majetich, *ibid.*, **27**, 4945 (1986).

3. B. Illesca, N. Martin, C. Seoane, P. Cruz, F. Langa and F. Wudl, *ibid.*, **36**, 8307 (1995); B. Herradon, A. Morcuende and S. Valverde, *Synlett*, 55 (1995).

4. D. Villemin and B. Labiad, *Synth. Commun.*, **20**, 3207 (1990); R. Gupta, S. Paul, A. K. Gupta and P. L. Kachroo, *Indian J. Chem.*, **33B**, 888 (1994).

5. A. Loupy, Pigeon, M. Ramdani, C. Yvanaeff, M. Majedoub, B. Labiad and D. Villemin, *Can. J. Chem.*, **71**, 90 (1993).

6. R. A. Abramovitch, *Org. Prep. Proced. Int.*, **23**, 685 (1991); G. Majetich, K. Wheless, *Microwave-Enhanced Chem.*, 455(1997); G. Bond, R. B. Moyes, *Microwave-Enhanced Chem.*, 551(1997).

7. Z. Huang and L. Zu, *Org. Prep. Proced. Int.*, **28**, 122 (1996); D. Villemin and B. Labiad, *Synth. Commun.*, **20**, 3207 (1990).

8. A. Loupy, P. Pigeon and M. Ramdani, *Tetrahedron*, **52**, 6705 (1996).

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SYNTHESIS OF 4-BORONO-2-FLUOROPHENYLALANINE

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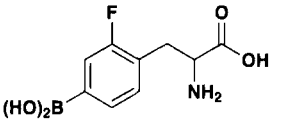
4-Boronophenylalanine (BPA) is one of only two boronated compounds approved for use in the U.S. Phase II Clinical Trials for boron neutron capture therapy.[1] This therapy is dependent on the interaction of boron-10 atoms with low energy (thermal) neutrons to generate cytotoxic alpha particles.[2] In an effort to determine the distribution of BPA *in vivo* utilizing both MRI[3] and positron emission tomography (PET),[4,5] 4-borono-2- fluorophenylalanine (**1**) was prepared. In MRI applications, **1**



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can be detected *in vivo* through the use of multinuclear, fluorine-19 MRI. Its primary role in PET studies is to serve in preliminary biodistribution studies in which tissue samples obtained at the time of tumor biopsy are analyzed for both fluorine and boron content. This data can then used to validate the fluorine-18 labeled BPA *in vivo* studies.[4,5] We now report the details of our synthesis of **1** starting from 4-bromo-2-fluorotoluene (**2**) (*Scheme 1*).

4-Bromo-2-fluorotoluene (**2**) was converted to the corresponding boronic acid **3** in 91% yield. Boronic acid **3** was then brominated using molecular bromine to form benzyl bromide **4** which was added directly to the sodium salt of diethyl acetamidomalonate to form **5** in 68% yield. The desired product, **1**, was formed in 55% yield from **5** via a one step hydrolysis/decarboxylation sequence.