

BENZOYLATION OF ARENES USING ENVIROCAT EPZG® CATALYST AND MICROWAVE IRRADIATION

Eva VEVERKOVÁ¹, Battsengel GOTOV², Róbert MITTERPACH¹ and Štefan TOMA^{3,*}

Department of Organic Chemistry, Faculty of Natural Sciences, Comenius University,
842 15 Bratislava, Slovak Republic; e-mail: ¹organika@fns.uniba.sk, ²gotovyn@fns.uniba.sk,
³toma@uniba.sk

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Dedicated to Professor Otakar Červinka on the occasion of his 75th birthday.

Benzoylations of several benzene, naphthalene and thiophene derivatives with benzoyl chloride or benzoic anhydride, catalyzed with EPZG® catalyst and in the absence of solvents were studied under microwave irradiation (MWI). Reasonable to good yields of products were achieved in short times.

Key words: Acylations; Benzoylations; Clays; Environmental chemistry; Heterogeneous catalysis; Microwave chemistry; Friedl–Crafts acylation.

Friedel–Crafts reactions are very important industrial processes with a considerable environmental drawback, which is caused primarily by using aluminum chloride as catalyst. The final step of the Friedel–Crafts acylation is work-up of the reaction mixture with water resulting in a great amount of waste water. This is the reason for the extensive search for a new, heterogeneous and environment-friendly catalyst. Acid clays with exchangeable cations were found to be very good Friedel–Crafts acylation catalysts^{1–3}. Clay-supported Lewis acids are especially good Friedel–Crafts catalysts^{4,5} and are therefore also commercialized, in spite of long reaction times⁶ (up to 20 h). The effect of structure of Clayzic catalyst on its catalytic activity was thoroughly studied⁷. Rare earth salts supported on clays were described as good Friedel–Crafts alkylation catalysts⁸, and Lewis acids supported on mesoporous silica were also used for the same reactions^{9,10}. Rare earth metal chloride supported on K-10 clay or silica gel are also very good catalysts for Friedel–Crafts acylation of different aromatic compounds, especially their methoxy derivatives¹¹. Even graphite was claimed to be a solid state Friedel–Crafts catalyst in methoxybenzene benzoylation¹², but it was

proved that the real catalysts are the metal, especially iron, impurities in graphite^{13,14}.

The beneficial effect of microwaves on many organic reactions was described¹⁵⁻²⁰, among them also on graphite catalyzed Friedel-Crafts benzoylation^{13,14} as well as different Lewis acids catalyzed Friedel-Crafts benzoylation of methoxyarenes²¹. An interesting microwave accelerated intramolecular Friedel-Crafts acylation catalyzed by K-10 clay was also described²². We decided therefore to examine if the application of microwave irradiation could shorten the reaction time of the Envirocat-catalyzed benzoylations. The second aim of our work was to find out whether isomer ratio of the products formed could be influenced by this unconventional energy source and whether the same catalyst can be reused several times.

EXPERIMENTAL

General

All microwave experiments were carried out in a Milestone Lavis 1000 reactor, power setting 400 W. Milestone Lavis 1000 reactor is a multimode microwave oven, with one magnetron, equipped with reflux condenser and an electromagnetic stirrer. Reactor is operating in a pulse mode (5 s on 5 s off) and power input can be regulated from 10 to 1 000 W. ¹H NMR spectra (300 MHz) were measured on a Varian Gemini 2000 instrument, GC-MS analyses were performed on a HP 5890A Series II gas chromatograph interfaced to HP 5971 A mass-selective detector. Melting points were determined on a Kofler hot-stage instrument and are uncorrected. Envirocat EPZG[®] catalyst⁶ is a ZnCl₂-clay supported catalyst similar to Clayzic. Envirocat EPZG[®] is a free flowing, yellow to green powder, bulk density 0.76 g/cm³, surface area approximately 250 m²/g.

Benzoylation with Benzoyl Chloride (Method A)

A microwave pre-dried EPZG[®] catalyst (0.5 g) was added to a mixture of arene (40 mmol) and benzoyl chloride (2.81 g, 20 mmol) in a 50 ml flask. (The catalyst was pre-dried either by azeotropic distillation with toluene or by exposing for 2 min to MWI at 270 W.) The mixture was then microwave-irradiated for a given time (Tables I and II), the final temperature was measured indicated by the IR thermometer which is in the reactor and checked by inserting a contact thermometer right after reaction was finished. The mixture was then cooled to room temperature. Dichloromethane was added and the catalyst was filtered off. The excess benzoyl chloride was destroyed by extraction with a water solution of triethylamine and the dichloromethane solution was dried over anhydrous sodium sulfate. The solvent was evaporated and the residue was subjected to GC-MS analysis or chromatographed on a silica gel column using hexane-ethyl acetate mixture as eluent.

TABLE I
Benzoylation of arenes with benzoyl chloride using EPZG® catalyst and MWI^a

| Arene | T_{fin} , °C | Yield, % | Isomers ratio ^b , % | | |
|-----------------------------|-----------------------|----------|--------------------------------|---------------|----------------|
| Benzene | 103 | 19 | | | |
| Bromobenzene | 152 | 12 | 13(<i>o</i>) | 4(<i>m</i>) | 83(<i>p</i>) |
| Fluorobenzene | 105 | 18 | 21(<i>o</i>) | 0(<i>m</i>) | 79(<i>p</i>) |
| Fluorobenzene ^c | 105 | 23 | 9(<i>o</i>) | 0(<i>m</i>) | 91(<i>p</i>) |
| Toluene | 130 | 36 | 17(<i>o</i>) | 6(<i>m</i>) | 77(<i>p</i>) |
| Toluene ^d | 136 | 41 | 20(<i>o</i>) | 8(<i>m</i>) | 72(<i>p</i>) |
| Methoxybenzene | 185 | 83 | 18(<i>o</i>) | 0(<i>m</i>) | 82(<i>p</i>) |
| Methoxybenzene ^e | 185 | 74 | 18(<i>o</i>) | 0(<i>m</i>) | 82(<i>p</i>) |
| Methoxybenzene ^f | 185 | 72 | 18(<i>o</i>) | 0(<i>m</i>) | 82(<i>p</i>) |
| Naphthalene | 165 | 68 | 66(1) | 34(2) | |
| 2-Methoxynaphthalene | 178 | 68 | 0(1) | 75(6) | 25(8) |
| Thiophene | 102 | 61 | 100(2) | 0(3) | |

^a Method A: Arene 40 mmol, benzoyl chloride 20 mmol, EPZG® 0.5 g, 20 min, MWI = microwave irradiation; ^b position of benzoyl in parentheses; ^c thermal heating for 72 h; ^d toluene : benzoyl chloride 1 : 2; ^e with recycled catalyst; ^f with twice recycled catalyst.

TABLE II
Benzoylation of arenes with benzoic anhydride using EPZG® catalyst and MWI^a

| Arene | T_{fin} , °C | Yield, % | Isomers ratio ^b , % | |
|----------------------|-----------------------|----------|--------------------------------|----------------|
| Benzene | 105 | 0 | | |
| Toluene | 130 | 0 | | |
| Methoxybenzene | 182 | 49 | 10(<i>o</i>) | 90(<i>p</i>) |
| Naphthalene | 166 | 33 | 66(1) | 34(2) |
| 2-Methoxynaphthalene | 183 | 32 | 82(6) | 18(8) |
| Thiophene | 106 | 44 | 100(2) | 0(3) |

^a Method B: Arene 20 mmol, benzoic anhydride 20 mmol, EPZG® 0.5 g, 20 min; ^b position of benzoyl in parentheses.

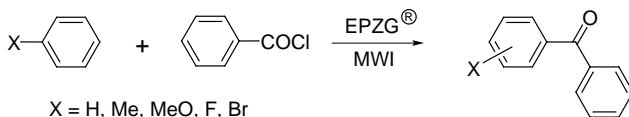
Benzoylation with Benzoic Anhydride (Method B)

A microwave pre-dried EPZG[®] catalyst (0.5 g) was added to a mixture of arene (20 mmol) and benzoic anhydride (4.53 g, 20 mmol) in a 50 ml flask. The mixture was microwave-irradiated for 20 min and then cooled to room temperature. (The final temperature was approximately the same as in method A.) Dichloromethane was added and the catalyst was filtered off. The solution was dried over anhydrous sodium sulfate, the solvent was evaporated and the residue subjected to GC-MS analysis or chromatographed on a silica gel column using hexane-ethyl acetate mixture as eluent.

The ¹H NMR spectra of isolated products are in accord with the published data: benzophenone²³, 4-fluorobenzophenone²⁴, 4-bromobenzophenone²⁵, 4-methylbenzophenone and 4-methoxybenzophenone²⁶, 1- and 2-benzyl-naphthalenes²⁷, X-benzoyl-2-methoxy-naphthalenes²⁸ and 2-benzoylthiophene²⁹.

RESULTS AND DISCUSSION

Several benzene derivatives, naphthalene, 2-methoxynaphthalene and thiophene were chosen as substrates for our Friedel-Crafts benzoylation study. The benzoylations were carried out either with benzoyl chloride or benzoic anhydride using different ratios of the substrate, benzoylation reagent and EPZG[®] catalyst ratio (Tables I-III). The general course of the reaction is outlined on the Scheme 1.



SCHEME 1

Structure of the products was established by ¹H NMR spectra and their comparison with the literature available data.

The first experiments were carried out with benzoyl chloride as an acylation agent (method A). After several trials, we found that 400 W input power of the microwave oven was the best for our experiments from the point of view of the reactants conversion and the reaction time. It is obvious (Table I) that yields were highly dependent on electronic effects of substituent as well as on the boiling point of the substrate. Synthesis of benzophenone in 67% yield using the EPZG[®] catalyst was described previously⁶: thermal heating was applied and the reaction time was 30 h. We achieved just a 19% yield after 20 min of microwave irradiation. This can be caused by performing the reaction on a small scale and most of benzene was probably evaporated into the reflux condenser. This is probably the reason why our benzoylation of toluene afforded just 36% yield of prod-

ucts. The obtained isomer ratio was (GC-MS) $o : m : p = 17 : 6 : 77$, which is slightly better than that described by Kodomari¹¹ ($o : p = 25 : 75$) using graphite as the catalyst and thermal heating. Our results are comparable with those obtained by Laporte *et al.*¹³ who used graphite as catalyst and microwave irradiation (MWI) (50% yield, $o : m : p = 13 : 3 : 84$). A rise in the benzoyl chloride substrate ratio to 1 : 2 did not change the picture. It is not surprising that benzylation of substrates like fluorobenzene and bromobenzene resulted in lower yields of the products (18 and 12%, respectively). We also performed benzylation of fluorobenzene under thermal heating. The reaction time was very long (72 h), the yield of the product was higher and the reaction was more selective than in the microwave experiment. This can be explained by superheating of the solid catalyst in the microwave experiment³⁰ which means that reaction takes place locally at higher temperature than is boiling point of fluorobenzene.

The benzylation of methoxybenzene led to virtually total conversion of the substrate (82% yield of isolated products) and the $o : p$ isomer ratio was 18 : 82. Our results are comparable with ref.¹³ (86%), but better than described for a conventional experiment with EPZG® catalyst⁶ (60%, 15 h). The reaction proceeded less selectively under our conditions, as we achieved the $o : p$ ratio 1 : 4.6 in contrast to the described^{6,13} 1 : 12. Benzylation of naphthalene resulted in a 78% yield of the mixture of benzoynaphthalenes; the observed ratio of 1- to 2-benzoynaphthalene was 2.3 : 1 (GC-MS). Benzylation of 2-methoxynaphthalene resulted in a total yield of 68% of the 75 : 25 mixture of 2-benzoyl-6-methoxynaphthalene and 1-benzoyl-7-methoxynaphthalene. The absence of 1-benzoylated product can be explained by results of Giordano *et al.*³¹, who found out that the isomer ratio was time-dependent and the acylation of 2-methoxynaphthalene is a reversible reaction.

An attempt at benzylation of thiophene was also made. The reaction went smoothly and 2-benzoylthiophene was isolated in 68% yield.

Very similar results were achieved using benzoic anhydride (method B) as the acylation agent (Table II).

The only difference is that, due to the less reactive acylation agent, no benzylation of benzene and toluene was observed and lower yields of products were obtained at benzylation of other substrates. The very low yields of benzylation of naphthalene and 2-methoxynaphthalene can also be explained by the fact that reaction is taking place in the melt where the local reaction temperature could be very high, destroying the catalyst. This could be judged from its black colour after the reaction.

Our second question was whether it is possible to observe a specific microwave effect and whether the same catalyst could be reused several times. The reaction with methoxybenzene as the substrate showed (Table I) that the same catalyst can be reused twice without considerable loss of its activity. It was also proved that the 20 min reaction time for benzoylation of methoxybenzene was overestimated. The same yield of benzoyl(methoxy)benzene was isolated just after 1 min of microwave irradiation. The reaction mixture reached temperature 148 °C after 1 min irradiation and 185 °C after 5 min irradiation (see Table III).

A much lower yield of the benzoyl(methoxy)benzene was isolated when the reaction was carried out under the same conditions (reaction time and temperature) but a thermal heating was applied with the reaction mixture immersed in an oil bath preheated to a chosen temperature. As it was rather a surprising result, experiments were repeated at lower power input (200 W), but even at such conditions the reaction was over after 5 min. An experiment with thermal heating was also performed, in which the reaction mixture was preheated to 100 °C without a catalyst, then an EPZG® catalyst was added and the mixture was heated to the same temperature for 10 min, but the yield of the benzoylated methoxybenzene was just 8%. This could be caused by a specific microwave effect or by the local overheating of the catalyst when exposed to microwave irradiation.

TABLE III
Benzoylation of methoxybenzene under different conditions^a

| Time, min | T_{fin} , °C | Heating | Isolated yield, % |
|-----------|-----------------------|----------|-------------------|
| 1 | 148 | MWI | 82 |
| 1 | 148 | Oil bath | 19 |
| 5 | 185 | MWI | 82 |
| 5 | 185 | Oil bath | 64 |

^a Methoxybenzene 40 mmol, benzoyl chloride 20 mmol, EPZG® 0.5 g.

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REFERENCES

1. Cornelis A., Gerstmans A., Laszlo P., Mathy A., Zieba I.: *Catal. Lett.* **1990**, *6*, 103.
2. Laszlo P., Mathy A.: *Helv. Chim. Acta* **1987**, *70*, 577.
3. Vaccari A.: *Catal. Today* **1998**, *41*, 53.
4. Clark J. H., Macquarrie D. J.: *Chem. Soc. Rev.* **1996**, 303.
5. Laszlo P.: *J. Phys. Org. Chem.* **1998**, *11*, 356.
6. Envirocats, Contract Catalysts, Knowsley Industrial Park, Prescott, UK L34 9HY.
7. Clark J. H., Cullen S. R., Barlow S. Y., Bastock T. W.: *J. Chem. Soc., Perkin Trans. 2* **1994**, 1117.
8. Baudry-Barbier D., Dormond A., Duriau-Montagne F.: *C. R. Acad. Sci., Ser. IIC* **1998**, *1*, 41.
9. Miller J. M., Wails D., Hartman J. S., Schebesh K., Belelie J. L.: *Can. J. Chem.* **1998**, *76*, 382.
10. Price P. M., Clark J. H., Martin K., Macquarrie D. J., Bastock T. W.: *Org. Proc. Res. Dev.* **1988**, *2*, 221.
11. Baudry-Baudier D., Dormond A., Duriau-Montagne F.: *J. Mol. Catal. A. Chemical* **1999**, *149*, 215.
12. Kodomari M., Suzuki Y., Yoshida K.: *Chem. Commun.* **1997**, 1567.
13. Laporte C., Baulès P., Laporterie A., Desmurs J. R., Dubac J.: *C. R. Acad. Sci., T. 1, Ser. IIC* **1998**, 141.
14. Desmurs J. R., Dubac J., Laporterie A., Desmurs J. R., Marquié J.: *Fr. Appl. 97/02917; Chem. Abstr.* **1998**, *129*, 244928.
15. Toma Š.: *Chem. Listy* **1993**, *87*, 627.
16. Baghurst D. R., Mingos D. M. P.: *Chem. Soc. Rev.* **1991**, *20*, 1.
17. Caddick S.: *Tetrahedron* **1995**, *51*, 10403.
18. Strauss C. R., Trainor R. W.: *Aust. J. Chem.* **1995**, *48*, 1665.
19. Loupy A., Petit A., Hamelin J., Texier-Boulett F., Jacqualt P., Mathé D.: *Synthesis* **1998**, 1213.
20. Gedye R. N., Wei J. B.: *Can. J. Chem.* **1998**, *76*, 525.
21. Laporte C., Marquié J., Laporterie A., Desmurs J. R., Dubac J.: *C. R. Acad. Sci., T. 2, Ser. IIC* **1999**, 455.
22. Costa A., de la Cruz P., De Miquel P., Diez-Barra E., de la Hoz A., Langa F., Loupy A., Majdoub M., Martín N., Sanchez C., Seoane C.: *Tetrahedron Lett.* **1995**, *36*, 2165.
23. Castellano S., Lorenc J. A.: *Chim. Ind.* **1965**, *47*, 643.
24. Adams D. J., Clark J. S., Nightingale D. J.: *Tetrahedron* **1999**, 7725.
25. Morley J. O.: *J. Chem. Soc., Perkin Trans. 2* **1977**, 601.
26. Kusama H., Narasaka K.: *Bull. Chem. Soc. Jpn.* **1995**, *68*, 2379.
27. Cerfontain H., Zou Y., Bakker B. H.: *Rec. Trav. Chim. Pays-Bas* **1994**, *113*, 403.
28. Pivsa-Art S., Okuro K., Miura M., Murata S., Nomura M.: *J. Chem. Soc., Perkin Trans. 1* **1994**, 1703.
29. Kang S. K., Lim K. H., Ho P. S., Yoon S. K., Son H. J.: *Synth. Commun.* **1998**, *28*, 1481.
30. Stuerger D., Gaillard P.: *Tetrahedron* **1996**, *52*, 5505.
31. Giordano C., Villa M., Annunziata R.: *Synth. Commun.* **1990**, *20*, 383.