Microwave-Assisted Isomerization of 2'-Aminochalcones on Clay: An Easy Route to 2-Aryl-1,2,3,4-tetrahydro-4-quinolones

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Abstract: A simple and environmentally benign method for the conversion of 2'-aminochalcones to 2-aryl-1,2,3,4-tetrahydro-4-quinolones is described which occurs under mild and solvent-free conditions on montmorillonite K 10 clay surface; microwave irradiation facilitates the procedure.

A growing interest in the synthesis[1-6] and oxidative cyclization of 2'-aminochalcones (**1**) has been stimulated, in part, by the possible transformation of such compounds into 2-aryl-1,2,3,4-tetrahydro-4-quinolones (**2**).[2-8] These tetrahydro-4-quinolones serve as valuable precursors[9,10] to medicinally important[11] but not readily accessible[11-16] 2-aryl-4-quinolones bearing substituents in either of the aromatic rings.

The formation of tetrahydro-4-quinolones is generally accomplished by acid or base catalyzed cyclization of 2'-aminochalcones.[2-8] These procedures involve the use of corrosive reagents such as orthophosphoric acid, acetic acid and strong alkalis. Consequently, it is desirable to develop manipulatively easy, preferentially environmental benign solvent-free protocol. In continuation of our studies on microwave-assisted reactions on solid surfaces,[17] herein we report a simple method for the formation of 2-aryl-1,2,3,4-tetrahydro-4-quinolones (**2**) under solvent free conditions on montmorillonite K10 clay, the reaction is further accelerated safely using irradiation in an unmodified household microwave (MW) oven.

Clay catalyzed organic reactions have generated considerable interest in recent years in view of their inexpensive nature and special catalytic attributes in heterogeneous reactions.[18] Microwave heating is used for a wide variety of organic reactions[19] and has found application in polymerization, depolymerization, rapid synthesis of organic compounds,[20] and for the induction of reactions under 'dry' conditions.[17,21,22] The salient features of the microwave approach are the rapid reaction rates, cleaner reactions and ease of manipulation. The reactions in dry media condition are specially appealing as they provide an opportunity to work with open vessels, thus avoiding the risk of high pressure development and with a possibility of upscaling the reactions on preparative scale.

We wish to report a rapid synthesis of tetrahydro-4-quinolones **2** under solvent-free mild reaction conditions. Upon MW irradiation of 2'-aminochalcones **1** adsorbed on montmorillonite K 10 clay for 1.5-2.5 min (temperature of alumina bath 110-140 °C), exclusive formation of cyclized products **2** takes place which is easily extractable into dichloromethane in high yields (**Table 1**). The alumina bath serves as a heat sink for the small amount of reactants normally employed in the study. We have explored this reaction on various other surfaces namely silica gel, silica gel doped with *p*-toluenesulfonic acid (*p*-TSA, 3g per 100g of silica) as well as neutral and basic alumina and found that the formation of **2** is ideally accomplished on K 10 surface without any side products. The reaction on silica supported *p*-TSA also provides reasonable yields of **2**, whereas the substrates are completely destroyed on basic alumina.

In order to determine the role of microwave in acceleration of this reaction, a comparable study was conducted in an oil bath at the same temperature. That the effect is not purely *thermal* [19,23] is borne out by the fact that similar reaction rates are not attainable at ~110 °C; relatively longer time is required for the conversion of starting *o*-aminochalcone **1a** to tetrahydro-4-quinolones **2a** (5-7 min) at ~110 °C in an oil bath. Although the nonthermal effects are not confirmed yet,[19g] we find the use of a microwave oven much efficient, convenient and cleaner.

The irradiation of *o*-aminochalcone (**1a**) is representative of the general procedure employed. Montmorillonite K 10 clay (1.0 g) is mixed with **1a** (0.1 g, 0.45 mmol) in solid state using a pestle and mortar or alternatively with a solution of **1a** in dichloromethane (2 mL). The adsorbed material is transferred to a glass tube and is inserted in an alumina bath (alumina: 100 g, mesh 65-325, Fisher scientific; bath: 5.7 cm diameter) inside the microwave oven. The compound is irradiated for 1.5 min (the temperature of alumina bath reached 110 °C at the end of this period) and the completion of the reaction is monitored by TLC examination. The product is extracted into dichloromethane (2 x 15 mL) and clay is filtered off. Removal of the solvent under reduced pressure affords 2-phenyl-1,2,3,4-tetrahydro-4-quinolone (**2a**), in 80 % yield, m.p.148-50 °C, (Lit. m.p. 149-50).[6]

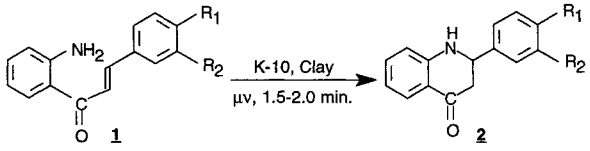

Table 1. Preparation of 2-aryl-1,2,3,4-tetrahydro-4-quinolones (**2a-g**) on montmorillonite K 10 clay under microwave irradiation.[a]

Entry	R_1	R_2	m.p. (°C)	Lit.m.p. (°C)	Yield (%)[b]
2a	H	H	148-50	149-50 [2,6]	80
2b	CH_3	H	148	149 [5]	77
2c	OCH_3	H	146-47	waxy solid [6]	78
2d	Cl	H	167-68	170-71	80
2e	Br	H	171	171 [5]	72
2f	NO_2	H	192-93	194 [5]	70
2g[c]	OCH_3	OCH_3	136-37	–	72

[a] A Sears Kenmore MW oven operating at 2450 MHz (power 900 W) was used.

[b] Yields refer to pure isolated products obtained and all products were identified by comparison of their TLC, IR and NMR spectra with those of authentic samples.

[c] ^{1}H NMR($CDCl_3$): 2.65 (m, 2H, H-3), 3.72 (s, 6H, 3',4'-OMe), 4.25-4.8 (m, 2H, H-2 & NH), 6.35-7.3 (m, 6H, aromatic), 7.56 (dd, 1H, H-5); IR(Nujol): 3225 (NH), 1625 (C=O) cm^{-1}.

In conclusion, the microwave irradiation of 2'-aminochalcone under solvent free 'dry' conditions on montmorillonite K 10 clay provides an easy and efficient procedure for the formation of 2-aryl-1,2,3,4-tetrahydro-4-quinolones in pure form and good yields.

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References and Notes

(1) Murphy, W.S.; Watanasin, S. *Synthesis* **1980**, 647.

(2) Mannich, C.; Dannehl, M. *Chem. Ber.* **1938**, *71*, 1899.

(3) Janzso, G.; *Topics in flavanoid Chemistry and Biochemistry*; Farkas, L.; Gabor, M.; Kallay, F., Ed.; Akad. Kiado Budapest, **1975**; p 144.

(4) Tokes, A.L.; Szilagyi, L. *Synth. Commun.* **1987**, *17*, 1235.

(5) a) Tokes, A.L.; Litkei, Gy.; Szilagyi, L. *Synth. Commun.* **1992**, *22*, 2433; b) Tokes, A.L.; Litkei, Gy. *Synth. Commun.* **1993**, *23*, 895.

(6) a) Donnelly, J.A.; Farrell, D.F. *J. Org. Chem.* **1990**, *55*, 1757; b) Donnelly, J.A.; Farrell, D.F.*Tetrahedron* **1990**, *46*, 885.

(7) Diesbach, H.; Kramer, H. *Helv. Chim. Acta.* **1945**, *28*, 1399.

(8) Tokes, A.L.; Janzso, G. *Synth. Commun.* **1989**, *19*, 3159.

(9) Singh, O.V.; Kapil, R.S. *Synth. Commun.* **1993**, *23*, 277.

(10) Prakash, O.; Kumar, D.; Saini, R.K.; Singh, S.P. *Synth. Commun.* **1994**, *24*, 2167.

(11) a) Osawa, T.; Ohta, H.; Akimoto, K.; Harada, K.; Soga, H.; Jinno, Y. Eur. Pat. Appl. EP 343547, *Chem. Abstr.* **1990**, *112*, 235197g; b) Hirak, U.; Hisashi, Y.; Hiroshi, Y.; Hitoshi, T. Eur. Pat. Appl. EP 287951, *Chem. Abstr.* **1989**, *110*, 173109k.

(12) a) Leonard, N.J.; Herbradson, H.F.; Van Heyningen, E.M. *J. Am. Chem. Soc.* **1946**, *68*, 1279; b) Reitsema, R.H. *Chem. Rev.* **1948**, *43*, 43.

(13) Chen, B.; Huang, X.; Wang, J. *Synthesis* **1987**, 482.

(14) Hormi, O.E.O.; Peltonen, C; Heikkila, L. *J. Org. Chem.* **1990**, *55*, 2513.

(15) Kasahara, A.; Izumi, T.; Watabe, H.; Takahashi, S. *Chem & Ind.* **1981**, 121.

(16) a) Kalinin, V.N.; Shostakovsky. M.V.; Ponomaryov, A.B. *Tetrahedron Lett.* **1992**, *33*, 373; b) Torii, S.; Okumoto, H.; HeXu, L. *Tetrahedron Lett.* **1991**, *32*, 237.

(17) a) Varma, R.S.; Varma, M. *Tetrahedron Lett.* **1992**, *33*, 5937; b) Varma, R.S.; Chatterjee, A.K.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 3207; c) Varma, R.S.; Chatterjee, A.K.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 4603; d) Varma, R.S.; Varma, M.; Chatterjee, A.K. *J. Chem. Soc.. Perkin. Trans.* **1993**, 999; e) Varma, R.S.; Lamture, J.B.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 3029.

(18) For references on clay-supported reagents a) Cornelis, A.; Laszlo, P. *Synthesis* **1985**, 909, and the references cited therein; b) Balogh, M.; Laszlo, P. *Organic Chemistry Using Clays*; Springer-Verlag: Berlin, **1993**; c) Delaude, L.; Laszlo, P. *J. Org. Chem.* **1996**, *61*, 6360 and the references cited therein.

(19) For recent reviews on microwave-assisted chemical reactions, see a) Abramovich, R. A. *Org. Prep. Proced. Int.* **1991**, *23*, 683; b) Mingos, D.M.P.; Baghurst, D.R. *Chem. Soc. Rev.* **1991**, *20*, 1; c) Whittaker, A. G.; Mingos, D. M. P. *J. Microwave Power Electromagn. Energy*; **1994**, *29*, 195; d) Majetich, G.; Hicks, R. *J. Microwave Power Electromagn. Energy*, **1995**, *30*, 27; e) Caddick, S. *Tetrahedron* **1995**, *51*, 10403; f) Strauss, C.R.; Trainor, R.W. *Aust. J. Chem.* **1995**, *48*, 1665; (g) For commentary on the First World Congress on Microwave Processing, see Dagani, D. *Chem. Eng. News* , February 10, **1997**, 26.

(20) a) Gedye, R.; Smith, F.; Westaway, K.; Ali, H.; Baldisera, L.; Laberge, L.; Rousell, J. *Tetrahedron Lett.* **1986**, *27*, 279; b) Giguere, R.J.; Bray, T.L.; Duncan, S.M.; Majetich, G. *Tetrahedron Lett.* **1986**, *27*, 4945; c) Giguere, R.J.; Namen, A.M.; Lopez, B.O.; Arepally, A.; Ramos, D.E.; Majetich, G.; Defrauw, J. *Tetrahedron Lett.* **1987**, *28*, 6553; d) Bose, A.K.; Manhas, M.S.; Ghosh, M.; Raju, V.S.; Tabei, K.; Urbanczyk-Lipkowska, Z. *Heterocycles* **1990**, *30*, 741; e) Bose, A.K.; Manhas, M.S.; Ghosh, M.; Shah, M.; Raju, V.S.; Bari, S.S.; Nawaz, S.N.; Banik, B.K.; Chaudhary, A.G.; Barakat, K.J. *J. Org. Chem.* **1991**, *56*, 6968; f) Banik, B.K.; Manhas, M.S.; Kaluza, Z.; Barakat, K.J.; Bose, A.K. *Tetrahedron Lett.* **1992**, *33*, 3603; g) Bose, A. K.; Jayaraman, M.; Okawa, A.; Bari, S. S.; Robb, E. W.; Manhas, M. S. *Tetrahedron Lett.*, **1996**, *37*, 6989 and references cited therein.

(21) a) Bram, G.; Loupy, A.; Majdoub, M.; Gutierrez, E.; Ruiz-Hitzky, E. *Tetrahedron* **1990**, *46*, 5167; b) Marrero-Terrero, A. L.; Loupy, A. *Synlett*, **1996**, 245.

(22) a) Benalloum, A.; Labiad, B.; Villemin, D. *J. Chem. Soc., Chem. Commun.* **1989**, 386; b) Villemin, D.; Labiad, B.; Ouhilal, Y. *Chem. Ind. (London)* **1989**, 607; c) Villemin, D.; Labiad, B. *Synth. Commun.* **1990**, *20*, 3325, 3333; d) Vallemin, D.; Benalloum, A. *Synth. Commun.* **1991**, *21*, 1, 63; e) Villemin, D.; Lalaoui, M.; Benalloum, A. *Chem. Ind. (London)* **1991**, 176.

(23) For a critical evaluation of activation process by microwaves see: Raner, K. D.; Strauss, C. R.; Vyskoc, F.; Mokbel, L. *J. Org. Chem.* **1993**, *58*, 950.