Pergamon

Tetrahedron Letters, Vol. 35, No. 26, pp. 4563-4564, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)00870-1

A New Route to Pyrimido [1,6-a] Benzimidazoles : Reactivity of Activated 2-Benzimidazoles with N-Acyl Imidates as β-Dielectrophiles under Microwave Irradiation.

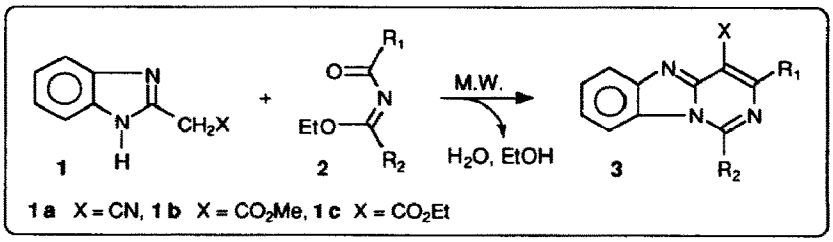
Mustapha Rahmouni[a], Aicha Derdour[b], Jean Pierre Bazureau*[c] and Jack Hamelin[c]

[a] *Centre Universitaire de Tiaret (C.U.T.), 14000 - Tiaret , Algérie.*
[b] *Université d'Oran, 31000 - Oran, Algérie*
[c] *Groupe de Recherches de Physico-Chimie Structurale 3 associé au CNRS, Campus de Beaulieu 35042 - Rennes, France.*

Key words : Benzimidazoles, N-Acyl imidates, Pyrimido [1,6-a] benzimidazoles, microwave irradiation.

Abstract : Activated 2-benzimidazoles react with a variety of N-Acyl imidates under microwave irradiation in open vessels to give the corresponding pyrimido [1,6-a] benzimidazoles.

Owing to their interesting biological activity[1] and their application as fluorescent dispersed dyes[2], we have investigated the synthesis of pyrimido [1,6-a] benzimidazoles from benzimidazoles **1** activated by electron withdrawing groups (such as CN, CO_2R with R = Me, Et). As part of a program in our laboratory related to the study of organic synthesis in dry media[3] and under microwave irradiation[4], we wish to report in this paper the first results obtained for the ring closure condensation of benzimidazoles[5,7] **1** with N-Acyl imidates[8] **2** as β-dielectrophiles with microwave activation. After heating compounds **1b** (X = CO_2Me) and **2** (R_1 = R_2 = Me) in toluene with continuous azeotropic elimination of water or in dry ethanol during 48 h, 95 % of **1b** was recovered unchanged with decomposition by-products of **2** (R_1 = R_2 = Me). In contrast when experiments[9] were performed without solvents in open vessels under microwave irradiation (400-510W, 15-30 min.), the reaction led to pyrimido [1,6-a] benzimidazoles **3** after ethanol and water elimination.



Structure of pyrimido [1,6-a] benzimidazoles **3** could be established by ^1H and ^{13}C NMR spectral analysis. For example in ^1H NMR, **3a**[9] (R_1 = R_2 = Me, X = CN) exhibits a lowfield singlet (2.76 ppm) assignable to the methyl group on C-3, the other methyl group is deshielded (3.19 ppm) by N-2 and N-10, an effect which is known in similar systems[10]. In ^{13}C NMR, two signals : one at δ = 153.29 ppm for C-3 and another at 160.61 ppm for C-1.

Entry	X	R_1	R_2	Power (W)	T. (min.)[a]	Yield (%)[b]
3a[9]	CN	Me	Me	510[d]	15	(86) 72
3b	CN	Me	Et	400[c]	30	65
3c	CN	Et	Me	510[d]	15	(38) 27
3d	CN	Me	Ph	510[d]	15	47
3e	CO_2Me	Me	Me	400[c]	30	86
3f	CO_2Et	Me	Et	400[c]	30	(42) 21
3g	CO_2Et	Me	Ph	510[d]	15	50

(a) Reaction time. (b) Crude and isolated yields.(c) domestic MW oven : Philips M705 (d) modified Moulinex 850W.

As a conclusion, this cyclocondensation reaction affords a new route to pyrimido [1,6-a] benzimidazoles and the present procedure appears to be very simple. The extension of this cyclocondensation strategy to other β-dinucleophiles on N-acyl imidates is actually under progress.

Acknowledgements : The authors thank Moulinex SA (France) for the generous gift of a modified 850W oven as a prototype.

REFERENCES AND NOTES :

1 Nawwar, Galal A.M.; Chabaka, Laila M.; Omar Mahmound, T.; *Phosphorus, Sulfur, Silicon, Relatd Elem.*, **1991**, *57*, 65-73.

2 Bechstein, U.; Liebsscher, J.; Kelboro, Y.; Paetzel, M.; **Ger.(East) DD 293,585** (Cl. C07D487/04), 05 Sep 1991, Appl. 312,530, 29 Jan 1988; *Chem. Abstr.*, **116** : 59393x.

3 Klein, B.; Texier-Boullet, F.; Hamelin, J.; *Synthesis*, **1986**, 409-410.

4 (a) Latouche, R.; Texier-Boullet, F.; Hamelin, J.; *Tetrahedron Lett.*; **1991**, *32*, 1179-82 (b) Pilard, J.F.; Klein, B.; Texier-Boullet, F.; Hamelin, J.; *Synlett*, **1992**, 219-220. (c) Lerestif, J.M.; Bazureau, J.P.; Hamelin, J.; *Tetrahedron Lett.*; **1993**, *34*, 4639-42.(d) Rechsteiner, B.; Texier-Boullet, F.; Hamelin, J.; *Tetrahedron Lett.*; **1993**, *34*, 5071-74.(e) Abdallah-El Ayoubi, S.; Texier-Boullet, F.; Hamelin, J.; *Synthesis*, **1994**, 258-60.

5 Methyl 2-benzimidazole ethanoate **1b** is synthetized in one step by condensation of *o*-phenylenediamine with the appropriate imino-ether[6] in CH_2Cl_2 at 41°C during 48h, in 87% yield (mp = 105°C).

6 King, F.E.; Acheson, R.M.; *J. Chem. Soc.*, **1949**, 1396-1400.

7 a) Copeland, R.A.B.; Day, A.R.; *J. Am. Chem. Soc.*, **1943**, *65*, 1072-1075 b) Ohta, S.; Yuasa, T.; Narita, Y.; Kawasaki, I.; Minamii, E.; Yamashita, M.; *Heterocycles*, **1991**, *32*, 1923-31.

8 Bader, H.; *J.Org.Chem.*, **1965**, *30*, 707-711.

9 Experimental procedure for the preparation of 1,3-dimethyl pyrimido [1,6-a] benzimidazole 4-carbonitrile (**3a**) : A mixture of **1a** (0.15 g - 0.96 mmol) and **2a** (0.25 g - 1.79 mmol) in a Pyrex glass, was irradiated at 510W during 15 min. After addition of 5 mL of methylene chloride, the resulting solution is adsorbed over Al_2O_3. Elution by ether and subsequent evaporation *in vacuo* gave 0.18 g of **3a** (Yield = 86%), then the crude residue is recristallized from chloroform in 72% yield (0.16 g) as yellow needles (mp = 241°C) - ^1H NMR ($CDCl_3$, 300 MHz) δ 2.76 (s, 3H); 3.19 (s, 3H); 7.45-7.50 (m, 1H, Ar); 7.60-7.62 (m, 1H, Ar); 7.98-8.03 (m, 2H, Ar).- ^{13}C NMR ($CDCl_3$,75 MHz) δ 23.24 (q, J = 129 Hz); 24.12 (q, J = 131 Hz); 95.13; 113.76; 114.57 (dd, J = 165, 8.2 Hz); 120.65 (dd, J = 164, 8.2 Hz); 123.35 (dd, J = 163, 7.5 Hz); 127.40 (dd, J = 161, 7.6 Hz); 127.81; 145.02; 146.42; 153.29 (q, J = 7.2 Hz, C-3); 160.64 (q, J = 6.8 Hz, C-1) - MS, *m/z* = 222.0909 found (calc. for $C_{13}H_{10}N_4$: 222.0905), M^+.

10 Hammad, H.A.; Mocin Nawwar, G.A.; Hamza Elgemeie, G.E.; Elnagdi, M.H.; *Heterocycles*, **1985**, *23*, 2177-81.

(*Received in France* 13 *April* 1994; *accepted* 5 *May* 1994)