Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Published online: 23 Aug 2006.

To cite this article: Didier Villemin , Beno[icaron]t Martin & Mohamed Khalid (1998) Dry Reaction on KF-Alumina: Synthesis of 4-Arylidene-1,3-(2H,4H) Isoquinolinediones, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 28:17, 3195-3200, DOI: 10.1080/00397919808004421

To link to this article: http://dx.doi.org/10.1080/00397919808004421

SYNTHETIC COMMUNICATIONS, 28(17), 3195-3200 (1998)

DRY REACTION ON KF-ALUMINA: SYNTHESIS OF 4-ARYLIDENE-1,3-(2H,4H) ISOQUINOLINEDIONES

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Abstract: 1,2,3,4-Tetrahydroisoquinoline-1,3-dione (**1**) and arylcarboxy-aldehydes (**2**) were condensed to 3-(arylmethylene)-1,2,3,4-tetraydroiso-quinoline-1,3-dione (**3**) in presence of potassium fluoride on alumina without solvent under focused microwave irradiation.

We have previously reported dry condensations of aldehydes with cyclic 6-ring compounds such as the Meldrum acid [1] and the barbituric acid (**4**) [2]. In these compounds the combination of electron withdrawing group and the quasi-planar structure 6-ring compounds gave a very acidic carbon . The analogy in structure of 1,2,3,4-tetrahydroisoquinoline-1,3-dione (**1**) with barbituric acid (**4**) suggest that (**1**) may react similarly to (**4**) with aldehydes.

The reaction of aromatic aldehydes (**2**) with (**1**) on basic catalyst potassium fluoride on alumina without solvent (dry reaction) under focused microwave irradiation [3] gave efficiently the condensation products (**3**) according the scheme 2.

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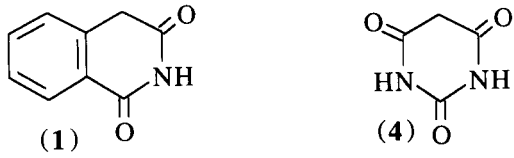
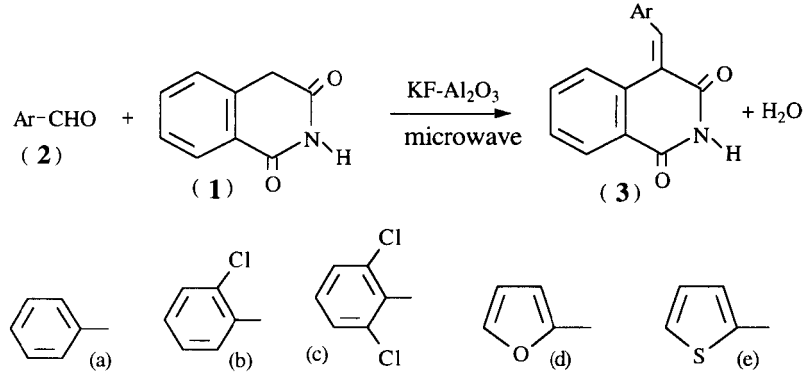
Scheme 1: Structural analogy



Scheme 2: Condensation of (**1**) with aldehyde under focused microwave irradiation



The reaction also took slowly place at room temperature, but the reaction was generally incomplete after 24h. The condensation products was obtained in good yields under focused microwave irradiation (2450 MHz, 60 W, 6 min.) with a resonance cavity [4] the results are reported in table I.

The yield of isolated products after crystallisation was generally good (82-93 %), but with the hindered aldehyde (**2c**), the reaction was more slow and prolonged microwave irradiation caused degradation of the product (**3c**). Only one isomer is obtained by analogy with other condensation the steoreochemistry Z was attributed. This stereochemistry corresponds to the thermodynamic more stable isomer according AM1 calculations. These condensation products are useful as intermediate in synthesis of isoquinoleine compounds[6].

In conclusion , we found a simple, fast, safe inexpensive and high yielding method for the preparation of 3-(arylmethylene)-1,2,3,4-tetraydroiso-quinoline-1,3-dione.

Table I: Condensation of 1,2,3,4-tetrahydroisoquinoline-1,3-dione (**1**) with arylcarboxyaldehydes (**2**) under focused microwave irradiation.

Entry	Aldehyde (**2**)	Yield [a] (%)	Mp(°C)	Lit.[ref.]
a	benzaldehyde	82	182	183-4 [6]
b	2-chlorobenzaldehyde	72	224	-
c	2,6-dichlorobenzaldehyde	64	188	-
d	2-furannecarboxaldehyde	93	210	210 [7]
e	2-thiophenecarboxaldehyde	88	166	-

Experimental

Proton NMR spectra (PMR) in ppm downfield from internal Me_4Si were recorded on a Brucker AC 250 instrument from a solution in DMSO-d_6 of the product. Mass spectra were recorded on Nermag R10.10H spectrometer. Melting point (Mp) in °C are uncorrected. AM1 calculation was effected with HyperChem® software[8] on Silicon Graphic workstation.

1,2,3,4-Tetrahydroisoquinoline-1,3-dione

It was obtained according to the literature[5] from homophtalic acid and aqueous ammonia. Yellow solid (dioxane); yield=72%; Mp=233(lit. 233); $C_9H_7NO_2$; NMR ^1H (DMSO-d_6) δ : 4.05(s, 2H, CH_2), 7.35(d, 1H, H arom, J=7.6 Hz), 7.43(t, 1H, H arom, J=7.6 Hz), 7.63(t, 1H, H arom, J=7.6 Hz), 8.0(d, 1H, H arom, J=7.6 Hz); MS m/z(%): 162 ($M^{+\cdot}$+1, 0.9), 161 ($M^{+\cdot}$, 2.9), 118 (30.6), 91 (10.0), 90 (100.0).

Synthesis of 4-(arylmethylene)-1,2,3,4-tetrahydroisoquinoline-1,3-dione

General procedure :

1,2,3,4-Tetrahydroisoquinoline-1,3-dione (**1**) (3 mmol, 0.483 g) and aldehyde (**2**) (3 mmol) were stirred 5 min at room temperature in acetonitrile (30 ml) with KF-Al_2O_3 (3 g), The solvent was then evaporated in vacuum and the solid was irradiated in an open Pyrex tube 8 mm diameter with focused microwaves in

resonance cavity [4] TE_{01} at 2450 MHz, with a universal generator MES 73-800. The product formed was extracted with acetonitrile (2X20ml). The solvent was evaporated in vacuum and the product (**3**) was crystallised in ethanol.

4-Phenylmethylene-1,2,3,4-tetrahydroisoquinoline-1,3-dione (3a)

Obtained from 1,2,3,4-tetrahydroisoquinoline-1,3-dione and benzaldehyde; irradiation 60 W, 6 min.; green solid; yield 82% ; Mp=182 (lit[6]. 183-184); $C_{16}H_{11}NO_2$; NMR ^1H (DMSO-d_6) δ : 7.3 to 7.6(b, 8H, H $_{arom}$), 7.9(d, 1H, H $_{arom}$, J=7.4 Hz), 8.1(s, 1H, CH=C), 10.4(b, 1H, NH); MS m/z(%) : 250 ($M^{+\cdot}$+1, 0.8), 249($M^{+\cdot}$, 1.0), 248 (3.3), 222 (2.6), 221 (1.8), 176(2.7), 147 (5.0), 105(7.7), 104 (44.1).

4-(2-Chlorophenylmethylene)-1,2,3,4-tetrahydroisoquinoline-1,3-dione (3b)

Obtained from 1,2,3,4-tetrahydroisoquinoline-1,3-dione and 2-chloro-benzaldehyde; irradiation 60 W, 6 min; yellow solid; yield 72%; Mp=224; $C_{16}H_{10}NO_2Cl$; NMR ^1H (DMSO-d_6) δ: 7.35(b, 2H, H $_{arom}$), 7.5 to 7.65(b, 3H, H $_{arom}$), 7.8(t, 1H, H $_{arom}$, J=7.6 Hz), 8.05(d, 1H, H $_{arom}$, J=7.6 Hz), 8.1(s, 1H, CH=C), 8.2(b, 1H, H $_{arom}$), 11.4(b, 1H, NH); MS m/z (%): 284 ($M^{+\cdot}$, 0.65), 282 (0.4), 266 (11.6), 258 (17.6), 257 (17.2), 256 (12.8), 255 (24.1), 220(16.2).

4-(2,6-Dichlorophenylmethylene)-1,2,3,4-tetrahydroisoquinoline-1,3-dione (3c)

Obtained from 1,2,3,4-tetrahydroisoquinoline-1,3-dione and 2,6-dichlorobenzaldehyde; irradiation 60 W, 3 min; orange solid; yield 64%; Mp 188; $C_{16}H_9NO_2Cl_2$; NMR ^1H (DMSO-d_6) δ: 7.2 to 7.6 (b, 6H, H $_{arom}$), 7.9 (s, 1H, CH=C), 8.1 (d, 1H, H $_{arom}$, J=7.6 Hz), 8.3 (b, 1H, NH); MS m/z (%): 318 ($M^{+\cdot}$, 2.7), 298 (15.2), 283 (5.8), 282 (11.2), 281 (12.7), 248 (11.2), 247 (45.5), 246 (5.7), 230 (13.6), 209 (12.4), 208 (22.7), 207 (75.4).

4-(Fur-2-ylmethylene)-1,2,3,4-tetrahydroisoquinoline-1,3-dione (3d)

Obtained from 1,2,3,4-tetrahydroisoquinoline-1,3-dione and 2-furaldehyde;

irradiation 60 W, 6 min; green solid; yield 93%; Mp 210 (lit[7]. 210°); $C_{14}H_9NO_3$; NMR ^1H (DMSO-d_6) δ: 6.7 (b, 1H, H arom), 7.2 to 7.5 (b, 2H, H arom), 7.7 to 7.8 (b, 1H, H arom), 7.9 (b, 1H, H arom), 8.05 (s, 1H, CH=C), 8.1 (b, 2H, H arom), 11.5 (b, 1H, NH); MS m/z (%): 240 (27.5), 239 (100.0), 238 (12.8), 222 (10.1), 211 (22.9), 196 (14.7), 186 (17.4).

4-(Thien-2-ylmethylene)-1,2,3,4-tetrahydroisoquinoline-1,3-dione (3e)

Obtained from 1,2,3,4-tetrahydroisoquinoline-1,3-dione and 2-thiophenecarboxaldehyde; irradiation 60 W, 6 min; green solid; yield=88%; Mp=166°C; $C_{14}H_9NO_2S$; NMR ^1H (DMSO-d_6) δ: 7.3 (b, 1H, H arom), 7.5 (t, 1H, H arom, J=7.6 Hz), 7.75 (t, 1H, H arom, J=7.6 Hz), 8.0 to 8.2 (b, 3H, H arom), 8.3 (b, 1H, H arom), 8.3 (s, 1H, CH=C), 10.6 (b, 1H, NH); MS m/z (%): 256 ($M^{+\cdot}$+1, 7.1), 255 ($M^{+\cdot}$, 18.8), 254 (12.0), 97 (12.1), 83 (11.1).

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Accepted February 8, 1998