

Application of Microwave in Organic Synthesis. Dry Synthesis of 2-Arylmethylene-3(2)-naphthofuranones

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Abstract: 3(2)-Naphthofuranone (**1**) was condensed in the presence of Al_2O_3 -KF with aromatic aldehydes (**4**) to give arylidenenaphthofuranones (**5a-f**) without solvent under focused microwave irradiation.

Keywords: Microwaves, organic synthesis, catalysis, dry reaction, furanone, aurone.

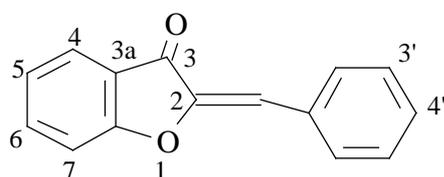
Introduction

Aurones (aurone, sulfuretol, maritimetol, leptosidol, etc.) are natural yellow pigments of plants related to flavonoids [1]. Aurones have a limited occurrence – the first aurone was discovered only in 1943 and, because of the limited methods of synthesis [1,3], aurones have received very limited attention. Analogy with flavonoids suggests that aurones could have interesting biological properties [2].

We have already reported that five-membered ring compounds with a carbonyl group, like tetrone acid [3a], pyrazolone [3b], thiohydanthoin [3c] or indanone [3d],

exhibit a high carbon acidity due to the pseudo-planar structure. These compounds consequently can be condensed easily with aldehydes in the presence of a solid catalyst (alumina, clay, Al_2O_3 -KF) without solvent (dry condensation).

We report herein the extension of this reaction to the synthesis of 2-arylmethylene-3(2)-naphthofuranones. Naphthofuranone (**1**), the homologue of 2-coumaranone (**2**), can be derived from 2-naphthoxyacetic acid (**3**), an useful auxin hormone [4]. We are also interested in studying the biological properties of such 3(2)-naphthofuranones described in older literature [5] but poorly studied to date.



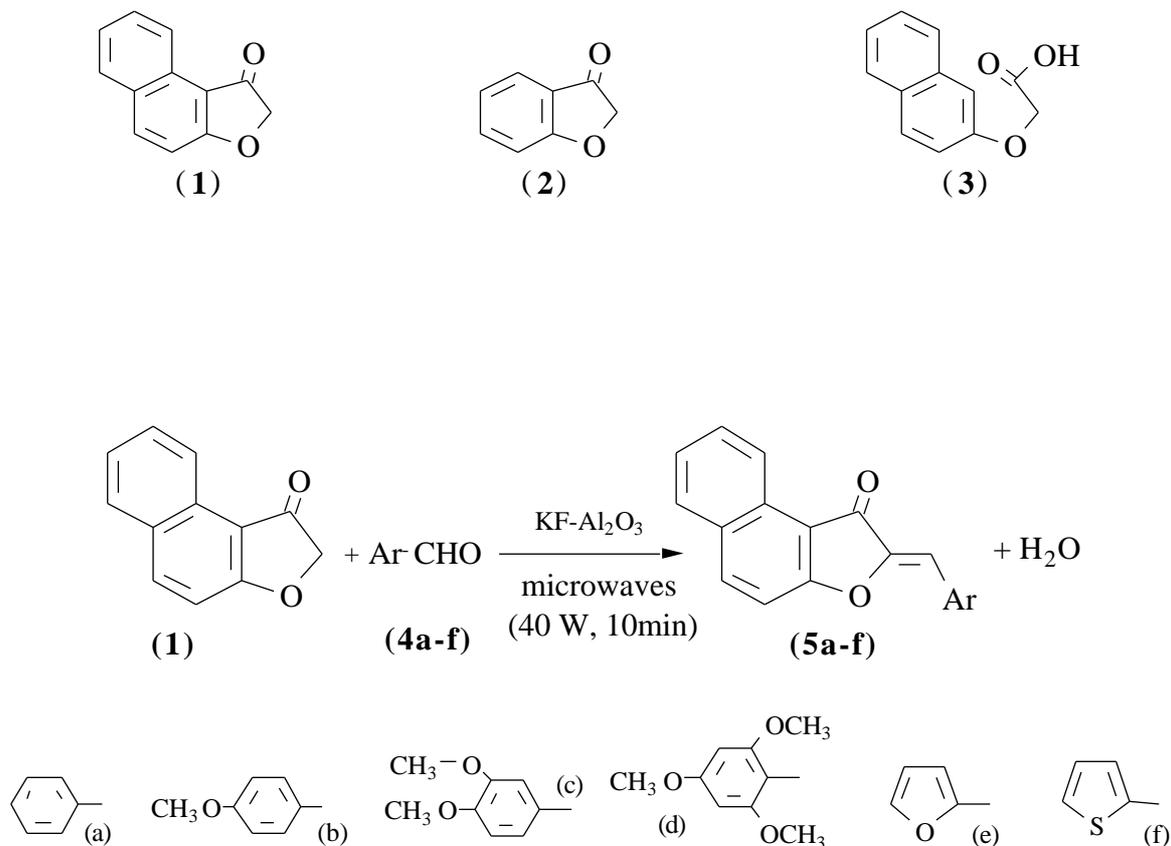
sulfuretol: 5 OH, 3' OH, 4' OH

maritimetol: 5 OH, 4 OH, 3' OH, 4' OH

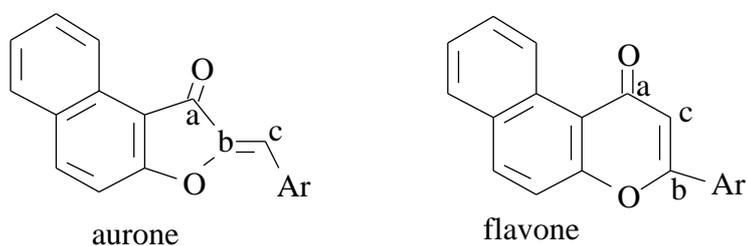
leptosidol: 5 OH, 4 OMe, 3' OH, 4' OH

Scheme 1. Aurones.

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Scheme 2. Condensation under focused microwave irradiation.



Results and Discussions

R. S. Varma and M. Varma have reported [6] a simple synthesis of aurones by dry condensation of 2-coumaranone (2) with arylaldehydes on basic alumina;

under these conditions, however, 3(2)-naphthofuranone (1) does not lead to the aurone derivatives. The more basic catalyst potassium fluoride on alumina is necessary in order to obtain condensation products. We have also used focused microwave irradiation [7,8] for increasing the rate

of the reaction without solvent. A moderate microwave focused irradiation of microwaves (10 min, 40 W) leads the condensation products (**5a-5f**) in good yield (57-96%), even with sterically hindered aldehydes such as 2,4,6-trimethoxybenzaldehyde (**4d**).

We have anticipated the possible rearrangement of aurone into flavone. Isomerisation of some aurones into flavones under basic conditions is known [9] and also the competitive formation of aurone and flavone takes place in flavonoid synthesis according to the published reaction conditions [10]. We have used ^{13}C NMR spectroscopy for the determination of the structure of the reaction products. According to the work of Ward et al. [11], significant chemical shift differences on carbon a,b,c, are characteristic of the aurone or flavone structure (table 1).

The chemical shifts of the product **4a** are very close to the chemical shifts observed in aurone. For compound **4d**, the chemical shifts of carbons a and b correspond to the aurone. Carbon c appears to be more shielded than those described in literature but, in our case, the phenyl group is more hindered than in the literature (table 2).

The condensation of naphthofuranone under our conditions seems to lead to aurones without rearrangement. All the olefinic protons have a chemical shift between 6.95 and 7.2 ppm. The reaction is stereospecific and the Z-stereochemistry was assigned by analogy of aurone obtained in the condition with coumaranone. Moreover the Z isomer corresponds to the more stable isomer according to AM1 calculations (see Figure 1).

Table 1. Comparison of chemical shifts of **4a** and literature data.

(ppm)	C=O (a)	=CH (c)	C=(b)
aurone	184.6	112.9	146.8
flavone	178.0	107.3	163.0
product 4a	184.7	113.1	147.6

Table 2. Comparison of chemical shifts of **4d** and literature data.

(ppm)	C=O (a)	=CH (c)	C= (b)
aurones (p-OMe)	183-185	111-113	145-148
flavones (o/p-OMe)	177-178	106-112	160-163
product 4d	184.3	106.8	147.5

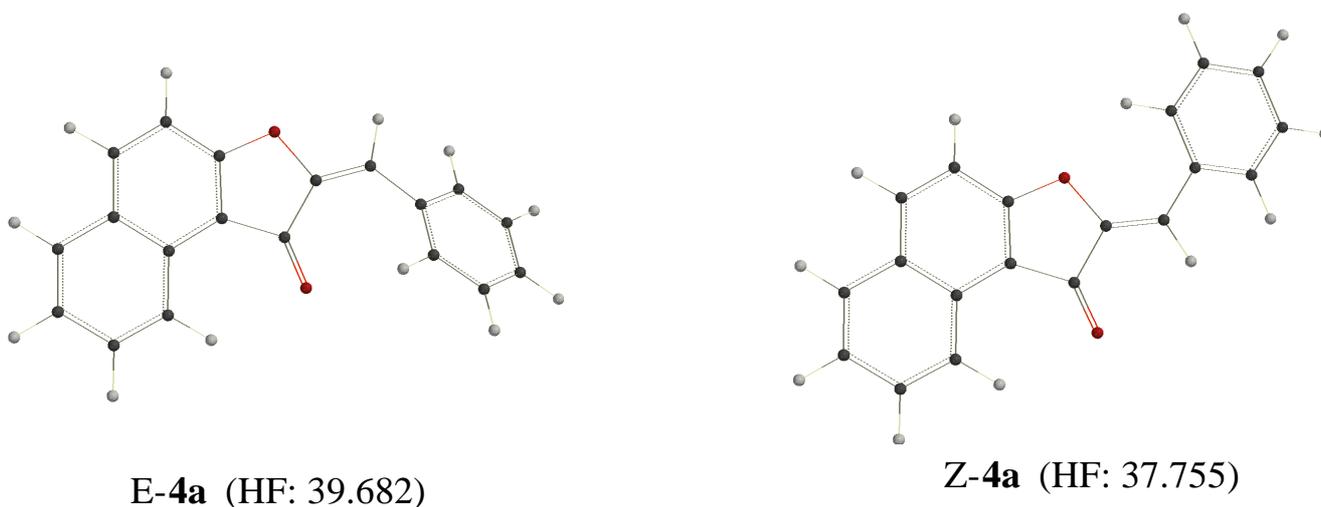


Figure 1. Energy minimised structure (AM1) generated by Spartan program [13].
HF= heat of formation (kcal/mol).

Conclusion

3(2)-Naphthofuranone (**1**) was condensed efficiently and rapidly in the presence of Al_2O_3 -KF with aromatic aldehydes (**4**) into Z-arylidene naphthofuranones (**5a-f**) without solvent under focused microwave irradiation. The method is very simple, safe and convenient.

Experimental Section

General

Proton NMR spectra (PMR) in ppm downfield from internal Me_4Si were recorded on a Bruker AC 250 instrument from a solution in CDCl_3 of the product. Mass spectra were recorded on a Nermag R10.10H spectrometer. Infrared spectra were recorded on Perkin Elmer 684 IR spectrophotometer in KBr with absorptions in cm^{-1} . Melting point (mp) in $^\circ\text{C}$ are uncorrected. AM1 calculations were carried out with HyperChem software [12] on a Silicon Graphics workstation and with Spartan software [13]. Satisfactory elemental analytical data have been obtained for all compounds described in this paper.

Synthesis of 2H-naphtho[2,1-b]furan-1-one (**1**)

2-Naphthoxyacetic acid [3b] (85 mmol, 17.2 g) was heated under reflux for 30 min with thionyl chloride in excess and a drop of dry DMF, in a 250 ml round-bottomed flask equipped with a condenser. The thionyl chloride was distilled off. The acid chloride obtained was slowly added dropwise to AlCl_3 (11.5 g) in CH_2Cl_2 (40 ml) cooled with ice water. The mixture was refluxed for

15 min; then the cake was treated with cold water under a hood. The product was then extracted into ether (4 x 100 ml). The organic layer was dried with magnesium sulphate and filtered on Celite. The solvent was evaporated in vacuum and the product was chromatographed on silica gel (eluent : $\text{AcOEt}/\text{C}_6\text{H}_{12}=20/80$).

Brown solid; yield 41%; mp 133; $\text{C}_{12}\text{H}_8\text{O}_2$; CAS registry number 19997-42-3; Beilstein registry number 133750; NMR ^1H (CDCl_3) : 4.8 (s, 2H, CH_2), 7.3 (d, 1H, H_{arom} , $J_1=7.7$ Hz), 7.5 (t, 1H, H_{arom} , $J_1=7.7$ Hz), 7.7 (t, 1H, H_{arom} , $J_1=7.7$ Hz), 7.85 (d, 1H, H_{arom} , $J_2=8.2$ Hz), 8.1 (d, 1H, H_{arom} , $J_1=7.7$ Hz), 8.75 (d, 1H, H_{arom} , $J_2=8.2$ Hz); MS m/z (%): 185 (M^{++1} , 13.0), 184 (M^+ , 88.4), 183 (13.0), 156 (11.6), 155 (43.5), 127 (20.3), 126 (27.6), 125 (30.4); IR (KBr): 1690 ($\text{C}=\text{O}$).

Synthesis of 2-(arylmethylene)-2H-naphtho[2,1-b]furan-1-one (**5a-f**)

General procedure

2H-Naphtho[2,1-b]furan-1-one (3 mmol, 0.552 g) and solid aldehyde (3 mmol) were stirred 5 min in 50 ml CH_2Cl_2 with $\text{KF-Al}_2\text{O}_3$ (3g). The solvent was then evaporated in vacuum, and the solid was irradiated in an open Pyrex tube (8 mm diameter) with focused microwaves (40 W) in resonance cavity TE₀₁ at 2450 MHz, with a universal generator MES 73-800, previously described [7]. Extraction was carried out with 40 ml acetonitrile. The product was filtered off and the solvent was evaporated. Recrystallisation from alcohol yielded the condensation product.

2-(Phenylmethylene)-2H-naphtho[2,1-b]furan-1-one (5a)

Obtained from benzaldehyde and 2H-naphtho[2,1-b]furan-1-one; irradiation 40 W, 10 min; yellow needles; yield 96%; mp 150; lit [14]; C₁₉H₁₂O₂; NMR ¹H (CDCl₃) : 6.95 (s, 1H, CH=C), 7.35 to 7.55 (b, 5H, H arom), 7.7 (t, 1H, H arom, J₁=7.7 Hz), 7.8 à 8.0 (b, 3H, H arom), 8.1 (d, 1H, H arom, J₁=7.7 Hz), 8.85 (d, 1H, H arom, J₂=8.2 Hz); MS m/z(%): 273 (M⁺+1, 3.5), 272 (M⁺, 24.2), 271 (35.0), 188 (6.9), 127 (23.8), 126 (12.9); IR (KBr): 1694 (C=O), 1628 (C=C).

2-(4-Methoxyphenylmethylene)-2H-naphtho[2,1-b]furan-1-one (5b)

Obtained from p-anisaldehyde and 2H-naphtho[2,1-b]furan-1-one; irradiation 40 W, 10 min; green solid; yield 73%; mp=168; lit [9]; C₂₀H₁₄O₃; NMR ¹H (CDCl₃) : 3.9 (s, 3H, CH₃O), 6.95 (s, 1H, CH=C), 7.05 (b, 2H, H arom), 7.45 to 7.6 (b, 2H, H arom), 7.7 (t, 1H, H arom, J₁=7.7 Hz), 7.8 to 8.0 (b, 3H, H arom), 8.1 (d, 1H, H arom, J₁=7.7 Hz), 8.9 (d, 1H, H arom, J₂=8.2 Hz); MS m/z(%): 303 (M⁺+1, 12.8), 302 (M⁺, 61.4), 301 (34.6), 287 (8.05), 271 (19.2), 259 (7.3), 202 (24.0), 185 (10.7), 135 (22.9), 126 (100.0); IR (KBr): 1690 (C=O), 1644 (C=C).

2-(Fur-2-ylmethylene)-2H-naphtho[2,1-b]furan-1-one (5c)

Obtained from 2-furaldehyde and 2H-naphtho[2,1-b]furan-1-one; irradiation 40 W, 10 min; green solid; yield 75%; mp 220; C₁₇H₁₀O₃; NMR ¹H (CDCl₃) : 6.65 (b, 1H, H arom), 7.0 (s, 1H, CH=C), 7.2 (b, 1H, H arom), 7.3 (d, 1H, H arom), 7.5 (b, 2H, H arom), 7.7 (b, 1H, H arom), 7.85 (b, 1H, H arom), 8.1 (b, 1H, H arom), 8.85 (d, 1H, H arom, J₂=8.2 Hz); MS m/z(%): 263 (M⁺+1, 5.65), 262 (M⁺, 36.9), 234 (7.4), 205 (7.5), 126 (41.9); IR (KBr): 1684 (C=O), 1630 (C=C).

2-(Thien-2-ylmethylene)-2H-naphtho[2,1-b]furan-1-one (5d)

Obtained from 2-thiophenecarboxaldehyde and 2H-naphtho[2,1-b]furan-1-one; irradiation 40 W, 10 min; green solid; yield 86%; mp 170; C₁₇H₁₀O₂S; NMR ¹H (CDCl₃) : 7.2 (b, 1H, H arom), 7.25 (s, 1H, CH=C), 7.5 à 7.75 (b, 5H, H arom), 7.9 (d, 1H, H arom, J₂=8.2 Hz), 8.15 (d, 1H, H arom, J₁=7.7 Hz), 8.9 (d, 1H, H arom, J₂=8.2 Hz); MS m/z(%): 279 (M⁺+1, 21.9), 278 (M⁺, 85.2), 277 (67.8), 250 (12.7), 221 (31.4), 171 (15.6), 142 (11.3), 126 (100.0); IR (KBr): 1684 (C=O), 1628 (C=C).

2-(3,4-Dimethoxyphenylmethylene)-2H-naphtho[2,1-b]furan-1-one (5e)

Obtained from 3,4-dimethoxybenzaldehyde and 2H-naphtho[2,1-b]furan-1-one; irradiation 40 W, 10 min; yellow solid; yield 81%; mp=201; C₂₁H₁₆O₄; NMR ¹H (CDCl₃) : 3.9 (s, 3H, CH₃O), 3.95 (s, 3H, CH₃O), 6.95 (s, 1H, CH=C), 7.0 (d, 1H, H arom, J₁=7.7 Hz), 7.45 to 7.6 (b, 4H, H arom), 7.75 (t, 1H, H arom, J₁=7.7 Hz), 7.9 (d, 1H, H arom, J₂=8.3 Hz), 8.15 (d, 1H, H arom, J₁=7.7 Hz), 8.9 (d, 1H, H arom, J₂=8.3 Hz); MS m/z(%): 333 (M⁺+1, 3.4), 332 (M⁺, 56.1), 331 (16.2), 317 (13.0), 301 (11.4), 289 (8.5), 274 (10.6), 258 (10.0), 246 (11.0), 220 (14.0), 202 (10.8), 189 (9.9), 167 (11.5), 127 (22.4), 126 (88.7); IR (KBr): 1680 (C=O), 1632 (C=C).

2-(2,4,6-Trimethoxyphenylmethylene)-2H-naphtho[2,1-b]furan-1-one (5f)

Obtained from 2,4,6-trimethoxybenzaldehyde and 2H-naphtho[2,1-b]furan-1-one; irradiation 40 W, 10 min; yellow needles; yield 57%; mp=124; C₂₂H₁₈O₅; NMR ¹H (CDCl₃) : 3.9 (b, 9H, CH₃O), 6.2 (b, 2H, H arom), 7.2 (s, 1H, CH=C), 7.35 (d, 1H, H arom, J₁=7.7 Hz), 7.5 (t, 1H, H arom, J₁=7.7 Hz), 7.7 (t, 1H, H arom, J₁=7.7 Hz), 7.9 (d, 1H, H arom, J₂=8.2 Hz), 8.05 (d, 1H, H arom, J₁=7.7 Hz), 8.9 (d, 1H, H arom, J₂=8.2 Hz); MS m/z(%): 363 (M⁺+1, 1.3), 362 (M⁺, 2.3), 332 (3.2), 331 (3.9), 197 (34.2), 196 (100.0); IR (KBr): 1686 (C=O), 1632 (C=C).

References and Notes

1. *The Chemistry of Flavonoid Compounds*, Ed. Geissman, T.A. Pergamon Press, London, 1962; *The Flavonoids*, J.B. Harbone, T.J. Mabry and H. Mabry, Chapman and Hall, London, 1975.
2. Orzalesi, H.; Castel, J.; Flandre, O.; Darmanaden, R.; Damon, M. *Ger. Offen.* 2,829,619; *Chem. Abstr.*, **1979**, 90, 197859z.
3. a) Villemin, D.; Labiad, B. *Synth. Commun.* **1990**, 20, 3207; b) Villemin, D.; Labiad, B. *Synth. Commun.* **1990**, 20, 3213; c) Villemin, D.; Ricard, M. *Synth. Commun.* **1987**, 17, 283; d) Villemin, D.; Ben Alloum, A.; Labiad, B. *J. Chem. Soc. Chem. Commun.* **1989**, 386.
4. a) *Index des Produits Phytosanitaires*, 20 ed., ACTA, Paris, **1982**; b) Villemin, D.; Hammadi, M. *Synth. Commun.* **1996**, 26, 4337.
5. Ullmann, G. *Ber.* **1897**, 30, 1468.
6. Varma, R. S.; Varma, M. *Tetrahedron Lett.* **1992**, 33, 5937, and references cited.
7. Villemin, D.; Martin, B. *Synth. Commun.* **1995**, 25, 2319.
8. (a) Review on microwave activation: Bram, G.; Loupy, A.; Villemin, D. in *Solid Supports and Catalysts in Organic Synthesis*, chap.12, p. 302-326. (b) Caddick, S. *Tetrahedron* **1995**, 51, 10403-1043;

- Smith, K. Ed., Ellis Horwood and Prentice Hall, 1992. (c) Langa, F.; de la Cruz, P.; de la Hoz, A.; Diaz-Ortiz, A.; Diez-Barra, E. *Contemporary Organic Synthesis* **1997**, 373-386.
9. Fitzgerald, D.M.; O'Sullivan, J.F.; Philbin, E.M.; Wheeler, T.S. *J. Chem. Soc.* **1955**, 860.
 10. Donnelly; J.A.; Emerson, G.M. *Tetrahedron* **1990**, *46*, 7227; Donnelly; J.A.; Doran, H.J. *Tetrahedron* **1975**, *31*, 1565; Dean, F.M.; Podimuang, V. *J. Chem. Soc.* **1965**, 3978.
 11. Pelter, A.; Ward, R.S.; Gray, T.I. *J. Chem. Soc. Perkin I*, **1976**, 2475; Pelter, A.; Ward, R.S.; Heller, H.G. *J. Chem. Soc. Perkin I*, **1979**, 328.
 12. HyperChem software from Hypercube Inc., Waterloo, Ontario, Canada.
 13. Spartan software from Wavefunction Inc., 18401 Von Karman Avenue, Suite 370, Irvine, CA 92612, USA.
 14. Ingham, B.H.; Stephen, H.; Timpe, R. *J. Chem. Soc.* **1931**, 895.

Sample Availability: available from the authors.