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Abstract: *p*-Toluenesulfonic acid (PTSA) in EtOH was used as a mild acid-catalyst for the annulation of various functionalized diarylalkynes under microwave irradiation. This free-metal process allowed the synthesis of a range of 3-arylsubstituted isocoumarins in good yields.

Key words: alkynes, annulations, isocoumarin, isochromene, microwaves activation

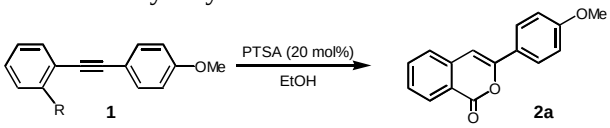
Isocoumarin structures are important components in many natural products that exhibit a broad range of biological activitities including antiallergic and antimicrobial,[1,2] antifungal,[3] antiinflammatory,[4] immunomodulatory,[5] cytotoxic,[6] and antiangiogenic.[7]Therefore, a number of methods have been reported in the literature for the synthesis of the isocoumarin ring.[8] The most common route is undoubtedly the cyclization of 2-(1-alkynyl)benzoic acids/esters under the triple bond activation.[9] A recent approach to the synthesis of isocoumarins from diarylalkynes using TFA[10] as a reagent and solvent prompted us to present our results in this field.

Previously, we reported a new and efficient *p*-toluenesulfonic acid-catalyzed hydration of unsymmetrical aliphatic alkynes in aqueous or alcoholic media.[11] Interestingly, this new environmentally metal-free procedure has been applied successfully to diarylalkynes to afford regioselectively a series of carbonyl compounds.[12] Following this work, we were interested to examine this mild and friendly procedure with diarylalkynes bearing an ortho alkoxycarbonyl function on the aromatic ring to give the corresponding 3-arylisocoumarins. Herein we report the results of this study.

First, we have studied the reaction with diarylalkyne **1a** bearing an ortho ethoxycarbonyl function on the aromatic ring as a model substrate. The results, summarized in Table 1, showed that treatment of **1a** with a catalytic amount of PTSA (20 mol%) in refluxing EtOH afforded the corresponding isocoumarin **2a** in a good yield but with a prolonged reaction time (70%, 24 h, entry 1). Next, in the continuation of our work to develop rapid and efficient methodologies,[13] we choose to promote and accelerate this reaction using microwaves irradiation.

In this way, we were pleased to observe that a reaction time of 30 minutes was sufficient to reach up to 98% conversion of starting diarylalkyne **1a** and isocoumarin **2a** was obtained in an excellent yield (89%, entry 2). As a control experiment, **1a** was heated in EtOH in a sealed tube at 160 °C for 30 minutes. Comparison of the results obtained using conventional or microwave heating indicated clearly the efficiency of the latter method (89%, entry 2 *vs* 30% entry 3). Other carboxyl groups were also examined for this annulation reaction. Interestingly, the yield of **2a** was remarkably increased by switching the ethoxycarbonyl group to a carboxylic acid function (98%, entry 4). The presence of an amide group on the aromatic ring smoothly affected the yield of this process. In this case, **2a** was isolated in a 74% isolated yield (entry 5) together with 19% of the 3-arylisoquinolin-1-one resulting from the 6-*endo-dig* nitrogen-cyclization. When **1d** (R = CN) was heated with PTSA in EtOH under microwave irradiation, **2a** was still isolated but in a modest yield (38%, entry 6).

Table 1. PTSA in EtOH promoted annulation of ortho-substituted arylalkynes **1**.



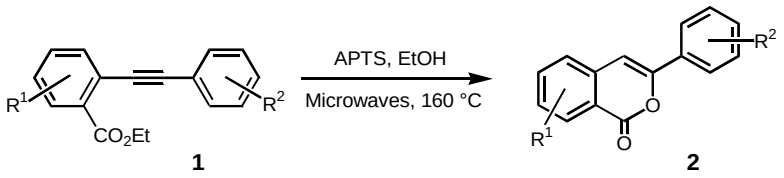
Entry	Alkyne **1**	Conditions	Time (h)	T (°C)	Yield[a] (%)
1	**1a**: R = CO_2Et	reflux	24	78	70
2	**1a**: R = CO_2Et	microwaves	0.5	160	89
3	**1a**: R = CO_2Et	sealed tube	0.5	160	30
4	**1b**: R = CO_2H	microwaves	0.5	160	98
5	**1c**: R = $CONH_2$	microwaves	0.5	160	74[b]
6	**1d**: R = CN	microwaves	0.5	160	38

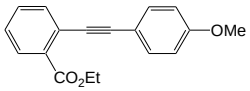
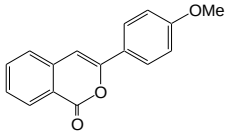
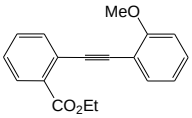
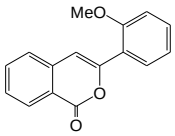
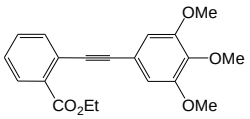
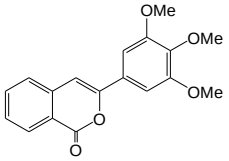
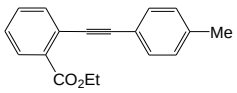
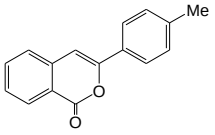
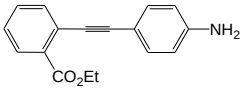
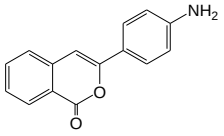
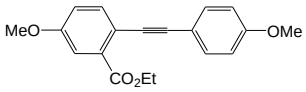
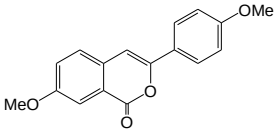
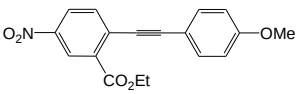
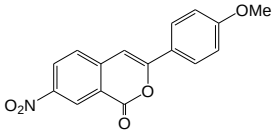
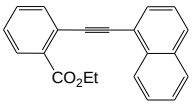
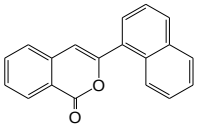
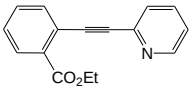
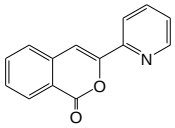
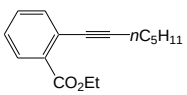
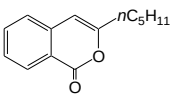
[a.] Isolated yield.
[b.] 19% of 3-(4-methoxyphenyl)isoquinolin-1-one were isolated.

Using our protocol, we were able to prepare a series of functionalized isocoumarins from various diarylalkynes **1** in good yields (Table 2). For practical considerations, we choose to prepare these isocoumarins **2** from diarylalkynes bearing an ortho ethoxycarbonyl group (rather than COOH), as they are easily available after Sonogashira-Linstrumelle couplings.[14]

As shown in entries 2 and 3, the presence of a methoxy group on the ortho or the meta position did not affected significantly the yield of this annulation process. A similar result was obtained starting from **1g**, **1h** or **1i** which provided the 3-arylisocoumarins **2d-f** in a satisfactory isolated yield (entry 4-6). The presence of a nitro group on the aromatic ring did not interfere with

Table 2. One pot synthesis of 3-aryl-isocoumarins **2** from diarylalkynes **1**



Entry	Alkyne **1**		Time (h)	Isocoumarin **2**		Yield[a] (%)
1		**1a**	0.5		**2a**	89
2		**1e**	1		**2b**	70
3		**1f**	1		**2c**	64
4		**1g**	1		**2d**	62
5		**1h**	1		**2e**	60
6		**1i**	2		**2f**	67
7		**1j**	1		**2g**	61
8		**1k**	2		**2h**	85
9		**1l**	2		**2i**	59
10		**1m**	2		**2j**	88[b]

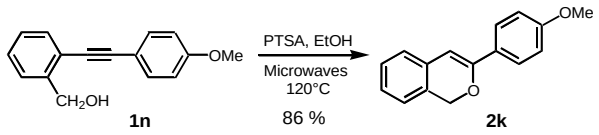
[a] Isolated yield.

[b] obtained as an inseparable 65/35 mixture with the Markovnikov ketone resulting from the triple bond hydration.

the outcome of this process as demonstrated with diarylalkyne **1j** (entry 7, 61%). Similarly, the arylnaphtlyl alkyne **1k** was successfully transformed into to the isocoumarin **2h** in an excellent 85% yield (entry 8). Finally, when replacing the phenyl substituent by a pyridine ring, this methodology was still efficient and the corresponding isocoumarin derivative **2i** was obtained in a satisfactory isolated yield and with a reasonable reaction time (entry 9, 2h, 59 %). Interestingly, we observed that our protocol was still efficient with the aliphatic arylalkyne **1m**. In that case, 3-pentylisocoumarin **2j** was obtained in a good yield (entry 10, 82%) suggesting that the presented protocol could be applied successfully to a range of aliphatic arylalkynes.

To show the high synthetic potential of this protocol, we have tested it with the diarylalkyne **1n** bearing a nucleophilic ortho hydroxymethyl substituent in place of the ethoxycarbonyl group (Scheme 1). We were pleased to observe that after stirring for 30 minutes at 120 °C under microwave heating, the annulation proceeded effectively to give in good yield the desired isochromene **2k**.

Scheme 1. Isochromene **2k** *via* PTSA-catalyzed annulation of **1n**.



1n **2k**

In conclusion, a novel and reliable procedure for the synthesis of isocoumarins was achieved *via* PTSA-catalyzed annulation of ortho substituted arylalkynes in EtOH under microwave irradiation. This metal-free procedure is characterized by the mildness of acidic conditions, short reaction times and good yields. The synthesis of other heterocycles such as isoquinolines and isothiochromenes from their corresponding ortho substituted benzylamine or thiol derivatives respectively is currently under investigation and will be presented in due course.

IR spectra were recorded on a Perkin-Elmer 841 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with a Bruker Avance 300 (300 MHz and 75 MHz, for ^{1}H and ^{13}C, respectively). ^{1}H chemical shifts are reported in ppm from an internal standard TMS or residual chloroform (7.27 ppm). ^{13}C chemical shifts are reported from the central peak of deuteriochloroform (77.1 ppm). ESI mass spectra were obtained with a LCT Waters-Micromass spectrometer Elemental analyses were performed with a Perkin-Elmer 240 analyzer. Melting points were recorded on Büchi B-450 apparatus and are uncorrected. Analytical TLC were performed on Merck precoated silica gel 60F plates. Merck silica gel 60 (230-400 mesh) was used for column chromatography. All microwave experiments were performed using an Emrys Optimizer in 2-5 mL pyrex reaction vessels. Each contained a Teflon stir bar and Teflon coated reaction vessel cap.

Typical procedure: To an Emrys Optimizer 2-5 mL pyrex reaction vessel were added diarylalkyne (0.5 mmol), PTSA (0.01 mmol), in EtOH (2.5 mL). The reaction vessel was then placed in the Emrys Optimizer and exposed to microwave irradiation according to the following specifications: temperature: 160°C, time (see Table 2), fixed hold time: on, sample absorption: high, pre-stirring: 60 s. After cooling to room temperature, H_2O (3 mL) was added to the crude and the mixture was extracted with EtOAc (3 x 2 mL). Organic layers were then washed with an aqueous saturated NH_4Cl solution, dried and concentrated. The crude mixture was then purified by column chromatography on silica gel.

3-(4-Methoxyphenyl)isocoumarin 2a:

White solid; mp 111-113 °C.

IR (neat): 2999, 2844, 1957, 1734, 1632, 1601, 1575, 1562, 1512, 1480, 1457, 1442, 1420, 1344, 1309, 1287, 1260, 1235, 1200, 1175, 1114, 1064, 1020, 925, 887, 835, 790 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.90 (s, 3H), 6.86 (s, 1H), 7.00 (d, 2H, *J* = 9.0 Hz), 7.44-7.50 (m, 2H), 7.75 (t, 1H, *J* = 7.8 Hz), 7.86 (d, 2H, *J* = 9.0 Hz), 8.32 (d, 1H, *J* = 7.8 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ 55.4 (CH_3), 100.2 (CH), 114.3 (2CH), 120.2 (C), 124.4 (C), 125.7 (CH), 126.8 (2CH), 127.7 (CH), 129.6 (CH), 134.8 (CH), 137.9 (C), 153.7 (C), 161.0 (C), 162.6 (C).

Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.00; H, 4.67.

MS *m/z* (ES+) 275.0 ($M+Na^+$).

3-(2-Methoxyphenyl)isocoumarin 2b:

White solid; mp 115-117 °C.

IR (neat): 3117, 3011, 2978, 2843, 1716, 1621, 1596, 1575, 1562, 1483, 1460, 1435, 1366, 1336, 1313, 1277, 1252, 1178, 1165, 1130, 1108, 1071, 1015, 963, 944, 924, 887, 854, cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.00 (s, 3H), 7.00-7.14 (m, 2H), 7.37-7.44 (m, 2H), 7.52 (d, 2H, *J* = 7.6 Hz), 7.70 (td, 1H, *J* = 7.9 Hz, *J* = 1.2 Hz), 8.00 (d, 1H, *J* = 7.9 Hz), 8.33 (d, 1H, *J* = 7.9 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ 55.7 (CH_3), 107.1 (CH), 111.4 (CH), 120.7 (CH), 120.9 (C), 126.3 (CH), 128.0 (CH), 128.9 (CH), 129.4 (CH), 130.8 (C), 134.6 (CH), 138.1 (CH), 145.1 (C), 150.5 (C), 157.3 (C), 162.6 (C).

Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.03; H, 4.66.

3-(3,4,5-Trimethoxyphenyl)isocoumarin 2c:

Beige solid; mp 171 °C.

IR (neat): 1716, 1635, 1580, 1501, 1416, 1240, 1170, 1119, 765, 750, 684 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.83 (s, 3H), 3.88 (s, 6H), 6.80 (s, 1H), 7.00 (s, 2H), 7.37-7.44 (m, 2H), 7.63 (dt, 1H, *J* = 7.6 Hz, *J* = 1.3 Hz), 8.22 (d, 1H, *J* = 4.4 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ 56.2 (2 CH_3), 60.8 (CH_3), 101.5 (CH), 102.7 (2 CH), 120.3 (C), 125.8 (CH), 127.5 (C), 128.0 (CH), 129.7 (CH), 134.9 (CH), 137.5 (C), 139.9 (C), 153.4 (C), 153.5 (2 C), 162.2 (C).

Anal. Calcd for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found: C, 69.15; H, 5.12.

MS *m/z* (ES+) 335.0 ($M+Na^+$).

3-(4-Methylphenyl)isocoumarin 2d:

White solid; mp 108-110 °C.

IR (neat): 2920, 1776, 1729, 1629, 1607, 1562, 1510, 1482, 1455, 1343, 1277, 1197, 1187, 1065, 845, 814 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 3H), 6.83 (s, 1H), 7.15-7.23 (m, 2H), 7.36-7.44 (m, 2H), 7.60 (t, 1H, *J* = 8.3 Hz), 7.70 (d, 2H, *J* = 8.3 Hz), 8.23 (d, 1H, *J* = 8.3 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5 (CH_3), 101.0 (CH), 120.5 (C), 125.3 (2CH), 125.9 (CH), 128.0 (CH), 129.3 (C), 129.7 (2CH), 129.8 (CH), 134.9 (CH), 137.8 (C), 140.4 (C), 154.0 (C), 162.5 (C).

Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found: C, 81.25; H, 5.08.

3-(4-Aminophenyl)isocoumarin 2e:

Yellow solid. mp 158 °C.

IR (neat): 3532-3482, 1705, 1601, 1524, 1072, 812, 748 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$)□: δ 3.78 (bs, 2H), 6.49 (d, 2H, *J* = 8.7 Hz), 6.59 (s, 1H), 7.29-7.23 (m, 2H), 7.51 (t, 1H, *J* = 7.8 Hz,), 7.56 (d, 2H, *J* = 8.7 Hz), 8.11 (d, 1H, *J* = 7.7 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ 98.5 (CH), 112.4 (2 CH),. 119.7 (C), 120.4 (C), 125.4 (CH), 126.7 (2 CH), 127.0 (CH), 129.5 (CH), 134.7 (CH), 138.5 (C), 149.8 (C), 154.6 (C), 162.8 (C)

Anal. Calcd for $C_{15}H_{11}NO_2$: C, 75.94; N, 5.90; H, 4.67. Found: C, 75.61; N, 5.74; H, 4.47.

MS *m/z* (ES+) 238.0 ($M+H^+$)

7-Methoxy-3-(4-methoxyphenyl)isocoumarin 2f:

White solid; mp 144-146 °C.

IR (neat): 2964, 2839, 1717, 1632, 1602, 1573, 1562, 1510, 1496, 1454, 1440, 1419, 1352, 1290, 1256, 1178, 1163, 1119, 1067, 1024, 935, 889, 867, 850, 837, 813 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.88 (s, 3H), 3.94 (s, 3H), 6.83 (s, 1H), 7.00 (d, 2H, *J* = 8.9 Hz), 7.32 (dd, 1H, *J* = 8.6 Hz, *J* = 2.6 Hz), 7.42 (d, 1H, *J* = 8.6 Hz), 7.73 (d, 1H, *J* = 2.6 Hz), 7.82 (d, 2H, *J* = 8.9 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ 55.5 (CH_3), 55.9 (CH_3), 100.2 (CH), 110.0 (CH), 114.3 (2 CH), 121.3 (C), 124.9 (CH), 126.6 (2 CH), 127.4 (CH), 131.5 (C), 131.8 (C), 134.2 (C), 159.4 (C), 160.9 (C).

Anal. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.27; H, 4.97.

3-(4-Methoxyphenyl)-7-nitro-isocoumarin 2g:

Yellow solid. mp 204 °C

IR (neat): 1729, 1599, 1481, 1336, 1178, 1093, 829 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.88 (s, 3H), 6.92 (s, 1H), 7.00 (d, 2H, *J* = 9.0 Hz), 7.60 (d, 1H, *J* = 8.6 Hz), 7.86 (d, 2H, *J* = 9.0 Hz), 8.42 (dd, 1H, *J* = 8.6 Hz, *J* = 2.4 Hz), 9.12 (d, 1H, *J* = 2.3 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ 55.5 (CH_3), 99.0 (CH), 114.5 (2 CH), 120.1 (C), 123.3 (C), 125.9 (CH), 126.8 (CH), 127.5 (2 CH), 129.0 (CH), 143.0 (C), 146.3 (C), 157.3 (C), 160.6 (C), 162.1 (C).

Anal. Calcd for $C_{16}H_{11}NO_5$: C, 64.65; N, 4.71; H, 3.73. Found: C, 64.45; N, 4.58; H, 3.68.

MS *m/z* (ES+) 298.0 ($M+H^+$).

3-Naphthalen-1-yl-isocoumarin 2h:

White solid; mp 120-122 °C.

IR (neat): 3091, 3042, 1938, 1715, 1638, 1606, 1566, 1508, 1486, 1454, 1396, 1352, 1310, 1241, 1200, 1178, 1154, 1116, 1065, 1023, 992, 956, 922, 881 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.80 (s, 1H), 7.47-7.61 (m, 5H), 7.70-7.81 (m, 2H), 7.86-8.00 (m, 2H), 8.21-8.30 (d, 1H, *J* = 9.7 Hz), 8.40 (d, 1H, *J* = 7.4 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ 107.1 (CH), 120.6 (C), 125.0 (CH), 125.1 (CH), 125.9 (CH), 126.3 (CH), 127.1 (CH), 127.7 (CH), 128.4 (CH), 128.6 (CH), 129.7 (CH), 130.6 (CH), 130.8 (C), 133.8 (2 C), 134.9 (CH), 137.5 (C), 154.7 (C), 162.6 (C).

Anal. Calcd for $C_{19}H_{12}O_2$: C, 83.81; H, 4.44. Found: C, 83.60; H, 4.27.

3-Pyridin-2-yl-isocoumarin 2i:

Yellow solid. mp 109-111°C.

IR (neat): 3059, 3011, 1963, 1737, 1641, 1600, 1582, 1568, 1472, 1453, 1431, 1346, 1316, 1282, 1232, 1183, 1153, 1075, 1012, 990, 932, 899 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47-7.65 (m, 1H), 7.72-7.88 (m, 2H), 7.90-8.14 (m, 3H), 8.30 (d, 1H, *J* = 8.0 Hz), 8.54-8.63 (m, 1H), 8.90-8.96 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 103.8 (CH), 120.0 (CH), 124.2 (C), 126.8 (CH), 127.0 (CH), 128.7 (CH), 129.8 (CH), 132.1 (C), 135.0 (CH), 137.1 (CH), 145.5 (C), 149.7 (CH), 152.2 (C), 168.7 (C).

Anal. Calcd for $C_{14}H_9NO_2$: C, 75.33; N, 6.27; H, 4.06. Found: C, 75.29; N, 6.21; H, 3.97.

3-*n*Pentyl-isocoumarin 2j

Yellow oil

IR (neat): 2927, 1729, 1657, 1342, 1287, 1108cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88-0.95 (t, 3H, *J* = 7.8 Hz), 1.05-1.40 (m, 6H), 1.51-1.70 (m, 2H), 6.20 (s, 1H), 7.38 (d, 1H,

J = 7.8 Hz), 7.42 (t, 1H, *J* = 7.8 Hz), 7.51 (t, 1H, *J* = 7.8 Hz), 8.17 (d, 1H, *J* = 7.8 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3 (CH_3), 22.5 (CH_2), 26.6 (CH_2), 31.2 (CH_2), 33.5 (CH_2), 102.9 (CH), 120.1 (C), 125.4 (CH), 127.8 (CH), 129.9 (CH), 134.4 (CH), 136.7 (C), 158.3 (C), 167.1 (C).

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.48; H, 7.27.

3-(4-Methoxyphenyl)-1*H*-isochromene 2k:

White solid; mp 126-128 °C.

IR (neat): 1602, 1501, 1443, 1250, 1170, 1114, 1025, 803, 720 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.54 (s, 3H), 5.20 (s, 2H), 6.35 (s, 1H), 6.91 (d, 2H, *J* = 8.4 Hz), 7.08-7.26 (m, 4H), 7.68 (d, 2H, *J* = 8.4 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ 55.3 (CH_3), 69.0 (CH_2), 99.5 (CH), 113.7 (2 CH), 123.5 (CH), 126.0 (CH), 126.6 (CH), 126.9 (2 CH), 127.8 (C), 128.2 (C), 129.1 (CH), 132.3 (C), 154.0 (C), 160.3 (C).

Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.51; H, 5.84.

MS *m/z* (ES+) 239.0 ($M+H^+$).

Acknowledgment

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Synthesis of isocoumarin *via* PTSA-catalyzed annulation of diarylalkynes

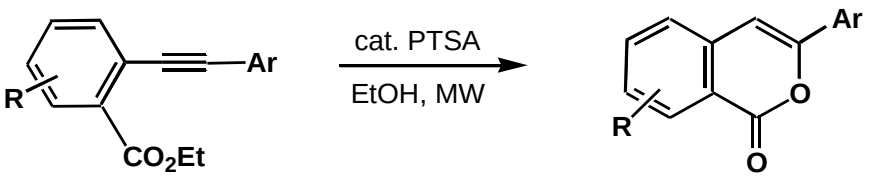
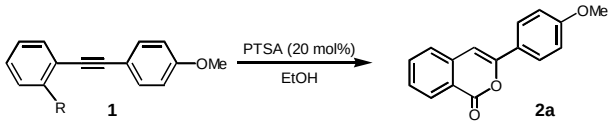


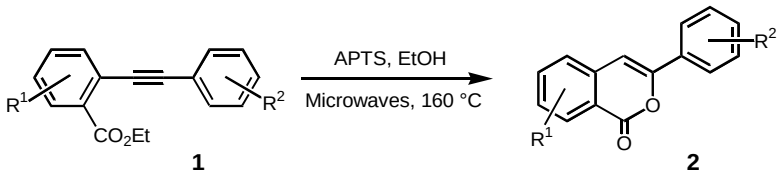
Table 1. PTSA in EtOH promoted annulation of ortho -substituted arylalkynes **1**.

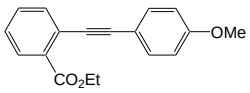
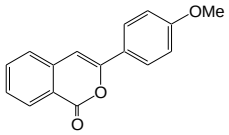
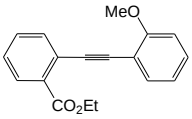
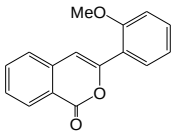
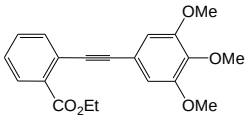
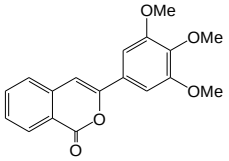
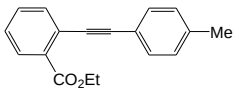
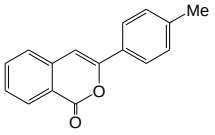
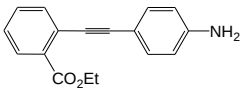
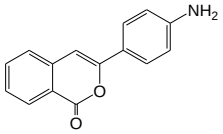
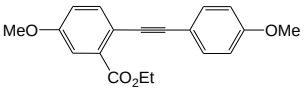
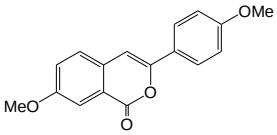
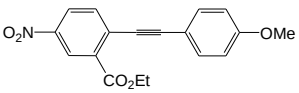
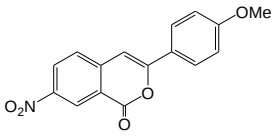
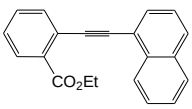
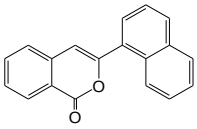
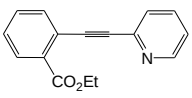
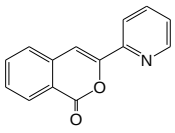
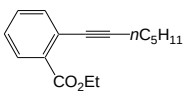
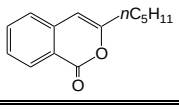


Entry	Alkyne **1**	Conditions	Time (h)	T (°C)	Yield[a] (%)
1	**1a**: R = CO_2Et	reflux	24	78	70
2	**1a**: R = CO_2Et	microwaves	0.5	160	89
3	**1a**: R = CO_2Et	sealed tube	0.5	160	30
)4	**1b**: R = CO_2H	microwaves	0.5	160	98
5	**1c**: R = $CONH_2$	microwaves	0.5	160	74[b]
6	**1d**: R = CN	microwaves	0.5	160	38

[a.] Isolated yield.
[b.] 19% of 3-(4-methoxyphenyl)isoquinolin-1-one were isolated.

Table 2. One pot synthesis of 3-aryl-isocoumarins **2** from diarylalkynes **1**

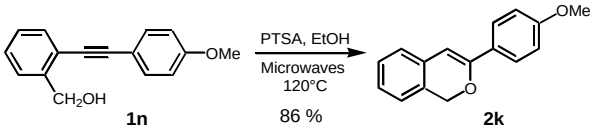


Entry	Alkyne **1**		Time (h)	Isocoumarin **2**		Yield[a] (%)
1		**1a**	0.5		**2a**	89
2		**1e**	1		**2b**	70
3		**1f**	1		**2c**	64
4		**1g**	1		**2d**	62
5		**1h**	1		**2e**	60
6		**1i**	2		**2f**	67
7		**1j**	1		**2g**	61
8		**1k**	2		**2h**	85
9		**1l**	2		**2i**	59
10		**1m**	2		**2j**	88[b]

[a] Isolated yield.

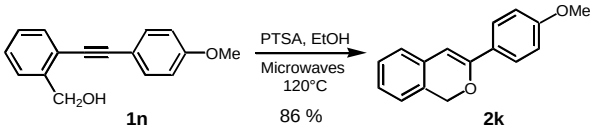
[b] obtained as an inseparable 65/35 mixture with the Markovnikov ketone resulting from the triple bond hydration

Scheme 1. Isochromene **2k** *via* PTSA-catalyzed annulation of **1n**.



1n **2k**

Scheme 1. Isochromene **2k** *via* PTSA-catalyzed annulation of **1n**.



1n **2k**