

Preparation of conjugated enynes and arylacetylenic compounds from arylalkynols using alumina in dry media

Ali Pourjavadi* and Gholam Bagheri Marandi

Department of Chemistry, Sharif University of Technology, PO Box 11365-9516, Azadi Ave., Tehran, Iran

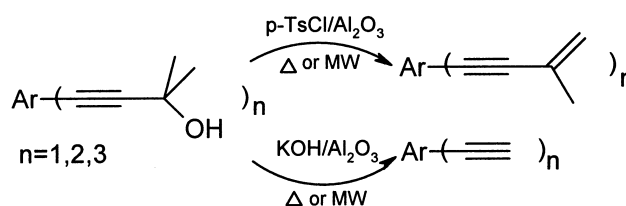
Arylalkynols were converted into both conjugated enynes and arylacetylenic compounds using *p*-TsCl/Al₂O₃ and KOH/Al₂O₃ respectively in classical heating or microwave irradiation methods in good yields.

Keyword: arylalkynol, alumina, conjugated enyne, arylacetylene, microwave

Conjugated enynes are attractive organic compounds that can be used in the synthesis of natural products,¹ polymers,² and selective construction of aromatic frameworks.³ They have been mainly constructed via coupling reactions of terminal alkynes with vinyl halides, triflates and organometallic compounds,⁴ and also homocoupling or cross-coupling of acetylenic compounds using metal catalysts such as Pd⁵ and Ru⁶ complexes. The dehydration of arylalkynols has also been used for preparation of conjugated enynes using reagents such as dicobalt hexacarbonyl complexes,⁷ acidic zeolites⁸ and polyphosphoric acid trimethylsilyl ester.⁹ The reagents selectively convert the propargylic alcohols into 1,3-enynes without producing α,β -unsaturated carbonyl compounds from Meyer-Schuster rearrangement¹⁰ of the corresponding alcohols.

On the other hand, arylacetylenic compounds are widely used in many areas of organic chemistry, for example, synthesis of natural products,¹¹ “molecular wires”,¹² dendrimers,¹³ cyclophanes,¹⁴ and nonlinear optical compounds.¹⁵ Several methods are available to generate the arylacetylenic compounds. The Sonogashira reaction^{4c, 4d} is of significant importance among them. This is the reaction of an arylhalide with a suitable terminal alkyne in the presence of a catalytic amount of a palladium(II) complex and copper(I) iodide dissolved in an amine as solvent and base. A couple of terminal alkynes are reported to be suitable for the preparation of arylacetylenes. They are trimethylsilylacetylene (TMSA) with subsequent desilylation from ArC \equiv CSiMe₃^{4c, 16} and 2-methylbut-3-yn-2-ol (MEBYNOL) with subsequent base-catalysed retro-Favorsky elimination of acetone from ArC \equiv C(CH₃)₂OH in solvents such as toluene.¹⁷ MEBYNOL is cheaper than TMSA and the resulting coupled products are frequently crystalline compounds but the required deprotection conditions (*i.e.*, high temperature, basic medium, and long reaction time) often result in polymerisation of the alkyne and a decrease in the reaction yield.

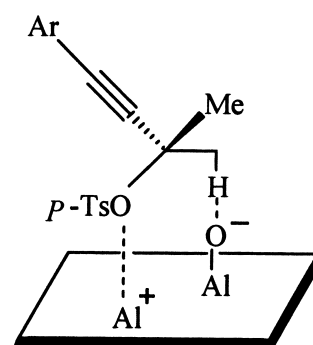
Organic reactions on solid supports have been widely used.¹⁸ Alumina is one of the most useful inorganic supports which has been used for the synthesis of organic compounds.¹⁹ It has large surface area and also contains acid and base sites on its surface. Therefore, alumina can be used as support, catalyst and reagent in organic reactions. We now report that arylalkynols, derivatives of MEBYNOL, can be converted into both conjugated enynes and acetylenic compounds in good yields using *p*-TsCl/Al₂O₃ and KOH/Al₂O₃ respectively. Reactions were performed in dry media using classical and microwave²⁰ (MW) heating methods, (Scheme 1).



Scheme 1

In our methodology, arylalkynols containing both electron donating and electron withdrawing substituents participated effectively. In order to compare the two methods, in the classical heating method conversion of arylalkynols **A**²¹ into conjugated enynes (see Table 1) and acetylenic compounds (see Table 2) was carried out at the final temperature of the MW experiments.

As shown in Table 1, in both methods, the dehydration of arylalkynols to enynes proceed quickly and good yields. It seems that the dehydration process may be achieved via the complex shown in Scheme 2. Herein neutral alumina is both a base and the activating agent of the leaving group.



Scheme 2

The production of the arylacetylenic compounds from the appropriate arylalkynols was accomplished via MW irradiation or classical heating the mixture of arylalkynol and neutral alumina coated by KOH. At the start of the MW irradiation or a few minutes after starting the reaction in a pre-heated oil bath, the arylacetylene rapidly built up from the supported mixture and settled down on the vessel wall while a volatile by-product (acetone) evaporated from the reaction mixture. These conditions, as well as the shortness of reaction time, retard the polymerisation or other side reactions of arylacetylenes and lead to the products in good yield. As shown in Table 2, yields of the

* To receive any correspondence. E-mail: AliPourjavadi@iup-ir.com

† This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1 Conversion of arylalkynols into conjugated enynes using *p*-TsCl and neutral Al₂O₃

Entry	Arylalkynol (A) ^a (ref.)	Enyne (B) ^b	Microwave ^c		Conventional			M.p./°C or phys. state	Lit. M.p./°C or phys. state
			Time /min	Yield /%	Temp. /°C	Time /min	Yield /%		
1			5.0	80	100	55	85	Colourless liquid	(Colourless liquid) ^{2c,23}
2			5.0	80	100	55	85	Pale yellow liquid	(Pale yellow liquid) ²³
3			–	–	100	60	90	30	(30) ²³
4			4.5	80	95	20	90	Pale yellow liquid	(Pale yellow liquid) ²³
5			4.0	85	105	60	80	42.5–43.5	(42.5–43.5) ²³
6			6.0	80	110	90	80	95.5–96.5	(95.5–96.5) ²³
7			6.0	85	105	90	85	62–63	
8			7.0	75	110	90	70	50–51	
9 ^d			3.0	90	110	25	85	97.5–98.5	(97.5–98.5) ²³
10 ^e			3.0	80	120	30	75	71.5–72.5	(71.5–72.5) ²³

^a Arylalkynol/*p*-TsCl ratio was 1 mmol/1 mmol on 2 g neutral Al₂O₃. ^b Eluent for purification of the enynes by plate chromatography was ratio 99/1 of hexane to ethylacetate unless of 7B that this ratio was 98/2. ^c **1A**, **2A** and **4A** were irradiated with level 7 (630 W) and **5A–10A** were irradiated with high power (900 W). ^d Arylalkynol/*p*-TsCl ratio was 1 mmol/2 mmol on 3 g Al₂O₃. ^e Arylalkynol/*p*-TsCl ratio was 1 mmol/3 mmol on 3 g Al₂O₃.

Table 2 Synthesis of arylacetylenic compounds from arylalkynols.

Entry	Arylalkynol (A) ^a (ref.)	Arylalkyne (C)	Microwave ^c		Conventional			M.p. /°C	Lit. M.p. /°C
			Time ^c /s	Yield ^d /%	Time /min	Temp /°C	Yield /%		
1			–	–	60	105	75(80)	Liquid	Liquid
2			–	–	60	105	75(80)	Liquid	(Liquid) ²⁹
3			–	–	60	105	75(80)	65	(61–65) ³⁰
4			55	89 (94)	45	95	83(88)	87	(86–87) ^{4c}
5			60	85 (92)	45	95	83(90)	29–30	(29) ³¹
6			25	81 (92)	30	90	80(85)	150	(150–151) ^{4c}
7			25	80 (89)	30	90	75(82)	69–70	(69–70) ^{4c}
8			30	81 (92)	30	90	80(85)	155–156	(156–157) ^{4c}
9			60	84 (95)	45	115	78(83)	95–96	(95–96) ^{4c}
10			75	85 (87)	60	130	75(80)	103	(102–103) ³²

^a Arylalkynol/KOH ratio was 1 mmol/0.7 g on 3 g neutral Al₂O₃ in except of compounds **9A** and **10A** that these ratios were 1 mmol/1.2 g and 1 mmol/2 g respectively. ^b Eluent for purification of the arylacetylenic compounds by column chromatography was ratio 99/5 of hexane to ethylacetate. ^c Irradiation was carried out in level 10 (high power-900 W) in except of compounds **7A** and **9A** that were irradiated with level 8. ^d Isolated yield and also the value in parentheses indicates yield based on the conversion of arylalkynol.

arylacetylenes using the MW technique are slightly greater than those of classical heating experiments.

In the cases of entry **3A** from Table 1 and entries **1A–3A** from Table 2, the MW method was not suitable, because before the completion of the reactions the starting compounds were sublimed (or evaporated) from the solid support and the corresponding product formed in low yield. However, in the classical heating method we achieved good yields by returning the built-up substance into the reaction mixture occasionally by a spatula.

In conclusion, our present methodology offers alternative features such as economic viability of the reagents, reduced reaction times and good yields to obtain conjugated enynes and arylacetylenic compounds from arylalkynols.

Experimental

IR spectra were recorded on a Mattson-1000 FTIR spectrophotometer. NMR spectra were recorded on a Bruker DRX-500 Avance or Bruker AC-80 spectrometer. Chemical shifts are expressed in ppm relative to TMS. Mass spectra were obtained on a Hewlett-Packard 5973 MSD. Elemental analyses (C, H, N) were performed on a Heraeus CHN-O-Rapid analyser. Melting points were obtained on a Buchi B-540 melting point apparatus and are uncorrected. MW experiments were performed in a Westinghouse 1400 W (900 W output) domestic MW oven. The arylalkynols were prepared using the Sonogashira reaction. The neutral Al₂O₃ used was Aluminium Oxide 1095-Merck.

Typical procedure for the preparation of a conjugated enyne by the classical heating method: *p*-TsCl (1 mmol) and neutral alumina (2 g) were well mixed then **8A** (1 mmol) was introduced to the mixture while it was being ground using a pestle and mortar. The mixture was transferred to a 25-ml round-bottomed flask attached to a short column (12 × 2 cm) and it was placed in a preheated oil bath (110°C). The solid mixture was vigorously stirred for 90 min. The oil bath was removed and the product mixture was allowed to cool to room temperature. After cooling the flask, the product was extracted with ethyl acetate and the solvent was then removed *in vacuo* to afford a crude product that was purified by thin layer chromatography on a silica plate (Merck-5715) using hexane/ethylacetate (99/1) as eluent. **8B** was obtained in 70% yield, as a white solid, m.p. 50–51°C; IR(KBr, cm⁻¹), 3055, 2923, 2223, 1608, 1500, 1377, 1307, 1179, 915, 838; ¹H NMR (CDCl₃, 500 MHz), δ(ppm) 2.00(s,3H), 5.40(s, 1H), 5.47(s, 1H), 7.51(d, 2H, *J* = 8.3 Hz), 7.60(d, 2H, *J* = 8.3 Hz); ¹³C NMR(CDCl₃, 125 MHz), δ(ppm) 32.58, 87.10, 95.30, 111.77, 118.94, 124.15, 126.59, 128.62, 132.39, 132.46; MS *m/e* 167, 166, 152, 140, 125, 113; Anal. calcd for C₁₂H₉N: C, 86.23; H, 5.39, found: C, 86.50; H, 5.25.

Typical procedure for the preparation of conjugated enyne by the MW method: *p*-TsCl (1 mmol) and neutral alumina (2 g) were well mixed, then **7A** (1 mmol) was introduced to the mixture while it was being ground. The mixture was transferred to a 200 ml Erlenmeyer flask attached to a short column (12 × 2 cm) and was irradiated by MW for 6 min. The procedure was used for the work-up and purification by plate chromatography with ratio 98/2 of hexane to ethyl acetate as mentioned above. **7B** was obtained in 85% yield, as a white solid, m.p. 62–63°C; IR(KBr, cm⁻¹), 3050, 2946, 2026, 1723, 1600, 1446, 1377, 1177, 1115, 882, 777; ¹H NMR (CDCl₃, 500 MHz), δ(ppm) 2.02 (s, 3H), 3.94 (s, 3H), 5.37(s, 1H), 5.46 (s, 1H), 7.51(d, 2H, *J* = 8.1 Hz), 8.00 (d, 2H, *J* = 8.1 Hz); ¹³C NMR(CDCl₃, 125 MHz), δ(ppm) 23.74, 52.65, 87.99, 93.90, 123.45, 126.91, 128.40, 129.76, 129.86, 131.89, 166.99; MS *m/e* 200, 185, 170, 169, 141, 139, 126, 115; Anal. calcd for C₁₃H₁₂O₂: C, 78.00; H, 6.00, found: C, 77.82; H, 6.20.

Typical procedure for the preparation of an arylacetylenic compound by the classical heating method: In a typical procedure for the classical heating method, KOH (0.7 g) was added onto neutral Al₂O₃ (3 g) and mixed well, then **6A** (1 mmol) was introduced to the mixture while it was being ground using a pestle and mortar. The mixture was transferred to a 25-ml round-bottomed flask attached to a short column (12 × 2 cm) and, it was placed in a preheated oil bath (90°C). The solid mixture was vigorously stirred for 30 min. The flask was cooled, and the mixture was extracted with hexane/ethylacetate (80/20), the solvent was removed *in vacuo* to afford a crude product that was purified by column chromatography on silica gel using hexane/ethylacetate (95/5) as eluent to give **6C** as a pale yellow solid, yield 80%, mp 150°C.

Typical procedure for the preparation of an arylacetylenic compound by the MW method: KOH (1.2 g) was added onto neutral Al₂O₃ (3 g) and mixed well, then **9A** (1 mmol) was introduced to the

mixture while it was being ground. The mixture was irradiated by MW (720 W, 60 s) in a 200 ml Erlenmeyer flask attached to short column (12 × 2 cm). The procedure was used for the work-up and purification as mentioned above. **9C** was obtained in 84% yield, as a white solid, m.p. 95–96°C.

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- 21 The physical and/or spectral data of arylalkynols 1A–10A. 1A: m.p. = 54–55°C (lit. m.p. = 51°C). 2A: m.p. = 50.5–51.5°C; IR (KBr, cm⁻¹), 3300, 2985, 2930, 1515, 1369, 1285, 1169, 969,

- 823; ^1H NMR (CDCl_3 , 500 MHz), $\delta(\text{ppm})$ 1.64 (s, 6H), 1.87 (brs, 1H), 2.37 (s, 3H), 7.13 (d, 2H, $J = 7.9$ Hz), 7.33 (d, 2H, $J = 7.9$ Hz); ^{13}C NMR (CDCl_3 , 125 MHz), $\delta(\text{ppm})$ 21.85, 31.95, 66.03, 82.64, 93.56, 120.88, 129.41, 131.95, 138.70; MS m/e 174, 159, 141, 131, 115, 91; Anal. calcd for $\text{C}_{12}\text{H}_{14}\text{O}$: C, 82.76; H, 8.05; found: C, 82.66; H, 8.24%. 3A: m.p. = 56.5–57.5°C (lit. m.p. = 56–57°C). [4A (Table 1) and 5A (Table 2)]: m.p. = 52–53°C. [4A (Table 2)]: m.p. = 115.5–116.5°C; IR (KBr, cm^{-1}), 3331, 2985, 1485, 1369, 1154, 969, 846, 769; ^1H NMR (CDCl_3 , 500 MHz), $\delta(\text{ppm})$ 1.69 (s, 6H), 2.30 (s, 1H), 7.38–7.62 (m, 9H); ^{13}C NMR (CDCl_3 , 125 MHz), $\delta(\text{ppm})$ 31.94, 66.11, 82.44, 94.82, 122.04, 127.35, 127.43, 129.27, 132.48, 140.73, 141.39; MS m/e 236, 221, 202, 178, 165, 152; Anal. calcd for $\text{C}_{17}\text{H}_{16}\text{O}$: C, 86.44; H, 6.78; found: C, 86.70; H, 6.90%. [5A (Table 1) and 7A (Table 2)]: colourless oil (lit. colourless oil). 6A: m.p. = 107.5–108.5°C (lit. colourless oil). [7A (Table 1)]: m.p. = 84.5–85°C (lit. m.p. = 84–85°C). 8A: m.p. = 68.5–69.5°C; IR (KBr, cm^{-1}), 3423, 2977, 2231, 1608, 1500, 1369, 1269, 1108, 969, 808; ^1H NMR (CDCl_3 , 500 MHz), $\delta(\text{ppm})$ 1.61 (s, 6H), 2.83 (s, 1H), 7.45 (d, 2H, $J = 8.4$ Hz), 7.55 (d, 2H, $J = 8.4$ Hz); ^{13}C NMR (CDCl_3 , 125MHz), $\delta(\text{ppm})$ 31.65, 65.90, 80.90, 98.89, 111.82, 118.83, 128.25, 132.33, 132.53; MS m/e 185, 184, 170, 154, 142, 127, 115; Anal. calcd for $\text{C}_{12}\text{H}_{11}\text{NO}$: C, 77.84; H, 5.95; N, 7.57; found: C, 77.50; H, 6.15%; N, 7.35. 9A: m.p. = 165–166°C (lit. m.p. = 162–163°C). 10A: m.p. = 177–178°C; IR (KBr, cm^{-1}), 3262, 2985, 2931, 1585, 1415, 1245, 1162, 962, 900, 654. ^1H NMR ($\text{DMSO}-d_6$, 500 MHz), $\delta(\text{ppm})$ 1.47 (s, 18H), 5.45 (s, 3H), 7.33 (s, 3H); ^{13}C NMR ($\text{DMSO}-d_6$, 125 MHz), $\delta(\text{ppm})$ 32.28, 64.47, 79.45, 98.50, 124.63, 133.96; MS m/e 324, 309, 291, 266, 251, 233, 189, 138; Anal. calcd for $\text{C}_{21}\text{H}_{24}\text{O}_3$: C, 77.78; H, 7.41; found: C, 77.62; H, 7.46%.
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