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Microwave-assisted Claisen rearrangement on a silica gel support

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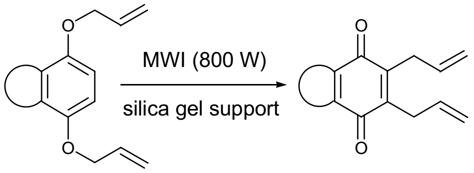
This paper is dedicated to Professor Srinivasan Chandrasekaran on the occasion of his 60th birthday

Abstract—A fast, efficient and environmentally benign solvent-free procedure has been developed for microwave-assisted Claisen rearrangement on a silica gel support. Various bis-allyl ketones were prepared using this protocol.

In recent years, solvent-free reactions using either organic or inorganic solid supports have received increasing attention.[1] There are several advantages to performing synthesis in dry media: (i) short reaction times, (ii) increased safety, (iii) economic advantages due to the absence of solvent. Silica gel is effective because the end products can easily be separated. Moreover, silica gel can function as a convenient medium and also act as a mild acidic catalyst.[2]

Microwave irradiation (MWI) has become an established tool in organic synthesis, because of the rate enhancements, higher yields and often, improved selectivity, with respect to the conventional reaction conditions.[3] In addition, solvent-free MWI processes are also clean and efficient.

Herein, we report a rapid procedure for the synthesis of bis-allyl ketones by microwave-assisted Claisen rearrangement[4] on a silica gel support (Scheme 1) under solvent-free conditions.

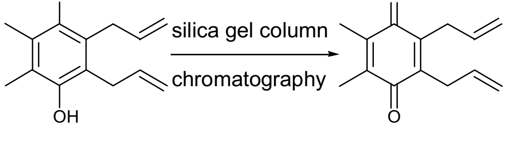


Scheme 1.

In connection with a project related to ring-closing metathesis, we observed that a tetra substituted 1,4-bis-hydroxybenzene derivative was partially transformed to the corresponding quinone derivative during purification on a silica gel column (Scheme 2).[5] This critical observation led to the development of a one-pot conversion of 1,4-bis-allyloxybenzene derivatives to 2,3-bis-allyl-1,4-quinone derivatives by taking advantage of the cumulative effect of the silica gel support and MWI under solvent-free conditions.

Among various solid supports, including silica gel, alumina and the highly acidic montmorillonite clay, silica gel was found to be the most efficient medium for this transformation. Here, the role of silica gel may be twofold: (i) Physisorption of reactants on the silica surface leading to an increase in local concentration, which in turn enhances the rate of reaction. (ii) The acidic nature of the silica surface promotes the oxidation of phenol to quinone. Some other oxidation processes induced by acidic silica gel have been reported in the literature.[6]

The required *O*-allylated starting materials were prepared by standard procedures as shown in Scheme 3. These *O*-allylated compounds were then heated in an unmodified domestic MW oven with a maximum power



Scheme 2.

Keywords: Claisen rearrangement; Microwave irradiation; Silica gel support; Solvent-free synthesis.

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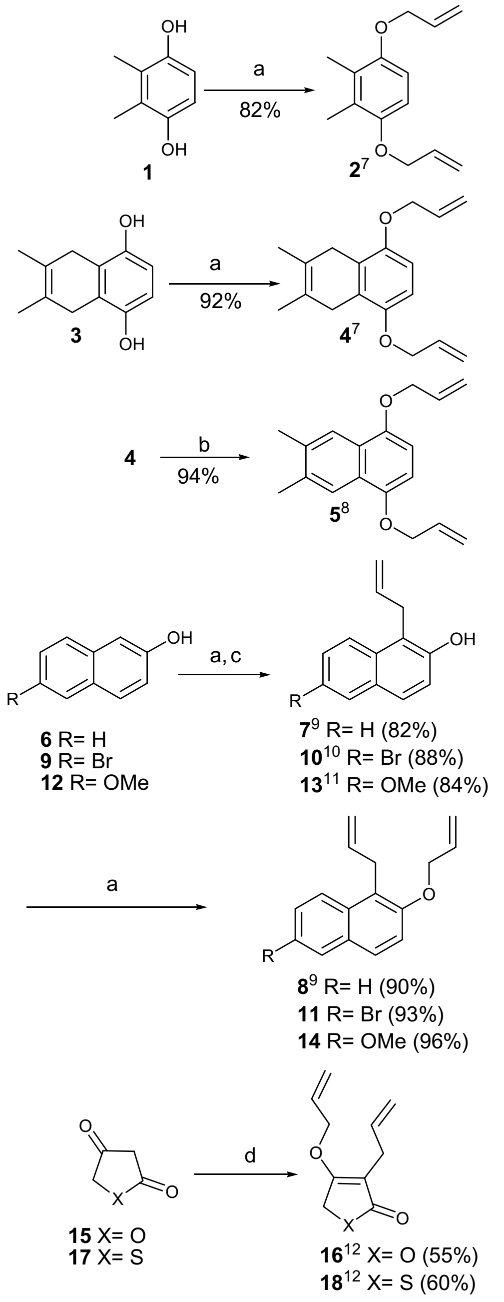
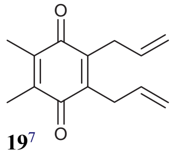
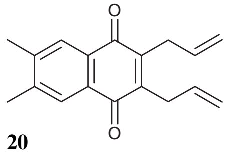
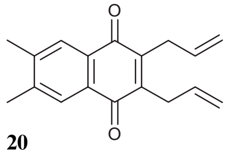
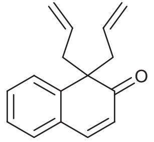
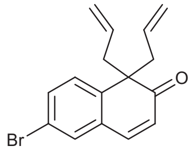
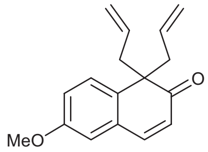
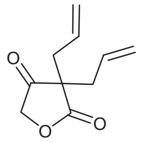
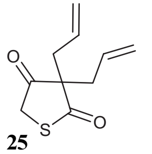


Scheme 3. Reagents and conditions: (a) allyl bromide, K_2CO_3, acetone, rt; (b) IBX, DMSO; (c) MWI/silica gel support; (d) allyl bromide, TBAF, THF/H_2O.[8–12]

of 800 W on silica gel support to produce the corresponding bis-allylated ketones in moderate to good yields (Table 1).

Table 1. Silica gel supported synthesis of bis-allyl ketones from the corresponding allyloxy compounds under microwave irradiation

Entry	Reactant (time, min)[a]	Product	Yield (%)[b]
1	**2** (7)	 **19**[7]	39
2	**4** (15)	 **20**	43
3	**5** (5)	 **20**	59
4	**8** (7)	 **21**[9]	73(96)[c]
5	**11** (7)	 **22**	75(95)[c]
6	**14** (7)	 **23**	78(95)[c]
7	**16** (7)	 **24**	75[d]
8	**18** (7)	 **25**	65

[a] Irradiation at 800 W using a Ken Star (OM-992E) household microwave oven.

[b] Isolated yield.

[c] Yields in the parentheses refer to the yield based on recovered starting material.

[d] GC yield.

Compound **4** on MWI gave the aromatized quinone **20**. The reaction times were optimized by monitoring the reaction mixture at different intervals by TLC. In some cases (entries 1–3, 7 and 8, Table 1) it was observed that prolonged irradiation gave an intractable polymeric material, thereby reducing the yield of the required product. Reducing the power level to avoid polymerization necessitated increased exposure times. Incomplete conversions of the starting materials were observed in entries 4–6 (Table 1). After 7 min (optimized time) exposure to MWI, the ratio of the starting material and the product remained constant. Even after prolonged exposure (>20 min) the starting material to product ratio remained the same (entries 4–6). Our earlier synthesis of **19** starting from **2** under conventional conditions gave a low yield (26%),[7] even prolonged heating (12 h) or forcing reaction conditions did not improve the yield of product. However, a significant rate enhancement and improved yield of the rearranged product was observed under MWI conditions on a silica gel support (entry 1, Table 1).

In summary, we have developed a safe, economical and green process for the synthesis of bis-allyl ketones via microwave-assisted Claisen rearrangement on a silica support under solvent-free conditions. A few notable advantages of this procedure are: (i) reasonably good yields (39–78%) of the rearranged products; (ii) fast reaction times (5–7 min); (iii) mild reaction conditions and (iv) avoidance of toxic solvents.

General procedure for Claisen rearrangement: To a dichloromethane solution of starting material in a beaker was added pre-activated (pre-activation of the silica gel was achieved by MWI [Ken Star, OM-992E] for 5 min) silica gel (100–200 mesh, 5–10 times the weight of the starting substrate) and then the solvent was evaporated. The resulting homogeneous mixture of the substrate and silica gel was then irradiated in a microwave oven, for the time given in Table 1. The reaction mixture was purified by flash chromatography. Elution of the column with a mixture of ethyl acetate and petroleum ether gave the required product.

Selected spectral data: **20**: yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 6H), 3.41 (dt, 4H, $J = 6.4$, 1.6 Hz), 5.02–5.09 (m, 4H), 5.82–5.92 (m, 2H), 7.82 (s, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 20.3, 30.9, 116.9, 127.5, 130.2, 134.2, 143.4, 144.9, 185.0; HRMS (QTOF): *m*/*z* calcd for $C_{18}H_{19}O_2$ (M+H): 267.1385. Found: 267.1382. **22**: colourless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.54 (dd, 2H, $J = 13.6$, 7.2 Hz), 2.89 (dd, 2H, $J = 13.6$, 7.2 Hz), 4.79–4.86 (m, 4H), 5.2–5.3 (m, 2H), 6.19 (d, 1H, $J = 10.4$ Hz), 7.30 (s, 1H), 7.32 (d, 1H, $J = 2.4$ Hz), 7.45 (d, 1H, $J = 2$ Hz), 7.55 (dd, 1H, $J = 8$ Hz, 2.2 Hz); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 46.1, 55.8, 118.5, 120.5, 127.2, 128.7, 131.9, 132.1, 132.5, 132.8, 142.5, 143.6, 202.4; HRMS (QTOF): *m*/*z* calcd for $C_{16}H_{16}OBr$ (M+H): 303.0385. Found: 303.0400. **23**: colourless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.55 (dd, 2H, $J = 13.4$, 7.0 Hz), 2.87 (dd, 2H, $J = 13.4$, 7.4 Hz), 3.85 (s, 3H), 4.77–4.87 (m, 4H), 5.22–5.32 (m, 2H), 6.16 (d, 1H, $J = 9.6$ Hz), 6.82 (d, 1H, $J = 2.8$ Hz), 7.0 (dd, 1H, $J = 2.8$, 8 Hz), 7.34 (d, 1H, $J = 9.2$ Hz), 7.35 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 46.3, 55.29, 55.33, 113.8, 115.9, 118.0, 126.5, 128.1, 131.8, 132.7, 135.5, 145.1, 158.0, 203.4; HRMS (QTOF): *m*/*z* calcd for $C_{17}H_{19}O_2$ (M+H): 255.1385. Found: 255.1381. **24**: colourless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.51 (d, 4H, $J = 6.4$ Hz), 4.41 (s, 2H), 5.14–5.19 (m, 4H), 5.59–5.69 (m, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 39.1, 54.1, 121.2, 130.2, 203.8, 209.8; Mass: (EI) *m*/*z* 180 (M^+). **25**: colourless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.41–2.53 (m, 4H), 3.79 (s, 2H), 5.09–5.13 (m, 4H), 5.57–5.67 (m, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 40.9, 41.2, 60.6, 120.7, 130.5, 203.5, 207.7; Mass: (EI) *m*/*z* 196 (M^+).

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