Silica sulfuric acid-catalyzed Claisen-Schmidt condensation of 1,3,4 trisubstituted pyrrole 2,5 dione to chalcones

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Abstract A series of 11 chalcones was synthesized from 1-(4-acetylphenyl)-3,4dibromo-1*H*-pyrrole-2,5-dione with various substituted benzaldehyde under solvent-free conditions using silica-sulphuric acid as a catalyst. The yields of chalcones are more than 90 %. All the compounds were characterized by physical, spectroscopic, and elemental analysis.

Keywords 1-(4-Acetylphenyl)-3,4-dibromo-1H-pyrrole-2,5-dione · Claisen-Schmidt reaction · SiO₂-H₂SO₄

Introduction

Since their development in the 1970s, Claisen-Schmidt reactions catalyzed by strong base or Lewis acids have become one of the most important tools for constructing chalcones. Traditionally, carbomethyls were widely studied and broadly used as the electrophile, both in the laboratory an in industry. However, with the further development of catalytic systems, a variety of electrophiles have now been successfully applied to the Claisen-Schmidt reaction.

The chalcones are α,β -unsaturated ketones containing the reactive ketoethylenic group –CO–CH=CH–. The presence of α,β -unsaturated carbonyl system in chalcone makes it biologically active [1]. Chalcones (α,β unsaturated ketone) are natural substances found in a number of plants or can also be synthetically prepared. They display many biological activities, for example, antiviral, anti-inflammatory, antimicrobial, antimitotic, antitumor, cytotoxicity, analgesic, and antipyretic properties. They also act as potential antiulcer, antifungal, anti-cancer, and antimalarial agents

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[2]. Recently there has been tremendous interest in the application of solvent-free methods in organic reactions such as the Claisen-Schmidt, Knoevenagel, aldol, and crossed-aldol [3]. There has been tremendous interest in the application of solvent-free aldol and crossed-aldol reactions, which are employed for synthesis of carbonyl compounds due to the operational simplicity, easier work-up, better yield, and eco-friendly nature [4]. Among reported solid acids, silica sulfuric acid has been used to catalyze a wide variety of reactions ranging from aldol condensation, acetalization, deacetalization, oxidation of alcohols, *N*-nitrosation of secondary amines, direct etherification of trimethylsilyl ethers [5] and formation of carbamate [6], and oxidation of alcohol [7]. The promoting effect of silica-sulphuric acid in their reaction was shown good performance and it is proved by obtaining higher percentage of yields. The product was isolated and the remaining catalyst was washed and reused with fresh substrate for further reactions. No decrease in the yield was observed, demonstrating that silica-sulphuric acid can be reused in the Claisen-Schmidt condensation reaction without environmental discharge [8].

Our group has worked to directly apply abundant and readily available oxygencontaining compounds such as *o*-and *p*-substituted acetophenones. In this account, we describe our recent efforts in silica-sulphuric acid-catalyzed Claisen-Schmidt reaction of 1-(4-acetylphenyl)-3,4-dibromo-1*H*-pyrrole-2,5-dione, a versatile electrophile.

Results and discussion

The important infrared spectral bands and their tentative assignments for dibromo compounds and its chalcones were recorded as KBr disks and are presented in experimental section. ¹H NMR spectra revealed signals 3.35 δ ppm for DMSO solvent and 3.53 δ & 8.12 δ ppm for DMF solvent. ¹H NMR data of compound revealed singlet at 2.58 δ ppm for -CH₃ group. The ¹H NMR data of compounds **2a–h** revealed signals between 6.78 and 8.50 δ ppm for aromatic protons. The IR spectra of compounds 2a-h revealed a characteristic band between 3,020 and 3,090 cm⁻¹ confirming the presence of (C=C) groups. The ¹H NMR data of compounds revealed signals between 2.48 and 2.53 δ ppm and 2.74–2.80 δ ppm for asymmetric aliphatic (C=C) of chalcones (Fig. 1). IR spectrum of the compounds showed a characteristic bands between 1.580 and 1.716 cm⁻¹, confirming the presence of C=O groups and C-Br present between 537 and 655 cm⁻¹ of dibromomaleimides. ¹³C NMR spectra of compounds showed a characteristic peak around 40.1, 77, 118, 124, 126.9, 127.85, 129, 130.22, 131.01, 138, 167.78, and 171 δ ppm (Fig. 2). IR spectrum of the compound **2c** showed a characteristic band at 1,410 cm $^{-1}\!,$ confirming the presence of $-NO_2$ group. ^{13}C NMR spectra of compounds 2c showed a characteristic peak around 39.91, 57.22, 76, 118, 124, 129, 130, 131, 138, 140, 143, 148, 168, and 172. In mass spectral studies, molecular ion peak for the compound 2e have been used to confirm the molecular formulae. The first peak at m/z 492 (M+) represents the molecular ion peak of the compound. Molecular ion peak again confirmed by fragments observed in mass spectra at m/ z 410, 386, 354, 254 until stable fragment is formed (Figs. 3, 4).



Fig. 1 1H NMR spectrum of compound 2b

Conclusions

This method is a very efficient and selective protocol for Claisen-Schmidt condensation of 1-(4-acetylphenyl)-3,4-dibromo-1*H*-pyrrole-2,5-dione in the presence of silica sulfuric acid catalyst. Operative simplicity and easy work-up process this approach provides better yielded products. The results obtained from this study reconfirmed that the product has formed.

Experimental

Materials and instrumentation

All reagents were of analytical reagent grade and were used without further purification. Solvents employed were purified by standard procedure before use. The melting points were determined in open capillary on Veego (Model: VMP-D) electronic apparatus and are uncorrected. To monitor the reactions as well as to establish the identity and purity of reactants and products, thin-layer chromatography was performed on microscopic glass slides (2×7.5 cm) coated with silica gel-G, using toluene-acetone and chloroform–methanol, as the solvent systems and spots were visualized under UV radiation. Elemental analysis (C, H, N) was



Fig. 2 13 C NMR spectrum of compound 2c



Fig. 3 ESI mass spectrum of compound 2e

performed using a PerkinElmer, USA 2400-II CHN analyzer. FTIR spectra $(4,000-400 \text{ cm}^{-1})$ recorded on a Simadzu 8400-S spectrophotometer using a KBr disk. Nuclear magnetic resonance spectra were recorded on a Varian 400-MHz model spectrometer using DMSO and or DMF as a solvent and TMS as internal reference (chemical shifts in δ ppm).





Preparation of chalcone from dibromomaleimide (2a-h)

The target compounds were prepared as shown in Scheme 1. An equimolar mixture of 1-(4-acetylphenyl)-3,4-dibromo-1H-pyrrole-2,5-dione **1** [9–11] (2 g), aromatic aldehydes (2.1 g) and silica sulfuric acid prepared by reported method [12] (1.5 g equal to 4 mmol of H+) were mixed thoroughly, placed in a glass tube, and capped (Scheme 1). The mixture was heated in an oven at 80 °C for 2–3.5 h. After complete conversion of the ketones, reactions were monitored by TLC, the mixture was cooled to room temperature. Dichloromethane (20–30 ml) was added and heated for 3–5 min. The reagent was removed by filtration. The filtrate was concentrated and the solid residue was recrystallized from ethanol to afford final product. The catalyst was recycled by washing ethyl acetate (20 ml) on solid remaining on the filter followed by drying in an oven at 50 °C for 2 h, which can be reusable for another reaction run. Spectral and microanalysis data of selective compounds are summarized below [13]. New compounds were completely characterized based on their spectroscopy data. Derivatives are shown in Table 1.

1-(4-((E)-3-arylacryloyl) phenyl)-3,4 dibromo-1H-pyrrole-2,5-dione 2a

Yellow solid, Yield 97 %; m.p. 149 °C; ¹H NMR (500 MHz, DMF), 3.52 δ and 8.23 δ ppm (DMF solvent), 7.45 δ ppm (1H, d, J = 15.5 Hz, *E*-vinylic-H), 7.66 δ ppm (2H, dd, Ar–H), 6.43–7.42 (5H, m, Ar–H), 7.75 δ ppm (1H, d, J = 15.5 Hz, *E*-vinylic-H); ¹³C NMR (500 MHz, DMF) 40.1, 77, 118, 124, 126.9, 127.85, 129, 130.22, 131.01, 138, 167.78, 171 δ ppm; FTIR (KBr) v_{max} cm⁻¹: 3028 (C=C), 1716 (C=O), 1527 (C=C of Ar), 835 (*p*-disubstituted Ar), 655 (C–Br); ESIMS *m*/*z* 462 (M + 1) Anal. Calcd for CHNOBr: C, 49.49; H, 2.40; N, 3.04 Found: C, 49.44; H, 2.38; N, 2.99.

1-(3',4'-Dimethoxy-4-((E)-3-arylacryloyl) phenyl)-3,4 dibromo-1H-pyrrole-2,5dione **2b**

Yellow solid, Yield 95 %; m.p. 116 °C; ¹H NMR (500 MHz, DMF) 2.9 δ ppm (3H, s, $-OCH_3$), 3.04 δ ppm (3H, s, $-OCH_3$), 3.55 δ and 8.063 δ ppm (DMF solvent),



Scheme 1 Synthesis of compounds 2a-k from 1-(4-acetylphenyl)-3,4-dibromo-1H-pyrrole-2,5-dione 1

Table 1 List of compounds 2a-k with their structures and groups

Structure of compounds



Table 1 continued

Structure of compounds



7.56 δ ppm (1H, d, J = 15.3 Hz, *E*-vinylic-H), 6.78–7.68 δ ppm (2H, dd, Ar–H), 7.81 δ ppm (1H, d, J = 15.3 Hz, *E*-vinylic-H), 6.38–8.37 δ ppm (3H, m, Ar–H); ¹³C NMR (500 MHz, DMF) 41.21, 58.2,62.3, 76.44, 118, 124, 129, 129.8, 131, 131.1, 132, 137.6, 139.9, 144, 167.8, 171 δ ppm; FTIR (KBr) v_{max} cm⁻¹: 3000 (C=C), 1580 (C=O), 1520 (C=C of Ar), 835 (*p*-disubstituted Ar), 650 (C–Br); ESIMS *m*/*z* 523 (M + 2) Anal. Calcd for CHNOBr: C, 48.40; H, 2.90; N, 2.69 Found: C, 48.39; H, 2.99; N, 2.64.

1-(3'-Nitro, 4'-methoxy-4-((E)-3-arylacryloyl) phenyl)-3,4 dibromo-1H-pyrrole-2,5dione **2c**

Orange solid, Yield 92 %; m.p. 118 °C; ¹H NMR (500 MHz, DMF) 3.0 δ ppm (3H, s, $-OCH_3$), 3.53 δ and 8.12 δ ppm (DMF solvent), 7.44 δ ppm (1H, d, J = 15.4 Hz, *E*-vinylic-H), 6.78–7.68 δ ppm (2H, dd, Ar–H), 7.78 δ ppm (1H, d, J = 15.4 Hz, *E*-vinylic-H) 6.55–8.45 δ ppm (3H, m, Ar–H); ¹³C NMR (500 MHz, DMF) 39.91,

57.22, 76, 118,124,127, 129, 130,131,138,140,143,148,168,172 δ ppm; FTIR (KBr) ν_{max} cm⁻¹: 2990 (C=C), 1589 (C=O), 1510 (C=C of Ar), 1250 (C–O), 840 (*p*-disubstituted Ar), 653 (C–Br); ESIMS *m*/*z* 537 (M + 1) Anal. Calcd for CHNOBr: C, 44.81; H, 2.26; N, 5.23 Found: C, 44.79; H, 2.23; N, 5.25.

1-(2'-Hydroxyl-4-((E)-3-arylacryloyl) phenyl)-3,4 dibromo-1H-pyrrole-2,5-dione 2d

Orange solid, Yield 93 %; m.p. 42 °C; ¹H NMR (500 MHz, DMF) 3.34 δ ppm (1H, s, –OH), 3.50 δ and 8.1 δ ppm (DMF solvent), 7.56 δ ppm (1H, d, J = 15.2 Hz, *E*-vinylic-H) 6.73–7.74 δ ppm (2H, dd, Ar–H), 7.77 δ ppm (1H, d, J = 15.2 Hz, *E*-vinylic-H) 6.45–8.2 δ ppm (4H, m, Ar–H), ¹³C NMR (500 MHz, DMF) 40, 75.77,118, 127, 128, 131, 127, 129, 130, 138, 140.2, 142, 168, 170.98 δ ppm; FTIR (KBr) v_{max} cm⁻¹: 3350 (–OH), 3084 (C=C), 1597 (C=O), 1525 (C=C of Ar), 1410 (NO₂), 1230 (C–O), 840 (*p*-disubstituted Ar), 537 (C–Br); ESIMS *m/z* 477 (M+) Anal. Calcd for CHNOBr: C, 47.83; H, 2.32; N, 2.92 Found: C, 47.85; H, 2.29; N, 2.96.

1-(4'-Chloro-4-((E)-3-arylacryloyl) phenyl)-3,4 dibromo-1H-pyrrole-2,5-dione 2e

Yellow solid, Yield 98 %; m.p. 163 °C; ¹H NMR (500 MHz, DMF) 3.55 δ and 8.063 δ ppm (DMF solvent), 7.6 δ ppm (1H, d, J = 15.3 Hz, *E*-vinylic-H), 6.78–7.68 δ ppm (2H, dd, Ar–H), 7.78 δ ppm (1H, d, J = 15.3 Hz, *E*-vinylic-H), 6.55–8.45 δ ppm (4H, m, Ar–H); ¹³C NMR (500 MHz, DMF) 39.9, 75.23, 118, 124, 127, 129, 129.4, 130, 140, 138, 140, 166.78, 171.2 δ ppm; FTIR (KBr) v_{max} cm⁻¹: 3020 (C=C), 1585 (C=O), 1525 (C=C of Ar), 835 (*p*-disubstituted Ar), 697 (C–Cl), 538 (C–Br); ESIMS *m*/*z* 492 (M+) Anal. Calcd for CHNOBr: C, 47.83; H, 2.32; N, 2.92 Found: C, 47.85; H, 2.29; N, 2.96.

1-(2'-Chloro-4-((E)-3-arylacryloyl) phenyl)-3, 4 dibromo-1H-pyrrole-2,5-dione 2f

Yellow solid, Yield 93 %; m.p. 166 °C; ¹H NMR (500 MHz, DMF) 3.53 δ and 8.063 δ ppm (DMF solvent), 7.54 δ ppm (1H, d, J = 15.5 Hz, *E*-vinylic-H), 6.77–7.66 δ ppm (2H, dd, Ar–H), 7.82 δ ppm (1H, d, J = 15.5 Hz, *E*-vinylic-H), 6.53–8.44 δ ppm (4H, m, Ar–H); ¹³C NMR (500 MHz, DMF) 40.01, 75.23, 118.5, 123, 128, 129,131,133, 137, 138, 140, 167, 171 δ ppm; FTIR (KBr) v_{max} cm⁻¹: 3022 (C=C), 1578 (C=O), 1527 (C=C of Ar), 836 (*p*-disubstituted Ar), 700 (C–Cl), 654(C–Br); ESIMS *m*/*z* 493 (M +1) Anal. Calcd for CHNOBr: C, 47.85; H, 2.29; N, 2.93 Found: C, 47.87; H, 2.31; N, 2.97.

1-(4'-Methyl-4-((E)-3-arylacryloyl) phenyl)-3,4 dibromo-1H-pyrrole-2,5-dione 2g

Pale yellow solid, Yield 96 %; m.p. 170 °C; ¹H NMR (500 MHz, DMF) 3.37 δ ppm (3H, s, -CH₃) 3.54 δ and 8.02 δ ppm (DMF solvent), 7.67 δ ppm (1H, d, J = 15.2 Hz, *E*-vinylic-H), 6.76–7.68 δ ppm (2H, dd, Ar–H), 7.77 δ ppm (1H, d, J = 15.2 Hz, *E*-vinylic-H), 6.51–8.43 δ ppm (4H, m, Ar–H); ¹³C NMR (500 MHz,

DMF) 40.12,57, 72, 118, 123.2, 128, 129, 131.1, 133, 137.2, 138, 140.1, 162.8, 171 δ ppm; FTIR (KBr) v_{max} cm⁻¹: 3030 (C=C), 1582 (C=O), 1529 (C=C of Ar), 839 (*p*-disubstituted Ar), 657(C–Br); ESIMS *m*/*z* 476 (M + 1) Anal. Calcd for CHNOBr: C, 50.56; H, 2.76; N, 2.95 Found: C, 50.53; H, 2.78; N, 2.93.

1-(4'-Methoxy-4-((E)-3-arylacryloyl) phenyl)-3,4 dibromo-1H-pyrrole-2,5-dione 2h

Yellow solid Yield, 92 %; m.p. 158 °C; ¹H NMR (500 MHz, DMF) 3.01 δ ppm (3H, s, -OCH₃), 3.53 δ and 8.13 δ ppm (DMF solvent), 7.68 δ ppm (1H, d, J = 15.5 Hz, *E*-vinylic-H), 6.72–7.63 δ ppm (2H, dd, Ar–H), 7.76 δ ppm (1H, d, J = 15.5 Hz, *E*-vinylic-H) 6.39–8.39 δ ppm (3H, m, Ar–H); ¹³C NMR (500 MHz, DMF) 41.2, 58.21, 76.43, 119, 125, 129, 129, 129.9, 131.2, 133, 137.6, 140, 143, 167, 173 δ ppm; FTIR (KBr) v_{max} cm⁻¹: 3000 (C=C), 1580 (C=O), 1600 (C=C of Ar), 835 (*p*-disubstituted Ar), 650 (C–Br); ESIMS *m*/*z* 492 (M + 1) Anal. Calcd for CHNOBr: C, 48.91; H, 2.67; N, 2.85 Found: C, 48.89; H, 2.64; N, 2.83.

1-(4'-Hydroxyl-4-((E)-3-arylacryloyl) phenyl)-3,4 dibromo-1H-pyrrole-2,5-dione 2i

Orange solid, Yield 48 %; m.p. 41–43 °C; ¹H NMR (500 MHz, DMF) 3.34 δ ppm (1H, s, –OH), 3.52 δ and 8.12 δ ppm (DMF solvent), 7.56 δ ppm (1H, d, J = 15.2 Hz, *E*-vinylic-H) 6.73–7.74 δ ppm (2H, dd, Ar–H), 7.77 δ ppm (1H, d, J = 15.2 Hz, *E*-vinylic-H) 6.45–8.2 δ ppm (4H, m, Ar–H), ¹³C NMR (500 MHz, DMF) 41, 75.7, 116, 126, 127, 131, 127, 129, 129.4, 130, 138, 139, 142, 167, 168.9 δ ppm; FTIR (KBr) v_{max} cm⁻¹: 3350 (–OH), 3084 (C=C), 1597 (C=O), 1525 (C=C of Ar), 1230 (C–O), 840 (*p*-disubstituted Ar), 537 (C–Br); ESIMS *m/z* 477 (M+) Anal. Calcd for CHNOBr: C, 47.83; H, 2.32; N, 2.92 Found: C, 47.80; H, 2.31; N, 2.94.

1-(3'-Nitro-4-((E)-3-arylacryloyl) phenyl)-3,4 dibromo-1H-pyrrole-2,5-dione 2j

Dark yellow solid, Yield 71 %; m.p. 146 °C; ¹H NMR (500 MHz, DMF) 3.53 δ and 8.12 δ ppm (DMF solvent), 7.44 δ ppm (1H, d, J = 15.4 Hz, *E*-vinylic-H), 6.78–7.68 δ ppm (2H, dd, Ar–H), 7.78 δ ppm (1H, d, J = 15.4 Hz, *E*-vinylic-H) 6.55–8.45 δ ppm (3H, m, Ar–H); ¹³C NMR (500 MHz, DMF) 38, 74, 117, 124, 128, 129.9, 131, 138, 141, 143, 146, 169, 171 δ ppm; FTIR (KBr) v_{max} cm⁻¹: 2990 (C=C), 1589 (C=O), 1510 (C=C of Ar), 1410 (NO₂), 1250 (C–O), 840 (*p*-disubstituted Ar), 653 (C–Br); ESIMS *m*/*z* 507 (M + 1) Anal. Calcd for CHNOBr: C, 45.09; H, 1.99; N, 5.54 Found: C, 44.99; H, 2.01; N, 5.54.

1-(2',4'-Dichloro-4-((E)-3-arylacryloyl) phenyl)-3,4 dibromo-1H-pyrrole-2,5-dione **2k**

Orange solid Yield 79 %; m.p. 158 °C; ¹H NMR (500 MHz, DMF) 3.55 δ and 8.063 δ ppm (DMF solvent), 7.6 δ ppm (1H, d, J = 15.3 Hz, *E*-vinylic-H), 6.78–7.68 δ ppm (2H, dd, Ar–H), 7.78 δ ppm (1H, d, J = 15.3 Hz, *E*-vinylic-H), 6.55–8.45 δ ppm (3H, m, Ar–H); ¹³C NMR (500 MHz, DMF) 40,77, 118, 123, 128,

129,130, 138,141,142,165, δ ppm; FTIR (KBr) v_{max} cm⁻¹: 3020 (C=C), 1585 (C=O), 1525 (C=C of Ar), 835 (*p*-disubstituted Ar), 697 (C–Cl), 538 (C–Br); ESIMS *m*/*z* 530 (M+) Anal. Calcd for CHNOBr: C, 43.06; H, 1.71; N, 2.64 Found: C, 42.93; H, 1.69; N, 2.65.

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