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A catalytic crossed-aldol condensation of ketones with aromatic and non-aromatic aldehydes by silica supported Preyssler heteropolyacids catalyst

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Synthesis of α,β-unsaturated aldol products by crossed-aldol condensation of aromatic aldehydes in the presence of heteropolyacids (HPAs) catalyst under reflux conditions and free of organic solvent is reported. Aldol condensation of 2-acetylthiophene, 2-acetylpyrrole and 2-acetylpyridine with different aromatic aldehydes was carried out in water in the presence of a silica supported Preyssler HPAs catalyst at room temperature. All reactions occur in a short time with excellent yields of cycloalkanones in water as an environmentally friendly solvent.

Keywords: α,β-unsaturated aldol, catalysts, aldehyde, ketone, condensation

INTRODUCTION

Aldol condensations are important in organic synthesis, providing a good way to form carbon–carbon bonds. The Robinson annulation reaction sequence features an aldol condensation; the Wieland-Miescher ketone product is an important starting material for many organic syntheses. In its usual form, it involves nucleophilic addition of a ketone enolate to an aldehyde to form a β-hydroxy ketone, a structural unit found in many naturally occurring molecules and pharmaceuticals [1–3]. Chalcones are α,β-unsaturated ketones and they have great abundance in the plant kingdom. It is well known that most of natural and synthetic chalcones are highly biologically active with multiple pharmaceutical and medicinal applications [4]. Recently they are used as anti-AIDS [5], cytotoxic with antiangiogenic activity [6,7], antimalarial [8,9], anti-inflammatory [10,11] and antitumor agents [12,13]. Recently, water has been considered as an attractive medium for many organic reactions [14]. With respect to organic solvents aqueous media are less expensive, healthy, safe and environmentally friendly. Also, water allows pH control and use of surfactants as micro aggregates. The hydrophilic effect and the large cohesive energy of water [15] are considered to be the main factors responsible for increasing reactivity and selectivity of the reactions [16]. Bis(p-methoxyphenyl) telluroxide and KF-Al_2O_3 have been used for crossed-condensation of cycloalkanones with aromatic aldehydes under microwave irradiation [17]. Anhydrous $RuCl_3$ and $TiCl_3(SO_3CF_3)$ have also been used for this purpose under solvent-free conditions [18]. The use of expensive and toxic reagents, long reaction times, low yields, and the formation of a mixture of products are among the drawbacks of the reported methods. Recently, more attention has been paid to the synthesis of α,α'-bis(substituted benzylidene) cycloalkanones [19]. Aldol condensation is a powerful tool for the formation of a carbon-carbon bond in many classes of carbonyl compounds [20]. Due to the importance of the methylene structural unit which is found in many naturally occurring compounds and antibiotics, and the use of α,α'-bis(substituted benzylidene)cycloalkanones as precursors for the synthesis of bioactive pyrimidine derivatives [21], condensation of cycloalkanones with aldehydes and ketones is of special interest and crossed-aldol condensation is an effective pathway for these preparations. However, traditional acid- or base-catalyzed reactions suffer from the reverse reaction [22], and from self-condensation of the starting materials [23]. Heteropolyacids (HPAs) are well defined molecular clusters that are remarkable for their molecular and electronic structural diversity and their significance in many areas, e.g., catalysis, medicine, and materials science [24,25]. The applications of

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HPAs in the field of catalysis are continuously growing. These compounds possess unique properties such as Brønsted acidity, possibility to modify their acid/base and redox properties by changing their chemical composition (substituted HPAs), ability to accept and release electrons, high proton mobility, easy work-up procedures, easy filtration, and minimization of cost and waste generation due to reuse and recycling of these catalysts [26-30]. Because of their stronger acidity, they generally exhibit higher catalytic activity than conventional catalysts such as mineral acids, ion exchange resins, mixed oxides, zeolites, etc. [31]. In the context of Green Chemistry, the substitution of harmful liquid acids by solid reusable HPAs as catalysts in organic synthesis is the most promising application of these acids [32,33]. HPAs are applied both in bulk or supported forms, homogeneous and heterogeneous catalysis being possible. HPAs have many advantages that make them environmentally attractive in the academic, industrial and economical signification. These are useful acids and oxidation catalysts in various reactions since their catalytic features can be varied at a molecular level [34]. Among them, the Keggin-type HPAs have long been known to be good catalysts for oxidation reactions [35]. They exhibit great advantages: for example, their catalytic properties can be tuned by changing the identity of the charge-compensating counter cations, heteroatoms and framework metal atoms [35]. Being stronger acids, heteropolyacids will have significantly higher catalytic activity than the conventional catalysts such as mineral acids, mixed oxides, zeolites, etc. In particular, in organic media, the molar catalytic activity of a heteropolyacid is often 100-1000 times higher than that of H_2SO_4 [34,36].

EXPERIMENTAL

Materials and Methods

All chemicals were obtained from Merck and used as received.

Instruments

^{1}H NMR spectra were recorded on a FT NMR Bruker 400 MHz spectrometer at 298 K. Melting points were recorded on an Electrothermal type 9100 melting point apparatus and were uncorrected. Chemical shifts were reported in ppm (δ-scale) relative to internal standard TMS (0.00 ppm) using $CDCl_3$ as a reference solvent. IR spectra were obtained with a Buck 500 scientific spectrometer (KBr pellets). The mass spectra (EI) were obtained on a Jeol JMS D-300 spectrometer operating at 70 eV. The products were identified by comparison of their mp., IR and NMR spectra with those of authentic samples. Elemental analyses were preformed on a Perkin Elmer 2400, series II microanalyzer.

Catalyst Preparation

Preyssler catalyst, $H_{14}[NaP_5W_{30}O_{110}]$ was prepared by passage of a solution of the potassium salt (30 mL) in water (30 mL) through a column (50 cm×1 cm) of Dowex 50W×8 in the H^+ form. The eluent was evaporated to dryness under vacuum [37,38]. Silica-supported Preyssler $H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ catalysts were prepared by impregnating Aerosil 300 silica with a methanolic solution of $H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ [39].

General procedure for crossed-aldol condensation of ketones with aromatic aldehydes:

Ketones (2.5 mmol), aromatic aldehydes (5 mmol), water (5 mL) and silica-supported Preyssler HPAs catalyst (0.05 g) were mixed. The mixture was refluxed for 3 h (Table 1). After complete conversion of the ketone, as monitored by TLC, the mixture was cooled to room temperature. Dichloromethane (30 mL) was added and heated for few minutes. The reagent was removed by filtration. The filtrate was concentrated, then the solid products were filtered off, washed with water (3×25 mL) and the solid residue was recrystallized from ethanol to afford the pure product. The catalyst was filtered off and recycled using a Buechner funnel (Ø = 6.0 cm) and washed with 20 mL dichloromethane followed by drying in an oven (90 ^{O}C) for 1 h.

Spectral data for selected compounds:

Compound (**15a)**: Anal. Calcd for $C_{19}H_{12}C_{l4}O$: C 57.32, H 3.04; Found C 57.21, H 3.14;

IR (KBr, cm^{-1}): 3060, 2932, 1705, 1635, 1578, 1553; ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 7.53 (s, 2H), 7.38 (m, 4H), 7.24 (m, 2H), 2.61 (s, 4H); ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 29.5, 126.3, 128.7, 132.2, 143.3, 146.5, 196.8.; MS (*m*/*z*, (relative abundance, %)): 361 (M+, 39.5), 325 (22.1), 291 (45.0), 226 (39.3), 161 (28.7).

Compound (**16a)**: Anal. Calcd for $C_{23}H_{20}O_3$: C 80.21, H 5.85; Found C 80.17, H 5.88;

IR (KBr, cm^{-1}): 2908, 1683, 1632, 1614, 1599; ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 7.35 (s, 2H), 7.24 (d, 4H, *J* = 8.8 Hz), 7.04 (d, 2H, *J* = 7.6 Hz), 6.12 (s, 4H), 3.05 (s, 4H); ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 29.5, 74.5, 125.2, 127.4, 132.2, 134.5, 139.9, 144.1, 197.2. MS (*m*/*z*, (relative

abundance, %)): 344 (M+, 41.3), 273 (56.4), 251 (62.3), 212 (41.6).

Compound (**17a)**: Anal. Calcd for $C_{19}H_{14}Br_2O$: C 54.58, H 3.38; Found C 54.52, H 3.43;

IR (KBr, cm^{-1}): 3058, 2925, 1686, 1624, 1603, 1555, 1180; ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 7.75 (s, 2H), 7.53 (m, 6 H), 7.33 (t, 2 H, J = 8.0 Hz), 3.12 (s, 4H); ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 29.7, 124.1, 127.9, 130.7, 132.9, 144.2, 196.4; MS (*m*/*z*, (relative abundance, %)): 416 (M+, 54.5), 345 (67.4), 337 (57.6), 339 (78.5), 326 (48.9), 325 (51.3), 311 (66.4), 129 (69.9).

Compound (**18a)**: Anal. Calcd for $C_{21}H_{20}O$: C, 87.46; H, 6.98; Found: C, 87.31; H, 7.02;

IR (KBr, cm^{-1}): 3023, 2962, 2927, 1660, 1605, 1572, 1485, 1442, 1240, 1144 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 7.80 (2H, dbr, J = 1.6 Hz), 7.45 (10H, Ar), 3.10 (2H, ddbr, J = 3.5, 15.8 Hz), 2.53 (2H, ddd, J = 2.6, 11.4, 15.8 Hz), 1.90 (1H, m), 1.10 (3H, d, J = 6 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 21.63, 29.40, 36.48, 128.35, 128.55, 130.37, 135.36, 135.95, 137.12, 190.15; MS (*m*/*z*, (relative abundance, %)): 288 (M+, 36.5), 217 (73.0), 197 (37.6), 191 (54.6), 183 (70.4).

Compound (**19a)**: Anal. Calcd for $C_{23}H_{24}O$: C, 87.29; H, 7.64; Found: C, 86.39; H, 7.69;

IR (KBr, cm^{-1}): 3025, 2964, 2930, 1663, 1596, 1575, 1514, 1243, 1180, 1146 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 7.78 (2H, dbr, J = 1.6 Hz), 7.32 (8H, Ar), 3.10 (2H, ddbr, J = 3.5, 15.7 Hz), 2.52 (2H, ddd, J =2.4, 11.3, 15.7 Hz), 2.37 (3H, s), 1.85 (1H, m), 1.06 (3H, d, J = 6.3 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 21.38, 21.65, 29.40, 36.55, 129.10, 130.45, 133.19, 134.66, 137.05, 138.77, 190.19; MS (*m*/*z*, (relative abundance, %)): 316 (M+, 42.5), 301 (46.7), 225 (76.5), 219 (81.4), 211 (38.7).

Compound (**20a)**: Anal. Calcd for $C_{23}H_{24}O_3$: C, 83.14; H, 7.22; Found: C, 82.39; H, 7.18;

IR (KBr, cm^{-1}): 2956, 2927, 1665, 1595, 1511, 1296, 1260, 1183, 1175, 1147 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 7.76 (2H, dbr, J = 1.6 Hz), 7.40 (8H, Ar), 3.83 (3H, s), 3.04 (2H, ddbr, J =3.5, 15.7 Hz), 2.50 (2H, ddd, J =2.4, 11.3, 15.7 Hz), 1.89 (1H, m), 1.12 (3H, d, J = 6.5 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 21.75, 29.39, 36.57, 55.30, 113.86, 128.72, 132.20, 133.55, 136.70, 159.84, 190.05; MS (*m*/*z*, (relative abundance, %)): 348 (M+, 43.2), 317 (58.7), 254 (44.7), 251 (85.1), 243 (63.2), 240 (38.6).

Compound (**21a)**: Anal. Calcd for $C_{21}H_{18}C_{l2}O$: C, 70.63; H, 5.04; Found: C, 70.54; H, 5.09; IR (KBr, cm^{-1}): 2960, 2927, 2870, 1662, 1604, 1571, 1485, 1405, 1247, 1148; ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 7.75 (2H, dbr, J = 1.6 Hz), 7.39 (8H, Ar), 2.97 (2H, ddbr, J = 3.5, 15.7 Hz), 2.49 (2H, ddd, J = 2.6, 11.2, 15.7 Hz), 1.90 (1H, m), 1.06 (3H, d, J = 6.5 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 21.60, 29.25, 36.34, 128.68, 131.55, 134.26, 134.57, 135.59, 135.99, 189.61; MS (*m*/*z*, (relative abundance, %)): 356 (M+, 35.5), 321 (57.5), 266 (68.4), 265 (45.4), 259 (42.2), 251 (41.4).

Compound (**2b)**: Anal. Calcd for $C_{16}H_{25}O$: C, 82.20; H, 11.36; Found: C, 82.16; H, 11.33;

IR (KBr, cm^{-1}): 1620, 1605; ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 6.50 (2H, d, J = 9.7 Hz), 2.40 (4H, m), 2.09 (2H, m), 1.66 (14 H, m), 1.19 (8H, m); ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 185.59, 144.25, 134.40, 40.21, 36.73, 31.75, 26.65, 23.70, 23.34; MS (*m*/*z*, (relative abundance, %)): 248 (M+, 21.3), 223 (63.2), 169 (35.6), 166 (49.8).

Compound (**3b)**: Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82; Found: C, 80.40; H, 9.87;

IR (KBr, cm^{-1}): 1620; ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 6.50 (2H, d, J = 9.7 Hz), 2.49 (4H, m), 2.09 (2H, m), 1.69 (14 H, m), 1.18 (8H, m); ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 185.56, 144.25, 134.40, 40.20, 36.72, 31.74, 26.65, 23.70, 23.35; MS (*m*/*z*, (relative abundance, %)): 164 (M+, 21.0), 135 (64.3), 82 (58.6).

Compound (**4b)**: Anal. Calcd for $C_{13}H_{16}O$: C, 81.20; H, 10.48; Found: C, 81.01; H, 10.30;

IR (KBr, cm^{-1}): 1621; ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 6.50 (2H, d, J = 9.7 Hz), 2.48 (4H, m), 2.10 (2H, m), 1.67 (14H, m), 1.20 (8H, m); ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 185.57, 144.24, 134.40, 40.21, 36.73, 31.71, 26.65, 23.70, 23.35; MS (*m*/*z*, (relative abundance, %)): 192 (M+, 19.1), 149 (49.9), 136 (67.8).

Compound (**1c)**: Anal. Calcd for $C_{13}H_{11}NO$ (197.24); calcd.: C, 79.16; H, 5.62; N, 7.10; found: C, 79.07; H, 5.54; N, 7.13; IR (KBr, cm^{-1}): 1641 (C=O), 2850, 2916, 3025 (CH), 3268 (NH). ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 6.36 (m, 1H), 7.05 (d, 1H), 7.18 (d, 1H), 7.30 (d, 1H, C_2-H; J=15.60), 7.58 (m, 5H), 7.85 (d, 1H, C_3-H; J=15.58), 10.30 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 35.2, 42.1, 110.7, 117.6, 125.2, 127.4, 128.0, 190.4. MS (*m*/*z*, (relative abundance, %)): 197 (M+, 29.4), 120 (52.4), 107 (49.9), 103 (52.6), 106 (32.9), 94 (43.0), 92 (41.4), 41 (44.6), 39 (23.1), 28 (38.7).

Compound (**2c)**: Anal. Calcd for $C_{14}H_{13}NO$ (211.26); calcd.: C, 79.60; H, 6.20; N, 6.63; found: C, 79.51; H, 6.13; N, 6.57; IR (KBr, cm^{-1}): 1642

(C=O), 2993 (CH), 3255 (NH). ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 2.40 (s, 3H), 6.36 (m, 1H), 7.12 (d, 1H), 7.25 (s, 1H), 7.28 (d, 2H), 7.35 (d, 1H, C_2-H, J=15.62), 7.55 (d, 2H), 7.85 (d, 1H, C_3-H; J=15.68), 10.32 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 22.2, 34.5, 41.5, 111.0, 127.8, 129.1, 135.4, 138.2, 190.2. MS (*m*/*z*, (relative abundance, %)): 211 (M+, 20.5), 196 (53.3), 120 (46.4), 117 (36.9), 106 (39.7), 92 (44.1), 41 (51.0), 39 (31.8), 28 (32.0).

Compound (**3c)**: Anal. Calcd for $C_{13}H_{10}ClNO$ (231.68); calcd.: C, 67.40; H, 4.35; N, 6.05; found: C, 67.32; H, 4.30; N, 5.97; IR (KBr, cm^{-1}): 1645 (C=O), 2875, 2984 (CH), 3272 (NH). ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 6.35 (m, 1H), 6.93 (d, 1H), 7.12 (s, 1H), 7.25 (s, 1H), 7.26 (d, 1H), 7.33 (d, 1H, C_2-H; J=15.69), 7.46 (d, 1H), 7.75 (t, 1H), 8.21 (d, 1H, C_3-H; J=15.69), 10.12 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 24.4, 40.8, 110.8, 117.3, 125.9, 133.0, 146.5, 190.1. MS (*m*/*z*, (relative abundance, %)): 231 (M+, 18.3), 196 (23.6), 137 35.3), 126 (46.8), 107 (34.7), 41 (31.6), 39 (53.7), 28 (44.6).

Compound (**4c)**: Anal. Calcd for $C_{13}H_{10}ClNO$ (231.68); calcd.: C, 67.40; H, 4.35; N, 6.05; found: C, 67.32; H, 4.30; N, 5.97; IR (KBr, cm^{-1}): 1645 (C=O), 2873, 2984 (CH), 3275 (NH). ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 6.35 (m, 1H), 7.12 (s, 1H), 7.15 (s, 1H), 7.34 (d, 1H, C_2-H; J=15.78), 7.40 (d, 2H), 7.55 (d, 2H), 7.80 (d, 1H, C_3-H; J=15.72), 10.36 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 111.33 (CH), 117.12 (CH), 122.83 (CH), 124.40 (CH), 128.12 (CH), 129.65 (C), 131.40 (2xCH), 134.17 (C_2-H), 134.67 (C), 137.23 (C), 142.30 (C_3-H), 179.79 (C=O). MS (*m*/*z*, (relative abundance, %)): 231 (M+, 16.2), 196 (39.8), 137 (31.5), 126 (49.7), 107 (63.3), 41 (50.7), 39 (28.9), 28 (41.4).

Compound (**5c)**: Anal. Calcd for $C_{13}H_{11}NO_2$ (213.23); calcd.: C, 73.23; H, 5.20; N, 6.57; found: C, 73.11; H, 5.14; N, 6.50;IR (KBr, cm^{-1}): 1630 (C=O), 2851, 2921 (CH), 3256 (NH), 3455 (OH). ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 6.27 (m, 1H), 6.61 (m, 1H), 6.84 (d, 1H), 7.09 (m, 1H), 7.12 (d, 1H), 7.25 (d, 1H, C_2-H; J=15.58), 7.36 (d, 1H), 7.65 (m, 1H), 8.16 (d, 1H, C_3-H; J=15.66), 10.07 (s, 1H), 10.36 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 25.6, 40.9, 110.6, 115.6, 117.3, 121.4, 125.3, 28.0, 130.3, 133.1, 154.4, 190.4. MS (*m*/*z*, (relative abundance, %)): 213 (M+, 19.7), 122 (36.8), 119 (49.6), 108 (21.6), 94 (28.9), 41 (48.6), 39 (37.6), 28 (50.9).

Compound (**6c)**: Anal. Calcd for $C_{14}H_{13}NO_2$ (227.26); calcd.: C, 73.99; H, 5.77; N, 6.16; found: C, 73.86; H, 5.71; N, 6.05; IR (KBr, cm^{-1}): 1642 (C=O), 2844, 2970 (CH), 3262 (NH). ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 3.87 (s, 3H), 6.35 (m, 1H), 6.95 (d, 2H), 7.12 (d, 1H), 7.17 (d, 1H), 7.26 (d, 1H, C_2-H; J=15.62), 7.60 (d, 2H), 7.80 (d, 1H, C_3-H; J=15.59), 10.45 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 57.85 (CH_3), 111.74 (CH), 115.33 (2xCH), 117.15 (CH), 118.96 (C), 121.60 (CH), 126.41 (C), 130.25 (2xCH), 131.76 (C_2-H), 143.81 (C_3-H), 163.20 (C), 180.95 (C=O). MS (*m*/*z*, (relative abundance, %)): 227 (M+, 23.3), 196 (71.6), 133 (67.0), 94 (58.9), 41 (53.5), 39 (44.3), 28 (66.2).

Compound (**7c)**: Anal. Calcd for $C_{14}H_{11}NO_3$ (241.42); calcd.: C, 69.65; H, 4.59; N, 5.80; found: C, 69.57; H, 4.53; N, 5.71; IR (KBr, cm^{-1}): 1640 (C=O), 2830, 2961 (CH), 3225 (NH). ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 6.05 (s, 2H), 6.38 (m, 1H), 6.87 (d, 1H), 7.11 (m, 3H), 7.15 (d, 1H), 7.20 (d, 1H, C_2-H; J=15.63), 7.94 (d, 1H, C_3-H; J=15.62), 10.47 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 103.25 (CH_2), 105.65 (CH), 107.60 (CH), 109.84 (CH), 116.20 (CH), 119.48 (C_2-H), 124.21 (CH), 129.43 (C), 133.10 (C), 142.52 (C_3-H), 148.25 (C), 148.30 (C), 178.85 (C=O). ^{13}C NMR ($CDCl_3$, 75 MHz): 30.8, 41.4, 101.3, 110.2, 117.2, 125.8, 126.7, 128.1, 132.5, 137.1, 138.8, 146.6, 148.4, 190.4. MS (*m*/*z*, (relative abundance, %)): 241 (M+, 30.1), 147 (48.9), 117 (59.7), 94 (74.6), 41 (69.7), 39 (35.6), 28 (41.1).

Compound (**8c)**: Anal. Calcd for $C_{15}H_{16}N_2O$ (240.30); calcd.: C, 74.98; H, 6.71; N, 11.58; found: C, 74.92; H, 6.65; N, 11.53. ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 34.6, 40.1, 41.4, 110.8, 112.9, 125.5, 128.8, 131.1, 132.8, 148.6, 190.4; IR (KBr, cm^{-1}): 1635 (C=O), 2906 (CH), 3240 (NH). ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 3.02 (s, 6H), 6.35 (m, 1H), 6.70 (d, 2H), 7.08 (m, 2H), 7.16 (d, 1H, C_2-H; J=15.58), 7.55 (d, 2H), 7.80 (d, 1H, C_3-H; J=15.53), 10.39 (s, 1H). MS (*m*/*z*, (relative abundance, %)): 240 (M+, 15.2), 146 (54.3), 107 (23.8), 94 (39.7), 41 (53.8), 39 (44.7), 28 (51).

Compound (**1d)**: Anal. Calcd for $C_{14}H_{12}OS$ (228.31); calcd.: C, 73.65; H, 5.30; S, 14.04; found: C, 73.58; H, 5.27; IR (KBr, cm^{-1}): 1590 (C=C), 1645 (C=O), 2919, 3085 (CH). ^{1}H-NMR (400 MHz, $CDCl_3$, δ/ppm): 2.40 (s, 3H), 7.17 (m, 1H), 7.20 (d, 2H), 7.40 (d, 1H, C_2-H; J=15.65), 7.55 (d, 2H), 7.66 (d, 1H), 7.85 (d, 1H, C_3-H; J=16.13), 7.87 (d, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, δ/ppm): 21.60 (CH_3), 120.59 (CH), 128.20 (CH), 128.55 (2xCH), 129.72 (2xCH), 131.70 (C_2-H), 131.95 (C), 133.78 (CH), 141.22 (C), 144.20 (C_3-H), 145.68 (C), 182.16 (C=O). MS (*m*/*z*, (relative abundance, %)): 228 (M+, 14.0), 213 (56.4), 124

(46.7), 117 (35.6), 111 (81.2), 58 (34.4), 41 (32.1), 39 (29.0).

Compound (**2d)**: Anal. Calcd for $C_{13}H_9ClOS$ (248.73); calcd.: C, 62.78; H, 3.65; S, 12.89; found: C, 62.66; H, 3.62; IR (KBr, cm^{-1}): 1593 (C=C), 1647 (C=O), 3091 (CH). ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 7.20 (m, 1H), 7.23 (d, 2H), 7.40 (d, 1H, C_2-H; *J*=15.65), 7.64 (d, 2H), 7.72 (d, 1H), 7.87 (d, 1H, C_3-H; *J*=15.79), 7.95 (d, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): 121.95 (CH), 128.26 (CH), 129.25 (2xCH), 129.62 (2xCH), 131.90 (C_2-H), 133.14 (C), 134.10 (CH), 136.45 (C), 142.53 (C_3-H), 145.30 (C), 181.74 (C=O). MS (*m*/*z*, (relative abundance, %)): 248 (M+, 22.7), 213 (32.4), 137 (56.4), 124 (43.5), 111 (81.1), 58 (23.7), 41 (44.3), 39 (31.7).

Compound (**3d)**: Anal. Calcd for $C_{13}H_9BrOS$ (293.18); calcd.: C, 53.26; H, 3.09; S, 10.94; found: C, 53.19; H, 3.05; IR (KBr, cm^{-1}): 1580 (C=C), 1647 (C=O), 3025 (CH). ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 7.20 (m, 1H), 7.46 (d, 1H, C_2-H; *J*=15.58), 7.50 (d, 2H), 7.57 (d, 2H), 7.73 (d, 1H), 7.80 (d, 1H, C_3-H; *J*=15.58), 7.87 (d, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 122.05 (CH), 124.85 (C), 128.29 (CH), 128.76 (2xCH), 131.96 (C_2-H), 132.18 (2xCH), 133.55 (C), 134.12 (CH), 142.60 (C_3-H), 145.31 (C), 181.70 (C=O). MS (*m*/*z*, (relative abundance, %)): 292 (M+, 31.2), 213 (37.6), 181 (42.8), 124 (29.7), 58 (56.8), 41 (43.6), 39 (42.6).

Compound (**4d)**: Anal. Calcd for $C_{14}H_{12}O_2S$ (244.31); calcd.: C, 68.83; H, 4.95; S, 13.13; found: C, 68.77; H, 4.90; IR (KBr, cm^{-1}): 1594 (C=C), 1645 (C=O), 3022 (CH). ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 3.85 (s, 3H), 6.95 (d, 2H), 7.24 (m, 1H), 7.30 (d, 1H, C_2-H; *J*=15.62), 7.39 (d, 1H), 7.66 (d, 2H), 7.77 (d, 1H), 7.89 (d, 1H, C_3-H; *J*=15.62). ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 34.6, 41.4, 55.8, 110.7, 114.4, 117.3, 125.6, 129.9, 132.8, 133.7, 190.3. MS (*m*/*z*, (relative abundance, %)): 244 (M+, 16.1), 213 (56.9), 133 (42.4), 124 (34.7), 65 (53.2), 58 (46.7), 41 (38.6), 39 (54.5).

Compound (**5d)**: Anal. Calcd for $C_{15}H_{14}O_3S$ (274.34); calcd.: C, 65.67; H, 5.14; S, 11.69; found: C, 65.58; H, 5.07; IR (KBr, cm^{-1}): 1565 (C=C), 1637 (C=O), 3021 (CH). ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 3.85 (s, 3H), 3.91 (s, 3H), 6.50 (d, 2H), 7.16 (m, 1H), 7.48 (d, 1H, C_2-H; *J*=15.62), 7.57 (d, 1H), 7.63 (m, 1H), 7.85 (s, 1H), 8.07 (d, 1H, C_3-H; *J*=15.62). ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 25.7, 41.5, 55.9, 56.6, 100.4, 111.1, 117.3, 125.5, 132.4, 159.0, 190.1. MS (*m*/*z*, (relative abundance, %)): 274 (M+, 41.2), 243 (56.5), 212 (34.4), 163 (29.7), 124 (38.6), 111 (76), 58 (67.5), 41 (53.4), 39 (43.1).

Compound (**6d)**: Anal. Calcd for $C_{15}H_{14}O_3S$ (274.34); calcd.: C, 65.67; H, 5.14; S, 11.69; found: C, 65.61; H, 5.10; IR (KBr, cm^{-1}): 1575 (C=C), 1648 (C=O), 2987 (CH). ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 3.86 (s, 3H), 3.95 (s, 3H), 6.85 (d, 1H), 6.98 (s, 1H), 7.12 (d, 1H), 7.17 (m, 1H), 7.35 (d, 1H, C_2-H; *J*=15.64), 7.59 (d, 1H), 7.67 (d, 1H, C_3-H; *J*=15.64), 7.69 (d, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 30.6, 41.4, 56.3, 11.1, 112.4, 117.2, 122.2, 132.5, 147.2, 149.8, 190.4. MS (*m*/*z*, (relative abundance, %)): 258 (M+, 17.2), 147 (43.7), 124 (56.9), 111 (76.5), 58 (64.9), 41 (42.3), 39 (39.0).

Compound (**7d)**: Anal. Calcd for $C_{14}H_{10}O_3S$ (258.30); calcd.: C, 65.10; H, 3.90; S, 12.41; found: C, 64.96; H, 3.85; IR (KBr, cm^{-1}): 1589 (C=C), 1646 (C=O), 2989 (CH). ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 6.05 (s, 2H), 6.77 (d, 1H), 7.19 (d, 1H), 7.29 (m, 2H), 7.34 (d, 1H, C_2-H; *J*=15.62), 7.62 (d, 1H), 7.78 (d, 1H, C_3-H; *J*=15.69), 7.85 (d, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 101.62 (CH_2), 106.67 (CH), 108.65 (CH), 119.83 (CH), 125.35 (C_2-H), 128.20 (CH), 129.18 (C), 131.56 (CH), 133.65 (CH), 143.90 (C_3-H), 145.67 (C), 148.35 (C), 149.95 (C), 181.94 (C=O). MS (*m*/*z*, (relative abundance, %)): 220 (M+, 16.3), 148 (67.8), 137 (73.3), 109 (43.7), 58 (52.1), 41 (41.5), 39 (23.7).

Compound (**8d)**: Anal. Calcd for $C_{11}H_8OS_2$ (220.32); calcd.: C, 59.97; H, 6.10; S, 29.11; found: C, 59.91; H, 6.07; IR (KBr, cm^{-1}): 1574 (C=C), 1640 (C=O), 3095 (CH). ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 7.08 (d, 1H), 7.19 (m, 1H), 7.27 (d, 1H, C_2-H; *J*=15.72), 7.41 (s, 1H), 7.51 (m, 1H), 7.76 (m, 1H), 7.89 (s, 1H), 8.09 (d, 1H, C_3-H; *J*=15.63). ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 120.38 (CH), 128.27 (CH), 128.36 (CH), 128.85 (C_2-H), 131.67 (C_3-H), 132.28 (CH), 133.86 (CH), 136.49 (CH), 141.52 (C), 149.99 (C), 181.59 (C=O). MS (*m*/*z*, (relative abundance, %)): 274 (M+,15.2), 243 (45.6), 212 (54.9), 163 (49.0), 124 (65.9), 111 (78.9), 58 (49.0), 41 (56.7), 39 (63.2).

Compound (**1e)**: Anal. Calcd for $C_{14}H_{10}ClNO$ (243.69); calcd.: C, 69.00; H, 4.14; N, 5.75; found: C, 68.91; H, 4.09; N, 5.70; IR (KBr, cm^{-1}): 1568, 1605 (C=C, C=N), 1676 (C=O), 3046 (CH). ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 7.38 (d, 2H), 7.52 (m, 1H), 7.67 (d, 2H), 7.89 (d, 1H, C_2-H; *J*=16.15), 7.87 (d, 1H), 8.20 (d, 1H), 8.29 (d, 1H, C_3-H; *J*=16.15), 8.77 (d, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 121.30 (CH), 122.99 (CH), 127.17 (C_2-H), 129.19 (CH), 129.98 (CH), 133.65 (C), 136.44 (C),

137.09 (C_3-H), 143.18 (CH), 148.88 (CH), 154.09 (C), 189.29 (C=O). MS (*m/z*, (relative abundance, %)): 243 (M+,12.1), 208 (54.7), 137 (75.4), 119 (34.6), 106 (56.8).

Compound (**2e)**: Anal. Calcd for $C_{15}H_{13}NO_2$ (239.27); calcd.: C, 75.30; H, 5.48; N, 5.85; found: C, 75.22; H, 5.43; N, 5.76; IR (KBr, cm^{-1}): 1572, 1596 (C=C, C=N), 1664 (C=O), 3050 (CH). ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 3.85 (s, 3H), 6.97 (d, 2H), 7.49 (m, 1H), 7.71 (d, 2H), 7.89 (m, 1H), 7.97 (d, 1H, C_2-H; *J*=15.95), 8.19 (d, 1H, C_3-H; *J*=15.89), 8.21 (d, 1H), 8.78 (d, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 55.42 (CH_3), 114.31 (CH), 118.47 (CH), 122.85 (CH), 126.74 (CH), 126.95 (C_2-H), 127.92 (C), 130.66 (CH), 136.99 (C_3-H), 144.70 (CH), 148.77 (CH), 154.45 (C), 161.71 (C), 189.42 (C=O). MS (*m/z*, (relative abundance, %)): 239 (M+,14.2), 133 (64.6), 119 (78.8), 106 (56.3).

Compound (**3e)**: Anal. Calcd for $C_{15}H_{11}NO_3$ (253.26); calcd.: C, 71.14; H, 4.38; N, 5.53; found: C, 71.08; H, 4.34; N, 5.47; IR (KBr, cm^{-1}): 1581 (C=C, C=N), 1655 (C=O), 3012 (CH). ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 6.02 (s, 2H), 6.87 (d, 1H), 7.23 (d, 1H), 7.29 (s, 1H), 7.49 (m, 1H), 7.85 (d, 1H), 7.87 (d, 1H, C_2-H; *J*=15.88), 8.06 (d, 1H, C_3-H; *J*= 15.93), 8.16 (m, 1H), 8.74 (d, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 101.60 (CH_2), 107.07 (CH), 108.60 (CH), 111.84 (CH), 118.90 (CH), 122.86 (CH), 125.65 (CH), 126.80 (C_2-H), 129.71 (C), 137.06 (C_3-H), 144.67 (CH), 148.35 (C), 148.80 (CH), 149.96 (C), 154.34 (C), 189.30 (C=O). MS (*m/z*, (relative abundance, %)): 253 (M+, 19.5), 147 (57.7), 119 (45.9), 106 (62.1).

Compound (**4e)**: Anal. Calcd for $C_{12}H_{10}N_2O$ (198.22); calcd.: C, 72.71; H, 5.08; N, 14.13; found: C, 72.64; H, 5.06 N, 14.08; IR (KBr, cm^{-1}): 1575 (C=C, C=N), 1653 (C=O), 3091 (CH), 3302 (NH). ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 6.34 (m, 1H), 6.73 (d, 1H), 7.02 (d, 1H), 7.28 (s, 1H), 7.51 (m, 1H), 7.89 (d, 1H, C_2-H; *J*=16.26), 7.98 (m, 1H), 8.39 (d, 1H, C_3-H; *J*=16.28), 8.79 (d, 1H), 8.98 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 111.45 (CH), 113.92 (CH), 116.80 (CH), 122.88 (CH), 123.27 (CH), 126.62 (C_2-H), 134.12 (CH), 136.29 (C), 137.07 (C_3-H), 148.59 (CH), 153.94 (C), 193.20 (C=O). MS (*m/z*, (relative abundance, %)): 198 (M+,14.0), 119 (56.9), 118 (67.8), 92 (49.8).

Compound (**5e)**: Anal. Calcd for $C_{12}H_9NOS$ (215.28); calcd.: C, 69.51; H, 4.21; N, 6.51; S, 14.90; found: C, 69.47; H, 4.19; N, 6.43; IR (KBr, cm^{-1}): 1580 (C=C, C=N), 1665 (C=O), 3031 (CH), 3319 (NH). ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 7.05 (m, 1H), 7.47 (m, 2H), 7.52 (m, 1H), 7.89 (d, 1H, C_2-H; *J*=15.54), 8.09 (s, 2H), 8.19 (d, 1H, C_3-H; *J*=15.52), 8.77 (d, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 119.75 (CH), 122.85 (CH), 126.83 (C_2-H), 128.22 (CH), 129.17 (CH), 132.15 (CH), 136.96 (C_3-H), 137.20 (CH), 140.98 (C), 148.84 (CH), 155.30 (C), 193.22 (C=O). MS (*m/z*, (relative abundance, %)): 215 (M+,16.1), 131 (67.9), 119 (75.4), 106 (56.8), 58 (8.7), 41 (44.6), 39 (43.8).

Compound (**1f)**: Anal. Calcd for $C_{16}H_{14}O_2$ (238.11): C, 80.64; H, 5.93; Found: C, 80.56; H, 5.88 Anal. Calcd for $C_{16}H_{13}ClO_2$ (272.56): C, 70.44; H, 4.81; Found: C, 70.37; H, 4.75; IR (KBr, cm^{-1}): 1596 (C=C), 1656 (C=O), 2933, 3055 (CH); ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 3.86 (s, 3H), 6.99 (d, 2H, *J*=7.6), 7.43 (m, 3H), 7.55 (d, 1H, C_2-H, *J*=15.7), 7.65 (d, 2H, *J*=5.7), 7.99 (d, 1H, C_3-H, *J*=15.7), 8.06 (d, 2H, *J*=7.6); ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 56.20, 114.01, 121.11, 127.56, 131.20, 135.56, 145.80, 166.84. MS (*m/z*, (relative abundance, %)): 238 (M+,26.4), 148 (75.3), 135 (45.9), 119 (41.2), 107 (32.3).

Compound (**2f)**: Anal. Calcd for $C_{16}H_{13}ClO_2$ (272.56): C, 70.44; H, 4.81; Found: C, 70.37; H, 4.75; IR (KBr, cm^{-1}): 1600 (C=C), 1656 (C=O), 2925, 3012 (CH); ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 3.91 (s, 3H), 6.99 (d, 2H, *J*=8.6), 7.41 (d, 2H, *J*=8.3), 7.50 (d, 1H, C_2-H, *J*=15.7), 7.55 (d, 2H, *J*=8.3), 7.77 (d, 1H, C_3-H, *J*=15.7), 8.06 (d, 2H, *J*=8.6); ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 55.7, 114.6, 121.1, 128.5, 129.1, 131.0, 133.4, 145.4, 166.6, 189.8. MS (*m/z*, (relative abundance, %)): 272 (M+, 22.7), 237 (45.8), 148 (67.8), 137 (54.3), 135 (39.7).

Compound (**3f)**: Anal. Calcd for $C_{17}H_{16}O_3$ (268.13): C, 76.08; H, 6.01; Found: C, 76.01; H, 5.95; IR (KBr, cm^{-1}): 1597 (C=C), 1656 (C=O), 2960, 3015, 3067 (CH); ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 3.84 (s, 3H), 3.89 (s, 3H), 6.97 (dd, 4H, *J*=8.3), 7.44 (d, 1H, C_2-H, *J*=15.5), 7.62 (d, 2H, *J*=8.4), 7.79 (d, 1H, C_3-H, *J*=15.6), 8.06 (d, 2H, *J*=8.4); ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm): 55.6, 115.1, 121.4, 127.7, 130.2, 130.9, 135.6, 145.4, 159.7, 166.7, 189.9. MS (*m/z*, (relative abundance, %)): 268 (M+,16.1), 148 (67.9), 137 (54.1), 135 (34.6).

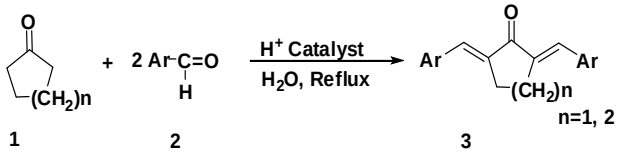
Compound (**4f)**: Anal. Calcd for $C_{17}H_{14}O_4$ (282.11): C, 72.31; H, 5.00; Found: C, 72.26; H, 4.95; IR (KBr, cm^{-1}): 1584 (C=C), 1655 (C=O), 2920, 3035 (CH); ^{1}H-NMR (400 MHz, $CDCl_3$, *δ*/ppm): 3.88 (s, 3H), 6.04 (s, 2H), 6.87 (d, 1H, *J*=8.0), 6.99 (d, 2H, *J*=8.6), 7.18 (m, 2H), 7.37 (d, 1H, C_2-H, *J*=15.4), 7.75 (d, 1H, C_3-H, *J*=15.4), 8.04 (d, 2H, *J*=8.6); ^{13}C-NMR (75 MHz, $CDCl_3$, *δ*/ppm):

55.6, 106.5, 108.2, 114.7, 122.4, 127.4, 131.1, 145.3, 148.0, 148.8,166.1, 189.8. MS (*m/z*, (relative abundance, %)): 282 (M+,26.2), 148 (65.9), 147 (52.9), 135 (23.8).

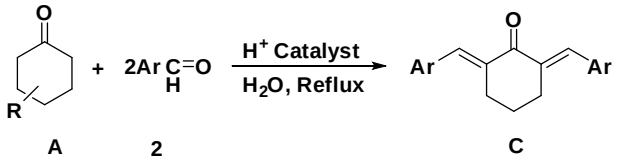
RESULTS AND DISCUSSION

We wish to report an efficient and selective method for condensation of cyclic and acyclic ketones with aromatic and non-aromatic aldehydes in aqueous medium, free of organic solvents. Different types of ketones were subjected to condensation with aromatic and non-aromatic aldehydes, containing either electron-releasing or electron-withdrawing groups, in the presence of the reagent under free of organic solvents conditions (Schemes 1, 2).

The results of crossed-aldol condensation of aromatic and non-aromatic aldehydes are summarized in Tables **1** and **2**. The reactions were completed within 1.5-6 h and high yields of α,α'-bis(substituted benzylidene and cinnamylidene) cyclopentanones and cyclohexanones were obtained (Table **1**, entries **1-12**).

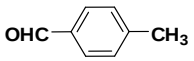
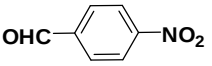
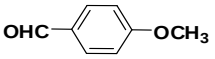
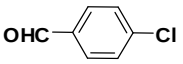
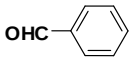
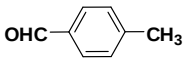
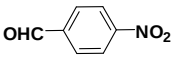
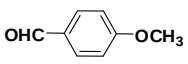
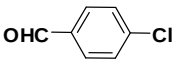
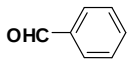


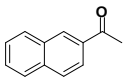
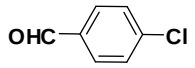
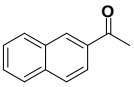
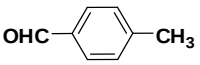
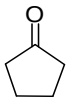
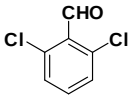
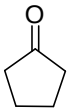
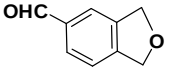
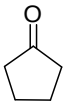
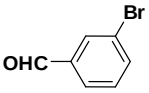
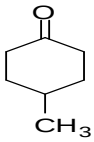
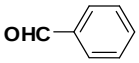
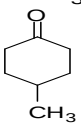
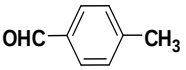
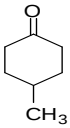
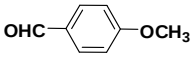
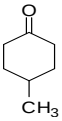
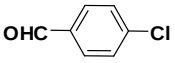
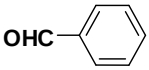
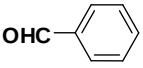
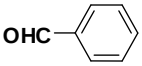
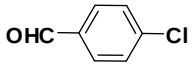
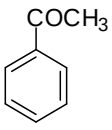
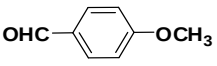
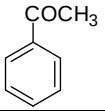
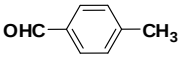
Scheme 1. Crossed-aldol condensation of ketones with aromatic aldehydes (**1**)



Scheme 2. Crossed-aldol condensation of ketones with non-aromatic aldehydes (**A**)

Table 1. Crossed-aldol condensation of ketones with aromatic aldehydes (**1**) in the presence of silica-supported Preyssler heteropolyacids catalyst under organic solvent-free and reflux conditions

Entry	Ketone	Aldehyde	Time, h	[a,b]Yield, %	M p (ºC)	
					Found	Reported
1a		$C_6H_5CH=CH-CHO$	2	97	225–227	222–224[17a]
2 a			2	98.5	217–219	220[17b]
3 a			2.5	95.5	229–230	230-231[17a]
4 a			1.5	97	212–214	210–211[17a]
5 a			2	96.5	223–225	225[17b]
6 a			1.5	96, 96[d], 95[d], 94[d]	190–191	188–191[17a]
7 a		$C_6H_4CH=CH-CHO$	3	92	181–183	180[17a]
8 a			2.5	94.5	167–169	170[18]
9 a			3	92.5	160–162	159[17a]
10 a			3	93	201–203	203–204[17a]
11 a			2.5	94, 93[d], 93[d], 92[d]	146–148	147–148[17a]
12 a			2	95, 94 [d], 93[d], 93[d]	115–118	117[17a]

13 a			1.5	97	162–164	163–165[17b]
14 a			1.5	98	143–145	142–143[17b]
15 a			1.5	82	182–188ºC (accomp. by decomp.)	–
16 a			1.5	91	247–249	
17 a			2.5	89	208–210	–
18 a			4	93.5	97–99	–
19 a			4.5	94	125–127	–
20 a			4	93	137-139	-
21 a			5	96	156-160	-
22 a			6	[c]28	115-118	117[17a]
23 a			5	[c]30	190-191	188-191[17a]
24 a			2.5	92.5	54-57	55-58[17c]
25 a			2.5	98	108-110	107-109[17b]
26 a			2.5	96.5	74-76	75-77[17c]
27 a			2.5	98	95-97	97-98[17c]

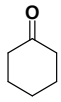
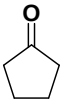
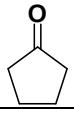
[a]Isolated yield; [b]Products were characterized by comparison of their spectroscopic data ([1]H-NMR and IR) and mps with those reported in the literature; [c]The reaction was performed in the absence of the catalyst; [d]The same catalyst was used for each of the four runs.

The results of crossed-aldol condensation of cyclic ketones with non-aromatic aldehydes in the presence of silica-supported Preyssler HPAs catalyst under free of organic solvents conditions was investigated at properiate times and under reflux (Table **2)**. In the crossed-aldol condensation

of cyclopentanone with hexanal the reaction yield is good (Table **2**, entry **2b)**, but in similar reactions for other cyclic ketones and with non-aromatic aldehydes the yields are lower (40-51%), (Table **2**, entries **1b, 3b** and **4b**).

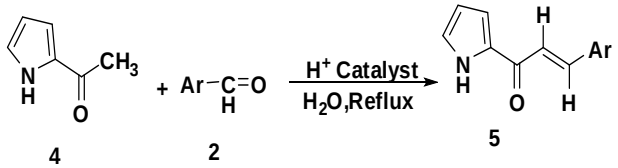
Reactions were also performed for acyclic ketones like 2-acetylnaphthalene and the corresponding products were obtained in excellent yields within 1.5 h (Table **1**, entries **13-14**, **24-27**). The promoting effect of silica-supported Preyssler HPAs catalyst in these reactions was shown by

Table 2. Crossed-aldol condensation of ketones with non-aromatic aldehydes (**A**) in the presence of silica-supported Preyssler heteropolyacids catalyst under organic solvent-free and reflux conditions

Entry	Ketone	Aldehyde	Time, h	[a,b]Yield, %	Bp (°C) Found	Bp (°C) Reported
1b		CH_3CHO	6	40	130	87–89 [40]
2b		*n*-$C_5H_{11}CHO$	5	81	140	–
3b		C_2H_5CHO	5	47	156	–
4b		*n*–PrCHO	6	51	170	–

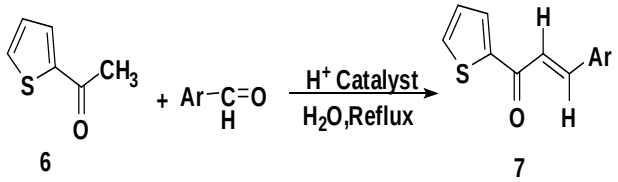
[a]Isolated yield; [b]Products were characterized by comparison of their spectroscopic data ([1]H-NMR and IR).

performing some reactions in the absence of the catalyst (Table **1**, entries **22, 23**). In these experiments the product was isolated and the remaining catalyst was washed and reloaded with fresh substrates for further runs. No decrease in the yield was observed, demonstrating that silica-supported Preyssler HPAs catalyst can be reused in crossed-aldol condensation (Table **1**, entries **6** and **11, 12**). We continued our research in this paper on the crossed-aldol condensation of some hetarylmethyl ketones with a variety of different aromatic aldehydes in water at reflux temperature and in the presence of silica-supported Preyssler HPAs as a catalyst for the synthesis of (2*E*)-3-aryl-1-hetarylprop-2-en-1-ones (**5, 7, 9** in Schemes **3, 4, 5**) and 1,3-disubstituted propenones (**11**, Scheme. **6**) in excellent yields with high stereoselectivity (**11**, Scheme **6**).



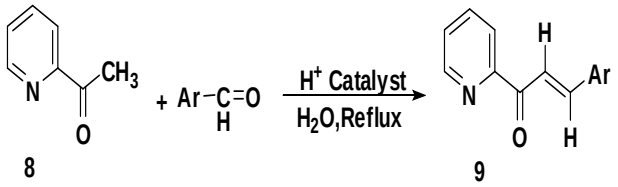
4 2 5

Scheme 3. Crossed-aldol condensation of 2-acetylpyrrol (**4**) with aromatic aldehydes and synthesis of (2*E*)-3-aryl-1-(pyrrol-2'-yl)prop-2-en-1-ones (**5**, **1-8c**).



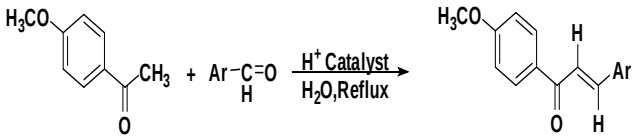
6 7

Scheme 4. Crossed-aldol condensation of 2-acetylthiophene (**6**) with aromatic aldehydes and synthesis of (2*E*)-3-aryl-1-(thien-2'-yl)prop-2-en-1-ones (**7**, **1-8d**).



8 9

Scheme 5. Crossed-aldol condensation of 2-acetylpyridine (8) with aromatic aldehydes and synthesis of (2*E*)-3-aryl-1-(pyrid-2'-yl)prop-2-en-1-ones (9, 1-5e).

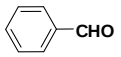
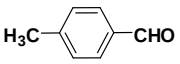
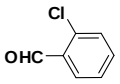
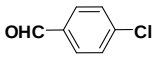
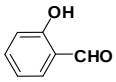
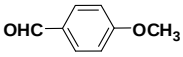
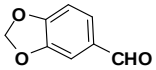
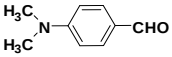


10 11

Scheme 6. Crossed-aldol condensation of 4-methoxyacetophenone (10) with aromatic aldehydes and synthesis of (2*E*)-3-aryl-1-(4`-methoxyphenyl)prop-2-en-1-ones (11, 1-4f).

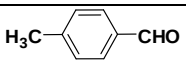
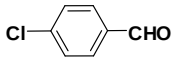
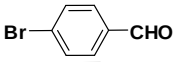
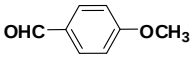
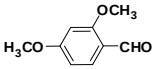
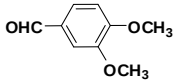
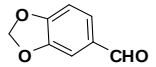
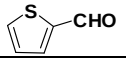
By efficient stirring of an equimolar amount of 2-hetarylmethyl ketones, 4-methoxyacetophenone (**4**, **6**, **8, 10**) and aromatic aldehydes in aqueous acidic (H^+) solution in the presence of silica-supported Preyssler catalysts as acidic catalyst at reflux temperature, stereoselective crossed-aldol condensation took place with precipitation of 3-aryl-1-hetarylprop-2-en-1-ones (**5, 7, 9** in Schemes **3, 4, 5**) and 1,3-disubstituted propenones in high yields within a short reaction time as shown in Tables **3, 4, 5, 6**.

Table 3. Crossed-aldol condensation of 2-acetylpyrrol (**4**) with aromatic aldehydes in the presence of silica-supported Preyssler heteropolyacids catalyst and water as a solvent at reflux conditions

Entry	Aldehyde	Time, min	[a,b]Yield, %	Mp (ºC)	
				Found	Reported
1c		100	78	136–138	–
2c		110	82	148–150	–
3c		94	88	121–123	–
4c		86	92	154–156	–
5c		135	69	167–168	-
6c		20	94, 94[c], 93[c], 91[c]	60–80	–
7c		15	98	140–142	–
8c		15	95	192–194	–

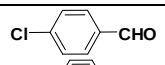
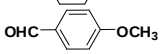
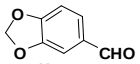
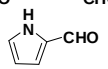
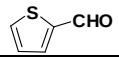
[a]Isolated yield; [b]Products were characterized by comparison of their spectroscopic data ([1]H-NMR and IR);
[c]The same catalyst was used for each of the four runs.

Table 4. Crossed-aldol condensation of 2-acetylthiophene (**6**) with aromatic aldehydes in the presence of silica-supported Preyssler heteropolyacids catalyst under organic solvent-free and reflux conditions

Entry	Aldehyde	Time, min	[a,b]Yield, %	Mp (ºC)	
				Found	Reported
1d		100	84	112–114	–
2d		76	81	118–120	–
3d		71	77	131–133	–
4d		30	94	144 –146	–
5d		12	96	113–115	–
6d		21	93.5	119–121	–
7d		23	92, 90[c], 90[c], 89[c]	117–119	–
8d		89	80.5	136–138	–

[a]Isolated yield; [b]Products were characterized by comparison of their spectroscopic data ([1]H-NMR and IR);
[c]The same catalyst was used for each of the four runs.

Table 5. Crossed-aldol condensation of 2-acetylpyridine (**8**) with aromatic aldehydes in the presence of silica-supported Preyssler heteropolyacids catalyst under organic solvent-free and reflux conditions

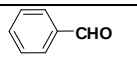
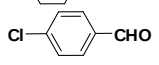
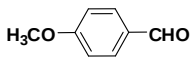
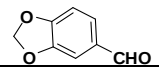
Entry	Aldehyde	Time, min	[a,b]Yield, %	Mp (ºC)	
				Found	Reported
1e		30	88	103–105	–
2e		36	97, 96c, 96c, 95c	120–122	–
3e		16	98, 97c, 96c, 96c	148–150	–
4e		69	80.5	124–126	–
5e		51	83	76–78	–

[a]Isolated yield; [b]Products were characterized by comparison of their spectroscopic data ([1]H-NMR and IR);
[c]The same catalyst was used for each of the four runs.

It is seen from Tables **3, 4, 5, 6** that electron-donating substituents of aromatic aldehydes reduce the reaction period and increase the yield of these ketones.

We found that the reaction proceeds efficiently and with good yields in the crossed-aldol condensation of 2-acetylpyrrol (**4**) with aromatic aldehydes (Table **3,** 1c-4c and 6c-8c) having electron-withdrawing and electron-donating substituents. In the crossed-aldol condensation of 2-acetylpyrrol (**4**) with 2-hydroxybenzaldehyde

Table 6. Crossed-aldol condensation of 4-methoxyacetophenone (**10**) with aromatic aldehydes in the presence of silica-supported Preyssler heteropolyacids catalyst under organic solvent-free and reflux conditions

Entry	Aldehyde	Time, min	[a,b]Yield, %	Mp (ºC)	
				Found	Reported
1f		88	70.5	119-121	–
2f		120	72, 71[c], 71[c], 69[c]	120-122	–
3f		28	89.5	89–91	–
4f		26	92.5	24–126	–

[a]Isolated yield; [b]Products were characterized by comparison of their spectroscopic data ([1]H-NMR and IR);
[c]The same catalyst was used for each of the four runs.

(Table **3**, entry **5c**) the reaction yields are lower, and probably an interaction between the ketone substituent and the hydroxyl group occurs (OH group in intermediate conditions of these reactions) (Table **3**, entry **5c**).

CONCLUSIONS

The present method is very suitable and efficient for crossed-aldol condensation of ketones, 2-acetylthiophene, 2-acetylpyrrole and 2-acetylpyridine with aromatic aldehydes. The synthesis of α,α'-bis(substituted benzylidene) cycloalkanones, (2*E*)-3-aryl-1-(thien-2'-yl)prop-2-en-1-ones, (2*E*)-3-aryl-1-(pyrrol-2'-yl)prop-2-en-1-ones and (2*E*)-3-aryl-1-(pyrid-2'-yl) prop-2-en-1-ones takes place with high yields in the presence of a reusable and environmentally benign catalyst. Simple work-up procedure, including washing the mixture followed by evaporation of the solvent, is another advantage of this method. $H_{14}[NaP_5W_{30}O_{110}]$, Preyssler type HPAs catalyst, is eco-friendly, inexpensive and efficient. High yields, relatively short reaction times, simplicity of operation and easy work-up procedure are some advantages of this protocol. $H_{14}[NaP_5W_{30}O_{110}]$ offers the advantages of higher hydrolytic and thermal stability. The salient features of Preyssler's anion are availability, non-toxicity and reusability. We believe this methodology can find usage in organic synthesis.

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КРЪСТОСАНА АЛДОЛНА КОНДЕНЗАЦИЯ НА КЕТОНИ С АРОМАТНИ И НЕ-АРОМАТНИ АЛДЕХИДИ С PREYSSLER‘ОВ ХЕТЕРОКИСЕЛИНЕН КАТАЛИЗАТОР ВЪРХУ СИЛИЦИЕВ ДИОКСИД КАТО НОСИТЕЛ

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(Резюме)

Съобщава се за синтезите на α,β-ненаситени алдолни продукти чрез кръстосана алдолна кондензация в присъствие на катализатор от хетерополикиселини (HPAs) при условия на рефлукс и без използванена органични разтворители. Алдолната кондензация на 2-ацетилтиофен, 2-ацетилпирол и 2-ацетилпиридин с различни ароматни алдехиди е извършвана вов вода в присъствие на Preyssler‘ов катализатор (HPAs) при обикновена температура. Всички реакции протичат с отлични добиви на стереоселективни хет-арилпропанони във вода кат екологично съвместим разтворител.