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Synthesis of benzazepine derivatives using multicomponent reaction of alkyl bromides

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Abstract: A novel procedure is investigated for the preparation of benzazepine derivatives using multicomponent reaction of imidazole, alkyl bromides, isatoic anhydride or its derivatives and activated acetylenic compounds in the presence of KF/Clinoptilolite nanoparticles as catalyst in water at room temperature. Some advantages of this procedure are: short time of reaction, high yields of product, easy separation of catalyst and products. KF/CP NPs show a good improvement in the yield of the product and displayed significant reusable activity.

Keywords: KF/CP NPs, Benzazepine derivatives, Three-component reaction, Alkyl bromide.

Introduction

Multicomponent reactions (MCRs) are important procedure for producing complex molecules from simple starting materials [1-5]. The molecules that were prepared by this method are attractive for medicinal and synthetic chemists [6-8]. Also, green procedure is finding method for saving resources and decrease prices. Use of ecologically solvents instead of toxic solvents, employing cheap reagents are the most attractive methods to expand a simple and green synthesis of organic compounds [9]. Azepines are prevalent motifs in several natural products possessing diverse biological properties. Benzazepines, which have a 7-membered aza-heterocyclic fused aromatic ring, are of interest because of their biological activity and use as building blocks for natural product synthesis and drug discovery [10-11].

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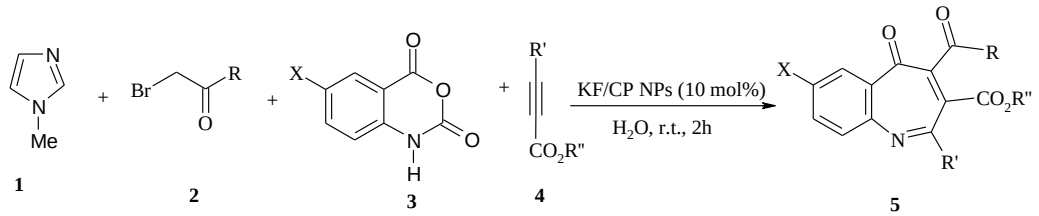
In the area of natural products synthesis, syntheses of alkaloids with a benzazepine skeleton, such as aphanorphine [12], cephalotaxine [13], and lennoxamine [14] have been investigated because of their interesting chemical structures and useful biological activities.

The most of methods utilize expensive organic solvents and catalysts which employ multi-step synthetic methodologies [15-28]. Recently, there has been enormous emphasis on the green and sustainable chemistry, where high importance has been given for the development of novel and eco-friendly methodologies which can reduce or eliminate the use and generation of hazardous industrial wastes [29]. Water as an available and cheap solvent in large amounts can increase the rate of organic reactions even for compounds that is water-insoluble. Also isolation of product in water is performed by simple filtration.

Recently, applications of potassium fluoride impregnated on zeolites and clays was considered a lot of attention because of new natural and inexpensive solid base system [30-38]. Among zeolites,

clinoptilolite, is a natural zeolite with a high internal surface area. It is much more valuable because of its high exchange ability for cations mainly for K+. Therefore, more free fluoride anions could be act as an effective base. In contrast, the preparation of potassium fluoride mixed with Clinoptilolite (KF/CP) is very simple and easy without any pre-activation [39-40]. In continuation of our attempts to expand new synthetic procedure for chief organic compounds [41-45] herein, we investigated a green procedure for the synthesis of some benzazepine derivatives **5** *via* an efficient four component reaction of *N*-methylimidazole **1**, α-haloalkanes **2**, isatoic anhydride or its derivatives **3** and activated acetylenic compounds **4** in the presence of a catalytic amount of PG-KF/CP NPs in water at room temperature with good yields (Scheme **1**).



1 **2** **3** **4** **5**

5	R	R'	R"	X	Yield (%) of **5**
a	4-MeO-C_6H_4	CO_2Me	Me	H	95
b	4-MeO-C_6H_4	CO_2Et	Et	H	93
c	4-Me-C_6H_4	H	Me	H	90
d	4-MeO-C_6H_4	H	Me	Me	92
e	4-MeO-C_6H_4	CO_2Me	Me	Me	95
f	4-Me-C_6H_4	CO_2Me	Me	H	87

Scheme 1: Synthesis of piperidine derivatives in the presence of lactic acid

Result and Discussion

In the starting stage of this work, condensation reaction of *N*-methylimidazole **1**, α-haloalkanes **2**, isatoic anhydride or its derivatives **3** and activated acetylenic compounds **4** was employed as a sample reaction to achieve the optimum conditions (Table **1**). This reaction wasn't performed without any catalyst even after 15h (entry 1, Table **1**) and very busy mixture in absence of cataltst. For this reasone, 10 mol% catalyst such as Fe_3O_4-MNPs was added to the reaction mixture. After 8 h, 45% yield of **5a** was produced (entry 4, Table 1). In order to more evaluate the catalytic activity, another catalyst such as ZnO-nanorods, CuO-NPs, TiO_2-NPs, Me_3N, Al_2O_3, Et_3N and KF/CP NPs were used in this reaction. Consequently, these results showed the KF/CP NPs is the best catalyst for this reaction. Then, the reaction was carried out in the presence of 15 mo% of KF/CP NPs as catalyst. By increasing the amount ofcatalyst from 10-20%, didn't seen any considerable change in the yields of reaction. Also, by increasing the reaction temperature to 80 ^oC, wasn't seen any change in the amount of **5a** after 15 h (entry 2, Table 1). As a result, to discover the optimal catalyst loading, different amounts (10–20 mol%) of KF/CP NPs were employed. The results displayed that 10 mol% of catalyst are enough for produce an excellent yield of **5a** (entry 5, Table **1**).

Table 1. Effect of catalyst, its loading and temperature on the condensation reaction of compound **5a**

Entry	Catalyst	Temp.(°C)	catalyst (mol%)	Time (h)	Yield%[a]
1	none	r.t.	-	15	-

2	none	80	-	15	10
3	none	90	-	15	10
4	Fe_3O_4-MNPs	r.t.	10	8	45
5	**KF/CP NPs**	**r.t.**	**10**	**2**	**95**
6	KF/CP NPs	80	10	5	95
7	KF/CP NPs	r.t.	15	5	95
8	KF/CP NPs	r.t.	20	5	95
9	Et_3N	r.t.	15	8	65
10	Me_3N	r.t.	10	7	76
11	Al_2O_3	r.t.	15	10	38
12	ZnO-NR	r.t.	10	8	78
13	ZnO-NR	90	15	8	78
14	CuO-NPs	r.t.	10	8	45
15	TiO_2-NPs	r.t.	10	10	68

As expected, the yield of product **5a** was achieved in 97% yield after 2 h (entry5, Table 1) in optimum conditions. The reason of selection of KF/CP-NPs as catalyst is inexpensive, safe than to other catalyst and abundance of CP. catalytic property of KF/CP include basic property by trapping the K^+ and successfully the F- performance as base in these reactions. Other catalyst such as ZnO-NPs, TiO_2-NPs is Lewis base and has low activity than F-. With triethyl amine as basic catalyst mixture of reaction is busy and separation of product is difficult. Trimethylamine is better than to triethylamine and yield of product is excellent. But F- because of small and free is better than all. Also, in this research the effects of some solvents was investigated on the production of sample reaction in the presence of 10 mol% of KF/CP NPs. The results tabulated in Table **2** display that H_2O is the best solvent for these reaction.

Table 2: Effects of solvent and temperature on generation of **5a** in presence of 10 mol% of KF/CP NPs

Entry	**Solvent**	**Temp. (°C)**	**Time (h)**	**Yield%[a]**
1	EtOH	r.t.	15	None
2	EtOH	90	15	None
3	CH_2Cl_2	r.t.	8	75
4	CH_2Cl_2	40	8	75
5	H_2O	r.t.	3	95
6	**H_2O**	**80**	**5**	**95**
7	Solvent-free	r.t.	8	90
8	DMf	r.t.	15	45
10	toluene	r.t.	12	78

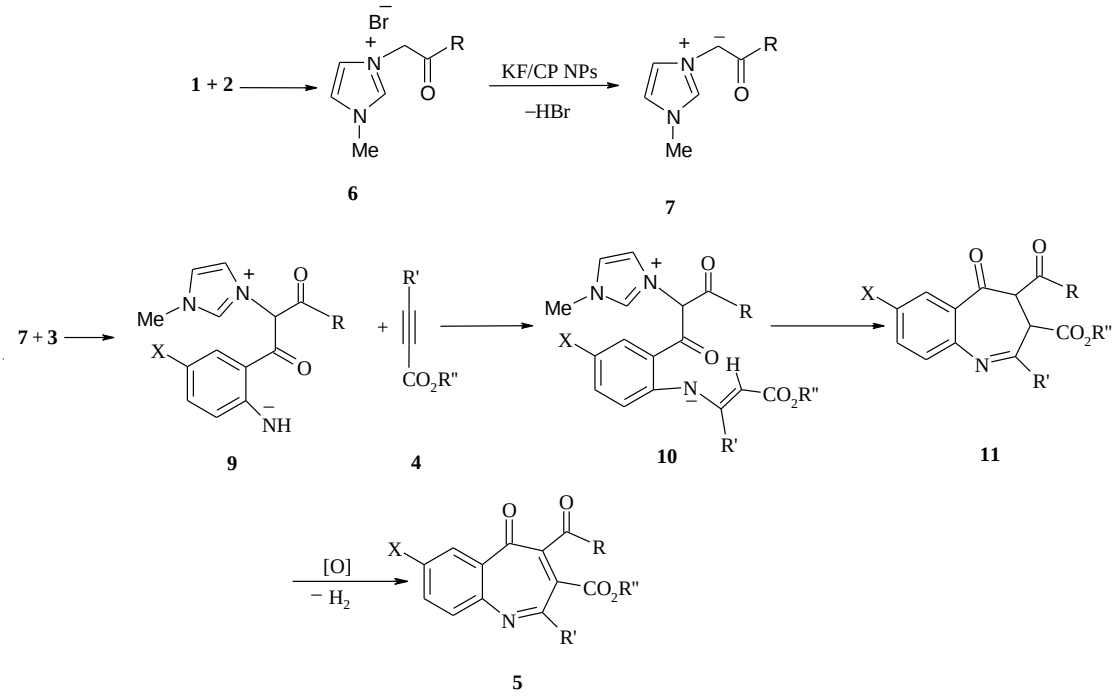
11	$CHCl_3$	r.t.	10	68

According to the outcomes of optimization reported in the Tables 1 and 2, KF/CP NPs (10 mol%) as catalyst, water as solvent, and room temperature were estimated to be the optimum reaction conditions. The reusability of the catalyst was confirmed in the model reaction (the synthesis of compound **5a**). The results showed that the catalyst can be reused five times without loss of activity (Table **3**). After each run, the catalyst was extracted by filteration and washed with water. It was then dried at ambient temperature for 24 h and employed for the next catalytic cycle.

Table 3: Activity of reused catalyst for synthesis of compound **5a**

Run	% Yield[a]
1st	95
2nd	95
3nd	93
4nd	93
5nd	90

The structures of compounds **5** were confirmed by IR, ^{1}H NMR, ^{13}C NMR, and mass spectral data. For example, the ^{1}H NMR spectrum of **5a** revealed three singlets at 3.75, 3.83 and 3.87 ppm for methoxy protons along with signals for aromatic moiety. In the ^{13}C NMR spectrum, the signals corresponding to the four carbonyl group of **5a** were observed at δ 160.2, 162.4, 178.2 and 189.3 ppm. The IR spectrum of **5a** was displayed characteristic C=O bands. Although there is no information about the mechanistic details, the reaction can be described by the mechanism proposed in Scheme **2**.



Scheme 2: Proposed mechanism for the formation of **5**.

First, *N*-methylimidazole **1** and alkyl bromides **2** is reacted in the presence of KF/CP NPs that is generated intermediate **7**. Intermediate **7** is attacked to compound **3** and produced intermediate **9**. Intermediate **9** react with compounds **4** and produced intermediate **10.** Intermolecular cyclization of intermediate **10** and elimination of isoquinoline generate compound **12**. Finally, intermediate **12** leads to the final product **5** by oxidation with air. The chief benefits of our method are high atom economy, green reaction conditions, use a small amount nanocatalyst, higher yield, shorter reaction times, and easy work-up, which are in good agreement with some principles of green chemistry.

The Bio-KF/Clinoptilolite nanoparticles were prepared by using *Punica Granatum* peel extract. The scanning electron microscopy images (SEM) Figure **1** and X-ray diffraction patterns (XRD) Figure **2** was employed for determination and confirmation of the construction and particle size of potassium fluoride/Clinoptilolite nanoparticles.

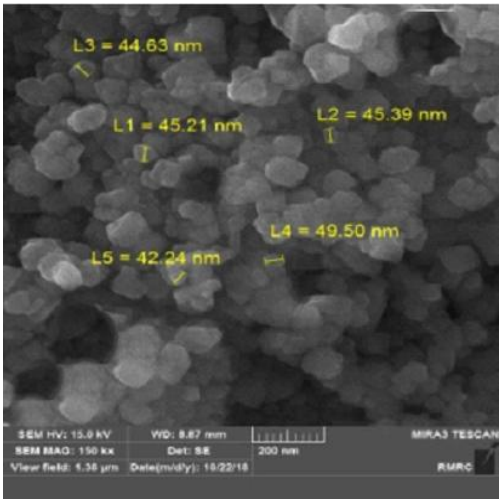


Figure 1: Scanning electron microscopy representation of green KF/CP nanoparticles

The KF/Clinoptilolite nanoparticles particles size has been found to be 35 nm employing the equation of Debye–Scherrer's ($D=K\lambda/\beta cos\theta$).

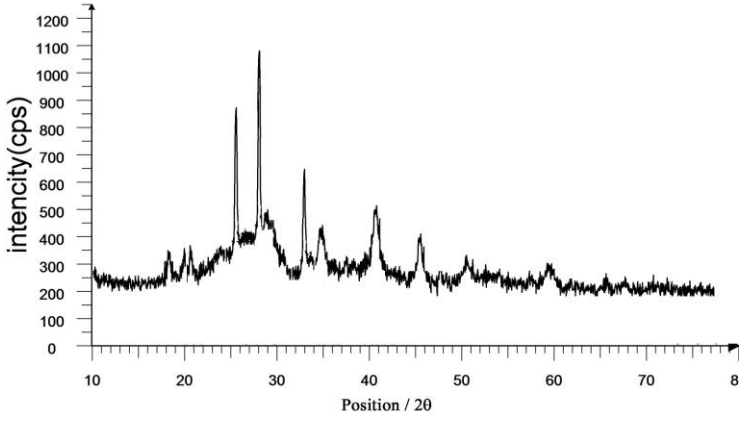


Figure 2: X-ray diffraction spectra of green KF/CP nanoparticles

Elemental analysis of the synthesized KF/CP NPs nanoparticles was performed using EDS technique (Figure 3). As shown in Figure 3, K and F peaks of KF/CP NPs nanoparticles indicate a successful synthesis. Also, the presence of peak carbon in the EDS spectrum indicates the presence of organic compounds at the nanoscale. To obtain a clear size, shape and structural image of the nanoparticles the sample was analyzed using transmission electron microscopy (Figure **4**). Transmission electron microscope image reveals the size of the synthesized KF/CP NPs to be less than 40 nm.

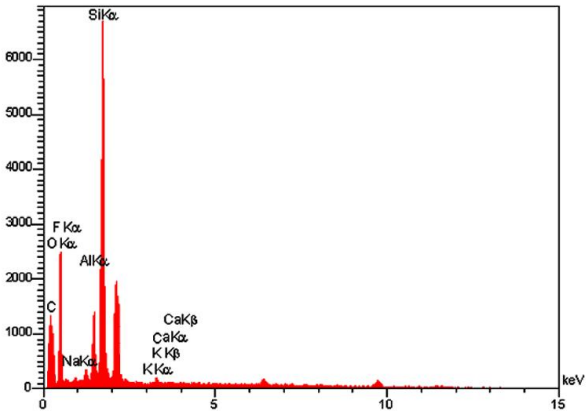


Figure 3: EDS image of green KF/CP NPs

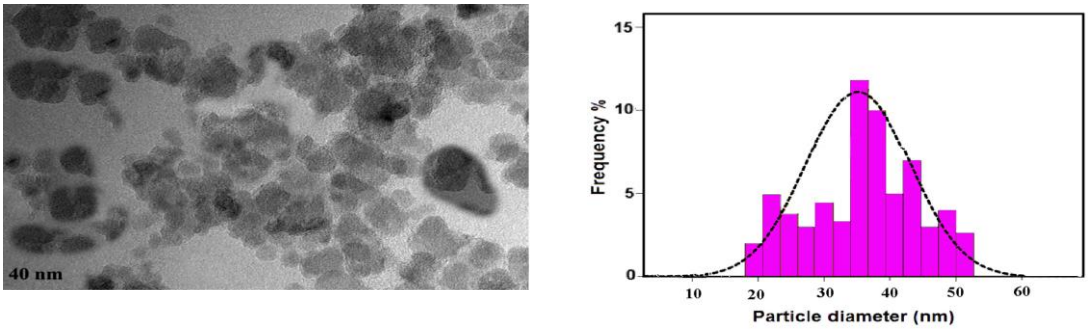


Figure 4: TEM image of the green KF/CP NPs

Conclusion

In summary, we investigate an useful, green, and environmentally procedure including imidazole, α-haloalkanes, alkyl bromides, isatoic anhydride or its derivatives and activated acetylenic compounds in the presence of PG-KF/CP NPs and acidic solution of H_2O_2 at room temperature in water which provides a new path to the synthesis of benzazepines. The present method has many advantages such as high atom economy and yield, mild and clean reaction condition, low catalyst loading, and short reaction time.

Experimental section

General procedure for preparation of green KF/CP NPs

The KF/CP (NPs) catalyst was prepared according to previously reported procedure.[30]Natural Clinoptilolite zeolite nano sized was produced using grinding in a planetary ball mill using a zirconia vial set in dry conditions with a time period of about 20 min. Thus, 1 g of KF and nano Clinoptilolite (9 g) was dissolved in *Punica Granatum Peel* water extract (10 ml). The mixture was stirred for 10 min. Then, precipitate was

filtered and washed with water. Then, KF/CP (NPs) was dried at 80 °C in a vacuum drying oven for 25 h. The yield of PG-KF/CP (NPs) by this procedure is more than using water for synthesis of KF/CP (NPs). The structure and particle size analysis of the KF/CP were performed by scanning electron microscopy images (SEM) and X-ray diffraction patterns (XRD). X-ray diffraction patterns (XRD) was used for calculating of the size of prepared KF/CP-NPs. The average crystallite size (D) for KF/CP-NPs was calculated based on peak with the strongest intensity using the Debye–Scherrer's equation ($D=K\lambda/\beta cos\theta$); where D is the grain size, β is full-width at half-maximum or half-width (FWHM) in radians and h is the position of the maximum of diffraction peak, *K* is the so-called shape factor (0.89), θ is Bragg's diffraction angle and λ is the X-ray wavelength used (1.5406 A˚ for CuK_{α}). Particles size of KF/CP has been found to be 40 nm.

General procedure for preparation of compounds 5a–f

In first pot isoquinoline **1** (2 mmol) mixed with alkyl bromide **2** (2 mmol) in the presence of *PG*-KF/CP NPs (15 mol%) in water (5 mL) for 30 min. In other pot, isatin or its derivatives **3** (2 mmol) mixed with acidic solution of H_2O_2 (10 mL) in water for 20 min. After this time, mixture in second pot was poured in first pot and mixture was stirred for 20 min. Then activated acetylenic compounds **4** (2mmol) was added to the magnetically stirred mixture and mixed for 1h. After 2 h, the reaction is completed and progress of the reaction is confirmed by TLC. Finally, the solid residue was collected by filtration and washed with EtOAc for separation of PG-KF/CP NPs. The solvent was evaporated and the product is separated as a solid form and purified by washing with Et_2O.

Dimethyl-4-(4-methoxybenzoyl)-5-oxo-5H-1-benzazepine-2,3-dicarboxylate (5a):

Yellow powder, mp 186-188˚C, Yield: 0.77 g (95%). IR (KBr) (ν_{max}/cm^{-1}): 1740, 1738, 1727, 1695, 1587, 1468, 1295 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): 3.75 (3 H, s, MeO), 3.83 (3 H, s, MeO), 3.87 (3 H, s, MeO), 7.35 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.48 (1 H, t, ^3J = 7.8 Hz, CH), 7.56 (1 H, t, ^3J = 7.8 Hz, CH), 7.98 (2 H, d, ^3J = 7.6 Hz, 2 CH), 8.12 (1 H, d, ^3J = 7.8 Hz, CH), 8.45 (1 H, d, ^3J = 7.8 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): 51.4 (MeO), 52.3 (MeO), 55.7 (MeO), 114.2 (2 CH), 122.3 (C), 125.4 (CH), 126.4 (CH), 127.2 (C), 129.2 (C), 130.4 (C), 132.5 (CH), 133.6 (2 CH), 137.2 (CH), 152.3 (C), 155.3 (C), 159.3 (C), 160.2 (C=O), 162.4 (C=O), 178.2 (C=O), 189.3 (C=O) ppm. EI-MS: 407 (M$^+$, 10), 376 (86), 31(100). Anal. Calcd for $C_{22}H_{17}NO_7$ (407.38): C 64.86, H 4.21, N 3.44; Found: C 64.98, H 4.38, N 3.58.

Diethyl-4-(4-methoxybenzoyl)-5-oxo-5H-1-benzazepine-2,3-dicarboxylate (5b):

Yellow powder, mp 192-194˚C, Yield: 0.81 g (93%). IR (KBr) (ν_{max}/cm^{-1}): 1739, 1735, 1726, 1692, 1583, 1475, 1286 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): 1.16 (3 H, t, ^3J = 7.4 Hz, CH_3), 1.23 (3 H, t, ^3J = 7.4 Hz, CH_3), 4.25 (2 H, q, ^3J = 7.4 Hz, CH_2O), 4.32 (2 H, q, ^3J = 7.4 Hz, CH_2O), 3.87 (3 H, s, MeO), 7.38 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.52 (1 H, t, ^3J = 7.8 Hz, CH), 7.63 (1 H, t, ^3J = 7.8 Hz, CH), 8.03 (2 H, d, ^3J = 7.6 Hz, 2 CH), 8.15 (1 H, d, ^3J = 7.8 Hz, CH), 8.52 (1 H, d, ^3J = 7.8 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): 13.8 (Me), 14.2 (Me), 61.3 (CH_2O), 62.4 (CH_2O), 55.6 (MeO), 114.3 (2 CH), 122.5 (C), 125.6 (CH), 126.7 (CH), 127.4 (C), 129.6 (C), 130.8 (C), 132.6 (CH), 134.2 (2 CH), 137.5 (CH), 152.6 (C), 155.8 (C), 159.6 (C), 160.4 (C=O), 162.7 (C=O), 178.7 (C=O), 189.5 (C=O) ppm. EI-MS: 435 (M$^+$, 10), 390 (78), 45(100). Anal. Calcd for $C_{24}H_{21}NO_7$ (435.43): C 66.20, H 4.86, N 3.22; Found: C 66.38, H 5.02, N 3.40.

Methyl-4-(4-methylbenzoyl)-5-oxo-5H-1-benzazepine-3-dicarboxylate (5c):

Yellow powder, mp 163-165˚C, Yield: 0.77 g (90%). IR (KBr) (ν_{max}/cm^{-1}): 1736, 1728, 1725, 1689, 1585, 1462, 1284 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): 2.48 (3 H, s, Me), 3.78 (3 H, s, MeO), 6.15 (1 H, s, CH), 7.38 (1 H, t, ^3J = 7.6 Hz, CH), 7.52 (1 H, t, ^3J = 7.6 Hz, CH), 7.86 (2 H, d, ^3J = 7.8 Hz, CH), 8.07 (2 H, d, ^3J = 7.8 Hz, 2 CH), 8.16 (1 H, d, ^3J = 7.6 Hz, CH), 8.28 (1 H, d, ^3J = 7.6 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): 22.3 (Me), 51.6 (MeO), 122.8 (C), 125.2 (CH), 126.4 (CH), 126.9 (C), 129.3 (C), 130.4 (2 CH), 131.5 (2 CH), 132.6 (CH), 136.3 (C), 137.4 (CH), 145.2 (C), 147.3 (CH), 154.2 (C), 160.6 (C=O), 178.4 (C=O), 190.2 (C=O) ppm. EI-MS: 333 (M$^+$, 15), 302 (82), 31(100). Anal. Calcd for $C_{20}H_{15}NO_4$ (333.34): C 72.06, H 4.54, N 4.20; Found: C 72.24, H 4.76, N 4.38.

Methyl-4-(4-methoxybenzoyl)-7-methyl-5-oxo-5H-1-benzazepine-3-dicarboxylate (5d):

Yellow powder, mp 172-174˚C, Yield: 0.67 g (92%). IR (KBr) (ν_{max}/cm^{-1}): 1738, 1725, 1696, 1587, 1484, 1293 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): 2.35 (3 H, s, Me), 3.75 (3 H, s, MeO), 3.87 (3 H, s, MeO), 6.23 (1 H, s, CH), 7.35 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.46 (1 H, t, ^3J = 7.7 Hz, CH), 7.68 (1 H, d, ^3J = 7.7 Hz, CH), 7.87 (1 H, s, CH), 8.06 (2 H, d, ^3J = 7.6 Hz, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): 21.4 (Me), 51.2 (MeO), 55.6 (MeO), 114.2 (2 CH), 123.6 (C), 126.3 (CH), 128.2 (C), 128.6 (C), 129.2 (C), 133.2 (2 CH), 134.3 (CH), 138.4 (C), 139.3 (CH), 145.4 (CH), 150.2 (C), 159.6 (C), 161.2 (C=O), 179.4 (C=O), 191.6 (C=O) ppm. EI-MS: 363 (M^+, 10), 332 (78), 31(100). Anal. Calcd for $C_{21}H_{17}NO_5$ (363.36): C 69.41, H 4.72, N 3.85; Found: C 69.63, H 4.93, N 3.98.

Dimethyl-4-(4-methoxybenzoyl)-7-methyl-5-oxo-5H-1-benzazepine-2,3-dicarboxylate (5e):

Yellow powder, mp 189-191˚C, Yield: 0.79 g (95%). IR (KBr) (ν_{max}/cm^{-1}): 1745, 1742, 1728, 1697, 1586, 1478, 1267 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): 2.25 (3 H, s, Me), 3.76 (3 H, s, MeO), 3.85 (3 H, s, MeO), 3.89 (3 H, s, MeO), 7.32 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.45 (1 H, t, ^3J = 7.7 Hz, CH), 7.64 (1 H, d, ^3J = 7.7 Hz, CH), 7.96 (1 H, s, CH), 8.16 (2 H, d, ^3J = 7.6 Hz, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): 21.4 (Me), 51.6 (MeO), 52.4 (MeO), 55.8 (MeO), 114.3 (2 CH), 122.5 (C), 126.3 (CH), 128.2 (C), 128.9 (C), 130.4 (C), 133.2 (2 CH), 134.3 (CH), 138.2 (C), 139.2 (CH), 148.2 (C), 155.6 (C), 159.7 (C), 160.8 (C=O), 161.8 (C=O), 179.2 (C=O), 190.4 (C=O) ppm. EI-MS: 421 (M^+, 15), 390 (78), 31(100). Anal. Calcd for $C_{23}H_{19}NO_7$ (421.39): C 65.55, H 4.54, N 3.32; Found: C 65.73, H 4.73, N 3.58.

Dimethyl-4-(4-methylbenzoyl)-7-nitro-5-oxo-5H-1-benzazepine-2,3-dicarboxylate (5f):

Yellow powder, mp 201-203˚C, Yield: 0.76 g (87%). IR (KBr) (ν_{max}/cm^{-1}): 1740, 1738, 1725, 1687, 1563, 1484, 1275 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): 2.48 (3 H, s, Me), 3.75 (3 H, s, MeO), 3.83 (3 H, s, MeO), 7.56 (1 H, d, ^3J = 7.8 Hz, CH), 7.78 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.93 (2 H, d, ^3J = 7.6 Hz, 2 CH), 8.23 (1 H, d, ^3J = 7.8 Hz, CH), 8.84 (1 H, s, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): 22.3 (Me), 51.4 (MeO), 52.6 (MeO), 122.3 (C), 125.2 (CH), 126.4 (CH), 127.6 (C), 128.3 (C), 129.6 (2 CH), 130.8 (2 CH), 131.4 (CH), 136.2 (C), 145.4 (C), 148.5 (C), 155.7 (C), 158.3 (C), 161.3 (C=O), 162.6 (C=O), 179.5 (C=O), 191.3 (C=O) ppm. EI-MS: 436 (M^+, 15), 405 (64), 31(100). Anal. Calcd for $C_{22}H_{16}N_2O_8$ (436.37): C 60.55, H 3.70, N 6.42; Found: C 60.73, H 3.86, N 6.68.

References

1. Domling, A. *Chem Rev* **2006**, *106*, 17.
2. Tietze, L. F.; Rackelmann, N. N. *Pure. Appl. Chem.* **2004**, *11*, 1967.
3. Domling, A.; Ugi, I. *Angew. Chem. Int. Ed.* **2000**, *39*, 3168.
4. Kolb, J.; Beck, B.; Almstetter, M.; Heck, S.; Herdtweck, E.; Domling, A. *Mol. Divers.* **2003**, *6*, 297.
5. Domling, A.; Ugi, I.; Werner, B. *Molecules* **2003**, *8*, 53..
6. Bon, R. S.; Vliet, B. V.; Sprenkels, N. E.; Schmitz, R. F.; Kanter, F. J. J.; Stevens, C. V.; Swart, M.; Bickelhaupt, F. M.; Groen, M. B.; Orru, R. V. *J. Org. Chem.* **2005**, *70*, 3542.
7. Banfi, L.; Basso, A.; Guanti, G.; Kielland, N.; Repeto, C.; Riva, R. Ugi *J. Org. Chem.* **2007**, *72*, 2151..
8. Galliford, C. V.; Scheidt, K. A. Catalytic Multicomponent Reactions for the Synthesis of N-Aryl Trisubstituted Pyrroles. *J. Org. Chem.* **2007**, *72*, 1811. DOI:10.1021/jo0624086
9. Erdmenger, T.; Guerrero-Sanchez, C.; Vitz, J.; Hoogenboom, R.; Schubert, U. S. *Chem. Soc. Rev.* **2010**, **39**, 3317–3333.
10. Kondo, K.; Kan, K.; Tanada, Y.; Bando, M.; Shinohara, T.; Kurimura, M.; Ogawa, H.; Nakamura, S.; Hirano, T.; Yamamura, Y.; Kido, M.; Mori, T.; Tominaga, M. *J. Med.Chem.* **2002**, *45*, 3805.
11. Schachtele, C.; Kubbutat, M. H.; Baumann, K.; Kunick, C. *J. Med. Chem.* **2010**, *53*, 2433.
12. Bower, J. F.; Szeto, P.; Gallagher, T. *Org. Biomol. Chem.* **2007**, *5*, 143−150.
13. Worden, S. M.; Mapitse, R.; Hayes, C. J. *Tetrahedron Lett*. **2002**, *43*, 6011−6014.
14. Couty, S.; Liegault, B.; Meyer, C.; Cossy, J. *Tetrahedron* **2006**, *62*, 3882−3895.
15. Plieninger, H.; Wild, D. *Chem. Ber.* **1966**, *99*, 3070–3075.
16. Sakan, T.; Matsubara, S.; Takagi, H.; Tokunaga, Y.; Miwa, T. *Tetrahedron Lett.* **1968**, 4925–4928.
17. Schroeter, G.; Gluschke, A.; Geotzky, S.; Huang, J.; Irmisch, G.; Laves, E.; Schrader, O.; Stier, G. *Ber. Dtsch. Chem. Ges.* **1930**, *63*, 1308–1329.

18. Briggs, L. H.; De Ath, G. C. *J. Chem. Soc.* **1937**, 456–457.
19. Cromarty, A.; Proctor, G. R. *J. Chem. Soc., Chem. Commun.* **1968**, 842–843.
20. Sato, Y.; Kojima, H.; Shirai, H. *J. Org. Chem.* **1976**, *41*, 195–200.
21. Quadir, M.; Priestley, R. E.; Rising, T. W. D. F.; Gelbrich, T.; Coles, S. J.; Hursthouse, M. B.; Sheldrake, P. W.; Whittall, N.; Hii, K. K. *Tetrahedron Lett.* **2003**, *44*, 3675–3678.
22. Dyker, G.; Markwitz, H. *Synthesis* **1998**, 1750–1754.
23. Martinez-Estibalez, U.; Sotomayor, N.; Lete, E. *Tetrahedron Lett.* **2007**, *48*, 2919–2922.
24. Kotha, S.; Lahiri, K. *Eur. J. Org. Chem.* **2007**, 1221–1236.
25. Jenny-Lee, P.; Pathak, R.; De Koning, C. B.; Van Otterlo, W. A. L. *Eur. J. Org. Chem.* **2007**, 4953–4961.
26. Kasparek, S. *Adv. Heterocycl. Chem*. **1974**, *17*, 45.
27. Gschwend, H. U.S. Patent 3,947,585, Mar 30, 1976.
28. Eugene, J. T.; Earl, R.; John, F. B.; Armin, W.; Ian Fryer, R. *J. Org. Chem.* **1982**, *47*, 2441–2447.
29. Clark, J. H.; Macquarrie, D. J. Handbook of Green Chemistry and Technology; Blackwell: Oxford, **2002**.
30. a) Khalilzadeh, M. A.; Hosseini, A.; Pilevar, A. *Eur. J. Org. Chem.* **2011**, 8, 1587. b) Salmanpour, S.; Khalilzadeh, M. A.; Hosseini, A. *Comb Chem High Throughput Screen* **2013**, *16*, 339 c) Khalilzadeh, M. A.; Keipour, H.; Hosseini, A.; Zareyee, D. *New J Chem* **2014**, *38*, 42. d) Hallajian, S.; Khalilzadeh, M. A.; Tajbakhsh, M.; Alipour, E.; Safaei, Z. Nano Clinoptilolite: Highly Efficient Catalyst for the Synthesis of Chromene Derivatives Under Solvent-Free Conditions. *Comb Chem High Throughput Screen* 2015, 18(5), 486.
31. Xie, W. L.; Huang, X. M. Synthesis of Biodiesel from Soybean Oil using Heterogeneous KF/ZnO Catalyst. *Catal Lett* **2006**, *107*, 53-59.
32. Gao, L. J.; Teng, G. Y.; Lv, J. H.; Xiao, G. M. Biodiesel Synthesis Catalyzed by the KF/Ca−Mg−Al Hydrotalcite Base Catalyst. *Energy Fuels* 201**0**, *24*, 646-651.
33. Hu, S.; Guan, Y.; Wang, Y.; Han, H. *Appl Energy* **2011**, *88*, 2685.
34. Ando, T.; Yamawaki, J. *Chem Lett* **1979**, *1*, 45
35. Zhu, J. H.; Chun, Y.; Qin, Y.; Xu, Q. H. *Microporous Mesoporous Mater* **1998**, *24*, 19-28.
36. Asseid, F. M.; Duke, C.V.A.; Miller, J.M.A. *Can J Chem* **1990**, *68*, 1420.
37. Zahouily, M.; Bahlaouane, B.; Aadil, M.; Rayadh, A.; Sebti, S. *Org Process Res Dev* **2004**, *8*, 275-278.
38. Gao, L.; Teng, G.; Xiao, G.; Wei, R. *Biomass Bioenergy* **2010**, *34*, 1283-1288.
39. Smith, J.V. *Chem Rev* **1998,** *88*, 149-182.
40. Ames, L.L. *Am Mineral* **1960**, *45*, 689
41. Hossaini, Z. S.; Zareyee, D.; Sheikholeslami-Farahani, F.; Vaseghi, S.; Zamani, A. *Heteroatom Chemistry*, **2017**, *28*, e21362.
42. Rostami-charati, F.; Hossaini, Z. S.; Zareyee, D.; Afrashteh,S.; Hosseinzadeh, M. *Journal of Heterocyclic Chemistry,* **2017**, *54*, 1937-1942.
43. Rostami-Charati, F.; Hossaini, Z. S.; Rostamian, R.; Zamani, A.; Abdoli, M. *Chemistry of Heterocyclic Compounds*, **2017**, *53*, 480-483.
44. Rezayati, S.; Sheikholeslami-Farahani, F.; Hossaini, Z. S.; Hajinasiri, R.; Afshari Sharif Abad, S *Combinatorial Chemistry and High Throughput Screening*, **2016**, *9*, 720-727. 45. Rostami-Charati, F.; Hossaini, Z. S.; Sheikholeslami-Farahani, F.; Azizi, Z.; Siadati, S. A. *Combinatorial Chemistry and High Troughput Screening*, **2015**, *18*, 872-880.
46. Sajjadi-Ghotbabadi, H.; Javanshir, Sh.; Rostami-Charati, F.; *Catal Lett* **2016**, *146*, 338–344.
47. a) M. A. Khalilzadeh, A. Hosseini, A. Pilevar, *Eur. J. Org. Chem.* **2011**, *8*, 1587 b) M. A. Khalilzadeh, H. Keipour, A. Hosseini, D. Zareyee, *New J Chem* **2014**, *38*, 42.