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Superelectrophilic nazarov cyclizations with *N*-heterocycles

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ABSTRACT

A series of Nazarov cyclizations has been studied involving *N*-heterocyclic-substituted 1-arylprop-2-en-1-one derivatives (aza-chalcones). Superacid catalyzed reactions of these derivatives provide good yields of heterocyclic-substituted 1-indanones. A mechanism is proposed involving diprotonated, super-electrophilic intermediates.

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1. Introduction

Olah and coworkers first recognized the concept of super-electrophilic activation [1]. It was proposed that monocationic electrophiles, such as nitronium (NO_2^+) and acetyl (CH_3CO^+) cations, could undergo further protonation in sufficiently acidic media and the resulting species should exhibit enhanced electrophilic reactivities [2]. This concept has been confirmed by numerous experimental studies with these multiply charged intermediates, or superelectrophiles [2]. As a result of the high reactivities of super-electrophiles, they have been used in many novel synthetic methods [2,3]. In previous studies, we and others have demonstrated that stable cationic charges – from protonated *N*-heterocyclic rings – have a profound activating effect in electrophilic reactions [4]. These *N*-heterocycle-based systems often have reactivities similar to Olah's superelectrophiles.

A number of recent studies have shown that strongly acidic media may be used to promote the Nazarov cyclization of chalcone derivatives to provide functionalized indanones [5]. For example, Koltunov and coworkers utilized zeolite and solid acid catalysts to convert chalcone to 3-phenyl-1-indanone (Scheme 1) [6]. A diprotonated superelectrophile was proposed as the possible intermediate leading to cyclization. Others have accomplished this transformation using forcing conditions and excess acids such as

AlCl_3 [7]. Several other reports describe chalcone cyclizations involving primarily electron rich aryl rings [8], such as Lawrence's microwave-assisted synthesis of potential tubulin-binding agents. [8a] In the following manuscript, we describe the use of protonated *N*-heterocyclic rings to facilitate the Nazarov reaction and provide functionalized 1-indanone products in good yields.

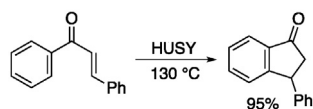
2. Results and discussion

In previous studies from our group, protonated *N*-heterocyclic rings have been shown to enhance the reactivities of carboxonium ion and carbenium ion electrophiles.[4b,c,d] Likewise, the presence of monocationic or dicationic protonated *N*-heterocyclic rings activated Diels-Alder dienes for cycloaddition reactions with ethylene [9]. In order to probe the effects of *N*-heterocyclic rings on the Nazarov reaction, a series of 1-arylprop-2-en-1-one derivatives (1) were prepared [10]. Derivatives of compound 1 were typically prepared using condensation chemistry, for example acetophenone reacts with 2-pyridinecarboxaldehyde to give 1-phenyl-3-(pyridin-2-yl)prop-2-en-1-one (1a, see Experimental Section). Upon treatment with excess superacid, $\text{CF}_3\text{SO}_3\text{H}$, substrate 1a provides the functionalized indanone (2) in quantitative yield (Table 1). The same substrate does not cyclize in excess H_2SO_4 or weaker acids at 80 °C. Likewise, the pyridyl isomers 1 b,c give the respective products 3 and 4 in good yields. Halogenated derivatives 5–6 and alkylated derivatives 7–8 are prepared in fair to good yields. Cyclization involving a 1-naphthyl ring provides product 9 in 92% yield, with cyclization occurring preferentially at the 2-position.

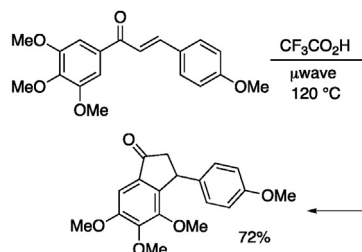
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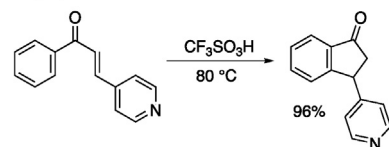
Koltunov, et al. 2005



Lawrence, et al. 2006

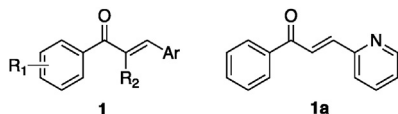


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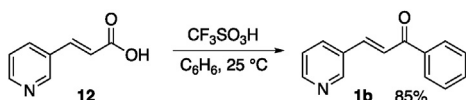


Scheme 1.

Other *N*-heterocyclic groups promote the cyclization, including the pyrazine and benzothiazole derivatives to give 10–11, respectively. Heterocycle-substituted 1-indanones have been useful as pharmaceutical intermediates and the above chemistry provides improved access to these structures. For example, the synthesis of compound 4 was described recently in a patent and an optimized procedure required no less than five synthetic steps (yields not given) [11]. Our methodology provides this compound in just two synthetic steps.



Some time ago, we reported the condensation reactions of acrylic acid derivatives with benzene in superacid [12]. It was observed that electron-deficient substrates, including those with *N*-heterocyclic derivatives, provide 1-phenylprop-2-en-1-ones.

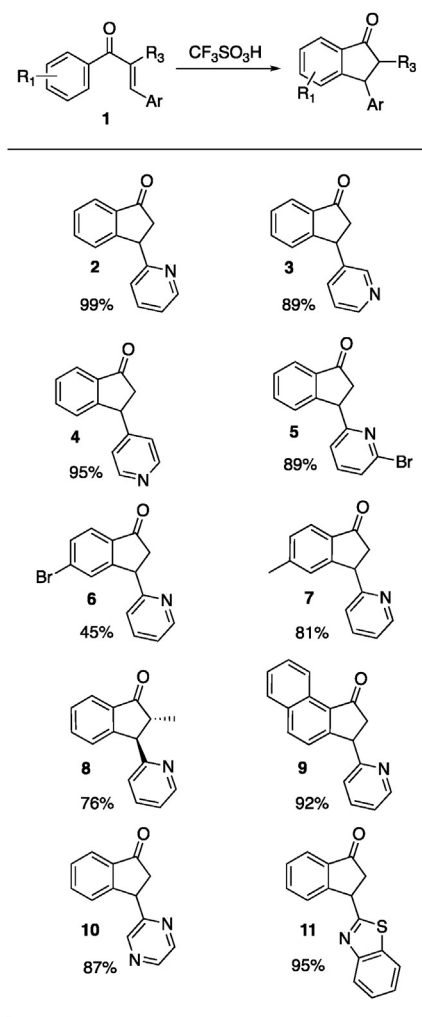


For example, 3-(pyridin-3-yl)acrylic acid (**12**) provides the azachalcone (**1b**) in 85% yield from a reaction with $\text{CF}_3\text{SO}_3\text{H}$ and C_6H_6 at 25 °C (eq 1).¹² We reasoned that the cyclization reaction conditions (80 °C) should provide substituted-indanones directly from the electron deficient acrylic acid derivatives. Thus, reaction of the imidazole derivative **13** provides the cyclization product **14** in a single synthetic step in 64% yield (Table 2). Likewise, the pyridine derivatives (**12**, **15**–**16**) give good yields of the respective indanones (**2**, **3**, and **4**). The previous study from our group also showed that pentafluorocinnamic acid (**17**) reacts with benzene in triflic acid to provide the fluorinated chalcone.¹² Similar to the heterocyclic derivatives, pentafluorocinnamic acid (**17**) provides the cyclization product (**18**) in high yield.

In the conversions to indanones, the cyclizations of the 1-

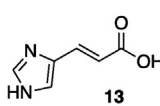
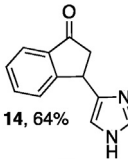
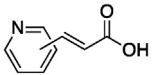
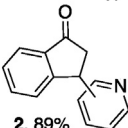
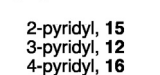
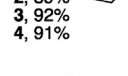
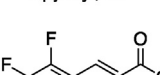
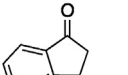
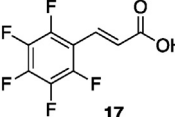
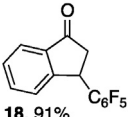
Table 1

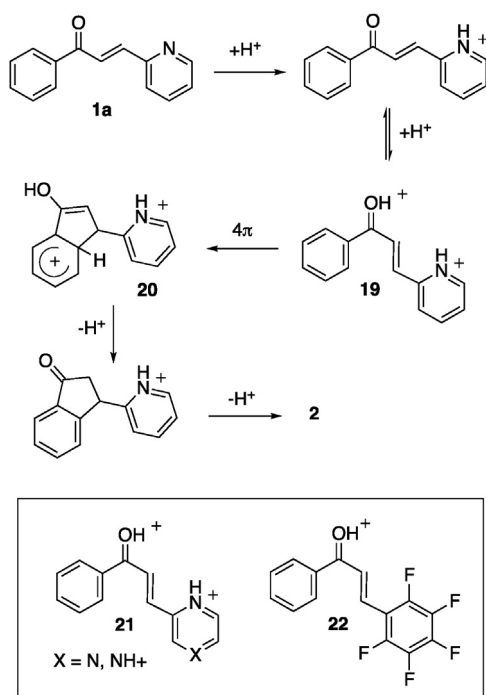
Products and isolated yields for the reactions of **1** and $\text{CF}_3\text{SO}_3\text{H}$ at 80 °C.



arylprop-2-en-1-one (**1**) derivatives likely involve diprotonated species or electron-deficient carboxonium ions. For example, compound **1a** is first protonated at the *N*-heterocycle and then at the carbonyl group to provide the dication **19** (Scheme 2). It is suggested that this superelectrophilic species triggers the 4 π electrocyclization - which leads to intermediate **20**. Deprotonation steps then provide the final product, indanone **2**. Previous work by Ohwada and coworkers has suggested that charge delocalization is an important driving force in the Nazarov cyclization with dicationic or superelectrophilic species [13]. The cyclization of dication **19** effectively separates the two cationic charges, wherein dication **20** has two monocation π -systems that are no longer in conjugation. In the case of the pyrazine substrate, protonation will likely give an equilibrium containing both the di- and triprotonated species (**21**). In the conversions involving pentafluorocinnamic acid (**17**), Friedel-Crafts chemistry gives the corresponding chalcone and the protonated derivative **22** is assumed to be the reactive intermediate leading to the Nazarov cyclization product. No other reasonably good base-site exists, so diprotonation is not likely with the pentafluorochalcone. With intermediate **22**, charge-charge repulsive effects are not a likely a driving force for the cyclization. Rather, cyclization is driven by the strongly electrophilic β -carbon of this species. A similar inductive effect may also be an important

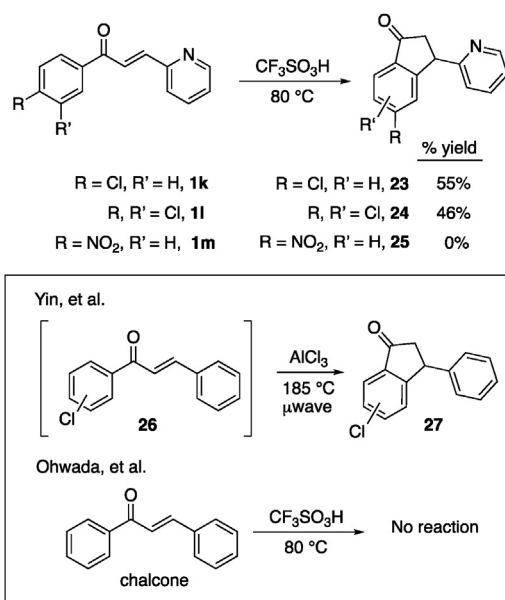
Table 2Products and yields from the reactions of acrylic acid derivatives with CF₃SO₃H and C₆H₆ at 80 °C.

starting material	product
 13	 14 , 64%
 2-pyridyl, 15	 2 , 89%
 3-pyridyl, 12	 3 , 92%
 4-pyridyl, 16	 4 , 91%
 17	 18 , 91%

**Scheme 2.**

contributing factor in the cyclizations of the aza-chalcones.

One of the hallmarks of superelectrophiles is their ability to react with weak nucleophiles and deactivated aromatic rings [2]. In order to examine this aspect of the chemistry, aza-chalcones (**1k-m**) were prepared with increasingly deactivated aryl groups (Scheme 3). Upon reaction in superacid, reasonable yields were obtained from both the chlorophenyl and 3,4-dichlorophenyl derivatives. Thus, substrate **1k** gives a 55% yield of the 5-chloro-1-indanone (**23**). While the dichlorophenyl derivative (**1l**) does undergo cyclization in fair yield, the two regioisomers (**24**) are formed. The 4-nitrophenyl derivative (**1m**) did not undergo

**Scheme 3.**

cyclization, even with elevated temperatures and prolonged reaction times. Substrate **1m** could be isolated quantitatively following the unsuccessful efforts. These results suggest a modest or slight increase in reactivity for the aza-chalcones over the chalcones. For example, Yin and coworkers studied the AlCl₃-promoted reactions of substituted benzenes with cinnamoyl chloride using microwave irradiation. [7a] In the case of chlorobenzene, the chloro-substituted chalcone (**26**) is formed as a mixture of regioisomers and the corresponding isomeric 1-indanones (**27**) are obtained in a crude yield of 88%. Purification of 5-chloro-3-phenyl-1-indanone (the phenyl analog of **23**) provides a 45% isolated yield of this indanone product. Considering the microwave induced transformation of **26** is done at 185 °C, while the aza-chalcone chemistry is done at a lower temperature (80 °C), this is consistent with a

somewhat higher level of reactivity for the aza-chalcone (**1k**). A reasonably good yield of the dichloroindanone product (**24**) is also obtained, despite the deactivating effects of the 3,4-dichlorophenyl group in the aza-chalcone **1l**. Nevertheless, attempts to obtain the cyclization product were unsuccessful with the 4-nitrophenyl derivative **1m**. In excess superacid, this system is likely protonated at the three good base sites – the pyridyl, carbonyl, and nitro groups. As such, the protonated 4-nitrophenyl group is expected to be highly deactivated, consequently even forcing conditions do not trigger the Nazarov cyclization. It has also been previously reported that chalcone does not undergo the Nazarov cyclization in excess $\text{CF}_3\text{SO}_3\text{H}$ at 80 °C,¹³ the same conditions used to provide good yields from the aza-chalcones (Table 1). This observation suggests an increase in reactivities for the aza-chalcone and a strong activating effect from the protonated *N*-heterocyclic groups.

3. Conclusion

In summary, we have found that aza-chalcones undergo efficient Nazarov cyclizations in the presence of superacidic $\text{CF}_3\text{SO}_3\text{H}$. The chemistry represents a simple method of preparing 1-indanones having *N*-heterocyclic substituents. A mechanism is proposed involving dicationic intermediates. Empirical evidence suggests that the protonated *N*-heterocyclic substituents activate the system towards cyclization - leading to good yields of products at modest temperatures.

4. Experimental

All reactions were performed using oven – dried glassware under an argon atmosphere. Trifluoromethanesulfonic acid (triflic acid) was freshly distilled prior to use. A previous report describes a procedure for the quantitative recycling of trifluoromethanesulfonic acid [14]. All commercially available compounds and solvents were used as received. ^1H and ^{13}C NMR were done using either 300 MHz or 500 MHz spectrometer. Reaction done with benzene at 80 °C were done in a high-pressure, glass reaction tube having a Teflon screw cap (obtained from a commercial glassware supplier). Low resolution mass spectra were obtained from a gas chromatography instrument equipped with a mass-selective detector. Ionization was accomplished with electron impact ionization. High resolution mass spectroscopy was done by a commercial laboratory (electron impact ionization or electrospray; sector instrument analyzer type). Aza-chalcones **1a** [15], **1b** [16], **1c** [16], **1f** [17], **1h** [18], **1k** [19], **1l** [20], and **1m** [19], are known compounds. Indanone **23** is a known compound. [7a] Compounds **12**, **13**, **15**–**17**, were purchased from a commercial supplier.

Procedure A: Synthesis of aza-chalcones, 1. A solution is prepared from 10 mL H_2O , 5 mL ethanol, pyridine (0.16 mL, 0.154 g, 2 mmol), and NaOH (0.2 g, 5 mmol). To this solution is added the aryl ketone (1 mmol) and heterocyclic aldehyde (1 mmol) and the solution is stirred at 25 °C for 12 h. A precipitate generally forms and this is filtered off, rinsed with water, and dried. The crude aza-chalcone is then further purified by silica gel column chromatography [14].

Procedure B: Synthesis of 1-indanones. In a vessel flushed with inert gas, the aza-chalcone (1 mmol) is added to 2 mL of $\text{CF}_3\text{SO}_3\text{H}$ (22 mmol). The vessel is sealed, heated to 80 °C, and the solution stirred for 18 h. Following the reaction period, the solution is cooled and then poured over ice. Chloroform (15 mL) is added to the mixture and the aqueous solution is made basic by the addition of saturated sodium bicarbonate. The organic extract is washed with water, then brine, and dried with anhydrous sodium sulfate. Filtration and removal of the solvent gives the crude indanone product - which is further purified by column chromatography

(hexanes:ethyl acetate).

Procedure C: Synthesis of 1-indanones. NOTE: this procedure is done near the boiling point of benzene, so adequate precautions should be made to handle the potential buildup of pressure in a closed reaction vessel. In a vessel flushed with inert gas, benzene (0.5 mL) and $\text{CF}_3\text{SO}_3\text{H}$ (2 mL, 22 mmol) are combined, into which is added the acrylic acid derivative (1 mmol). The vessel is sealed, heated to 80 °C, and the solution stirred for 18 h. Following the reaction period, the solution is cooled and then poured over ice. Chloroform (15 mL) is added to the mixture and the aqueous solution is made basic by the addition of saturated sodium bicarbonate. The organic extract is washed with water, then brine, and dried with anhydrous sodium sulfate. Filtration and removal of the solvent gives the crude indanone product - which is further purified by column chromatography (hexanes:ethyl acetate).

4.1. (*E*)-3-(6-Bromopyridin-2-yl)-1-phenylprop-2-en-1-one (**1d**)

Using General Procedure A, acetophenone (120 mg, 1 mmol) and 6-bromopicolinaldehyde (186 mg, 1 mmol) provides aza-chalcone **1d** (259 mg, 0.90 mmol, 90%) as yellow solid, R_f = 0.6 (hexane: ethyl acetate, 1:1). ^1H NMR (500 MHz CDCl_3) δ = 8.09 (1H, s), 8.05 (2H, t, J = 7 Hz), 7.65 (1H, s), 7.62–7.55 (2H, m), 7.49 (2H, t, J = 7.5 Hz), 7.44 (1H, d, J = 7.5 Hz), 7.39 (1H, d, J = 7.5 Hz). ^{13}C NMR (125 MHz, CDCl_3) δ = 190.0, 154.4, 142.6, 140.8, 139.1, 137.6, 133.2, 128.8, 128.75, 128.72, 126.9, 124.0. Mass spectrum (low resolution, EI): 287 [M+], 260, 210, 180, 105, 77, 51. HRMS calculated for $\text{C}_{14}\text{H}_{11}\text{BrNO}$, 288.0024 (MH⁺). Found 288.0012.

4.2. (*E*)-1-(4-Bromophenyl)-3-(pyridin-2-yl)prop-2-en-1-one (**1e**)

Using General Procedure A, 4-bromoacetophenone (199 mg, 1 mmol) and 2-pyridinecarboxaldehyde (107 mg, 1 mmol) provides aza-chalcone (**1e**) (259 mg, 0.90 mmol, 90%) as yellow solid, R_f = 0.7 (hexane: ethyl acetate, 1:1). ^1H NMR (500 MHz CDCl_3) δ = 8.62 (1H, d, J = 3 Hz), 8.01 (1H, d, J = 15 Hz), 7.89 (2H, d, J = 8 Hz), 7.73–7.65 (2H, m), 7.56 (2H, d, 8 Hz), 7.40 (1H, d, J = 7.5 Hz), 7.23 (1H, t, J = 5 Hz). ^{13}C NMR (125 MHz, CDCl_3) δ = 189.1, 152.9, 150.2, 143.2, 136.9, 136.5, 131.9, 130.2, 128.2, 125.5, 124.8, 124.5. HRMS calculated for $\text{C}_{14}\text{H}_{11}\text{BrNO}$, 288.0024 (MH⁺). Found 288.0014.

4.3. (*E*)-2-Methyl-1-phenyl-3-(pyridin-2-yl)prop-2-en-1-one (**1g**)

Propiophenone (134.2 mg, 1 mmol) is dissolved in 10 mL of ethyl ether and sodium hydride (36 mg, 1.5 mmol) is added to the mixture at 0 °C. After stirring for 30 min, 2-pyridinecarboxaldehyde (109 mg, 1 mmol) is added to the mixture. The solution is allowed to warm to room temperature, stirred for another 12 h and then 5 mL of 1 M HCl is added to the mixture. The solution is stirred for 5 h and then poured over 10 g of ice, neutralized by saturated NaHCO_3 , and the organic product is extracted into diethyl ether. The organic extract is washed with water and then (2x) with brine solution, followed by drying with sodium sulfate, filtration, and concentrating under vacuum. The crude product mixture is purified by flask chromatography (hexane: ethyl acetate) to provide aza-chalcone (**1g**). ^1H NMR (500 MHz CDCl_3) δ = 8.70 (1H, s), 7.79 (2H, t, J = 5 Hz), 7.70 (1H, dd, J = 1.5, J = 7.5 Hz), 7.53 (1H, dd, J = 2, J = 6 Hz), 7.46 (2H, d, J = 4.5 Hz), 7.36 (1H, d, J = 5.5 Hz), 7.21 (1H, t, J = 1 Hz), 7.12 (1H, d, J = 0.5 Hz), 2.45 (3H, d, J = 1.5 Hz). ^{13}C NMR (125 MHz, CDCl_3) δ = 199.6, 155.1, 149.7, 140.3, 139.4, 137.9, 136.3, 131.9, 129.5, 128.3, 125.5, 122.6, 14.7. HRMS calculated for $\text{C}_{15}\text{H}_{14}\text{NO}$, 224.1075 (MH⁺). Found 224.1069.

4.4. (E)-1-(Naphthalen-1-yl)-3-(pyridin-2-yl)prop-2-en-1-one (**1h**)

Known compound, but unreported characterization data. [21] Using General Procedure A, compound **1h** was isolated. ^1H NMR (500 MHz CDCl_3) δ = 8.68 (1H, d, J = 4 Hz), 8.47 (1H, d, J = 8.5 Hz), 8.01 (1H, d, J = 8 Hz), 7.93–7.85 (3H, m), 7.73–7.70 (1H, m), 7.66–7.53 (4H, m), 7.47 (1H, d, J = 8 Hz), 7.29–7.27 (1H, m). ^{13}C NMR (125 MHz, CDCl_3) δ = 195.2, 153.2, 150.2, 143.9, 136.8, 136.5, 133.9, 132.1, 130.6, 130.3, 128.5, 127.9, 127.6, 126.5, 125.7, 124.9, 124.5, 124.4. Mass spectrum (low resolution, EI): 258 [M^+], 230, 181, 127, 104, 78, 51. HRMS calculated for $\text{C}_{18}\text{H}_{14}\text{NO}$, 260.1075 (MH^+). Found 260.1062.

4.5. (E)-1-Phenyl-3-(pyrazin-2-yl)prop-2-en-1-one (**1i**)

1-Phenylprop-2-yn-1-ol (159 mg, 1.2 mmol), 2-iodopyrazine (205 mg, 1 mmol), triethyl amine (0.2 mL), 1.5 mL THF are added in a 5 mL microwave vial. The mixture is then degassed by an argon gas stream. To this solution, CuI (19 mg, 0.1 mmol) and palladium bis triphenylphosphine dichloride (70 mg, 0.1 mmol) is added, the vial is sealed, and placed in microwave reactor. The reaction is run for 15 min at 150 °C, after which the product mixture is diluted with 10 mL of diethyl ether and washed with brine (10 mL). The aqueous phase is back extracted with diethyl ether (2 \times 5 mL), the organic extracts are combined, and dried over anhydrous MgSO_4 . Removal of the solvent is followed by purification of the product with flash column chromatography (ethyl acetate:hexanes, 1:1) to provide aza-chalcone **1i** (99 mg, 0.47 mmol, 47%). ^1H NMR (300 MHz CDCl_3) δ = 8.68 (1H, d, J = 1.2 Hz), 8.59 (1H, t, J = 2.1 Hz), 8.52 (1H, d, J = 2.4 Hz), 8.15 (1H, d, J = 15.3 Hz), 8.03 (2H, t, J = 6.9 Hz), 7.75 (1H, d, J = 15.3 Hz), 7.59–7.53 (1H, m), 7.49–7.44 (2H, m). ^{13}C NMR (75 MHz, CDCl_3) δ = 189.6, 148.8, 145.8, 145.2, 144.8, 138.7, 137.4, 133.3, 128.72, 128.70, 127.5. HRMS calculated for $\text{C}_{13}\text{H}_{11}\text{N}_2\text{O}$, 211.0871 (MH^+). Found 211.0870.

4.6. (E)-3-(Benzo[d]thiazol-2-yl)-1-phenylprop-2-en-1-one (**1j**)

Using General Procedure A, acetophenone (120 mg, 1 mmol) and 2-pyridinecarboxyaldehyde (163 mg, 1 mmol) in 25 mL of water provide aza-chalcone **1j** (164.5 mg, 0.62 mmol, 62%) as yellow solid; R_f = 0.56 (hexane: ethyl acetate, 3:1). ^1H NMR (500 MHz CDCl_3) δ = 8.07 (1H, d, J = 8 Hz), 8.03 (2H, d, J = 8 Hz), 7.89 (2H, d, J = 7.5 Hz), 7.86 (1H, d, J = 8.5 Hz), 7.58 (1H, t, J = 7.5 Hz), 7.48 (3H, t, J = 7.5 Hz), 7.40 (1H, t, J = 7.5 Hz). ^{13}C NMR (125 MHz, CDCl_3) δ = 189.1, 163.8, 154.0, 137.2, 135.9, 135.4, 133.4, 128.8, 128.7, 128.6, 126.9, 126.5, 124.0, 121.8. Mass spectrum (low resolution, EI): 265 [M^+], 236, 160, 116, 105, 77, 51. HRMS calculated for $\text{C}_{16}\text{H}_{11}\text{NOS}$, 266.0640 (MH^+). Found 266.0636.

4.7. 3-(2-Pyridyl)-1-indanone (**2**)

Using General Method B, aza-chalcone **1a** (209.1 mg, 1 mmol) provides indanone **2** (198.6 mg, 0.95 mmol, 95%). Alternatively, General Method C also provides indanone **2**. Thus, arylclic acid **15** (149.1 mg, 1 mmol) provides indanone **2** (186.1 mg, 0.89 mmol, 89%) as yellow solid, R_f = 0.5 (hexane: ethyl acetate, 1: 1). ^1H NMR (300 MHz CDCl_3) δ = 8.53 (1H, dd, J = 1.8, J = 5.7 Hz), 7.80 (1H, d, J = 7.5 Hz), 7.64 (1H, td, J = 1.8, J = 9.3 Hz), 7.55 (1H, td, J = 1.2, J = 7.5 Hz), 7.40 (1H, t, J = 7.5 Hz), 7.28 (1H, dd, J = 0.9, J = 7.8 Hz), 7.18–7.14 (2H, m), 4.77–4.73 (1H, m), 3.23–3.14 (1H, m), 3.03–2.95 (1H, m). ^{13}C NMR (75 MHz, CDCl_3) δ = 205.7, 162.1, 156.6, 149.9, 136.9, 136.7, 134.9, 128.0, 126.5, 123.7, 122.1, 122.0, 46.5, 44.5. Mass spectrum (low resolution, EI): 209 [M^+], 180, 152, 131, 77, 51. HRMS

calculated for $\text{C}_{14}\text{H}_{12}\text{NO}$, 210.0919 (MH^+). Found 210.0910.

4.8. 3-(3-Pyridinyl)-1-indanone (**3**)

Using General Method B, aza-chalcone **1b** (209.1 mg, 1 mmol) provides indanone **3** (194.3 mg, 0.93 mmol, 93%). Alternatively, General Method C also provides indanone **3**. Thus, arylclic acid **12** (149.1 mg, 1 mmol) provides indanone **3** (192.3 mg, 0.92 mmol, 92%) as a yellow oil. R_f = 0.3 (hexane: ethyl acetate, 1: 1). ^1H NMR (300 MHz CDCl_3) δ = 8.51 (2H, s), 7.79 (1H, d, J = 7.5 Hz), 7.57 (1H, td, J = 0.9, J = 7.5 Hz), 7.43 (1H, t, J = 7.5 Hz), 7.32 (1H, t, J = 5.7 Hz), 7.27–7.19 (3H, m), 4.62–4.59 (1H, m), 3.29–3.22 (1H, m), 2.67–2.59 (1H, m). ^{13}C NMR (75 MHz, CDCl_3) δ = 204.8, 156.6, 149.3, 148.6, 139.2, 136.8, 135.3, 134.7, 128.3, 126.7, 129.6, 46.4, 41.8. Mass spectrum (low resolution, EI): 209 [M^+], 180, 152, 131, 103, 77, 51. HRMS calculated for $\text{C}_{14}\text{H}_{12}\text{NO}$, 210.0919 (MH^+). Found 210.0908.

4.9. 3-(4-Pyridyl)-1-indanone (**4**)

Using General Method B, aza-chalcone **1a** (209.1 mg, 1 mmol) provides indanone **4** (194.3 mg, 0.93 mmol, 93%). Alternatively, General Method C also provides indanone **4**. Thus, arylclic acid **16** (149.1 mg, 1 mmol) provides indanone **4** (192.3 mg, 0.92 mmol, 92%) as yellow oil. R_f = 0.6 (hexane: ethyl acetate, 1: 1). ^1H NMR (300 MHz CDCl_3) δ = 8.53 (2H, d, J = 5.7 Hz), 7.82 (1H, d, J = 7.5 Hz), 7.59 (1H, td, J = 0.9, J = 7.5 Hz), 7.45 (1H, t, J = 6 Hz), 7.26 (2H, d, J = 8.1 Hz), 7.05 (2H, d, J = 6 Hz), 4.58–4.53 (1H, m), 3.27–3.18 (1H, m), 2.68–2.60 (1H, m). ^{13}C NMR (75 MHz, CDCl_3) δ = 204.5, 155.9, 152.4, 150.3, 136.8, 135.3, 128.4, 126.7, 123.7, 122.8, 45.9, 43.7. Mass spectrum (low resolution, EI): 209 [M^+], 180, 131, 103, 77, 51. HRMS calculated for $\text{C}_{14}\text{H}_{12}\text{NO}$, 210.0919 (MH^+). Found 210.0918.

4.10. 3-(6-Bromo-2-pyridyl)-1-indanone (**5**)

Using General Method B, aza-chalcone **1d** (289.0 mg, 1 mmol) provides indanone **5** (257.2 mg, 0.89 mmol, 89%) as white solid. ^1H NMR (500 MHz CDCl_3) δ = 7.79 (1H, d, J = 7.5 Hz), 7.57 (1H, t, J = 7.2 Hz), 7.51–7.39 (2H, m), 7.34 (2H, t, J = 8.4 Hz), 7.03 (1H, J = 7.5 Hz), 4.77–4.73 (1H, m), 3.23–3.14 (1H, m), 2.98–2.90 (1H, m). ^{13}C NMR (125 MHz, CDCl_3) δ = 205.0, 163.8, 155.6, 142.0, 139.2, 136.7, 135.0, 128.3, 126.5, 123.8, 120.6, 46.1, 44.3. Mass spectrum (low resolution, EI): 287 [M^+], 260, 210, 180, 105, 77, 51. HRMS calculated for $\text{C}_{14}\text{H}_{11}\text{BrNO}$, 288.0024 (MH^+). Found 288.0021.

4.11. 5-Bromo-3-(2-pyridyl)-1-indanone (**6**)

Using General Method B, aza-chalcone **1e** (289.1 mg, 1 mmol) provides indanone (**6**) (130 mg, 0.45 mmol, 45%) as a light yellow solid, MP = 119–121 °C, R_f = 0.45 (hexane: ethyl acetate, 1:1). ^1H NMR (500 MHz CDCl_3) δ = 8.58 (1H, s), 7.72 (1H, s), 7.69 (1H, d, J = 8.5 Hz), 7.57 (1H, d, J = 8.5 Hz), 7.47 (1H, s), 7.28–7.21 (2H, m), 4.75 (1H, t, J = 3.5 Hz), 3.21–3.17 (1H, m), 3.07–3.03 (1H, m). ^{13}C NMR (125 MHz, CDCl_3) δ = 204.2, 161.2, 158.1, 150.1, 137.1, 135.6, 131.7, 130.2, 129.8, 124.9, 122.3, 122.3, 46.2, 44.4. Mass spectrum (low resolution, EI): 289 [M^+], 258, 155, 132, 104, 78, 51. HRMS calculated for $\text{C}_{14}\text{H}_{11}\text{BrNO}$, 288.0024 (MH^+). Found 288.0011.

4.12. 5-Methyl-3-(2-pyridyl)-1-indanone (**7**)

Using General Method B, aza-chalcone **1f** (223 mg, 1 mmol) provides indanone **7** as dark orange solid (180 mg, 0.81 mmol, 81%), MP: 102–104 °C, R_f = 0.38 (hexane: ethyl acetate, 1:2). ^1H NMR (500 MHz CDCl_3) δ = 8.55 (1H, d, J = 4.5 Hz), 7.70 (1H, d, J = 8 Hz), 7.67–7.63 (1H, m), 7.21 (1H, d, J = 7.5 Hz), 7.18–7.14 (2H, m), 7.08

(1H, s), 4.72–4.69 (1H, m), 3.19–3.13 (1H, m), 3.00–2.95 (1H, m), 2.37 (3H, s). ^{13}C NMR (125 MHz, CDCl_3) δ = 205.2, 162.3, 157.1, 149.9, 146.1, 136.9, 134.5, 129.3, 126.7, 123.5, 122.1, 122.0, 46.4, 44.7, 22.1. Mass spectrum (low resolution, EI): 223 [M⁺], 194, 115, 89, 78, 51. HRMS calculated for $\text{C}_{15}\text{H}_{14}\text{NO}$, 224.1075 (MH^+). Found 224.1065.

4.13. *Trans*-2-Methyl-3-(2-pyridyl)-1-indanone (**8**)

Using General Method B, aza-chalcone **1g** (224 mg, 1 mmol) provided indanone **8** (170.2 mg, 0.76 mmol, 76%) as an oil. R_f = 0.36 (hexane: ethyl acetate/1:1). ^1H NMR (500 MHz CDCl_3) δ = 8.59 (1H, dd, J = 2, J = 5.5 Hz), 7.82 (1H, d, J = 8 Hz), 7.72–7.68 (1H, m), 7.57 (1H, td, J = 1, J = 8.5 Hz), 7.42 (1H, t, J = 7.5 Hz), 7.23–7.21 (3H, m), 4.26 (1H, d, J = 5 Hz), 3.03–2.97 (1H, m), 1.41 (3H, d, J = 7.5 Hz). ^{13}C NMR (125 MHz, CDCl_3) δ = 207.7, 161.5, 154.9, 149.7, 136.9, 136.2, 134.9, 128.1, 126.2, 123.8, 122.8, 122.2, 55.6, 51.3, 14.3. Mass spectrum (low resolution, EI): 223 [M⁺], 208, 194, 180, 167, 115, 78, 51. HRMS calculated for $\text{C}_{15}\text{H}_{14}\text{NO}$, 224.1075 (MH^+). Found 224.1067.

4.14. 3-(Pyridin-2-yl)-2,3-dihydro-1H-cyclopenta[*a*]naphthalen-1-one (**9**)

Using General Method B, aza-chalcone **1h** (259 mg, 1 mmol) provides ketone **9** (238 mg, 0.92 mmol, 92%) as yellow solid, MP: 115–117 °C, R_f = 0.48 (hexane: ethyl acetate/1:2). ^1H NMR (500 MHz CDCl_3) δ = 9.21 (1H, d, J = 8.5 Hz), 8.52 (1H, d, J = 4.5 Hz), 7.94 (1H, d, J = 8.5 Hz), 7.82 (1H, d, J = 8 Hz), 7.65 (1H, t, J = 7 Hz), 7.61–7.59 (1H, m), 7.53 (1H, t, J = 8 Hz), 7.27 (1H, d, J = 8.5 Hz), 7.13 (2H, t, J = 5 Hz), 4.77–4.75 (1H, m), 3.28–3.23 (1H, m), 3.08–3.03 (1H, m). ^{13}C NMR (125 MHz, CDCl_3) δ = 206.2, 161.9, 159.3, 149.9, 136.9, 136.0, 132.8, 130.8, 129.2, 129.0, 128.1, 126.9, 124.3, 123.5, 122.3, 122.1, 46.5, 45.2. Mass spectrum (low resolution, EI): 259 [M⁺], 230, 152, 126, 78, 51. HRMS calculated for $\text{C}_{18}\text{H}_{14}\text{NO}$, 260.1075 (MH^+). Found 260.1072.

4.15. 3-(2-Pyrazinyl)-1-indanone (**10**)

Using General Method B, aza-chalcone **1i** (210 mg, 1 mmol) provides indanone **10** (182.8 mg, 0.87 mmol, 87%) as brown oil. R_f = 0.16 (hexane: ethyl acetate/1:1). ^1H NMR (500 MHz CDCl_3) δ = 8.63 (1H, s), 8.54 (2H, s), 7.86 (1H, d, J = 8 Hz), 7.61 (1H, td, J = 1.5, J = 7.5 Hz), 7.47 (1H, t, J = 7.5 Hz), 7.30 (1H, dd, J = 1, J = 8 Hz), 4.83 (1H, dd, J = 4, J = 8 Hz), 3.22 (1H, dd, J = 8, J = 10.5 Hz), 3.05 (1H, dd, J = 4, J = 15 Hz). ^{13}C NMR (125 MHz, CDCl_3) δ = 204.8, 155.3, 144.8, 143.8, 143.4, 136.7, 135.1, 128.4, 126.3, 123.9, 43.9, 43.8. Mass spectrum (low resolution, EI): 210 [M⁺], 181, 127, 102, 77, 51. HRMS calculated for $\text{C}_{13}\text{H}_{11}\text{N}_2\text{O}$, 211.0871 (MH^+). Found 211.0869.

4.16. 3-(2-Benzthiazolyl)-1-indanone (**11**)

Using General Method B, aza-chalcone **1j** (264 mg, 1 mmol) provided indanone **11** as yellow solid (250 mg, 0.95 mmol, 95%), MP: 139–143 °C R_f = 0.47 (hexane: ethyl acetate, 3:1). ^1H NMR (300 MHz CDCl_3) δ = 8.01 (1H, d, J = 8.4 Hz), 7.85 (2H, t, J = 6.6 Hz), 7.65–7.61 (2H, m), 7.53–7.47 (2H, m), 7.41–7.36 (1H, m), 5.18–5.16 (1H, m), 3.41–3.32 (1H, m), 3.22–3.14 (1H, m). ^{13}C NMR (75 MHz, CDCl_3) δ = 203.6, 172.4, 153.9, 153.1, 136.4, 135.2, 135.0, 128.9, 126.9, 126.3, 125.3, 123.9, 123.0, 121.7, 44.3, 43.2. Mass spectrum (low resolution, EI): 265 [M⁺], 236, 103, 77, 63, 51. HRMS calculated for $\text{C}_{16}\text{H}_{11}\text{NOS}$, 266.0640 (MH^+). Found 266.0633.

4.17. 3-(1H-imidazole-4-yl)-1-indanone (**14**)

Using General Method C, acrylic acid derivative **13** (138 mg,

1 mmol) provides indanone **14** (126.7 mg, 0.64 mmol, 64%) as yellow oil, R_f = 0.4 (ethyl acetate: methanol, 9:1). ^1H NMR (500 MHz CDCl_3) δ = 7.75 (1H, d, J = 7.5 Hz), 7.62 (1H, t, J = 8 Hz), 7.53 (1H, s), 7.49 (1H, d, J = 8 Hz), 7.40 (1H, t, J = 7.5 Hz), 6.79 (1H, s), 4.69–4.66 (1H, m), 3.19–3.14 (1H, m), 2.88–2.83 (1H, m). ^{13}C NMR (125 MHz, CDCl_3) δ = 205.9, 156.6, 136.6, 135.4, 134.9, 128.5, 128.4, 127.9, 126.6, 123.5, 44.7, 37.3. HRMS calculated for $\text{C}_{12}\text{H}_{11}\text{N}_2\text{O}$, 199.0871 (MH^+). Found 199.0864.

4.18. 3-(Pentafluorophenyl)-1-indanone (**18**)

Using General Method C, pentafluorocinnamic acid **17** (238.2 mg, 1 mmol) provides indanone **18** (271.3 mg, 0.91 mmol, 91%) as white solid, MP = 101–103, R_f = 0.75 (hexane: ethyl acetate, 4:1). ^1H NMR (500 MHz CDCl_3) δ = 7.84 (1H, d, J = 7.5 Hz), 7.64–7.60 (1H, m), 7.47 (1H, t, J = 7.5 Hz), 7.27 (1H, d, J = 7.5 Hz), 5.01–4.99 (1H, m), 3.24–3.19 (1H, m), 2.86–2.82 (1H, m). ^{13}C NMR (125 MHz, CDCl_3) δ = 203.4, 154.1, 136.3, 135.3, 128.5, 125.5, 123.9, 43.0, 33.0, and 146–116 (pentafluorophenyl multiplets). Mass spectrum (low resolution, EI): 298 [M⁺], 250, 219, 201, 131, 76, 50. HRMS calculated for $\text{C}_{15}\text{H}_9\text{F}_5\text{O}$, 299.0495 (MH^+). Found 299.0501.

4.19. Dichloro-3-(pyridin-2-yl)-2,3-dihydro-1H-inden-1-one (**24a,b**)

Using General Procedure B, aza-chalcone **11** (0.28 g, 1 mmol) provides indanone **24** as an inseparable mixture of regioisomers (**24a,b**, 128 mg, 0.46 mmol, 46%). ^1H NMR (300 MHz, CDCl_3 , 25 °C): δ 8.48 (dd, J = 5.38 Hz, J = 1.52 Hz, 1H), 8.43 (dq, J = 3.98 Hz, J = 0.78 Hz, 1H), 7.79 (s, 1H), 7.65–7.54 (m, 3H), 7.49 (d, J = 8.07 Hz, 1H), 7.32 (d, J = 0.85 Hz, 1H), 7.19 (s, 1H), 7.16–7.12 (m, 2H), 7.08 (qd, J = 2.72 Hz, J = 1.06 Hz, 2H), 4.76 (dd, J = 8.25 Hz, J = 2.63 Hz, 1H), 4.63 (dd, J = 7.89 Hz, J = 4.06 Hz, 1H), 3.20–3.08 (m, 2H), 2.98 (dd, J = 18.90 Hz, J = 4.20 Hz, 1H), 2.77 (dd, J = 18.90 Hz, J = 2.80 Hz, 1H).; ^{13}C NMR (300 MHz, CDCl_3 , 25 °C): δ 203.43, 202.99, 160.71, 155.34, 154.76, 150.17, 149.93, 139.74, 139.36, 137.61, 137.18, 136.73, 136.29, 133.29, 131.56, 130.96, 128.47, 125.17, 122.98, 122.48, 122.36, 122.26, 122.05, 46.11, 45.77, 45.72, 44.61. High-Resolution MS (EI) (M + H), calcd for $\text{C}_{14}\text{H}_{10}\text{NOCl}_2$, 278.0139, found, 278.0137.

5. Experimental

The paper must include the following: (1) Introduction, (2) Results/Discussion, (3) Conclusion, (4) Experimental Section and (5) References. Supplementary data and other sections are optional. You will usually want to divide your article into (numbered) sections and subsections (perhaps even subsubsections). Code section headings using the options in the 'Styles' menu. Headings should reflect the relative importance of the sections. Note that text runs on after a 4th order heading. Use the heading style for the whole paragraph, but remove the italic coding except for the actual heading.

Ensure that all tables, figures and schemes are cited in the text in numerical order. Trade names should have an initial capital letter, and trademark protection should be acknowledged in the standard fashion, using the superscripted characters for trademarks and registered trademarks respectively. All measurements and data should be given in SI units where possible, or other internationally accepted units. Abbreviations should be used consistently throughout the text, and all nonstandard abbreviations should be defined on first usage. Authors are requested to draw attention to hazardous materials or procedures by adding the word CAUTION followed by a brief descriptive phrase and literature references if appropriate. The experimental information should be as concise as

possible, while containing all the information necessary to guarantee reproducibility.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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References

- [1] G.A. Olah, A. Germain, H.C. Lin, D.A. Forsyth, *J. Am. Chem. Soc.* 97 (1975) 2928–2929.
- [2] G.A. Olah, D.A. Klumpp, *Superelectrophiles and Their Chemistry*, Wiley & Sons, New York, NY, 2008.
- [3] a H. Albright, P.S. Riehl, C.C. McAtee, J.P. Reid, J.R. Ludwig, L.A. Karp, P.M. Zimmerman, M.S. Sigman, C.S. Schindler, *J. Am. Chem. Soc.* 141 (2019) 1690–1700;
b U. Castelli, J.-F. Lohier, I. Drukenmgller, A. Mingot, C. Bachman, C. Alayrac, J. Marrot, K. Stierstorfer, A. Kornath, A.-C. Gaumont, S. Thibaudeau, *Angew. Chem. Int. Ed.* 58 (2019) 1355–1360;
c N.A. Devleshova, S.V. Lozovskiy, V.V. Vasilyev, *Tetrahedron* 75 (2019) article 130517 (1–13);
d A. Djurovic, M. Vayer, Z. Li, R. Guillot, J.-P. Baltaze, V. Gandon, C. Bour, *Org. Lett.* 21 (2019) 8132–8137;
e Y. Wei, X. Zheng, D. Lin, H. Yuan, Z. Yin, L. Yang, Y. Yu, S. Wang, L.-H. Xie, W. Huang, *Org. Lett.* 84 (2019) 10701–10709;
f Z. Zhu, G.E. Salnikov, K.Y. Koltunov, *Tetrahedron Lett.* 60 (2019) 857–859;
g Z. Zhu, A.M. Genaeve, G.E. Salnikov, K.Y. Koltunov, *Org. Biomol. Chem.* 16 (2018) 9129–9132;
h A. Narayanan, A. Nirmalchandar, F. Paknia, G. Rasul, T. Mathew, G.K.S. Prakash, *Top. Catal.* 61 (2018) 652–663;
i A.H. Soltan, T. Verheyen, M. Smet, W.M. De Borggraeve, J. Patterson, *Polym. Chem.* 9 (2018) 2775–2784;
j D.S. Ryabukhin, A.D. Lisakova, A.S. Zalivatskaya, I.A. Boyarskaya, G.L. Starova, R.E. Trifonov, V.A. Ostrovskii, A.V. Vasilyev, *Tetrahedron* 74 (2018) 1838–1849;
k I.S. Akhrem, D.V. Avetisyan, L.V. Afanas'eva, O.I. Artyushin, N.D. Kagramanov, A.L. Sigan, *Tetrahedron Lett.* 58 (2017) 4014–4019;
l H. Vuong, B.P. Dash, S.O. Nilsson Lill, D.A. Klumpp, *Org. Lett.* 20 (2018) 1849–1852;
m D. Lin, Y. Wei, C. Ou, H. Huang, L. Xie, L. Tang, W. Huang, *Org. Lett.* 18 (2017) 6220–6223;
n L.J. Bonazaba Milandou, H. Carreyre, S. Alazet, G. Greco, A. Martin-Mingot, C. Nkounkou Loumpangou, J.M. Ouamba, F. Bouazza, T. Billard, S. Thibaudeau, *Angew. Chem. Int. Ed.* 56 (2017) 169–172;
o D.S. Ryabukhin, D.Z. Zakusilo, M.O. Kompanets, A.A. Tarakanov, I.A. Boyarskaya, T.A. Artamonova, M.A. Khohodorkovskiy, I.O. Opeida, A.V. Vasilyev, *Beilstein J. Org. Chem.* 12 (2016) 2125–2135;
p D.A. Klumpp, S. Kennedy, *ARKIVOC* (2018) 215–232, part ii;
q S. Thibaudeau, H. Carreyre, A. Mingot, in: H. Groult, F.R. Leroux, A. Tressaud (Eds.), *Modern Synthesis Processes and Reactivity of Fluorinated Compounds*, Elsevier, London, UK, 2017, pp. 349–388;
r D.A. Klumpp, *Beilstein J. Org. Chem.* 7 (2011) 346–363.
- [4] a M. Gasonoo, A. Sumita, K. Giuffre, K. Boblak, T. Ohwada, D.A. Klumpp, *J. Org. Chem.* 82 (2017) 6044–6053;
b K.N. Boblak, D.A. Klumpp, *J. Org. Chem.* 79 (2014) 5852–5857;
c D.A. Klumpp, G. Garza, G.V. Sanchez, S. Lau, S. DeLeon, *J. Org. Chem.* 65 (2000) 8997–9000;
d Y. Zhang, A. McElrea, G.V. Sanchez Jr., D.A. Klumpp, D. Do, A. Gomez, S.L. Aguirre, R.J. Rendy, *Org. Chem.* 68 (2003) 5119–5124;
e S.E. Denmark, Z.J. Wu, *Org. Chem.* 63 (1998) 2810–2811;
f E.J. Corey, T. Shibata, T.W. Lee, *J. Am. Chem. Soc.* 124 (2002) 3808–3809;
g D.A. Klumpp, S. Lau, *J. Org. Chem.* 64 (1999) 7309–7311.
- [5] a J. Zhu, C. Zhong, H.-F. Lu, G.-Y. Li, X. Sun, *Synlett* (2008) 458–462;
b A. Saito, M. Umakoshi, N. Yagyu, Y. Hanzawa, *Org. Lett.* 10 (2008) 1783–1785;
c Y. Liu, P. Zhao, B. Zhang, C. Xi, *Org. Chem. Front.* 3 (2016) 1116–1119;
d J.L. Marco, *Synth. Commun.* 26 (1996) 4225–4231;
e E. McDonald, P.J. Smith, *Chem. Soc., Perkin Trans. 1* (1980) 837–842;
f J.M. Allen, K.M. Johnston, J.F. Jones, R.G. Shotton, *Tetrahedron* 33 (1977) 2083–2087;
g H.J. Williams, R.L. Harlow, *J. Chem. Soc., Perkin Trans. 1* (1975) 1537–1539.
- [6] a K.Y. Koltunov, S. Walspurger, J. Sommer, *Tetrahedron Lett.* 46 (2005) 8391–8394;
b A.S. Souna Sido, S. Chassaing, M. Kumarraja, P. Pale, J. Sommer, *Tetrahedron Lett.* 48 (2007) 5911–5914.
- [7] a W. Yin, Y. Ma, J. Xu, Y. Zhao, *J. Org. Chem.* 71 (2006) 4312–4315;
b A. Sani-Souna-Sido, S. Chassaing, P. Pale, Sommer, *J. Appl. Catal. A* 336 (2008) 101–108.
- [8] a N.J. Lawrence, E. Armitage, M. Simon, B. Greedy, D. Cook, S. Ducki, A.T. McGown, *Tetrahedron Lett.* 47 (2006) 1637–1640;
b A.P. Prakasham, A.K. Saxena, S. Luqman, C. Debabrata, T. Kaur, A. Gupta, D.K. Yadav, C.S. Chanotiya, K. Shanker, F. Khan, A.S. Negi, *Bioorg. Med. Chem.* 20 (2012) 3049–3057;
c H.O. Saxena, U. Faridi, S. Srivastava, J.K. Kumar, M.P. Darokar, S. Luqman, C.S. Chanotiya, V. Krishna, A.S. Negi, S.P.S. Khanuja, *Bioorg. Med. Chem. Lett.* 18 (2008) 3914–3918.
- [9] H. Vuong, B.P. Dash, S.O. Nilsson Lill, D.A. Klumpp, *Org. Lett.* 20 (2018) 1849–1852.
- [10] Aza-chalcones in this study: 1a, R1=H, R2=H, R3= 2-pyridyl; 1b, R1=H, R2=H, R3= 3-pyridyl; 1c, R1=H, R2=H, R3= 4-pyridyl; 1d, R1=H, R2=H, R3= 2-(6-bromopyridyl); 1e, R1=4-bromophenyl, R2=H, R3= 2-pyridyl; 1f, R1=4-tolyl, R2=H, R3= 2-pyridyl; 1g, R1=H, R2=methyl, R3= 2-pyridyl; 1h, R1=1-naphyl, R2=H, R3= 2-pyridyl; 1i, R1=H, R2=H, R3= 2-pyrazinyl; 1j, R1=H, R2=H, R3= 2-benzothiazolyl; 1k, R1=4-chlorophenyl, R2=H, R3= 2-pyridyl; 1l, R1=3,4-dichlorophenyl, R2=H, R3= 2-pyridyl; 1m, R1=4-nitrophenyl, R2=H, R3= 2-pyridyl.
- [11] P.T. Lansbury, C.J. Justman, Preparation of analogs of indatraline for treatment of neurodegenerative diseases, 150, 2009, p. 351758. Patent WO 2009036275 A1; CAN.
- [12] R. Rendy, Y. Zhang, A. McElrea, A. Gomez, D.A. Klumpp, *J. Org. Chem.* 69 (2004) 2340–2347.
- [13] T. Suzuki, T. Ohwada, K. Shudo, *J. Am. Chem. Soc.* 119 (1997) 6774–6780.
- [14] B.L. Booth, T.A. El-Fekky, *J. Chem. Soc. Perkin I* (1979) 2441–2443.
- [15] S. Pai, M. Moos, M.H. Schreck, C. Lambert, D.G. Kurth, *Inorg. Chem.* 56 (2017) 1418–1432.
- [16] T.P. Robinson, R.B. Hubbard, T.J. Ehlers, J.L. Arbiser, D.J. Goldsmith, J.P. Bowen, *Bioorg. Med. Chem.* 13 (2005) 4007–4013.
- [17] L.E. Downs, D.M. Wolfe, P.R. Schreiner, *Adv. Synth. Catal.* 347 (2005) 235–238.
- [18] A. Rosas-Sanchez, R.A. Toscano, J.G. Lopez-Cortes, M.C. Ortega-Alfaro, *Dalton Trans.* 44 (2015) 578–590.
- [19] S. Otto, F. Bertoncin, J.B.F.N. Engberts, *J. Am. Chem. Soc.* 118 (1996) 7702–7707.
- [20] M.G. Mamolo, V. Falagiani, L. Vio, E. Banfi, *Farmaco* 54 (1999) 761–767.
- [21] A. Rosas-Sanchez, R.A. Toscano, J.G. Lopez-Cortes, M.C. Ortega-Alfaro, *Dalton Trans.* 44 (2015) 578–590.