Research on Chemical Intermediates
https://doi.org/10.1007/s11164-019-04014-9

An expeditious and green one-pot synthesis of 12-substituted-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[*b*]acridine-1,6,11(2*H*)-triones

Saiedeh Kamalifar[1] · **Hamzeh Kiyani**[1]

Received: 3 September 2019 / Accepted: 3 October 2019

Abstract
In this study, several new 12-aryl/heteroaryl-3,3-dimethyl-tetrahydrobenzo[*b*]acridine-1,6,11(2*H*)-trione heterocyclic compounds that can be considered as 1,4-naphthoquinone fused with 4-substituted 7,7-dimethyl-4,6,7,8-tetrahydroquinolin-5(1*H*)-ones, have been synthesized through the three-component cyclocondensation of benzaldehydes/heteroaldehydes, 2-amino-1,4-naphthoquinone, and dimedone. The pot-, atom-, and step-economy reactions were implemented under reflux conditions. One of the most important aspects of this reaction is the use of ethanol as the reaction medium taking into account the principles of green chemistry. Not using a catalyst in this type of reactions is also significant from the standpoint of green chemistry. The protocol developed in this study has the benefits of the simplicity, no use of chromatographic methods for purification, structural diversity, employing non-toxic solvent, good-to-high yields, safety, and using cost-effective solvent. The structures of the newly synthesized 1,4-naphthoquinone fused with 4-substituted 7,7-dimethyl-4,6,7,8-tetrahydroquinolin-5(1*H*)-ones were confirmed employing spectroscopic data as well as elemental analysis.

Keywords 2-Amino-1,4-naphthoquinone · Dimedone · Green synthesis · 12-Substituted-tetrahydrobenzo[*b*]acridine-1,6,11(2*H*)-trione · Three-component cyclocondensation

Introduction

Multicomponent reactions (MCRs) are characterized by the combination of three or more starting materials in a one-pot sequence to the production of various chemical compounds in high chemical yields and bond-forming economy. The products which

✉ Hamzeh Kiyani
hkiyani@du.ac.ir

[1] School of Chemistry, Damghan University, Damghan 36716-41167, Iran

Published online: 26 October 2019

are synthesized via an MCR contain portions of all the reactants. These highly efficient reactions are powerful and atom-efficient and have been successfully employed to the synthesis of heterocycles without isolation of intermediates. Besides the characteristics as mentioned earlier, these environmentally friendly processes have many major advantages over conventional synthesis that can be seen in Fig. 1 [1–20].

N-Polyheterocycles are present in several natural products, various important synthetic bioactive compounds, dyes, vitamins, agrochemicals, functional materials, and drug-like candidates. Therefore, the synthesis of *N*-containing heterocyclic compounds as "privileged" structures has received noteworthy consideration and significant interest in the fields of bioorganic, modern organic synthetic, and medicinal chemistry as well as drug discovery [21–30].

On the other hand, the fused 1,4-naphthoquinones (1,4-NQs) and related substances, as indispensable organic compounds, are endowed with a wide range of remarkable physiological properties, specifically for their antioxidant [31], antimicrobial [32], antimalarial [33], fungicidal [34], anti-inflammatory [35], and indoleamine 2,3-dioxygenase 1 inhibitory [36] activities. It has been mentioned that the 1,4-NQ structure is an important compound found in several synthetic and natural products with a wide range of pharmacological activities, including anti-inflammatory, antifungal, antiviral, anti-atherosclerosis, antileishmanial, and antitumor effects [37–41]. 1,4-NQs are also extensively employed as raw materials in the pharmaceutical industry as well as in the preparation of pesticides in agriculture [40].

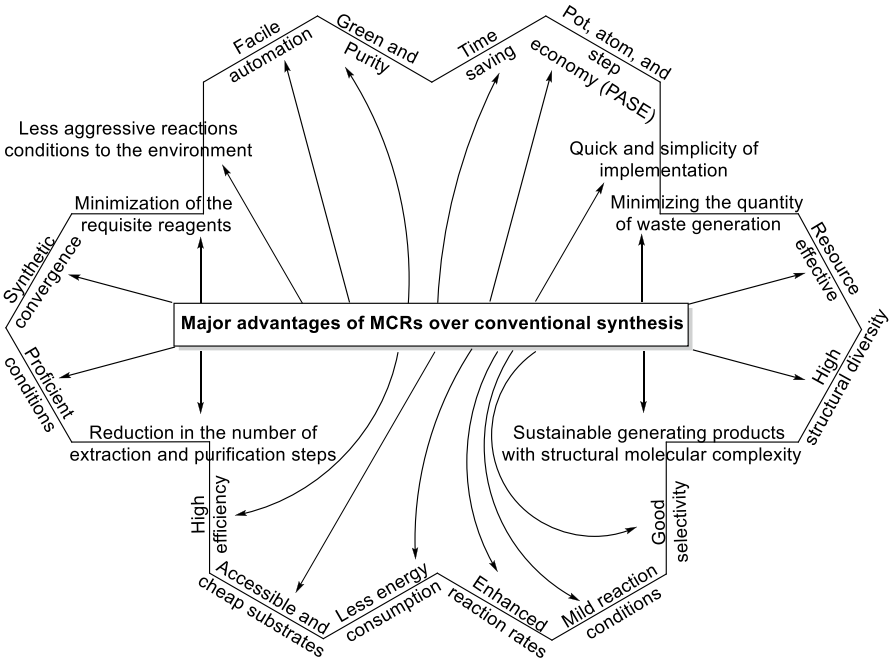


Fig. 1 Major benefits of MCRs

Recently, 2-amino-1,4-naphthoquinones (A-1,4-NQs) have received attention for their broad scope of bioactivities, mostly such as antimicrobial, antifungal, antibiotic, antimalarial, antioxidant, antiplatelet, and tyrosinase inhibitory activities [42–55]. It should be underlined that the great majority of the A-1,4-NQs are employed as attractive starting materials for the synthesis of a broad spectrum of biologically active compounds [42–55]. Studying anticancer, antibacterial as well as antifungal activities of these drug-like compounds is also of attention to researchers [56–67]. In addition to that, amino-1,4-naphthoquinones are a promising family of drug candidates for wound healing agent in diabetic conditions [68].

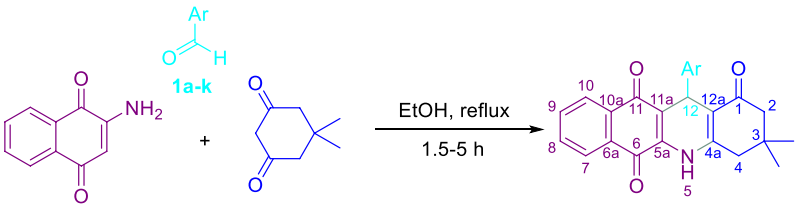
Benzoacridine-based molecules containing 1,4-dihydropyridine nucleus constitute well-known classes of bioactive compounds with biological effects, including antifungal, anticancer, antibacterial, and antimalarial activities [38, 69–73]. Multihydroacridineone derivatives can be used as fluorescent molecular probes for monitoring polymerization process. The framework of benzoacridineone has also attracted much interest because it is structurally similar to the well-known 1,4-dihydropyridines [74].

Keeping the importance of *N*-containing heterocyclic compounds and derivatives of 1,4-naphthoquinones, we report herein the synthesis of 3,3-dimethyl-12-aryl-heteroaryl-hexahydrobenzo[*b*]acridine-1,6,11(2*H*)-triones through the one-pot three-multicomponent-reaction (3-MCR) synthetic methodology (Scheme 1).

Experimental

General

All chemicals were purchased from Alfa Aesar and Aldrich and were used without further purification, except for liquid aldehydes which were distilled and purified before using. All solvents were distilled before use. Melting points were measured on a Buchi 510 melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR



Ar = C_6H_5 (**1a**, **4a**), 4-MeO-C_6H_4 (**1b**, **4b**), 3,4-di-MeO-C_6H_3 (**1c**, **4c**), 3,4,5-tri-MeO-C_6H_2 (**1d**, **4d**), 4-HO-C_6H_4 (**1e**, **4e**), 4-HO-3-EtO-C_6H_3 (**1f**, **4f**), 4-NO_2-C_6H_4 (**1g**, **4g**), 4-Cl-C_6H_4 (**1h**, **4h**), 4-F-C_6H_4 (**1i**, **4i**), 4-CF_3-C_6H_4 (**1j**, **4j**), 3-pyridyl (**1k**, **4k**)

Scheme 1 Three-component synthesis of 12-substituted-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[*b*]acridine-1,6,11(2*H*)-triones (**4a–k**)

measurements were performed by a Bruker Avance DRX-300 MHz operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C using DMSO-d_6 as the solvent. The development of reactions was monitored by thin-layer chromatography (TLC) analysis on Merck pre-coated silica gel 60 F_{254} aluminum sheets, visualized by UV light.

General procedure for the synthesis of 12-substituted-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[*b*]acridine-1,6,11(2*H*)-trione (4a–k)

A mixture of substituted benzaldehydes (**1a**–**k**, 1 mmol), 2-amino-1,4-naphthoquinone (**2**, 0.173 g, 1 mmol), and 5,5-dimethylcyclohexane-1,3-dione, dimedone, (**3**, 0.140 g, 1 mmol) was stirred in EtOH (5 mL) under reflux conditions for appropriate times (TLC analysis). After completion of the reaction, the reaction mixture was cooled to room temperature, and the solvent was then removed under reduced pressure. The resulting solid residue was collected and recrystallized with chloroform to give heterocyclic products (**4a**–**k**).

3,3-Dimethyl-12-phenyl-3,4,5,12-tetrahydrobenzo[*b*]acridine-1,6,11(2*H*)-trione (4a)

Yield: 90%, reaction time: 3 h, m.p. 297–300 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.05 (s, 3H, CH_3), 1.14 (s, 3H, CH_3), 2.24 (d, J = 16.4 Hz, 1H, H_4), 2.31 (d, J = 16.4, 1H, H_4), 2.47 (d, J = 16.9 Hz, 1H, H_2), 2.54 (d, J = 16.8 Hz, 1H, H_2), 5.43 (s, 1H, CH), 7.13 (td, J = 2.0, 7.4 Hz, 1H, $H_{4'}$), 7.24 (td, J = 1.7, 7.6 Hz, 2H, $H_{3', 5'}$), 7.41 (dd, J = 1.3, 7.11 Hz, 2H, $H_{2', 6'}$), 7.62–7.74 (m, 2H, $H_{8, 9}$)[a], 8.02–8.08 (m, 2H, $H_{7, 10}$)[a], 9.78 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 27.0 (CH_3), 29.6 (C_3), 32.6 (C_4), 34.1 (CH), 50.7 (C_2), 111.0 (C_{12a}), 119.5 (C_{11a}), 126.1 (C_7), 126.4 (C_{10}), 126.7 ($C_{4'}$), 128.4 ($C_{2', 6'}$), 126.6 ($C_{3', 5'}$), 130.8 (C_{6a}), 132.3 (C_{10a}), 133.7 (C_8), 135.3 (C_9), 138.9 (C_{5a}), 146.1 ($C_{1'}$), 150.2 (C_{4a}), 180.0 (C_6, C=O)[a], 182.5 (C_{11}, C=O)[a], 195.2 (C_1, C=O of dimedone moiety). Anal. Calcd. For $C_{19}H_{13}NO_3$ (%): C, 75.24; H, 4.32; N, 4.62; Found: C, 75.22; H, 4.30; N, 4.62.

[a]In this and other cases, the signals were assigned adapting to the literature [75, 76].

12-(4-Methoxyphenyl)-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[*b*]acridine-1,6,11(2*H*)-trione (4b)

Yield: 90%, reaction time: 3 h, m.p. 284–286 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.89 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 2.04 (d, J = 16.1 Hz, 1H, H_4), 2.22 (d, J = 16.2, 1H, H_4), 2.54 (d, J = 17.6 Hz, 1H, H_2), 2.66 (d, J = 17.5 Hz, 1H, H_2), 3.63 (s, 3H, OCH_3), 5.10 (s, 1H, CH), 6.74 (d, J = 8.5 Hz, 2H, $H_{3', 5'}$), 7.14 (d, J = 8.5 Hz, 2H, $H_{2', 6'}$), 7.52–7.81 (m, 2H, $H_{8, 9}$), 7.87 (d, J = 7.2 Hz, 1H, H_7), 7.98 (d, J = 7.7 Hz, 1H, H_{10}), 9.79 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 26.5 (CH_3), 29.1 (C_3), 32.1 (C_4), 32.6 (CH), 50.2 (C_2), 54.9 (OCH_3), 110.6 (C_{12a}), 113.4 ($C_{3', 5'}$), 119.3 (C_{11a}), 125.6 (C_7), 125.9 (C_{10}), 128.9 ($C_{2', 6'}$), 130.2 (C_{6a}), 131.9 (C_{10a}), 133.2 (C_8), 134.7 (C_9), 138.0 (C_{5a}), 138.03 ($C_{1'}$), 149.5 (C_{4a}), 157.6 (C_{Ar}-OCH_3), 179.6 (C_6,

C═O), 182.0 (C_{11}, C═O), 194.7 (C_1, C═O of dimedone moiety). Anal. Calcd. For $C_{19}H_{13}NO_3$ (%): C, 75.24; H, 4.32; N, 4.62; Found: C, 75.22; H, 4.30; N, 4.62.

12-(3,4-Dimethoxyphenyl)-3,3-dimethyl-3,4,5,12,-tetrahydrobenzo[*b*]acridine-1,6,11(2*H*)-trione (**4c**)

Yield: 95%, reaction time: 2 h, m.p. 239–240 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.92 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 2.06 (d, J = 16.1 Hz, 1H, H_4), 2.24 (d, J = 16.2, 1H, H_4), 2.55 (d, J = 17.6 Hz, 1H, H_2), 2.68 (d, J = 17.5 Hz, 1H, H_2), 3.63 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3), 5.10 (s, 1H, CH), 6.71 (d, J = 8.2 Hz, 2H, $H_{3', 5'}$), 7.76 (d, J = 8.3 Hz, 2H, $H_{2', 6'}$), 6.83 (s, 1H, $H_{2'}$), 7.73–7.82 (m, 2H, $H_{8, 9}$), 7.89 (d, J = 6.8 Hz, 1H, H_7), 7.98 (d, J = 6.2 Hz, 1H, H_{10}), 9.79 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 26.4 (CH_3), 29.2 (C_3), 32.1 (C_4), 32.9 (CH), 50.2 (C_2), 55.3 (OCH_3), 110.5 (C_{12a}), 111.5 ($C_{5'}$), 112.0 ($C_{2'}$), 119.2 (C_{11a}), 119.9 ($_{6'}$), 125.6 (C_7), 125.8 (C_{10}), 130.3 (C_{6a}), 131.9 (C_{10a}), 133.2 (C_8), 134.7 (C_9), 137.9 (C_{5a}), 138.3 ($C_{1'}$), 147.3 (C_{4a}), 148.2 ($C_{4'}$, C_{Ar}-OCH_3), 149.6 ($C_{3'}$, C_{Ar}-OCH_3), 179.5 (C_6, C═O), 182.1 (C_{11}, C═O), 194.7 (C_1, C═O of dimedone moiety). Anal. Calcd. For $C_{19}H_{13}NO_3$ (%): C, 75.24; H, 4.32; N, 4.62; Found: C, 75.22; H, 4.30; N, 4.62.

(3,4,5-Trimethoxyphenyl)-3,4,5,12-tetrahydrobenzo[*b*]acridine-1,6,11(2*H*)-trione (**4d**)

Yield: 95%, reaction time: 1.5 h, m.p. 224–226 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.97 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 2.08 (d, J = 16.2 Hz, 1H, H_4), 2.24 (d, J = 16.2, 1H, H_4), 2.56 (d, J = 17.5 Hz, 1H, H_2), 2.72 (d, J = 17.5 Hz, 1H, H_2), 3.55 (s, 3H, p-OCH_3), 3.67 (s, 6H, 2×m-OCH_3), 5.11 (s, 1H, CH), 6.50 (s, 2H, $H_{2', 6'}$), 7.73–7.83 (m, 2H, $H_{8, 9}$), 7.95 (d, J = 7.4 Hz, 1H, H_7), 7.99 (dd, J = 1.4, 7.5 Hz, 1H, H_{10}), 9.81 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 26.4 (CH_3), 29.3 (C_3), 32.1 (C_4), 33.6 (CH), 50.2 (C_2), 55.7 (OCH_3), 59.8 (OCH_3), 105.3 ($C_{2', 6'}$), 110.1 (C_{12a}), 118.8 (C_{11a}), 125.7 (C_7), 125.9 (C_{10}), 130.3 (C_{6a}), 131.9 (C_{10a}), 133.2 (C_8), 134.7 (C_9), 136.7 ($C_{4'}$, C_{Ar}-p-OCH_3), 138.1 ($C_{1'}$), 141.2 (C_{5a}), 149.9 (C_{4a}), 152.5 ($C_{3', 5'}$, C_{Ar}-m-OCH_3), 179.5 (C_6, C═O), 182.2 (C_{11}, C═O), 194.8 (C_1, C═O of dimedone moiety). Anal. Calcd. For $C_{19}H_{13}NO_3$ (%): C, 75.24; H, 4.32; N, 4.62; Found: C, 75.22; H, 4.30; N, 4.62.

12-(4-Hydroxyphenyl)-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[*b*]acridine-1,6,11(2*H*)-trione (**4e**)

Yield: 95%, reaction time: 2 h, m.p. 288–290 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.90 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 2.05 (d, J = 16.1 Hz, 1H, H_4), 2.22 (d, J = 16.2, 1H, H_4), 2.53 (d, J = 18.5 Hz, 1H, H_2), 2.66 (d, J = 17.4 Hz, 1H, H_2), 5.06 (s, 1H, CH), 6.57 (d, J = 8.4 Hz, 2H, $H_{3', 5'}$), 7.02 (d, J = 8.4 Hz, 2H, $H_{2', 6'}$), 7.70–7.79 (m, 2H, $H_{8, 9}$), 7.87 (d, J = 7.1 Hz, 1H, H_7), 7.97 (dd, J = 1.4, 7.4 Hz, 1H, H_{10}), 9.12 (s, 1H, OH), 9.71 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 26.5 (CH_3), 29.1 (C_3), 32.1 (C_4), 32.4 (CH), 50.3 (C_2), 110.8 (C_{12a}), 114.8 ($C_{3', 5'}$), 119.5 (C_{11a}), 125.5 (C_7), 125.8 (C_{10}), 128.8 ($C_{2', 6'}$), 130.2 (C_{6a}), 131.9 (C_{10a}), 133.1 (C_8), 134.7 (C_9), 136.4

($C_{1'}$), 137.9 (C_{5a}), 149.3 (C_{4a}), 155.7 (C_{Ar}-OH), 179.6 (C_6, C═O), 182.0 (C_{11}, C═O), 194.7 (C_1, C═O of dimedone moiety). Anal. Calcd. For $C_{19}H_{13}NO_3$ (%): C, 75.24; H, 4.32; N, 4.62; Found: C, 75.22; H, 4.30; N, 4.62.

12-(3-Ethoxy-4-hydroxyphenyl)-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[*b*] acridine-1,6,11(2*H*)-trione (4f)

Yield: 90%, reaction time: 4 h, m.p. 262–264 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.91 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.27 (t, 3H, J = 6.9 Hz, $OCH_2\underline{CH_3}$), 2.06 (d, J = 16.1 Hz, 1H, H_4), 2.2 (d, J = 16.2, 1H, H_4), 2.53 (d, J = 18.2 Hz, 1H, H_2), 2.67 (d, J = 17.4 Hz, 1H, H_2), 3.86–3.95 (m, 2H, OCH_2), 5.05 (s, 1H, CH), 6.58 (s, 2H, $H_{2', 6'}$), 6.77 (s, 1H, $H_{5'}$), 7.71–7.81 (m, 2H, $H_{8, 9}$), 7.90 (dd, J = 1.4, 8.6 Hz, 1H, H_7), 7.98 (dd, J = 1.4, 7.1 Hz, 1H, H_{10}), 8.65 (s, 1H, OH), 9.74 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 14.7 ($CH_2\underline{C}H_3$), 26.4 (CH_3), 29.2 (C_3), 32.1 (C_4), 32.7 (CH), 50.3 (C_2), 63.8 (OCH_2), 110.7 (C_{12a}), 113.9 ($C_{2'}$), 115.2 ($C_{5'}$), 119.4 (C_{11a}), 120.2 ($C_{6'}$), 125.6 (C_7), 125.8 (C_{10}), 130.3 (C_{6a}), 131.9 (C_{10a}), 133.2 (C_8), 134.7 (C_9), 136.8 ($C_{1'}$), 137.9 (C_{5a}), 145.4 (C_{Ar}-OH), 146.1 (C_{Ar}-OEt), 149.4 (C_{4a}), 179.6 (C_6, C═O), 182.1 (C_{11}, C═O), 194.7 (C_1, C═O of dimedone moiety). Anal. Calcd. For $C_{19}H_{13}NO_3$ (%): C, 75.24; H, 4.32; N, 4.62; Found: C, 75.22; H, 4.30; N, 4.62.

3,3-Dimethyl-12-(4-nitrophenyl)-3,4,5,12-tetrahydrobenzo[*b*] acridine-1,6,11(2*H*)-trione (4g)

Yield: 95%, reaction time: 2 h, m.p. 293–295 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.86 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 2.05 (d, J = 16.1 Hz, 1H, H_4), 2.24 (d, J = 16.2, 1H, H_4), 2.57 (d, J = 17.5 Hz, 1H, H_2), 2.68 (d, J = 17.6 Hz, 1H, H_2), 5.28 (s, 1H, CH), 7.54 (d, J = 8.7 Hz, 2H, $H_{2', 6'}$), 7.75–7.88 (m, 3H, $H_{7, 8, 9}$), 7.98–8.04 (m, 1H, H_{10}), 8.07 (d, J = 8.6 Hz, 2H, $H_{3', 5'}$), 9.98 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 26.5 (CH_3), 28.9 (C_3), 32.1 (C_4), 34.4 (CH), 50.1 (C_2), 109.6 (C_{12a}), 117.6 (C_{11a}), 123.3 ($C_{3', 5'}$), 125.6 (C_7), 126.0 (C_{10}), 129.3 ($C_{2', 6'}$), 130.4 (C_{6a}), 131.7 (C_{10a}), 133.3 (C_8), 134.8 (C_9), 138.9 (C_{5a}), 146.0 ($C_{4'}$, C_{Ar}-NO_2), 150.3 (C_{4a}), 152.8 ($C_{1'}$), 179.3 (C_6, C═O), 181.9 (C_{11}, C═O), 194.6 (C_1, C═O of dimedone moiety). Anal. Calcd. For $C_{19}H_{13}NO_3$ (%): C, 75.24; H, 4.32; N, 4.62; Found: C, 75.22; H, 4.30; N, 4.62.

12-(4-Chlorophenyl)-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[*b*] acridine-1,6,11(2*H*)-trione (4h)

Yield: 90%, reaction time: 3 h, m.p. 287–288 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.87 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 2.05 (d, J = 16.1 Hz, 1H, H_4), 2.23 (d, J = 16.2, 1H, H_4), 2.55 (d, J = 17.5 Hz, 1H, H_2), 2.67 (d, J = 17.5 Hz, 1H, H_2), 5.15 (s, 1H, CH), 7.25 (m, 4H, $H_{2', 3', 5'}$), 7.76–7.82 (m, 2H, $H_{8, 9}$), 7.87 (d, J = 6.7 Hz, 1H, H_7), 8.00 (d, J = 6.8 Hz, 1H, H_{10}), 9.85 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 26.5 (CH_3), 29.0 (C_3), 32.0 (C_4), 33.3 (CH), 50.1 (C_2), 110.2 (C_{12a}), 118.4 (C_{11a}), 125.5 (C_7), 125.8 (C_{10}), 127.9 ($C_{3', 5'}$), 129.8 ($C_{2', 6'}$), 130.3 (C_{6a}), 130.7 ($C_{4'}$), 131.8 (C_{10a}), 133.2 (C_8), 134.7 (C_9), 138.5 (C_{5a}), 144.5 ($C_{1'}$), 149.8 (C_{4a}), 179.4 (C_6,

C═O), 181.9 (C_{11}, C═O), 194.6 (C_1, C═O of dimedone moiety). Anal. Calcd. For $C_{19}H_{13}NO_3$ (%): C, 75.24; H, 4.32; N, 4.62; Found: C, 75.22; H, 4.30; N, 4.62.

12-(4-Fluorophenyl)-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[*b*] acridine-1,6,11(2*H*)-trione (**4i**)

Yield: 90%, reaction time: 3 h, m.p. 294–296 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.87 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 2.05 (d, J = 16.1 Hz, 1H, H_4), 2.23 (d, J = 16.2, 1H, H_4), 2.56 (d, J = 17.5 Hz, 1H, H_2), 2.66 (d, J = 17.5 Hz, 1H, H_2), 5.16 (s, 1H, CH), 7.00 (t, J = 8.7 Hz, 2H, $H_{3', 5'}$), 7.24–7.29 (m, 2H, $H_{2', 6'}$), 7.69–7.81 (m, 2H, $H_{8, 9}$), 7.86 (d, J = 7.0 Hz, 1H, H_7), 7.99 (d, J = 6.9 Hz, 1H, H_{10}), 9.86 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 26.5 (CH_3), 29.0 (C_3), 32.1 (C_4), 33.0 (CH), 50.2 (C_2), 110.4 (C_{12a}), 114.7 (d, $^2J_{C\text{-}F}$ = 84.0 Hz, $C_{3', 5'}$), 118.7 (C_{11a}), 125.6 (C_7), 125.9 (C_{10}), 129.7 (d, $^3J_{C\text{-}F}$ = 32.1 Hz, $C_{2', 6'}$), 130.3 (C_{6a}), 131.8 (C_{10a}), 133.3 (C_8), 134.7 (C_9), 138.4 (C_{5a}), 141.9 ($^4J_{C\text{-}F}$ = 12.0 Hz, $C_{1'}$), 149.7 (C_{4a}), 130.7 ($^1J_{C\text{-}F}$ = 962.7 Hz, $C_{4'}$, C_{Ar}-F), 179.5 (C_6, C═O), 182.0 (C_{11}, C═O), 194.7 (C_1, C═O of dimedone moiety). Anal. Calcd. For $C_{19}H_{13}NO_3$ (%): C, 75.24; H, 4.32; N, 4.62; Found: C, 75.22; H, 4.30; N, 4.62.

3,3-Dimethyl-12-(4-(trifluoromethyl)phenyl)-3,4,5,12-tetrahydrobenzo[*b*] acridine-1,6,11(2*H*)-trione (**4j**)

Yield: 95%, reaction time: 2 h, m.p. 283–284 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.87 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 2.06 (d, J = 16.1 Hz, 1H, H_4), 2.24 (d, J = 16.2, 1H, H_4), 2.56 (d, J = 17.5 Hz, 1H, H_2), 2.68 (d, J = 17.6 Hz, 1H, H_2), 5.24 (s, 1H, CH), 7.48 (d, J = 8.1 Hz, 2H, $H_{2', 6'}$), 7.56 (d, J = 8.3 Hz, 2H, $H_{3', 5'}$), 7.38–7.81 (m, 2H, $H_{8, 9}$), 7.86–7.89 (m, 1H, H_7), 78.00–8.03 (m, 1H, H_{10}), 9.94 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 26.6 (CH_3), 28.9 (C_3), 32.1 (C_4), 34.1 (CH), 50.1 (C_2), 109.9 (C_{12a}), 118.1 (C_{11a}), 124.9 (CF_3), 125.0 ($C_{3', 5'}$), 125.6 (C_7), 125.9 (C_{10}), 126.6 ($C_{4'}$), 128.8 ($C_{2', 6'}$), 130.4 (C_{6a}), 131.8 (C_{10a}), 133.3 (C_8), 134.8 (C_9), 138.8 (C_{5a}), 150.0 ($C_{1'}$), 150.2 (C_{4a}), 179.4 (C_6, C═O), 181.9 (C_{11}, C═O), 194.7 (C_1, C═O of dimedone moiety). Anal. Calcd. For $C_{19}H_{13}NO_3$ (%): C, 75.24; H, 4.32; N, 4.62; Found: C, 75.22; H, 4.30; N, 4.62.

3,3-Dimethyl-12-(pyridin-3-yl)-3,4,5,12-tetrahydrobenzo[*b*] acridine-1,6,11(2*H*)-trione (**4k**)

Yield: 80%, reaction time: 5 h, m.p. 275–278 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.86 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 2.05 (d, J = 16.1 Hz, 1H, H_4), 2.23 (d, J = 16.2, 1H, H_4), 2.55 (d, J = 17.4 Hz, 1H, H_2), 2.68 (d, J = 17.5 Hz, 1H, H_2), 5.16 (s, 1H, CH), 7.21–7.25 (m, 1H, $H_{5'}$), 7.61 (d, J = 7.9 Hz, 1H, $H_{4'}$), 7.73–7.82 (m, 2H, $H_{8, 9}$), 7.86–7.88 (m, 1H, H_7), 7.99–8.02 (m, 1H, H_{10}), 8.28 (d, J = 3.8 Hz, 1H. $H_{6'}$), 8.49 (s, 1H, $H_{2'}$), 9.91 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 26.5 (CH_3), 29.0 (C_3), 32.0 (CH), 32.1 (C_4), 50.1 (C_2), 109.8 (C_{12a}), 117.9 (C_{11a}), 123.5 ($C_{5'}$), 125.6 (C_7), 125.9 (C_{10}), 130.4 (C_{6a}), 131.8 (C_{10a}), 133.3 (C_8), 134.7 (C_9), 135.4 ($C_{4'}$), 138.8 (C_{5a}), 141.0 ($C_{3'}$), 147.3 (C_{4a}), 149.2 ($C_{6'}$), 150.1 ($C_{2'}$), 179.3 (C_6, C═O), 181.9 (C_{11},

C=O), 194.6 (C_1, C=O of dimedone moiety). Anal. Calcd. For $C_{19}H_{13}NO_3$ (%): C, 75.24; H, 4.32; N, 4.62; Found: C, 75.22; H, 4.30; N, 4.62.

Results and discussion

2-Amino-1,4-naphthoquinone (**2**) was synthesized as the brown crystalline material from the commercially available 1,4-naphthoquinone and sodium azide in aqueous acetic acid at 40 °C for 2 h according to the method reported in the literature [77]. A series of 12-substituted-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[*b*] acridine-1,6,11(2*H*)-triones, 1,4-naphthoquinone fused with 7,7-dimethyl-4,6,7,8-tetrahydroquinolin-5(1*H*)-ones, (**4a**–**k**) were synthesized from an equimolar mixture of aromatic aldehydes (**1a**–**k**) with 2-amino-1,4-naphthoquinone (**2**) and 5,5-dimethylcyclohexane-1,3-dione, dimedone, (**3**) via the one-pot 3-MCR of in EtOH as a green solvent under reflux conditions (Scheme 1). The initial attempt began with the 3-MCR of benzaldehyde (**1a**, 1 mmol), 2-amino-1,4-naphthoquinone (**2**, 1 mmol), and dimedone (**3**, 1 mmol) in EtOH without adding any catalyst or additives. The reaction was subjected to reflux conditions, and thin-layer chromatography (TLC) analysis revealed that the reaction was completed within 3 h. After workup, the desired product 3,3-dimethyl-12-phenyl-3,4,5,12-tetrahydrobenzo[*b*] acridine-1,6,11(2*H*)-trione (**4a**) was isolated in 90% yield. The temperature reaction was altered to understand the effect of temperature on the reaction yield and reaction time. Satisfactory results were not obtained from this study. The influence of the solvent on the reaction time and product yield was also screened in the MCR of benzaldehyde (**1a**), A-1,4-NQ (**2**), and dimedone (**3**) using several solvents such as ethanol, water, dichloromethane, and acetonitrile under reflux conditions. The results are presented in Table 1. Among the different solvents explored, EtOH was found to be an excellent choice of the solvent. Under refluxing ethanol, to show the versatility of this 3-MCR, a set of 12-substituted-3,3-dimethyl-3,4,5,12-tetrahydrobenzo[*b*] acridine-1,6,11(2*H*)-triones was synthesized by changing the structure of aromatic aldehydes. Substituted benzaldehydes containing electron-donating (–Me, –OMe, OH, OEt) and electron-withdrawing groups (–F, Cl, NO_2 $–CF_3$) as well as a heteroaromatic aldehyde (pyridine-3-carbaldehyde) were employed. In all experiments,

Table 1 Screening of the solvent effect on the synthesis of 3,3-dimethyl-12-phenyl-3,4,5,12-tetrahydrobenzo[*b*] acridine-1,6,11(2*H*)-trione (**4a**)

Entry	Solvent (5 mL)	Time (h)	Isolated yields (%)
1	EtOH	3	90
2	H_2O	3.5	50
3	CH_2Cl_2	4	60
4	CH_3CN	4	60

The reaction was implemented using benzaldehyde (**1a**, 1 mmol), 2-amino-1,4-naphthoquinone (**2**, 1 mmol), and dimedone (**3**, 1 mmol) under reflux temperature of the solvent

the reaction proceeds efficiently under the same reaction conditions, and the corresponding heterocyclic products were obtained in 80–95% isolated yields.

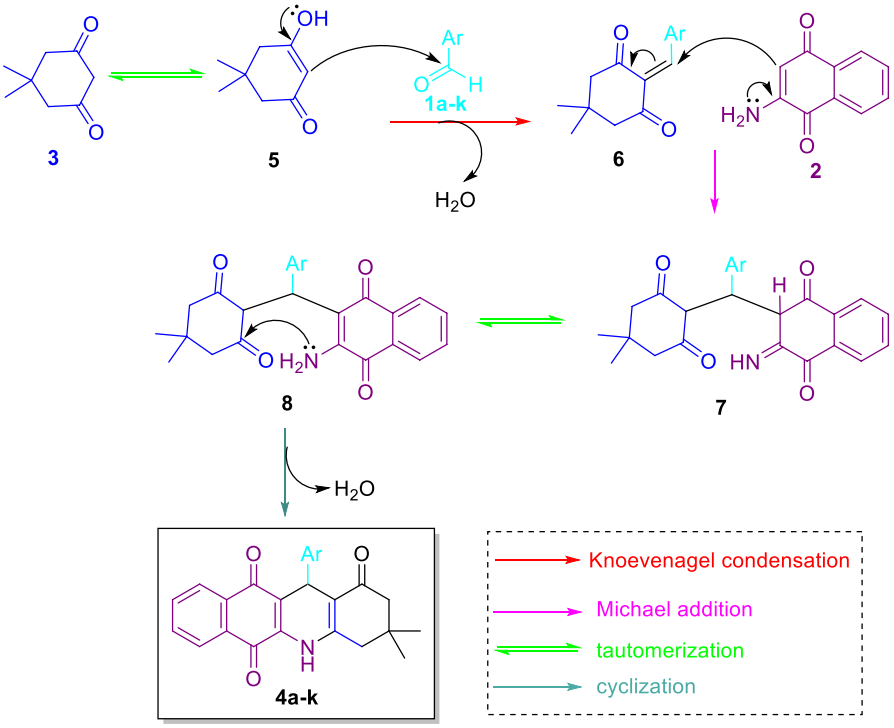
The structural confirmation of numerous synthesized heterocyclic compounds has been done based on the corresponding analytical and spectroscopic data analysis. For example, in the proton nuclear magnetic resonance (^{1}H NMR) of compound **4b**, CH_3 protons showed two separate singlets at δ_H 0.89 and 1.02 ppm. CH_3 proton signals of synthesized heterocycles were observed in a range of δ_H 0.86–1.14 ppm. The protons of CH_2 at the position C4 of dimedone moiety appeared at δ_H 2.04 and 2.22 ppm as two separate doublets with $^2J_{HH}$ = 16.1 Hz and 16.2 Hz because of geminal coupling [78]. Two doublets at δ_H 2.54 ($^2J_{HH}$ = 17.6 Hz) and 2.66 ($^2J_{HH}$ = 17.5 Hz) were attributed to CH_2 protons of the position C2 of dimedone ring. In the ^{1}H NMR spectra of other synthesized compounds, the dimedone moiety signals also appeared in the same region, *i.e.*, from 2.04 to 2.72 ppm. The spectrum displayed a singlet at δ_H 3.63 ppm, which indicates the presence of a methoxy group. It is noteworthy that compounds **4c** and **4d** contain the methoxy groups and their corresponding proton signals appeared at δ_H 3.63 and 3.66 ppm for **4c**, and δ_H 3.55 (*p*-OCH_3) and 3.67 (*m*-OCH_3) ppm, respectively. In other heterocyclic compounds that do not contain the methoxy group, these signals are not seen. Furthermore, in compounds **4e** and **4f** containing hydroxyl group instead of a methoxy in *para*-position, the resonances of the OH protons were determined as singlets at δ_H 9.12 and 8.65 ppm, respectively. A singlet at δ_H 5.10 ppm, integrating for one hydrogen, is owing to CH (H-12) of 1,4-dihydropyridine scaffold. The characteristic singlet in the range from 5.05 to 5.28 ppm for CH of 1,4-dihydropyridine section was present in the ^{1}H NMR spectra of all the target compounds. The protons of *ortho*-position (H-3′, 5′) and *meta*-position (H-2′, 6′) of *p*-methoxyphenyl ring showed two doublets centered at δ_H 6.74 (2H, J = 8.5 Hz), 7.14 (2H, J = 8.5 Hz), respectively. Resonated multiplet signal at δ_H 7.52–7.81 ppm and two doublets at δ_H 7.87 (J = 7.2 Hz) and 7.98 (J = 7.7 Hz) ppm, integrating for four protons, were attributed to 1,4-NQ hydrogens [40] in the desired compound. The resonance of the NH proton signal belonging to the 1,4-dihydropyridine nucleus was found as a singlet signal at δ_H 9.79 ppm. Also, singlet signals observed in the downfield region, ranging from 9.71 to 9.98 ppm, each with integrating for one hydrogen and characteristic of NH proton confirmed the formation of 1,4-dihydropyridine ring in the all heterocyclic compounds.

The ^{13}C NMR spectrum of compound **4b** showed a peak from the two methyl-group carbons (3-CH_3) at 26.5 ppm. The two methylene carbon signals at δ_C 32.1 (4-CH_2) and 50.2 (2-CH_2) ppm, the signal at δ_C 29.1 ppm (C-3), and a carbonyl signal at δ_C 194.7 ppm suggested a dimedone moiety in the molecule. The corresponding chemical shift of the *p*-methoxy group was observed at δ_C 54.9 ppm. Two signals, observed at 179.6 and 182.0 ppm, were assigned to the carbonyl groups of 1,4-naphthoquinone moiety. The chemical shifts of the carbonyl functional groups at the position C11 are higher than those of C6, which can be attributed to the resonance effect between nitrogen and the carbonyl groups at C-11 [75, 76]. The expected resonance signals for other carbons were detected in the range of δ_C 110.6–157.6 ppm. The NMR data, except for the aryl and heteroaryl rings on position C4 of 1,4-dihydropyridine moiety, were similar to those of compound **4b**.

The plausible mechanism of the reaction is outlined in Scheme 2. The reaction possibly starts with a keto-enol tautomerization of dimedone (**3**), and the reaction of generated enol (**5**) with the aldehydes (**1**) via the Knoevenagel condensation to give the corresponding α,β-unsaturated dicarbonyl intermediates **6**. Michael addition between 2-amino-1,4-naphthoquinone (**2**) and intermediates **6** affords the Michael adducts **7**. The tautomerization of **7** gives intermediate **8** with a 1° amine group which is then converted into the desired 1,4-naphthoquinone fused with 4-substituted 7,7-dimethyl-4,6,7,8-tetrahydroquinolin-5(1*H*)–one polyheterocyclic compounds (**4a**–**k**) through intramolecular nucleophilic cyclization.

Conclusions

In summary, the green and expeditious synthesis of a series of new 12-aryl/heteroaryl-3,3-dimethyl-tetrahydrobenzo[*b*]acridine-1,6,11(2*H*)-trione derivatives from aromatic aldehydes, 2-amino-1,4-naphthoquinone, and dimedone via 3-CR approach has been described. Among several solvents tested in this reaction, the best results were obtained when ethanol was employed as the reaction medium.



Scheme 2 Possible mechanism for the synthesis of 12-substituted-3,3-dimethyl-tetrahydrobenzo[*b*]acridine-1,6,11(2*H*)-trione (**4a**–**k**)

Structural elucidation of the newly synthesized fused tetracyclic compounds containing substituents at position 4 of 1,4-dihydropyridine ring was implemented utilizing recorded spectroscopic data analysis. The simplicity of operation under mild conditions, simple workup and purification process, inexpensiveness, atom economy, convenience, the use of ethanol as an environmentally benign solvent, and very good-to-high yields make this approach attractive for the synthesis of a variety of such heterocyclic compounds.

Acknowledgements The authors are thankful to Damghan University Research Council for financial support of this study.

References

1. J.F.A. Filho, B.C. Lemos, A.S. de Souza, S. Pinheiro, S.J. Greco, Tetrahedron **73**, 6977 (2017)
2. I. Khan, A. Ibrar, N. Abbas, A. Saeed, Res. Chem. Intermed. **42**, 5147 (2016)
3. S. Das, A.K. Bagdi, S. Santra, A. Majee, A. Hajra, Res. Chem. Intermed. **41**, 6749 (2015)
4. R. Jiang, M. Liu, H. Huang, L. Mao, Q. Huang, Y. Wen, Q.Y. Cao, J. Tian, X. Zhang, Y. Wei, J. Colloid Interface Sci. **519**, 137 (2018)
5. M.R. Bhosle, D. Nipte, J. Gaikwad, M.A. Shaikh, G.M. Bondle, J.N. Sangshetti, Res. Chem. Intermed. **44**, 7047 (2018)
6. P. Mane, B. Shinde, P. Mundada, V. Gawade, B. Karale, A. Burungale, Res. Chem. Intermed. (2019). https://doi.org/10.1007/s11164-019-03945-7
7. C. Lambruschini, A. Basso, L. Banf, Drug Discov. Today Technol. **29**, 3 (2018)
8. S. Saranya, K.R. Rohit, S. Radhika, G. Anilkumar, Org. Biomol. Chem. **17**, 8048 (2019)
9. S. Zhi, X. Ma, W. Zhang, Org. Biomol. Chem. **17**, 7632 (2019)
10. A. Al Otaibi, F.M. Deane, C.C. Russell, L. Hizartzidis, S.N. McCluskey, J.A. Sakoff, A. McCluskey, RSC Adv. **9**, 7652 (2019)
11. M. de Souza Siqueira, L.C. da Silva-Filho, Tetrahedron Lett. **57**, 5050 (2016)
12. N.G. Salunkhe, C.A. Ladole, N.V. Thakare, A.S. Aswar, Res. Chem. Intermed. **44**, 355 (2018)
13. C. Altuğ, L.Y. Saleh, E. Caner, H. Güneş, M. Sameeullah, Phosphorus Sulfur Silicon Relat. Elem. **194**, 111 (2019)
14. M.R. Bhosle, M.A. Shaikh, D. Nipate, L.D. Khillare, G.M. Bondle, J.N. Sangshetti, Polycycl. Aromat. Compd. (2019). https://doi.org/10.1080/10406638.2018.1533875
15. C.C. Jiao, Y.C. Tian, H.L. Cong, Y.Q. Shen, B. Yu, Integr. Ferroelectr. **198**, 55 (2019)
16. V. Arandkar, R.R. Vedula, Phosphorus Sulfur Silicon Relat. Elem. **194**, 533 (2019)
17. S.P.N. Sudhan, R. Nasir Ahmed, H. Kiyani, S. Sheik Mansoor, J. Saudi Chem. Soc. **22**, 269 (2018)
18. H. Kiyani, Curr. Org. Synth. **15**, 1043 (2018)
19. H. Kiyani, M. Bamdad, Res. Chem. Intermed. **44**, 2761 (2018)
20. H. Kiyani, A. Mosallanezhad, Curr. Org. Synth. **15**, 715 (2018)
21. A. Jana, P. Bhaumick, A.K. Panday, R. Mishra, L.H. Choudhury, Org. Biomol. Chem. **17**, 5316 (2019)
22. S. Saigal, H. Khan, S. Rahman, M.M. Khan, RSC Adv. **9**, 14477 (2019)
23. T.B. Aquino, J.E.R. do Nascimento, I.F.C. Dias, D.H. de Oliveira, T. Barcellos, E.J. Lenardão, G. Perin, D. Alves, R.G. Jacob, Tetrahedron Lett. **59**, 1080 (2018)
24. A. Malhotra, T. Kaur, R. Bansal, J. Heterocycl. Chem. (2019). https://doi.org/10.1002/jhet.3683
25. R. Nongrum, G.K. Kharmawlong, J.W.S. Rani, N. Rahman, A. Dutta, R. Nongkhlaw, J. Heterocycl. Chem. (2019). https://doi.org/10.1002/jhet.3680
26. C. Sambandam, S. Dhanavel, M. Haridoss, G. Mannuthusamy, J. Heterocycl. Chem. (2019). https://doi.org/10.1002/jhet.3656
27. M.A. Abozeid, M.R. El-Kholany, L.A. Abouzeid, A.R.H. Abdel-Rahman, E.S.I. El-Desoky, J. Heterocycl. Chem. (2019). https://doi.org/10.1002/jhet.3686
28. N. Aljaar, R. Gujjarappa, M. Al-Refai, M. Shtaiwi, C.C. Malakar, J. Heterocycl. Chem. (2019). https://doi.org/10.1002/jhet.3673

29. K.M. Sim, P.Q. Chan, X.L. Boo, K.S. Heng, K.W. Lye, K.C. Teo, Lett. Org. Chem. **15**, 575 (2018)
30. A.V. Chate, R.M. Dongre, M.K. Khaire, G.M. Bondle, J.N. Sangshetti, M. Damale, Res. Chem. Intermed. **44**, 6119 (2018)
31. N.A. Akwu, Y. Naidoo, M. Singh, N. Nundkumar, J. Lin, S. Afr, J. Bot. **123**, 180 (2019)
32. B.M. Mbala, J. Jacobs, P. Claes, V. Mudogo, N. De Kimpe, Tetrahedron **67**, 8747 (2011)
33. M.S. Abdelfattah, K. Toume, M.A. Arai, H. Masu, M. Ishibashi, Tetrahedron Lett. **53**, 3346 (2012)
34. E.A. Kolodina, N.I. Lebedeva, M.S. Shvartsberg, Mendeleev Commun. **22**, 332 (2012)
35. J. Wang, W. Li, J. Qin, L. Wang, S. Wei, H. Tang, Bioorg. Chem. **83**, 477 (2019)
36. R. Yang, Y. Chen, L. Pan, Y. Yang, Q. Zheng, Y. Hu, Y. Wang, L. Zhang, Y. Sun, Z. Li, X. Meng, Bioorg. Med. Chem. **26**, 4886 (2018)
37. B. Du, G. Cai, B. Zhao, X. Meng, X. Wang, Y. Li, Res. Chem. Intermed. **39**, 1323 (2013)
38. Y. Li, X. Xu, D. Shi, S. Ji, Chin. J. Chem. **27**, 1510 (2009)
39. W.F. Rabêlo, R. Echemendía, Synth. Commun. **49**, 515 (2019)
40. Z. Gokmen, M.E. Onan, N.G. Deniz, D. Karakas, E. Ulukaya, Synth. Commun. **40**, 3008 (2019)
41. V. Vairaperumal, M. Perumal, P. Sengodu, S. Shanumuganthan, M. Paramasivam, ChemistrySelect **4**, 3006 (2019)
42. X.L. Chen, Y. Dong, S. He, R. Zhang, H. Zhang, L. Tang, K.M. Zhang, J.U. Wang, Synlett **30**, 615 (2019)
43. M. Gholampour, S. Ranjbar, N. Edraki, M. Mohabbati, O. Firuzi, M. Khoshneviszadeh, Bioorg. Chem. **88**, 102967 (2019)
44. A. Kacmaz, Z. Hamurcu, Phosphorus Sulfur Silicon Relat. Element. **193**, 831 (2018)
45. A. Sharma, I.O. Santos, P. Gaur, V.F. Ferreira, C.R.S. Garcia, D.R. da Rocha, Eur. J. Med. Chem. **59**, 48 (2013)
46. S. Ullah, J. Akter, S.J. Kim, J. Yang, Y. Park, P. Chun, H.R. Moon, Med. Chem. Res. **28**, 95 (2019)
47. B.J. Josey, E.S. Inks, X. Wen, C.J. Chou, J. Med. Chem. **56**, 1007 (2013)
48. J. Guo, I.N.C. Kiran, R.S. Reddy, J. Gao, M. Tang, Y. Liu, Y. He, Org. Lett. **18**, 2499 (2016)
49. A. Kosiha, C. Parthiban, K.P. Elango, J. Photochem. Photobiol. B **168**, 165 (2017)
50. A.A. Aly, E.A. Ishak, M.A. Alsharari, N.S. Al-Muaikel, T.M.I. Bedair, J. Heterocycl. Chem. **49**, 9 (2012)
51. W.O. Valenc, T.V. Baiju, F.G. Brito, M.H. Araujo, C. Pessoa, B.C. Cavalcanti, C.A. de Simone, C. Jacob, I.N.N. Namboothiri, E.N. da Silva Junior, ChemistrySelect **2**, 4301 (2017)
52. A.A. Osowole, A.C. Ekennia, O.O. Olubiyi, M. Olagunju, Res. Chem. Intermed. **43**, 2565 (2017)
53. D.Y. Yuk, C.K. Ryu, J.T. Hong, K.H. Chung, W.S. Kang, Y. Kim, H.S. Yoo, M.K. Lee, C.K. Lee, Y.P. Yun, Biochem. Pharmacol. **60**, 1001 (2000)
54. Y.L. Hsu, C.P. Chuang, Synthesis **46**, 3374 (2014)
55. C. Festus, A.C. Ekennia, A.A. Osowole, L.O. Olasunkanmi, D.C. Onwudiwe, O.T. Ujam, Res. Chem. Intermed. **44**, 5857 (2018)
56. A. Kosiha, K.M. Lo, C. Parthiban, K.P. Elango, Mater. Sci. Eng. C **94**, 778 (2019)
57. C. Festus, A.C. Ekennia, C.U. Ibeji, S.N. Okafor, D.C. Onwudiwe, A.A. Osowole, O.T. Ujam, J. Mol. Struct. **1163**, 455 (2018)
58. C. Ibis, Z. Ozsoy-Gunes, A.F. Tuyun, S.S. Ala, H. Bahar, M.V. Stasevych, R.Y. Musyanovych, O. Komarovska-Porokhnyavets, V. Novikov, J. Sulfur Chem. **37**, 477 (2016)
59. J. Li, X. Zhang, H. Xiang, L. Tong, F. Feng, H. Xie, J. Ding, C. Yang, J. Org. Chem. **82**, 6795 (2017)
60. M. Manickam, P.R. Boggu, J. Cho, Y.J. Nam, S.J. Lee, S.H. Jung, Bioorg. Med. Chem. Lett. **28**, 2023 (2018)
61. E.O. Olawode, R. Tandlich, E. Prinsloo, M. Isaacs, H. Hoppe, R. Seldon, D.F. Warner, V. Steenkamp, P.T. Kaye, Bioorg. Med. Chem. Lett. **29**, 1572 (2019)
62. E. Leyva, L.I. Lopez, R.F.G. de la Cruz, C.G. Espinosa-Gonzalez, Res. Chem. Intermed. **43**, 1813 (2017)
63. U. Sharma, D. Katoch, S. Sood, N. Kumar, B. Singh, A. Thakur, A. Gulati, Indian J. Chem. **52B**, 1431 (2013)
64. P. Ravichandiran, S.A. Subramaniyan, S.Y. Kim, J.S. Kim, B.H. Park, K.S. Shim, D.J. Yo, ChemMedChem **14**, 532 (2019)
65. P. Ravichandiran, M. Masłyk, S. Sheet, M. Janeczko, D. Premnath, A.R. Kim, B.H. Park, M.K. Han, D.J. Yoo, ChemistryOpen **8**, 589 (2019)
66. N. Bayrak, H. Yıldırım, A.F. Tuyun, E.M. Kara, B.O. Celik, G.K. Gupta, H.I. Ciftci, M. Fujita, M. Otsuka, H.R. Nasiri, Lett. Drug Des. Discov. **14**, 647 (2017)

67. L.I. Lopez-Lopez, J.J.V. Garcia, A. Saenz-Galindo, S.Y. Silva-Belmares, Lett. Org. Chem. **11**, 573 (2014)
68. S.H. Cardoso, C.R. de Oliveira, A.S. Guimarães, J. Nascimento, J. de Oliveira dos Santos Carmo, J.N. de Souza Ferro, A.C. de Carvalho Correia, E. Barreto, Chem. Biol. Interact. **291**, 55 (2018)
69. A. Murugesan, R.M. Gengan, A. Krishnan, Mater. Chem. Phys. **188**, 154 (2017)
70. G. Mohammadi Ziarani, S. Mousavi, M. Rahimifard, A. Badiei, J. Mex. Chem. Soc. **58**, 168 (2014)
71. S. Janke, S. Boldt, K. Ghazargan, P. Ehlers, A. Villinger, P. Lange, Eur. J. Org. Chem. **2019**, 6177 (2019)
72. F. Shaebani Behbahani, J. Tabeshpour, S. Mirzaei, S. Golmakaniyoon, Z. Tayarani-Najaran, A. Ghasemi, R. Ghodsi, Arch. Pharm. Chem. Life Sci. **352**, e1800307 (2019)
73. I. Antonini, P. Polucci, A. Magnano, S. Martelli, J. Med. Chem. **44**, 3329 (2001)
74. S. Tu, R. Jia, B. Jiang, Y. Zhang, J. Zhang, J. Heterocycl. Chem. **43**, 1621 (2006)
75. T.F. Borgati, J.D. de Souza Filho, A.B. de Oliveira, J. Braz. Chem. Soc. **30**, 1138 (2019)
76. S. Bhand, R. Patil, Y. Shinde, D.N. Lande, S.S. Rao, L. Kathawate, S.P. Gejji, T. Weyhermüller, S. Salunke-Gawali, J. Mol. Struct. **1123**, 245 (2016)
77. J. Mattay, A.G. Griesbeck, *Photochemical Key Steps in Organic Synthesis: An Experimental Course Book* (Wiley-VCH Verlagsgesellschaft mbH, Weinheim, 1994), p. 105
78. M. Bayat, F.S. Hosseini, S. Nasri, J. Sulfur Chem. **39**, 99 (2018)