Black Sea Journal of Engineering and Science
doi: 10.34248/bsengineering.1545551

Open Access Journal
e-ISSN: 2619 – 8991

Research Article
Volume 7 - Issue 6: 1204-1216 / November 2024

SYNTHESIS OF HETARYL SUBSTITUTED PYRAZOLO[3,4-*b*]QUINOLINONE SYSTEMS BY MULTICOMPONENT CYCLOCONDENSATION REACTION

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Abstract: In this study, the synthesis of pyrazolo[3,4-*b*]quinolinone compounds was carried out via one-pot three-component reactions. These reactions proceed as domino processes, making them easier to occur than the conventional multistep organic reactions. By employing this method, new organic molecules can be synthesized in a single step, using minimal time and number of trials. In the first phase of this two-step study, heteroaromatic carbaldehydes (quinoline-8-carboxaldehyde and quinoline-4-carboxaldehyde) were prepared to be used as substrates in subsequent reactions by oxidation of 8-methylquinoline and 4-methylquinoline with selenium dioxide, a mild oxidant. In the second step, heteroaromatic carbaldehyde reacted with aminopyrazole and dimedone in anhydrous ethanol by one-pot multicomponent condensation method to synthesize six compounds with heteryl-substituted pyrazolo[3,4-*b*]quinolinone ring system. The crude products were obtained in excellent yields and further purified by crystallization. The structures of the compounds, which were found to be completely pure as a result of chromatographic studies, were elucidated by spectroscopic methods and elemental analysis.

Keywords: One-Pot reactions, Quinolinone, Selenium dioxide, Methylquinoline, Multicomponent reactions (MCRs), Biological activity

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Received: September 08, 2024
Accepted: October 10, 2024
Published: November 15, 2024

Cite as: Gümüş MK, Kaban Ş. 2024. Synthesis of hetaryl substituted pyrazolo[3,4-b]quinolinone systems by multicomponent cyclocondensation reaction. BSJ Eng Sci, 7(6): 1204-1216.

1. Introduction

Presently, chemical research is preponderantly focused on synthesizing new compounds that potentially have biological activity and measuring this activity. Heterocyclic systems and their substituted derivatives, which are among the most important classes of organic chemistry, are widely used in medicine as well as in industry (Desenko et al., 2024; Doğan et al., 2022; Gümüş et al., 2024). Multicomponent reactions take place when three or more starting materials react in a reaction vessel to form a target product containing portions of all the initial materials (Zhu and Bienayme, 2005). It is well known that heterocyclic compounds are generally formed by intramolecular or intermolecular cyclization reactions (cyclocondensation) of straight-chain substances (Gümüş et al., 2018).

In previous research concerning the preparation of quinolinone rings, they were synthesized via one-pot three-component reactions using dimedone and benzaldehyde derivatives with aminopyrazole derivatives (Quiroga et al., 1998a; Quiroga et al., 2001; Danel et al., 2022), aminopyrimidine derivatives (Quiroga et al., 1998b), and aminobenzimidazole derivatives (Lipson et al., 2003a; Chebanov et al., 2010), and pyrazolo[3,4-*b*]quinolinone ring system was investigated as inhibitors of glycogen synthase kinase 3 with exquisite kinomewide selectivity and their functional effects (Wagner et al. 2016).

Furthermore, it was observed that mostly the phenyl group and its derivatives were found in the quinolinone systems since benzaldehyde and its derivatives were used as substituents. In light of this information, this study aimed to synthesize new heteryl-substituted quinolinone derivatives by multicomponent cyclocondensation reaction technique.

In the first step, heteroaromatic carbaldehydes were synthesized by oxidation of methylquinolines with selenium dioxide, which is a weak oxidant (Kaplan, 1941; Seyhan and Fernelius, 1957). In the second step, heteroaromatic carbaldehyde reacted with corresponding aminopyrazole and dimedone in anhydrous ethanol by one-pot multicomponent condensation method to synthesize six compounds with heteryl-substituted pyrazolo[3,4-*b*]quinolinone ring system.

2. Materials and Methods

2.1. Equipment and Supplies

Fourier Transform Infrared (FTIR) spectra of the products were obtained on a Perkin Emler Spectrum One FTIR spectrophotometer by tableting with potassium bromide. Nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR) spectra were obtained in DMSO-d_6 (using tetramethylsilane (TMS) standard) on a Varian Mercury 400 MHz spectrophotometer. Mass spectra were obtained using a Hewlett Packard GC/MS 6890/5973 70 eV spectrometer. Elemental analysis was performed using a Thermo Electron Corporation, CHNS-O Analyzer.

Solvent recovery during extraction and crystallization of the products was performed in a Heidolph VV 2000 rotary evaporator. In thin layer chromatography (TLC), "Merck silica gel 60 F254 aluminum layer" with fluorescent indicator and "Desega Min UVIS, 50 Hz UVP" 254 nm ultraviolet lamp were used. The melting points of the isolated pure substances were determined in a "Gallenkamp" model melting point apparatus with open capillary tubes and no thermometer correction was made.

2.2. Preparation of Selenium dioxide for use as an Oxidant in the Preparation of Carbaldehydes

Selenium dioxide was prepared by oxidation of metallic selenium with nitric acid or by combustion in oxygen and nitrogen dioxide. Purification can be performed by crystallization or sublimation; however, sublimation is preferable. Since selenium dioxide and selenious acid are very expensive substances, it is important to recover metallic selenium. The recovered metallic selenium was pulverized, washed with suitable solvents to remove organic impurities, and then dried so that it can be reused. While concentrated nitric acid (20 g, 14.1 mL) in a porcelain capsule was heated in a fume hood and burner flame, metallic selenium (10 g) was slowly added in portions. The resulting solution was heated at a temperature not exceeding 200 °C until the selenous acid was completely evaporated. The crude product was purified by sublimation (Blatt, 1986).

2.3. Preparation and Properties of Hetaryl Substituted Carbaldehydes

2.3.1. Synthesis of quinoline-4-carboxaldehyde

After adding selenium dioxide to the solution of 4-methylquinoline in dioxane, the reaction mixture was boiled in an oil bath at 105-110 °C for two hours under refluxing. The mixture, which turned dark brown during boiling, was filtered while hot to remove the metallic selenium and the solvent was removed in a rotary evaporator. Water vapor distillation was applied to the residue to obtain the crude product. Quinoline-4-carboxaldehyde hydrate was crystallized from a mixture of ethanol/water (50:50) (Kaplan, 1941). Analysis data: Colorless needle crystals (%50), mp. 82-3 °C. IR (KBr): 3100-3000 (=C–H aromatic stretching), 2860 and 2760 (C–H aldehyde stretching), 1680 (C=O aldehyde stretching), 1580 and 1497 (C=N and C=C stretching), 1210, 1035, 845 and 750 (C–H bendings) cm^{-1}.

2.3.2. Synthesis of quinolin-8-carboxaldehyde

The mixture of 8-methylquinoline and selenium dioxide was moderately heated dry to 145-150 °C in a system equipped with an oxidizing tube. From this temperature, the reaction mixture was heated to 220 °C within 20 minutes and then raised to 250 °C within 2-3 minutes to remove unreacted 8-methylquinoline. The aldehyde was extracted from the cooled mixture with ether and crystallized from water (Seyhan and Fernelius, 1957). Analysis data: Light yellow needle crystals (%45), mp. 93-4 °C. IR (KBr): 3120–2980 (=C–H aromatic stretching), 2860 (C–H aldehyde stretching), 1670 (C=O aldehyde stretching), 1565 and 1500 (C=N and C=C stretching), 1240, 1165,1130, 860, 830 and 790 (C–H bendings) cm^{-1}.

2.3.3. Preparation of anhydrous ethanol

To 1 L of 95% ethanol in a 2 L round-bottomed flask, 250 g of calcium oxide was added which has been heated in an oven at high temperature for about six hours and cooled without contact with air. The mixture was boiled for six hours under a reflux condenser for 12 hours and then the alcohol was removed by distillation (Blatt, 1986).

2.3.4. Synthesis of pyrazolo[3,4-b]quinolinone compounds

To a solution of (1.0 mmol) heterylcarbaldehyde in anhydrous ethanol in a round bottom flask (1.0 mmol), a solution of the amine compound in anhydrous ethanol (1.0 mmol) and a solution of the dimedone compound in anhydrous ethanol (1.0 mmol) were added and brought to boiling over a water bath under a reflux condenser equipped with a $CaCl_2$ tube. The mixture was boiled for different time intervals for each compound under TLC control until the reaction was terminated. The crude product obtained from the cooled dark solution was filtered and purified by crystallization using appropriate solvents (Figure 1), (Gümüş 2009).

3. Results

Using each heterocyclic aldehyde, corresponding amines (3-methyl-5-aminopyrazole, 3-phenyl-5-aminopyrazole) and dimedone, six pyrazolo[3,4-*b*]quinolinone compounds (Compounds 1-6) containing the hetaryl group as a substituent were synthesized by one-pot multicomponent reaction (3-MCR) in anhydrous ethanol medium.

3.1. Spectroscopic Analysis Data of Compounds 1-6

3,7,7-Trimethyl-4-(pyridin-3-yl)-2,4,6,7,8,9-hexahydro-5H-pyrazolo[3,4-b]quinolin-5-one (Compound 1, Wagner et al. 2016, yield, 32%). FT-IR (KBr) cm^{-1}: 3223 (NH stretching), 3128-3026 (aromatic, =C-H stretching), 2964-2893 (alifatic, CH, CH_2 and CH_3, stretching), 1628-1474 (heteroaromatic ring, C=N and C=C stretching), 1380-1253 (C-H bendings). ^{1}H-NMR (DMSO-d_6) δ ppm: 11.76 (s, 2-NH, 1H), 9.92 (s, 9-NH, 1H), 8.38 (m, 2'-CH, 1H), 8.23 (m, 6'-CH, 1H), 7.42 (m, 4'-CH, 1H), 7.18 (m, 5'-CH, 1H), 4.95 (s, 4-CH, 1H), 2.45 (d, 8-CH, J=16.9 Hz, 1H), 2.39 (d, 8-CH, J=16.9 Hz, 1H), 2.1 (d, 6-CH, J=16.1 Hz, 1H),

1.93 (d, 6-CH, J=16.1 Hz, 1H), 1.86 (s, 3-CH_3, 3H), 0.98 and 0.90 (2s, 7-$(CH_3)_2$, 6H). ^{13}C-NMR (DMSO-d_6) δ ppm: 9.98 (3C-CH_3), 27.56 and 29.42 (7C-$(CH_3)_2$), 32.65 (4-CH), 33.56 (7-C), 41.64 (8-CH_2), 50.99 (6-CH_2), 103.69, 106.82, 123.92, 135.20, 135.83, 144.08, 146.89, 147.15, 149.29, 153.88 (carbons of aromatic and olefinic rings, 10C), 193.51 (5-C carbonyl carbon). GC-MS (MeOH) m/z (%): 309 (10), 308 (90, M^+), 250 (100, -C_4H_{10}), 230 (60, -C_5H_4N), 78 (32, -$C_{13}H_{16}N_3O$). Elemental Analysis Results: $C_{18}H_{20}N_4O$, Found, %: C 70.03; H 6.48; N 18.21. Calculated, %: C 70.11; H 6.48; N 18.21.

3.2. *3,7,7-Trimethyl-4-(quinolin-4-yl)-2,4,6,7,8,9-hexahydro-5H-pyrazolo[3,4-b]quinolin-5-one* (Compound 2)

FT-IR (KBr) cm^{-1}: 3230-3195 (NH stretching), 3125-3040 (=C-H aromatic stretching), 2958-2893 (alifatic, CH, CH_2 and CH_3 stretching), 1618-1421 (aromatic and heteroaromatic ring, C=C and C=N stretching), 1382-1252 (C-H bendings). ^{1}H-NMR (DMSO-d_6) δ ppm: 11.76 (br.s, 2-NH, 1H), 9.92 (s, 9-NH, 1H), 8.70-7.22 (m, aromatik, 6H), 5.72 (br.s, 4-CH, 1H), 2.51 (d, 8-CH, J=16.6 Hz, 1H), 2.44 (d, 8-CH, J=16.6 Hz, 1H), 2.08 (d, 6-CH, J=16.1 Hz, 1H), 1.86 (d, 6-CH, J=16.1 Hz, 1H), 1.61 (s, 3-CH_3, 3H), 0.99 and 0.90 (2s, 7-$(CH_3)_2$, 6H). ^{13}C-NMR (DMSO-d_6) δ ppm: 10.33 (3C-CH_3), 27.59 and 29.47 (7C–$(CH_3)_2$), 32.57 (4-CH), 41.70 (8-CH_2), 50.96 (6-CH_2), 107.40, 121.81, 125.27, 126.37, 126.62, 129.39, 130.17, 136.16, 146.75, 150.73, 154.05 (carbons of aromatic and olefinic rings, 14C), 193.69 (5-C carbonyl carbon). GC-MS (MeOH) m/z (%): 359 (10), 358 (60, M^+), 230 (100, -C_9H_6N), 129 (32, -$C_{13}H_{16}N_3O$). Elemental Analysis Results: $C_{22}H_{22}N_4O$, Found, %: C 73.80; H 6.13; N 15.54. Calculated, %: C 73.72; H 6.19; N 15.63.

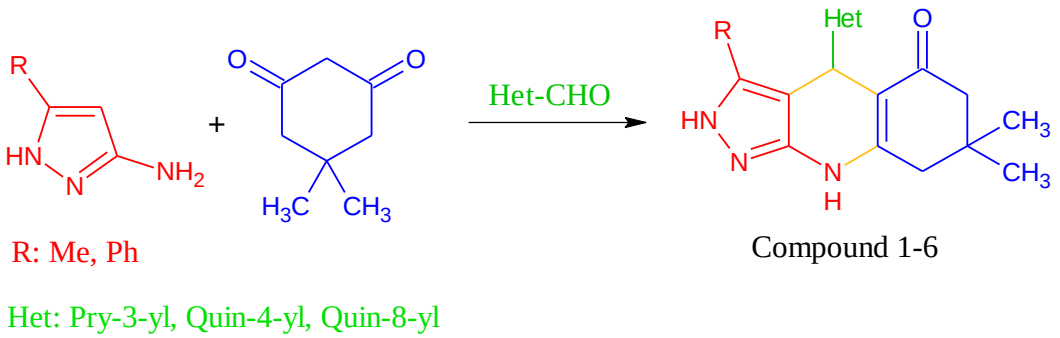


Figure 1. Synthesis of six novel hetaryl substituted pyrazolo[3,4-*b*]quinolinone compounds.

3.3. *3,7,7-Trimethyl-4-(quinolin-8-yl)-2,4,6,7,8,9-hexahydro-5H-pyrazolo[3,4-b]quinolin-5-one* (Compound 3)

FT-IR (KBr) cm^{-1}: 3220 (NH stretching, 3126-3046 (aromatic, =C-H stretching), 2971-2867 (alifatic, CH, CH_2 and CH_3 stretching), 1599-1431 (heteroaromatic ring, C=N and C=C stretching), 1382-1251 (C-H bendings). ^{1}H-NMR (DMSO-d_6) δ ppm: 11.51 (br.s, 2-NH, 1H), 9.59 (s, 9-NH, 1H), 8.99-7.37 (m, aromatic, 6H), 6.46 (s, 4-CH, 1H), 2.52 (d, 8-CH, J=17.9 Hz, 1H), 2.48 (d, 8-CH, J=17.9 Hz, 1H), 2.09 (d, 6-CH, J=16.1 Hz, 1H), 1.88 (d, 6-CH, J=16.1 Hz, 1H), 1.66 (s, 3-CH_3, 3H), 1.02 and 1.01 (2s, 7-$(CH_3)_2$, 6H). ^{13}C-NMR (DMSO-d_6) δ ppm: 10.48 (3C-CH_3), 27.81 and 29.62 (7C-$(CH_3)_2$), 28.85 (7-C), 32.66 (4-CH), 41.88 (8-CH_2), 51.32 (6-CH_2), 105.65, 108.65, 121.75, 125.99, 127.20, 128.14, 135.69, 136.76, 145.19, 147.05, 148.71, 149.83, 154.11 (carbons of aromatic and olefinic rings, 14C), 193.31 (5-C carbonyl carbon). GC-MS (MeOH) m/z (%): 358 (100, M^+), 220 (66, -C_9H_6N), 130 (46, -$C_{13}H_{16}N_3O$). Elemental Analysis Results: $C_{22}H_{22}N_4O$, Found, %: C 73.65; H 6.24; N 15.71. Calculated, %: C 73.72; H 6.19; N 15.63.

3.4. *7,7-Dimethyl-3-phenyl-4-(pyridin-3-yl)-2,4,6,7,8,9-hexahydro-5H-pyrazolo[3,4-b]quinolin-5-one* (Compound 4)

FT-IR (KBr) cm^{-1}: 3299-3175 (NH stretching), 3125-3051 (=C-H aromatic stretching), 2950-2866 (alifatic, CH, CH_2 and CH_3 stretching), 1604-1425 (heteroaromatic ring, C=C and C=N stretching), 1373-1142 (C-H bendings). ^{1}H-NMR (DMSO-d_6) δ ppm: 12.64 (s, 2-NH, 1H) 10.05 (s, 9-NH, 1H), 7.07-8.33 (m, aromatic, 6H), 5.36 (s, 4-CH, 1H), 2.48 (d, 8-CH, J=16.6 Hz, 1H), 2.38 (d, 8-CH, J=16.6 Hz, 1H), 2.14 (d, 6-CH, J=16.1 Hz, 1H), 1.94 (d, 6-CH, J=16.1 Hz, 1H), 0.99 and 0.82 (2s, 7-$(CH_3)_2$, 6H). ^{13}C-NMR (DMSO-d_6) δ ppm: 27.22 and 29.52 (7C–$(CH_3)_2$), 32.66 (7-C), 33.88 (4-CH), 41.48 (8-CH_2), 50.95 (6-CH_2), 103.07, 107.41, 123.82, 126.67, 128.71, 129.47, 129.87, 135.39, 143.23, 147.26, 149.28, 153.26 (aromatic and olefinic ring carbons, 16C), 193.45 (5-C carbonyl carbon). GC-MS (MeOH) m/z (%): 371 (21), 370 (100, M^+), 292 (55, -C_4H_5N), 78 (45, -$C_{18}H_{18}N_3O$). Elemental Analysis Results: $C_{23}H_{22}N_4O$, Found, %: C 74.65; H 5.89; N 15.19. Calculated, %: C 74.57; H 5.99; N 15.12.

3.5. *7,7-Dimethyl-3-phenyl-4-(quinolin-4-yl)-2,4,6,7,8,9-hexahydro-5H-pyrazolo[3,4-b]quinolin-5-one* (Compound 5)

FT-IR (KBr) cm^{-1}: 3300-3195 (NH stretching), 3125-3040 (aromatic, =C-H stretching), 2958-2893 (alifatic, CH_3, CH_2 and CH stretching), 1585-1421 (heteroaromatic ring, C=C and C=N stretching), 1382-1252 (C-H bendings). ^{1}H-NMR (DMSO-d_6) δ ppm: 12.53 (br.s, 2-NH, 1H), 10.20 (s, 9-NH, 1H), 8.60-7.13 (m, aromatic, 11H), 6.06 (br.s, 4-CH, 1H), 2.55 (d, 8-CH, J=16.5 Hz, 1H), 2.42 (d, 8-CH, J=16.5 Hz, 1H), 2.11 (d, 6-CH, J=16.1 Hz, 1H), 1.85 (d, 6-CH, J=16.1

Hz, 1H), 0.99 and 0.79 (2s, 7-$(CH_3)_2$, 6H). ^{13}C-NMR (DMSO-d_6) δ ppm: 27.14 and 29.61 (7C-$(CH_3)_2$), 32.52 (7-C), 40.82 (4-CH), 41.60 (8-CH_2), 50.96 (6-CH_2), 103.76, 107.96, 122.86, 125.90, 126.04, 127.39, 128.63, 128.99, 129.18, 129.57, 129.75, 139.05, 148.16, 148.50, 150.33, 153.40 (carbons of aromatic and olefinic rings, 20C), 193.71 (5-C carbonyl carbon). GC-MS (MeOH) m/z (%): 421 (20, M+1), 420 (100, M^+), 296 (55, -C_9H_6N), 128 (50, -$C_{18}H_{18}N_3O$). Elemental Analysis Results: $C_{27}H_{24}N_4O$, Found, %: C 77.19; H 5.68; N 13.37. Calculated, %: C 77.12; H 5.75; N 13.32.

3.6. *7,7-Dimethyl-3-phenyl-4-(quinolin-8-yl)-2,4,6,7,8,9-hexahydro-5H-pyrazolo[3,4-b]quinolin-5-one* (Compound 6)

FT-IR (KBr) cm^{-1}: 3300-3195 (NH stretching), 3125-3040 (aromatic, =C-H stretching), 2958-2893 (alifatic, CH_3, CH_2 and CH stretching), 1585-1421 (heteroaromatic ring, C=C and C=N stretching), 1382-1252 (C-H bendings). ^{1}H-NMR (DMSO-d_6) δ ppm: 12.53 (br.s, 2-NH, 1H) 10.20 (s, 9-NH, 1H), 8.60-7.13 (m, aromatik, 11H), 6.06 (br.s, 4-CH, 1H), 2.55 (d, 8-CH, J=16.5 Hz, 1H), 2.42 (d, 8-CH, J=16.5 Hz, 1H), 2.11 (d, 6-CH, J=16.1 Hz, 1H), 1.85 (d, 6-CH, J=16.1 Hz, 1H), 0.99 and 0.79 (2s, 7-$(CH_3)_2$, 6H). ^{13}C-NMR (DMSO-d_6) δ ppm: 27.14 and 29.61 (7C-$(CH_3)_2$), 32.52 (7-C), 40.82 (4-CH), 41.60 (8-CH_2), 50.96 (6-CH_2), 103.76, 107.96, 122.86, 125.90, 126.04, 127.39, 128.63, 128.99, 129.18, 129.57, 129.75, 139.05, 148.16, 148.50, 150.33, 153.40 (carbons of aromatic and olefinic rings, 20C), 193.71 (5-C carbonyl carbon). GC-MS (MeOH) m/z (%): 421 (20, M+1), 420 (100, M^+), 296 (55, -C_9H_6N), 128 (50, -$C_{18}H_{18}N_3O$). Elemental Analysis Results: $C_{27}H_{24}N_4O$, Found, %: C 77.19; H 5.68; N 13.37. Calculated, %: C 77.12; H 5.75; N 13.32.

4. Discussion

Cyclocondensation can theoretically occur via two pathways. However, in the studies performed so far, it has been reported that pathway B is not followed during the reaction and only products via pathway A are formed (Quiroga et al., 1998a; Quiroga et al., 1998b; Quiroga et al., 2001; Lipson et al., 2003b).

Since there will be no interaction between 4-H and 9-NH in the NMR data of the linear products formed by pathway A, they will give singlet peaks when they resonate (Gümüş 2009). In fact, in the ^{1}H NMR spectra of compounds 1, 2, 3, 4, 5, and 6, 4-H and 9-NH gave singlet peaks with integration ratios of 1:1. This situation is inconsistent with the product being formed in the angular structure via pathway B, since H and NH are adjacent in the angular structure and spin-spin interactions would be expected between them. Since no such interaction was observed, the product formed is the linear product (Figure 2).

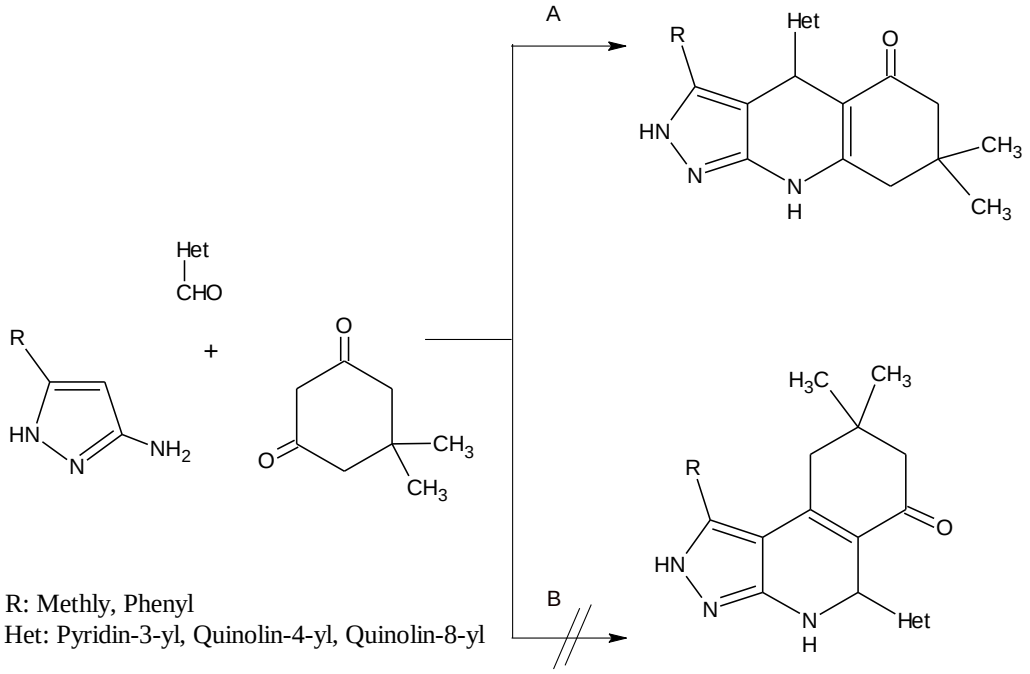


Figure 2. Theoretical possibilities of the cyclocondenzation reaction.

When the resonance structures of 3(5)-Amino-5(3)-methylpyrazole are examined, it is seen that the electron density on the fourth carbon is quite high as indicated in the resonance structures, so it has the ability to attack as a nucleophile (Figure 3). In addition, the electron density on the fourth carbon increases again because the amino group substituted on the pyrazole activates the ring by giving electrons to the ring (Figure 4).

Based on this information, we can propose the following mechanisms (Figure 5) for the formation of compound 1.

In pathway A, a Knoevenagel intermediate is formed between the aldehyde and the dimedone, and then another intermediate is formed by Michael addition to this α,β-unsaturated intermediate by the attack of

electrons at the fourth carbon of the pyrazole. Due to resonance, this intermediate is formed to a higher degree in pathway B, which we will discuss later, and therefore the reaction only follows pathway A. In the next step of the reaction, an intramolecular ring condensation takes place between the substituted amino group of the pyrazole and the keto-group of the dimedone to form the main product. We can propose the following mechanism for path B.

As a result of Michael's addition to the α, β-unsaturated Knoevenagel intermediate, an intermediate is formed by attacking the lone pair in the amino group as a substituent in the pyrazole ring. When this intermediate is studied, it is believed that the nitrogen atom is positively charged, and since nitrogen is an electronegative atom, it will avoid this road. Therefore, the reaction will not follow pathway B (Figure 6) and will proceed via pathway A. Indeed, the NMR data of the products formed as a result of the reaction support these views (Table 1 and Table 2).

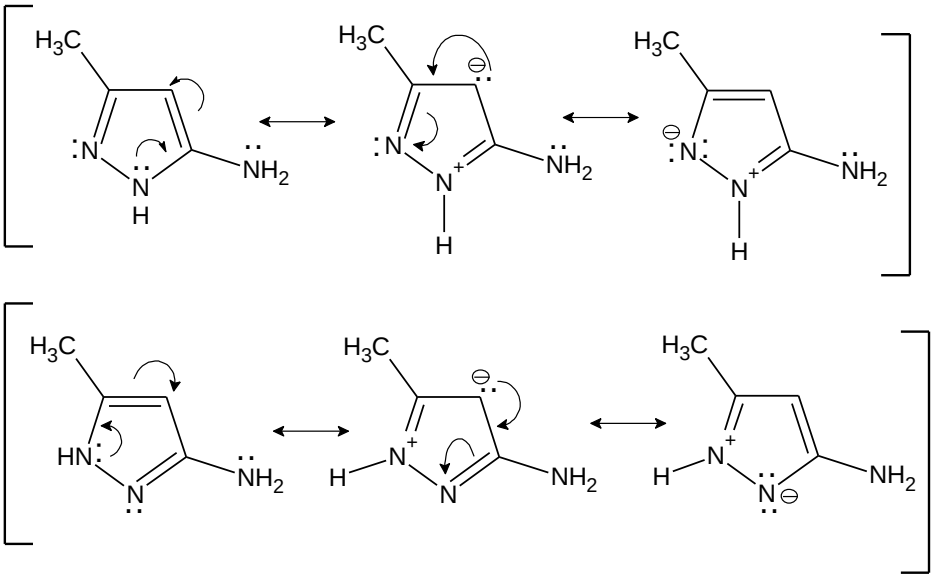


Figure 3. Resonance structures of 3(5)-Amino-5(3)-methylpyrazole.

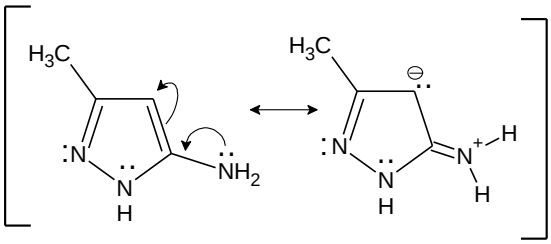


Figure 4. The amino group substituted on the pyrazole activates the ring by giving electrons.

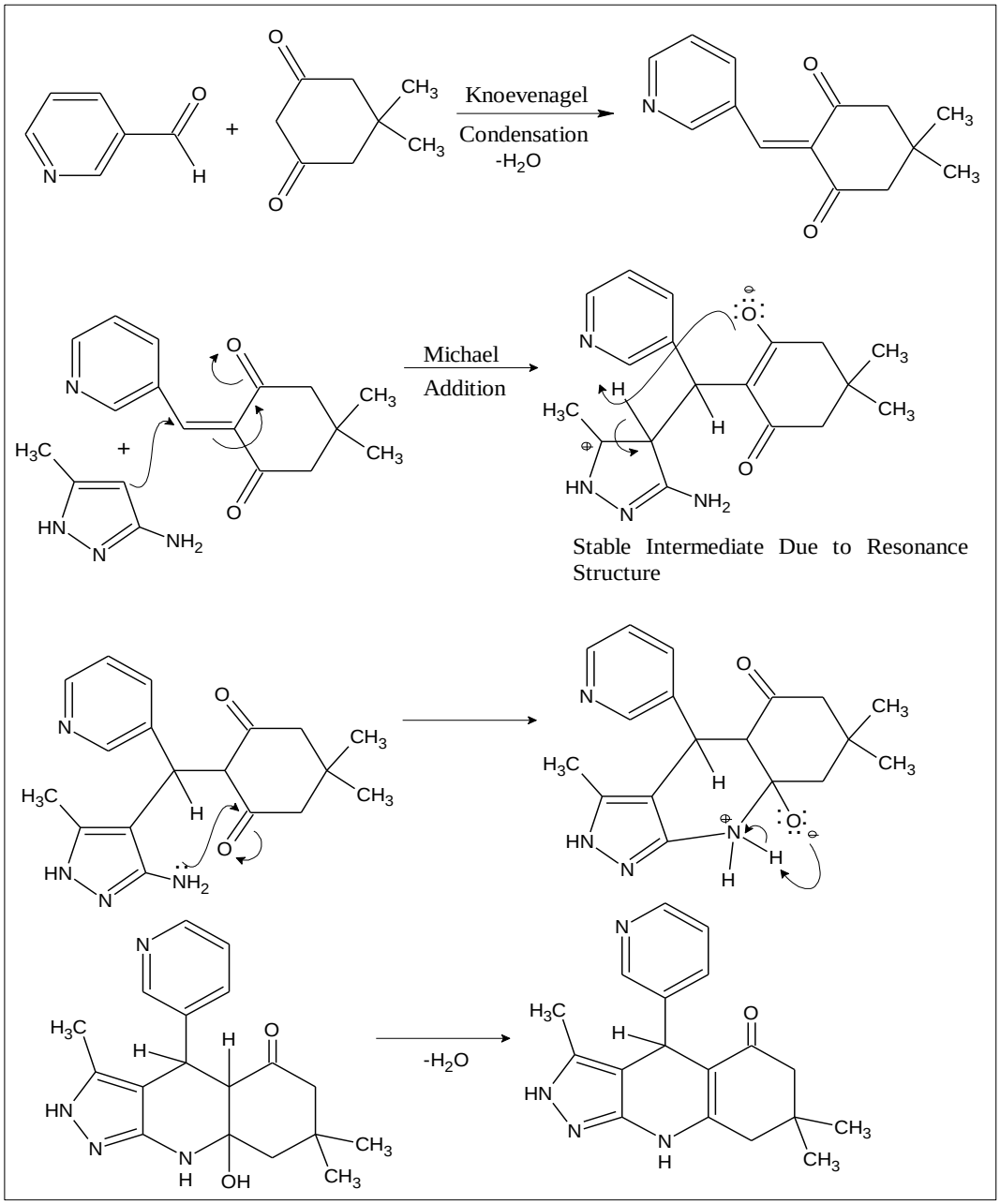


Figure 5. Mechanism of the product formed via pathway A.

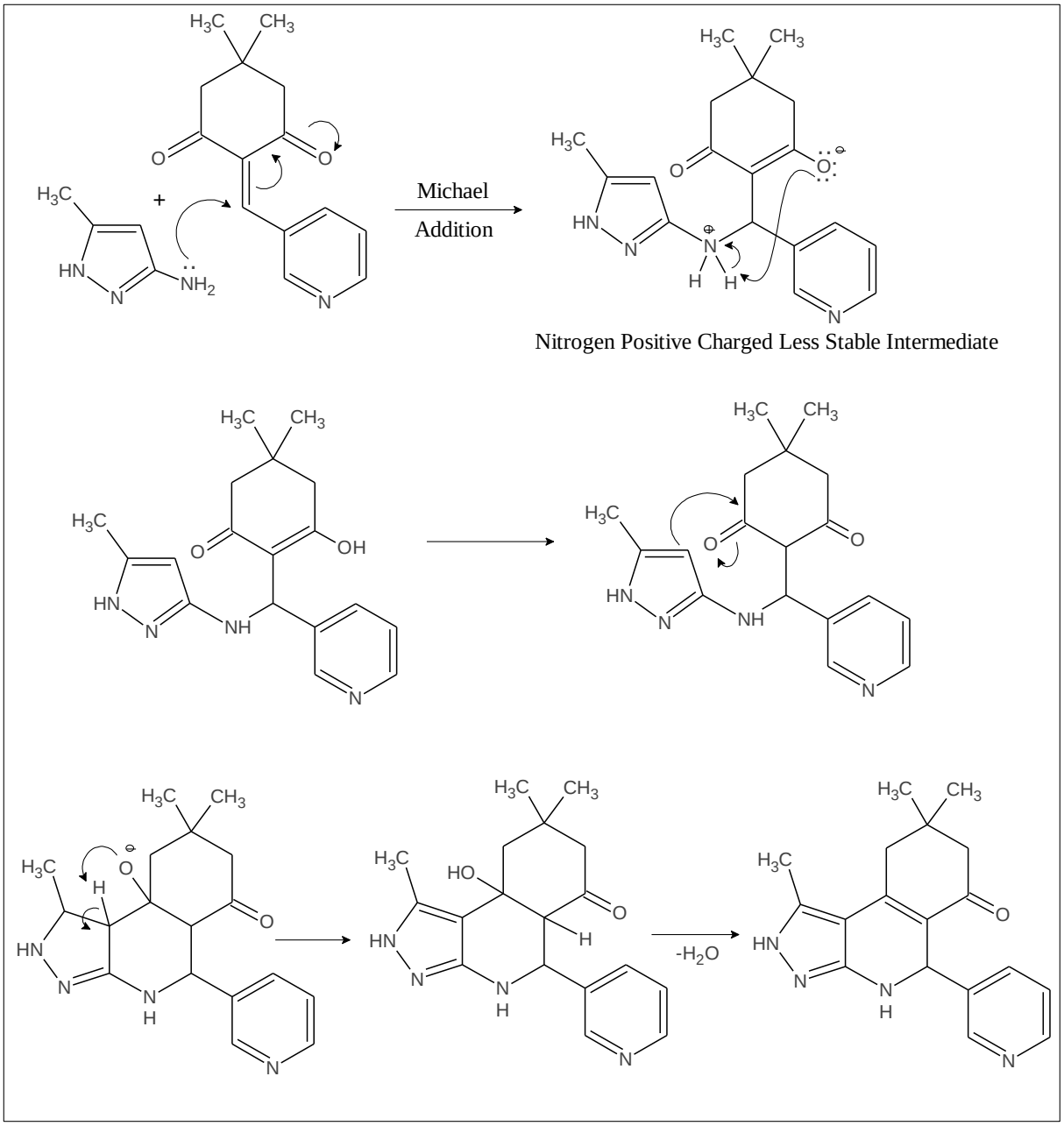
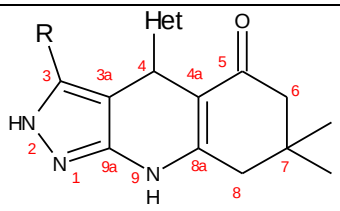


Figure 6. Mechanism of the product formed via pathway B.

Table 1. ^{1}H-NMR values of compounds 1-6 δ (ppm)



R: Methyl, Phenyl

Het: Pyr-3-yl, Quin-4-yl, Quin-8-yl

Compound	2-H br.s, 1H	3-CH_3 s, 3H	4-Het. m	4-H s, 1H	6-H 2d, 2H	7-C(Me)$_2$ 2s, 6H	8-H 2d, 2H	9-H br.s, 1H
1	11.76	1.86	7.18-8.38	4.95	1.93 2.10	0.90 0.98	2.39 2.45	9.92
2	11.76	1.61	7.22-8.70	5.72	1.86 2.08	0.90 0.99	2.44 2.51	9.92
3	11.51	1.66	7.37-8.99	6.46	1.88 2.09	1.01 1.02	2.48 2.52	9.59
	2-H br.s, 1H	3-Ph m, 5H	4-Het. m	4-H s, 1H	6-H 2d, 2H	7-C(Me)$_2$ s, 6H	8-H 2d, 2H	9-H br.s, 1H
4	12.64	7.38-7.48	7.07-8.33	5.36	1.94 2.14	0.82 0.99	2.38 2.48	10.05
5	12.53	7.30-7.43	7.13-8.60	6.06	1.85 2.11	0.79 0.99	2.42 2.55	10.20
6	12.35	7.33-7.38	7.10-8.88	6.75	1.80 2.10	0.85 1.00	2.42 2.54	9.91

Table 2. ^{13}C-NMR values of compounds 1-6 δ (ppm)

Compound	1	2	3	4	5	6
7-C(Me)$_2$	27.56 29.42	27.59 29.47	27.81 29.62	27.22 29.52	27.14 29.61	27.19 29.80
3-Me	9.98	10.33	10.48	-	-	-
C-8	41.64	41.70	41.88	41.48	41.60	41.71
C-7	33.56	32.57	28.85	32.66	32.52	32.60
C-6	50.99	50.96	51.32	50.95	50.96	51.31
C-5	193.51	193.69	193.31	193.45	193.71	193.69
C-4	32.65	32.57	32.66	33.88	32.70	32.60

Mass spectral analyses of these synthesized compounds were performed to confirm their structures. The MS spectra of compounds 1, 2, 3, 4, 5 and 6 revealed that, the m/z ratios obtained from the observed molecular ion peaks are 385, 358, 358, 370, 420 and 420, respectively. These values determine the molecular weights of the synthesized products. Both these molecular peaks and their subsequent general (a-a') fragmentation prove the proposed structures of the compounds (Figure 7 and Figure 8).

When the FT-IR spectra of the obtained compounds are examined, aromatic =C-H stretching, aliphatic C-H stretching, C=O stretching, C=N and C-N stretching vibrations characteristic for nitrogen-containing heterocyclic compounds are observed in the region characteristic for them. The strong primary amine absorption bands of the heteroaromatic amines used as starting materials in the reactions were not observed in the spectra of the products (Figure 9). Physical properties, yields and elemental analysis values of all synthesized compounds are given in Table 3.

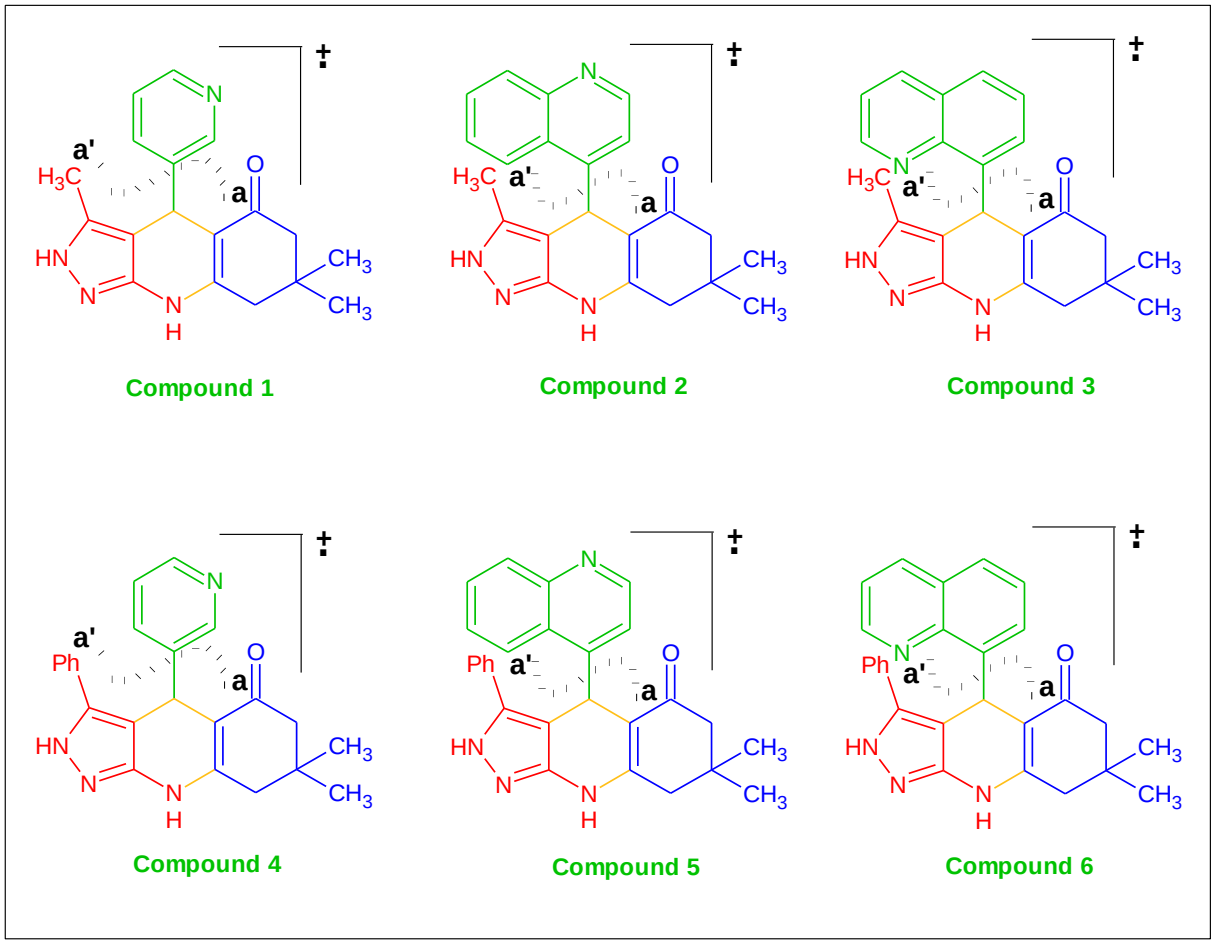


Figure 7. General fragmentations of compounds 1-6.

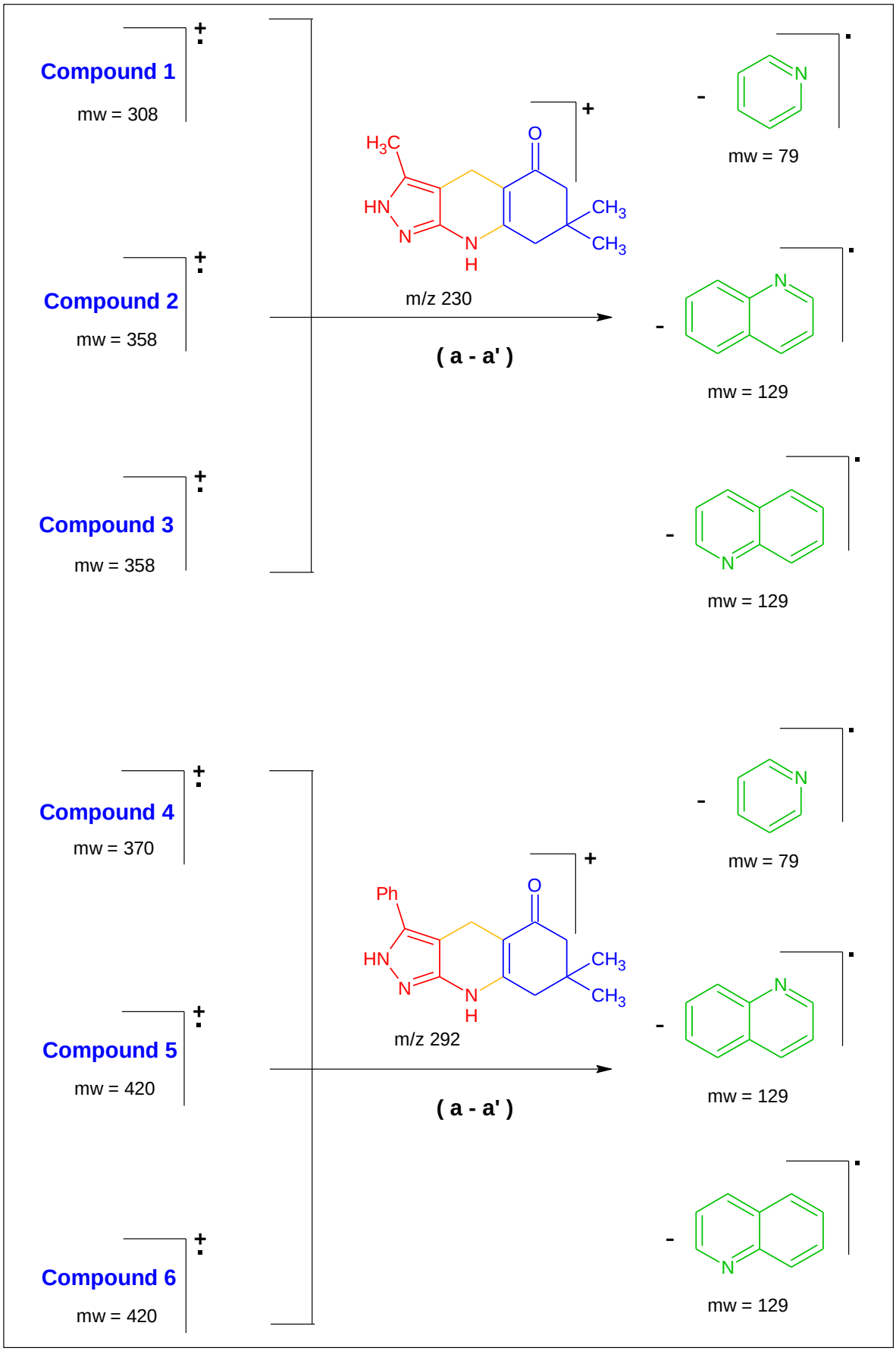


Figure 8. Comparison of fragmentation values of compounds 1-6.

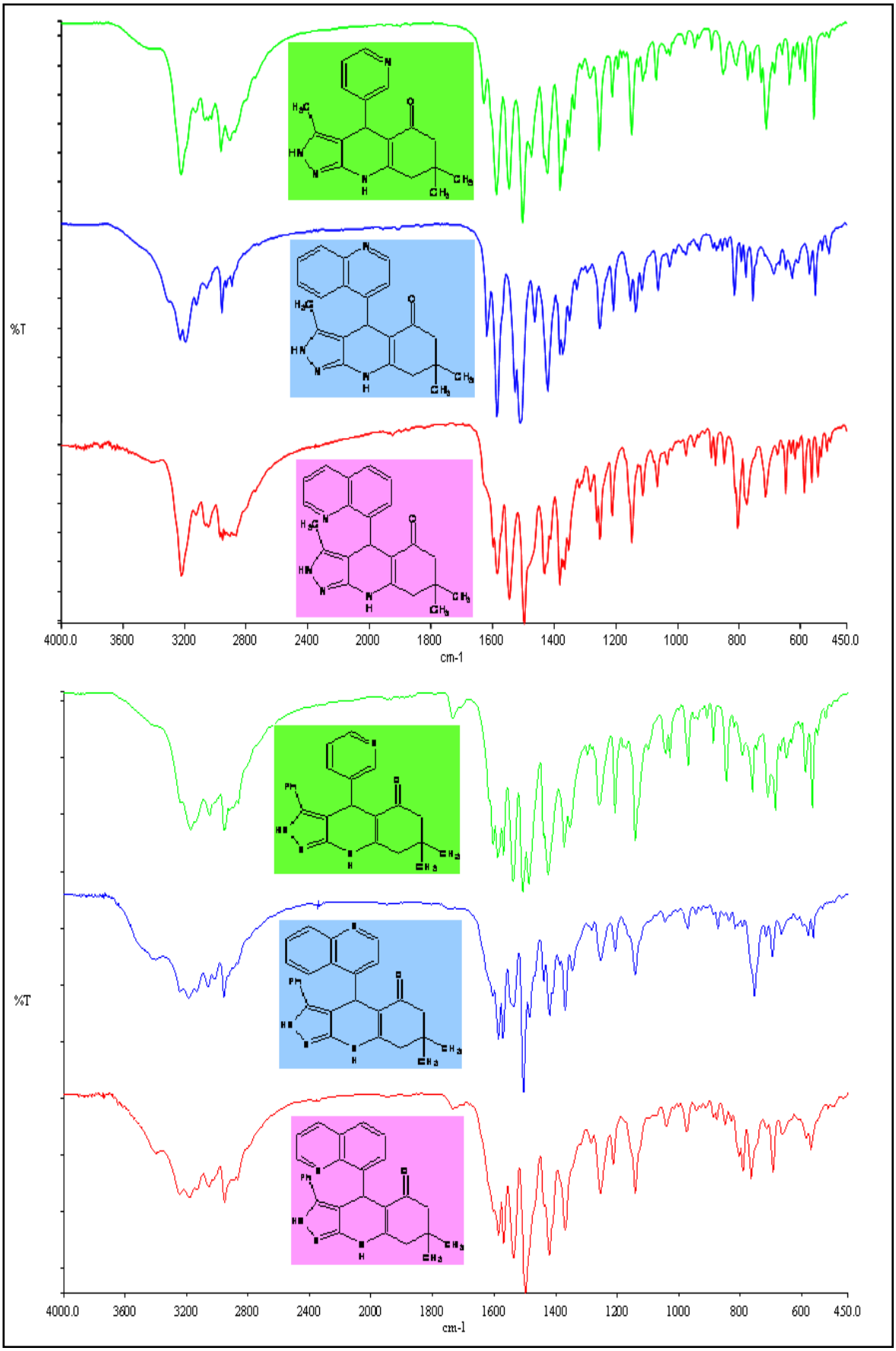


Figure 9. Comparison of FT-IR spectra of compounds 1-6.

Table 3. Physical properties, yields and elemental analysis values of compounds 1-6

Compound	Molecular formula	mw (g/mol)	Melting point (°C)	Yield (%)	Crystal shape	Crystal color	Elemental Analysis Calculated/Found		
							C	H	N
1	$C_{18}H_{20}N_4O$	308	307-8	83	powdered	light yellow	70.11 70.03	6.54 6.48	18.17 18.21
2	$C_{22}H_{22}N_4O$	358	304-5	72	powdered	light yellow	73.72 73.80	6.19 6.13	15.63 15.54
3	$C_{22}H_{22}N_4O$	358	301-2	78	powdered	light yellow	73.72 73.65	6.19 6.24	15.63 15.71
4	$C_{23}H_{22}N_4O$	370	298-9	70	powdered	light yellow	74.57 74.65	5.99 5.89	15.12 15.19
5	$C_{27}H_{24}N_4O$	420	225-6	63	powdered	light yellow	77.12 77.19	5.75 5.68	13.32 13.37
6	$C_{27}H_{24}N_4O$	420	270-1	68	powdered	light yellow	77.12 77.05	5.75 5.81	13.32 13.40

4. Conclusion

In conclusion, the synthesis of six compounds by one-pot multicomponent cycloaddition reaction technique was successfully carried out in this study. The crude products were obtained in very good yields and purified by crystallization. The structures of the compounds, which were found to be completely pure as a result of chromatographic studies, were elucidated by spectroscopic methods and elemental analysis.

Author Contributions

The percentages of the authors' contributions are presented below. All authors reviewed and approved the final version of the manuscript.

	M.K.G.	S.K.
C	80	20
D	80	20
S	10	90
DCP	90	10
DAI	80	20
L	90	10
W	80	20
CR	80	20
SR	80	20
PM	20	80
FA	20	80

C=Concept, D= design, S= supervision, DCP= data collection and/or processing, DAI= data analysis and/or interpretation, L= literature search, W= writing, CR= critical review, SR= submission and revision, PM= project management, FA= funding acquisition.

Conflict of Interest

The authors declared no conflict of interest.

Ethical Consideration

Ethics committee approval was not required for this study since there was no study on animals or humans.

Acknowledgements

This study is based on Mustafa Kemal Gümüş's doctorate thesis, conducted under the supervision of Şeniz Kaban.

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