



*Dedicated to the memory of
Academician Bogdan C. Simionescu (1948–2024)*

NEW SYNTHESIS ROUTE TOWARD UNEXPECTED QUINOLINE – SULFONAMIDE COMPOUND

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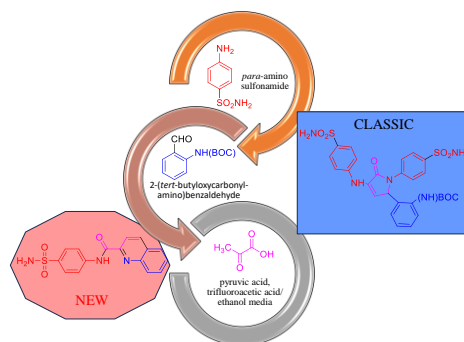
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In this investigation, we detail the conception and formation of an innovative sulfonamide-N-heterocycle framework. Employing a one-pot, three-component approach, we synthesized two new compounds, using trifluoroacetic acid as a highly effective catalyst. This method represents a progression in the Doebner reaction, leveraging aniline with electron-withdrawing substituents to yield quinolines. The technology provides numerous advantages, such as shortened reaction durations, a streamlined purification process, the use of a cost-effective catalyst, and the attainment of high product yields.

To validate both the structure and synthesis protocol, we employed various physicochemical techniques, including NMR, MS, FT-IR, and melting point analysis.



INTRODUCTION

Within the domain of drug design, nitrogenous molecules occupy a prominent role owing to their manifold advantages in comparison to their non-nitrogenous counterparts.¹ The introduction of nitrogen into a molecule elevates its basicity, thereby significantly augmenting its reactivity and interactions with other molecules.² Additionally, nitrogen atoms exhibit an exceptional ability to form robust hydrogen bonds with specific molecules, leading to an intensified affinity for

binding. Another noteworthy attribute of nitrogenous compounds is their inherent polarity. This characteristic can be strategically harnessed to finely adjust properties such as lipophilicity, water solubility, and oral absorption, thereby optimizing their overall pharmacological profile.³

Within the varied spectrum of nitrogenous heterocycles, the quinoline motif distinguishes itself as a pivotal element found in natural alkaloids exhibiting diverse biological functions.¹ The quinoline ring serves as the basis for potent malaria treatments, including quinine, chloroquine, mefloquine, and

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amodiaquine.⁴ Additionally, quinoline analogs exhibit potential in addressing cancer⁵ through various pathways,³ such as inhibiting tyrosine kinase, acting as alkylating agents, and inhibiting tubulin.⁶

Because altering the structure of a favored moiety with therapeutic properties significantly impacts its therapeutic value, developing new synthetic medicines based on the quinoline scaffold remains an active area of research.

Since the early discovery of sulfonamide-containing antibacterial medicines, the sulfonamide or sulfonyl functional groups have been crucial motifs in medicinal chemistry. The use of these groups in medicinal chemistry is indispensable, as they define a significant class of medications widely utilized in both agricultural and pharmaceutical applications.⁷ Due to their numerous biological applications, such as antibacterial,⁴ antifungal,⁸ anti-inflammatory,⁹ antioxidant,¹⁰ diuretics,¹¹ anticancer,¹² carbonic anhydrases,¹³ and antitumor and GSK inhibitors,¹⁴ sulfonamides have recently attracted significant interest in biology and medicine.

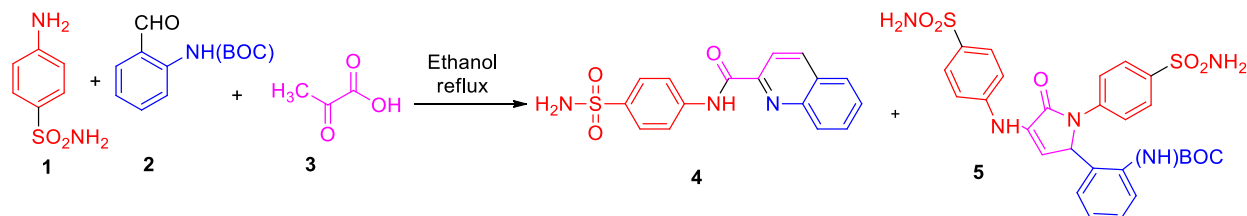
As part of our ongoing research in the area of nitrogen heterocyclic derivatives,^{15–20} we present herein the unexpected formation of a quinoline-sulfonamide derivative that emerged during our

attempt to synthesize a library of quinoline-4-carboxylic acids.

RESULTS AND DISCUSSION

In our previous attempts, starting from *para*-iodoaniline's reaction with different aldehydes, we successfully synthesized a library of 1H-pyrrol-2(5H)-one derivatives when ethanol was used as solvent¹⁶ and quinoline-4-carboxylic acids, when the reaction medium was changed to acetic acid²¹ as well as an unexpected structure when we used *ortho*-substituted aldehydes.

Under similar experimental conditions, starting from *para*-amino sulfonamide²² or *meta*-amino-sulfonamide²³ reacted with the same aldehydes we obtained in both solvents only 1H-pyrrol-2(5H)-one derivatives or, less frequently, 2-oxo-2,5-dihydrofuran derivatives.²² However, when we reacted *para*-amino sulfonamide (1) with the particular 2-(*tert*-butyloxycarbonyl-amino)benzaldehyde (2), pyruvic acid (3) and catalytic amount of trifluoroacetic acid in ethanol media (Scheme 1), a surprisingly new quinoline derivative **4** was formed, along with pyrrole derivative **5**.



Scheme 1 – Synthesis of compounds **4** and **5**.

Since this was not the first time for us when interesting compounds emerged from Doebner type reaction when “the right” *ortho*-substituted aldehyde was used,²⁴ we continued our investigation in elucidating the structure of this new quinoline derivative and explaining its formation.

Thus, for compound **4**, we can speculate that the presence of trifluoroacetic acid led to the *in situ* deprotection of the amine group which further underwent a convenient cyclization due to the favorable position of the nitrogen. On the other side, the amine group from sulfonamide reacted with the other part of the trifluoroacetic acid and led in the end to the formation of compound **4**, which features a quinolinic structure bearing a sulfonamide moiety.

Both newly synthesized compounds were analyzed by NMR (¹H-NMR, ¹³C-NMR, ¹H,¹H-

COSY, ¹H,¹³C-HSQC, ¹H,¹³C-HMBC, ¹H,¹⁵N-HMBC), FT-IR spectroscopies and mass spectrometry MALDI-MS.

The chemical structure for the compound **4** was deduced from 1D and 2D NMR spectra. Compared with the previous NMR profiles obtained by us from different Doebner type synthesis, the striking difference was the absence of the two doublets with 2 to 3 Hz vicinal coupling constant, resonating in the interval 6.00–6.80 ppm, excluding thus a potential 1H-pyrrol-2(5H)-one derivative.^{16,22} After a close inspection of the proton spectrum, we also excluded the formation of a quinoline-4-carboxylic acid derivative based on the absence of the characteristic substitution proton-pattern previously described by us for these compounds.²⁴ The proton spectrum (Fig. 1) recorded for compound **4** presents nine signals,

visible in the interval 7.2–11.2 ppm, suggesting an aromatic / heteroaromatic compound. All the signals

are well separated, with splitting patterns dictated by the first-order proton-proton couplings.

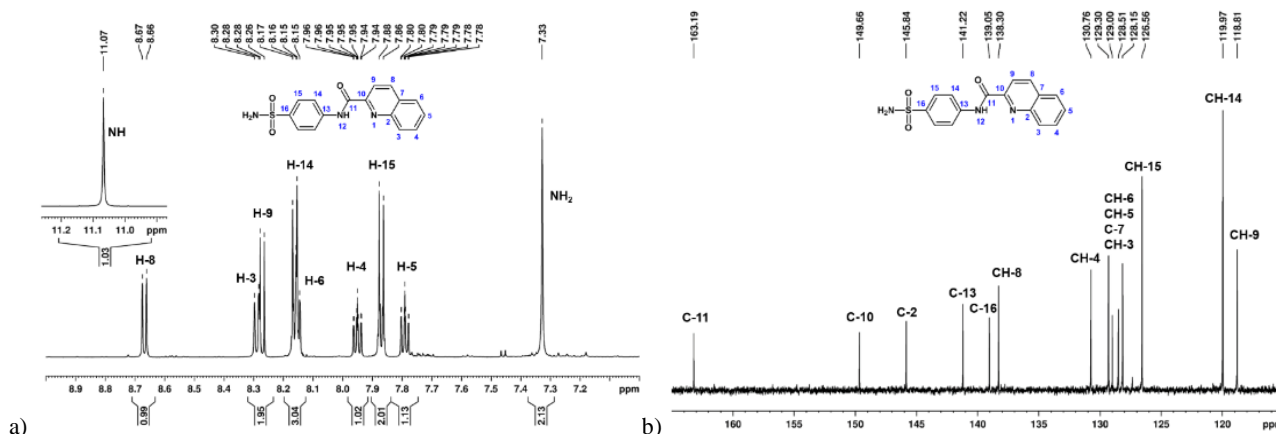


Fig. 1 – a) Display around the signal of interest from ^1H -NMR spectrum corresponding to newly synthesized compound **4**, recorded in DMSO-d_6 at 600 MHz. The signal resonating 11.07 ppm, assigned to NH proton, is included in the left-side insert; b) Display around the signal of interest from ^{13}C -NMR spectrum recorded for compound **4**, in DMSO-d_6 at 150 MHz.

The proton-proton correlations obtained in 2D COSY spectrum (Fig. 2) indicated three isolated spin systems. The first spin system was readily assigned to the 2-NH(BOC)benzaldehyde residue as it connected the two triplets of doublets from 7.79 ppm (H-5) and 7.95 ppm (H-4) with the two doublets from 8.14 ppm (H-6) and 8.29 ppm (H-3).

The second spin system, associated with amino-sulfonamide residue, contains the two doublets from 7.87 ppm (H-15) and 8.17 ppm (H-14), showing the roof-effect pattern characteristic to *para*-substitution. The remaining two doublets, from 8.27 ppm (H-9) and 8.67 ppm (H-8), form the last spin system present in the isolated derivative **4**.

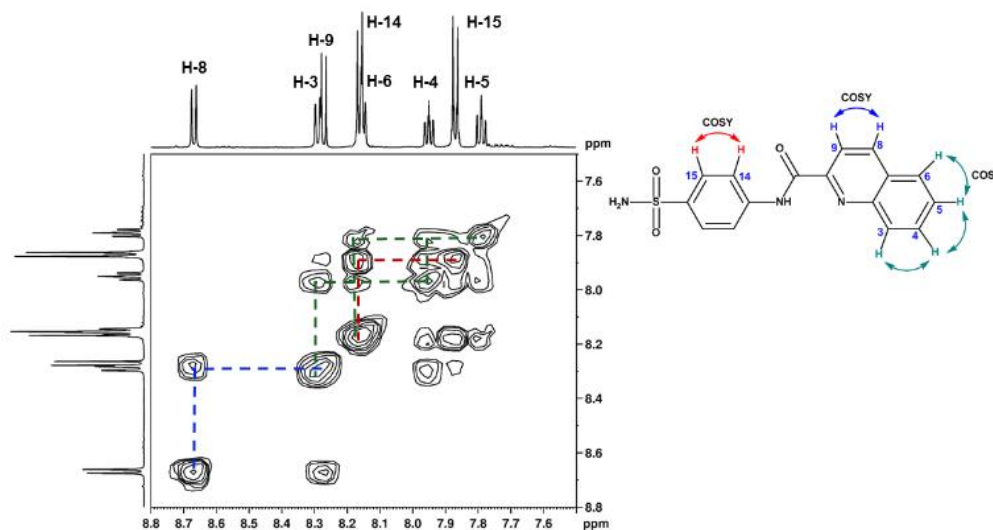


Fig. 2 – Detailed regions of H,H-COSY spectrum around the signals of interest, recorded for compound **4**, showing the three isolated spin systems.

In the proton-carbon direct correlations HSQC spectrum it was found that the two singlets from 7.33 and 11.07 ppm are not covalently linked to any carbon atom. This information, corroborated with the integral's ratio of 2:1, indicated us the existence of NH_2 and NH groups. In our previous studies, we used ^{15}N NMR to underline different structural modifications of newly

synthesized nitrogen-containing compounds.^{16,22–25} Thus, we recorded the proton-nitrogen HMBC spectrum for compound **4** (Fig. 3) to better understand the elements that build-up this new structure. Several correlation signals were visible in the 2D proton-nitrogen HMBC spectrum indicating the presence of three nitrogen atoms at 95.6, 125.0 and 302.5 ppm.

Based on the direct couplings generated by the presence of proton-nitrogen covalent bond (annotated on the spectrum in Fig. 3), we assigned the nitrogen atom from 95.6 ppm to sulfonamide NH₂ group and the nitrogen atom from 125.0 ppm to carboxamide NH group. The third nitrogen atom, resonating at 302.5 ppm, has a

three-bond interaction with protons H-3 and H-9 from two different spin systems, supporting a quinoline-like structure, as suggested in Scheme 1. It also has a four-bond correlation with the amidic NH proton, which validates the proximity of *para*-amino-sulfonamide residue.

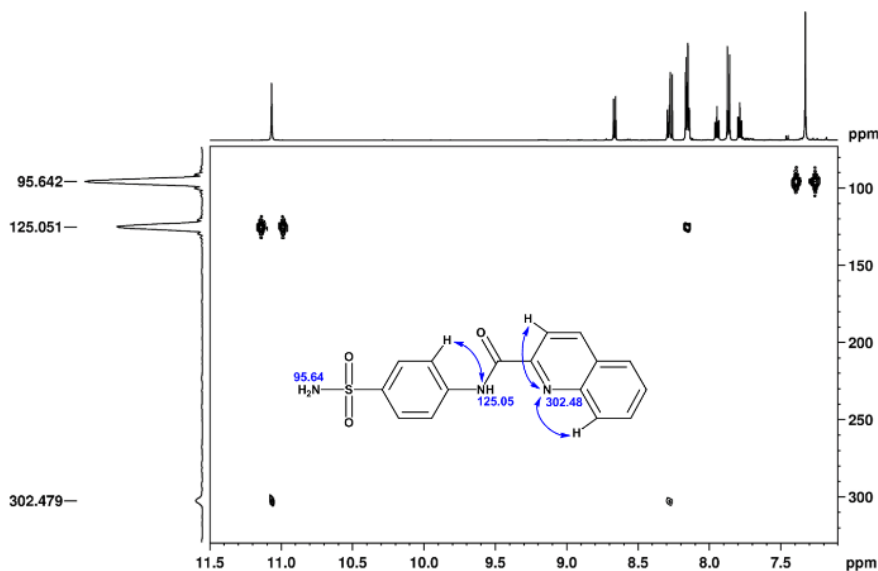


Fig. 3 – Detailed region of the ¹H,¹⁵N-HMBC spectrum around the signals of interest, recorded for compound **4**, showing the correlation signals generated by the three bonds proton-nitrogen couplings. The schematic representation of compound **4** structure with illustration of the proton-nitrogen HMBC couplings.

Valuable information that allowed us to deduce the structure proposed for compound **4** was obtained from long-range proton-carbon HMBC experiment,

all the correlations visible this spectrum as well as the direct proton-carbon correlations from HSQC, being centralized in Table 1.

Table 1

Proton-carbon interactions obtained experimentally in HSQC and HMBC spectra.

HSQC direct correlations (chemical shift, ppm)		
H-5 (7.79) – C-5 (128.5)	H-6 (8.14) – C-6 (128.1)	H-3 (8.29) – C-3 (129.3)
H-15 (7.87) – C-15 (126.5)	H-14 (8.17) – C-14 (119.9)	H-8 (8.67) – C-8 (138.3)
H-4 (7.95) – C-4 (130.4)	H-9 (8.27) – C-9 (118.8)	
HMBC long range correlations (chemical shift, ppm)		
C-14 (119.9) – NH	C-3 (129.3) – H-5	C-13 (141.2) – H-15, NH
C-6(128.1) – H-4, H-8	C-4 (130.7) – H-6	C-2 (145.8) – H-4, H-6, H-8
C-5 (128.5) – H-3	C-8 (138.3) – H-6	C-10 (149.7) – H-8
C-7 (129.0) – H-3, H-5, H-9	C-16 (139.0) – H-14, NH ₂	C-11 (163.2) – NH, H-8, H-9

For the second compound isolated from this reaction, compound **5**, the presence in the proton spectrum of two doublets at 6.19 and 6.56 ppm, with 3 Hz vicinal coupling constant, prompted us towards the 1H-pyrrol-2(5H)-one structure proposed in Scheme 1. This proposed chemical structure is based on the our previous experience with similar proton and

carbon spectral profiles, as we previously described in detail the algorithm for NMR characterization of several 1H-pyrrol-2(5H)-one derivatives bearing *para*-iodo-aniline¹⁶ or *para*-amino-sulfonamide residues.^{22,23} Herein, we included in Experimental Section the NMR parameters associated with compound **5**, without giving details about the signals

assignments that are based on proton-proton and proton-carbon bidimensional correlations.

The FTIR spectra of the obtained compounds shown important differences (Fig. 4) as follows: in the first part of the spectra (2800–3600 cm^{-1}) for compound **4** (quinolinic structure) we observed a split band in the range 3469–3440 cm^{-1} associated with an N-H band while for compound **5** this band appears at 3423 cm^{-1} as a single broad peak. Both spectra show small peaks associated with aromatic C-H bond and derivative **5** also shows a peak attributed to C-H aliphatic band.

The second region (400–1800 cm^{-1}) also displays differences in term of wavelength and shape of the peaks as follows: the amidic C=O and

N-H group appear at 1637 cm^{-1} in quinoline **4** while for compound **5** the band attributed to the tert-butoxycarbonyl protecting group appears in the interval 1599–1697 as a split band. Next interval is associated with sulphonamides moieties and C-N band and they appear both shifted and with modified appearance. All the other signals are in good agreement with the proposed structures.

We also performed MS to both compounds, to verify their molecular mass and as expected we found the signal corresponding to m/z 328 for compound **4** and at m/z 600 corresponding to compound **5** ($[M+H]^+$), thus verifying the proposed structures.

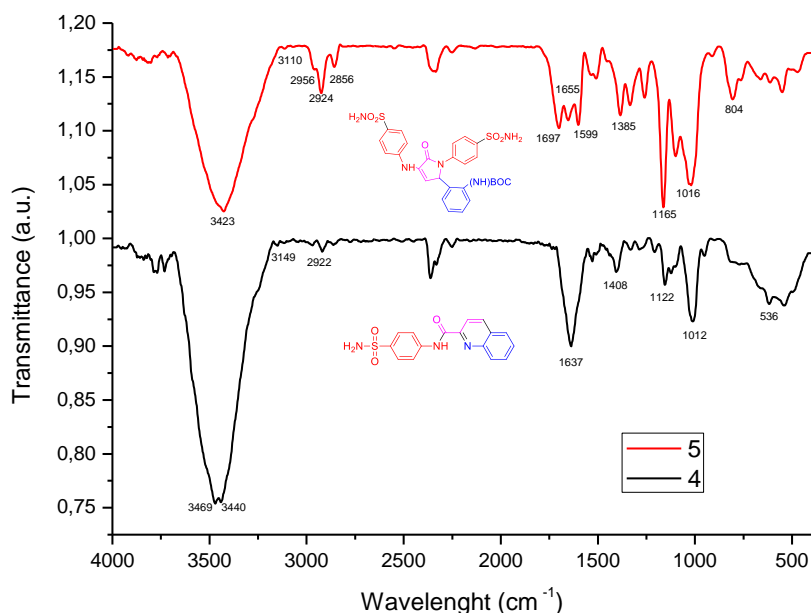


Fig. 4 – FT-IR spectra of compounds **4** and **5**.

EXPERIMENTAL

Chemistry

Analytical thin-layer chromatography was performed with commercial silica gel plates 60 F254 (Merck Darmstadt, Germany) and visualized with UV light ($\lambda_{\text{max}} = 254$ or 365 nm). The NMR spectra included in this study were recorded on Bruker Avance NEO 400 and 600 MHz spectrometers equipped with 5 mm four nuclei direct detection z-gradient probe (^1H , ^{13}C , ^1F , ^{29}Si -QNP) and 5 mm inverse detection multinuclear z-gradient probe respectively. Proton and carbon chemical shifts are reported in

δ units (ppm) relative to the residual solvent signal (ref: $\text{DMSO-}d_6$ ^1H , 2.51 ppm and ^{13}C , 39.47 ppm). ^1H , ^1H -COSY, ^1H , ^{13}C -HSQC and ^1H , ^{13}C -HMBC experiments were recorded using standard pulse sequences as delivered by Bruker with TopSpin 4.0.8 spectrometer control and processing software. The ^{15}N chemical shifts were obtained as projections from the 2D indirectly detected ^1H , ^{15}N -HMBC spectra and are referred to external liquid ammonia (0.0 ppm) using as external standard nitromethane (380.2 ppm). IR spectra were recorded on a Shimadzu IRTracer-100 instrument (Shimadzu U.S.A. Manufacturing, Inc., Canby, OR, USA). The melting point of the compounds measured on a MEL-TEMP capillary

melting point apparatus from ambient temperature up to 400 °C. All commercially available products were used without further purification unless otherwise specified.

Mass spectra were acquired on a Bruker Rapiflex MALDI-TOF (Bruker Daltonics, Bremen-GERMANY) equipped with a Smartbeam 3D laser.

The samples were dissolved in DMSO and then diluted 10 times in methanol. For the MALDI matrix solutions, 20 mg of α -cyano-4-hydroxycinnamic acid (HCCA) was dissolved in 1 ml methanol. Then, MALDI matrix solution and sample solution was mixed each other in 1:1, 2:1 and 4:1 ration and finally 1 μ L from each final solution was deposited onto the MALDI target, dried at room temperature and analyzed in MALDI-TOF-MS. Mass calibration of MALDI-TOF-MS was performed by the peptide mixture standard solution (Bruker Daltonics, Bremen-GERMANY).

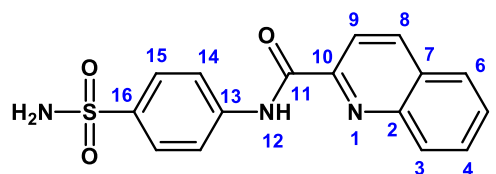
FlexControl (Bruker Daltonics, Version 4.0) was used to optimize and acquire data using the following parameters: positive ion polarity in reflector mode, mass scan range m/z 100–1600 Da), digitizer 1.25 GHz, detector voltage 2117 V, 1000 shots per pixel, and 5 kHz laser frequency. The laser power was set at 60% to 80% of the maximum and 1000 laser shots were accumulated for each spectrum. MS/MS fragmentation experiments were performed in LIFT mode using a Bruker standard fragmentation method.

General procedure for synthesis of compounds 4 and 5

In a 4 mL amount of ethanol, the NH(BOC)-benzaldehyde **2** (1 mmol) was combined with 1 mmol of *p*-amino benzenesulfonamide **1**. The

reaction mixture was stirred at room temperature for 20 minutes. Trifluoroacetic acid (20 μ L) and pyruvic acid **3** (1.5 mmol) in ethanol were then added to the mixture, which was then allowed to reflux for 12 hours at a catalytic rate. By removing the resultant suspension and washing the solid with ethanol, the necessary compound was produced. To aid in crystallization, dichloromethane and ethanol were utilized.

***N*-(4-Sulfamoylphenyl)quinoline-2-carboxamide 4**: Yellow solid; 23% yield; mp 205–208 °C; IR ATR $\nu(\text{cm}^{-1})$: 3469, 3440, 3149, 2922, 1637, 1527, 1408, 1336, 1284, 1207, 1155, 1122, 1012, 949, 766, 619, 536, 490.

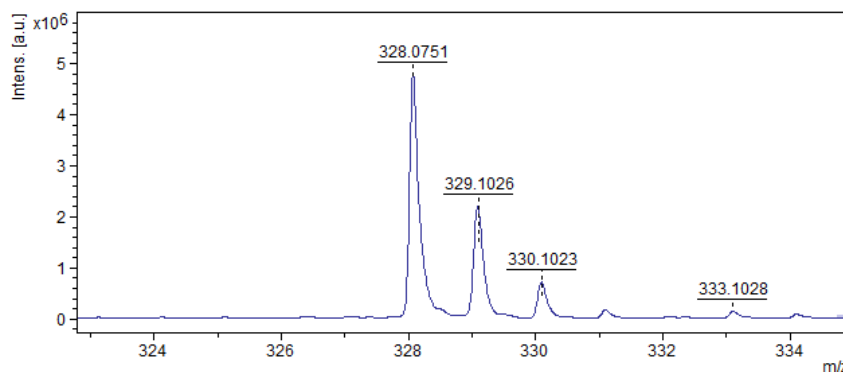


^1H NMR (DMSO- d_6 , 600.1 MHz, δ (ppm)): 7.32 (2H, s, NH₂), 7.79 (1H, td, $^3J = 7$ Hz, $^4J = 1$ Hz, H-5), 7.87 (2H, d, $^3J = 9$ Hz, H-15), 7.95 (1H, td, $^3J = 7$ Hz, $^4J = 1$ Hz, H-4), 8.14 (1H, d, $^3J = 7$ Hz, H-6), 8.17 (2H, d, $^3J = 9$ Hz, H-14), 8.27 (1H, d, $^3J = 9$ Hz, H-9), 8.29 (1H, d, $^3J = 7$ Hz, H-3), 8.67 (1H, d, $^3J = 9$ Hz, H-8), 11.07 (1H, s, NH-12).

^{13}C NMR (DMSO- d_6 , 150.9 MHz, δ (ppm)): 118.8 (CH-9), 119.9 (CH-14), 126.5 (CH-15), 128.1 (CH-6), 128.5 (CH-5), 129.0 (C-7), 129.3 (CH-3), 130.7 (CH-4), 138.3 (CH-8), 139.0 (C-16), 141.2 (C-13), 145.8 (C-2), 149.7 (C-10), 163.2 (CO-11).

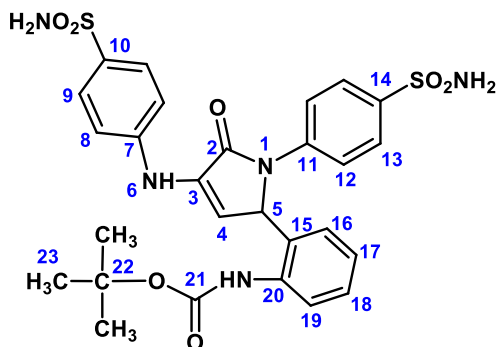
^{15}N NMR (DMSO- d_6 , 60.8 MHz, δ (ppm)): 95.6 (NH₂), 125.0 (NH), 302.5 (N)

HRMS (MALDI-TOF/TOF) m/z calcd for $[\text{M}+\text{H}]^+$ 328.0755, found 328.0751.



Tert-butyl (2-(5-oxo-1-(4-sulfamoylphenyl)-4-((4-sulfamoylphenyl)amino)-2,5-dihydro-1H-pyrrol-2-yl)phenyl)carbamate 5: Brown solid; 40 %

yield; mp 270–271 °C; IR ATR $\nu(\text{cm}^{-1})$: 3423, 3110, 2956, 2924, 2856, 1697, 1655, 1599, 1508, 1385, 1331, 1255, 1165, 1095, 1016, 804, 761, 663, 613, 549, 469.

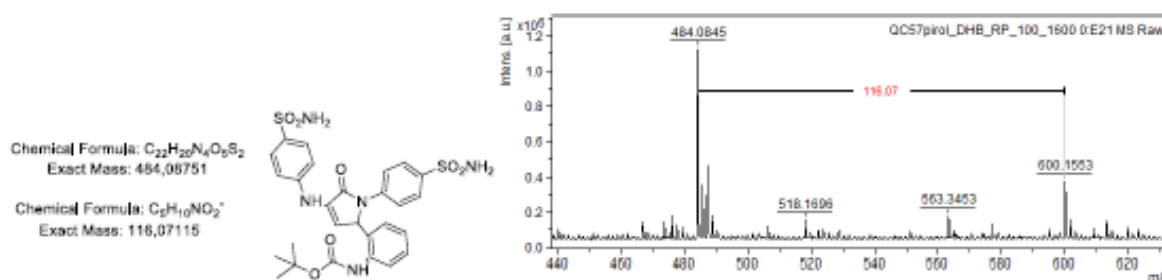


^1H NMR (DMSO- d_6 , 600.1 MHz, δ (ppm)): 1.54 (9H, s, $3\times\text{CH}_3$ -23), 6.19 (1H, d, $^3J = 3$ Hz, H-5), 6.56 (1H, d, $^3J = 3$ Hz, H-4), 6.86 (1H, d, $^3J = 8$ Hz, H-16), 7.07 (1H, t, $^3J = 8$ Hz, H-17), 7.18 (2H, s, NH_2 -10), 7.22 (1H, t, $^3J = 8$ Hz, H-18), 7.27 (2H, s, NH_2 -14), 7.29 (1H, d, $^3J = 8$ Hz, H-19), 7.35 (2H, d, $^3J = 9$ Hz, H-8), 7.70 (2H, d, $^3J = 9$ Hz, H-9), 7.72 (2H, d, $^3J = 9$ Hz, H-13), 7.77 (2H, d, $^3J = 9$ Hz, H-12), 8.73 (1H, s, NH -6), 9.17 (1H, bs, NH -20).

^{13}C NMR (DMSO- d_6 , 100.6 MHz, δ (ppm)):

28.1 ($3\times\text{CH}_3$), 57.9 (CH-5), 79.3 (C-22), 112.5 (CH-4), 115.9 (CH-8), 119.7 (CH-12), 125.2 (CH-16), 126.4 (CH-13), 126.7 (CH-17), 127.0 (CH-9), 127.8 (CH-19), 128.2 (CH-18), 131.5 (C-3), 132.3 (C-15), 135.3 (C-10), 136.3 (C-20), 139.1 (C-14), 139.9 (C-11), 144.9 (C-7), 154.6 (CO-21), 166.7 (CO-2).

HRMS (MALDI-TOF/TOF) m/z calcd for $[[\text{M}+\text{H}]^+ 600.15419$, found 600.1553 (we highlighted the fragmentation due to tert-butoxycarbonyl protecting group).



CONCLUSIONS

This study presents the design and synthesis of a novel sulfonamide-quinoline scaffold. The compound was produced utilizing a one-pot, two-component technique, with trifluoroacetic acid serving as an efficient catalyst. The applicable method is an advancement in the Doebner reaction, which involves aniline derivatives with electron-withdrawing substituents to produce quinolines. This technology offers many benefits, including reduced reaction times, simplified purification process, use of cost-effective catalyst, and high product yields.

The obtained compounds were characterized by physicochemical techniques (^1H -NMR, ^{13}C -NMR, MS, FT-IR and melting point) in order to confirm the structure and the synthesis procedure.

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REFERENCES

1. Diaconu, D.; Antoci, V.; Mangalagiu, V.; Amariucăi-Mantu, D.; Mangalagiu, I., *Sci. Rep.*, **2022**, *12*, 1–17. <https://doi.org/10.1038/s41598-022-21435-6>.
2. Tiglani, D.; Salahuddin; Mazumder, A.; Yar, M. S.; Kumar, R.; Ahsan, M. J., *Polycycl. Aromat. Compd.*, **2021**, *0*, 1–23. <https://doi.org/10.1080/10406638.2021.1942933>.
3. Li, W.; Xu, F.; Shuai, W.; Sun, H.; Yao, H.; Ma, C.; Xu, S.; Yao, H.; Zhu, Z.; Yang, D. H.; Chen, Z. S.; Xu, J., *J. Med. Chem.*, **2019**, *62*, 993–1013. <https://doi.org/10.1021/acs.jmedchem.8b01755>.
4. Konda, S.; Raparthi, S.; Bhaskar, K.; Munaganti, R. K.; Guguloth, V.; Nagarapu, L.; Akkewar, D. M., *Bioorg. Med. Chem. Lett.*, **2015**, *25*, 1643–1646. <https://doi.org/10.1016/j.bmcl.2015.01.026>.
5. Moldoveanu, C.; Mangalagiu, I. I.; Zbancioc, G.; Danac, R.; Tataringa, G.; Zbancioc, A. M., *Molecules*, **2025**, *30*, 702. <https://doi.org/10.3390/molecules30030702>.
6. Oniciuc, L.; Amăriucăi-Mantu, D.; Diaconu, D.; Mangalagiu, V.; Danac, R.; Antoci, V.; Mangalagiu, I., *Int.*

- J. Mol. Sci.*, **2023**, *24*, 8124. <https://doi.org/10.3390/ijms24098124>.
7. Majumdar, K. C.; Mondal, S., *Chem. Rev.*, **2011**, *111*, 7749–7773. <https://doi.org/10.1021/cr1003776>.
 8. Lal, J.; Gupta, S. K.; Thavaselvam, D.; Agarwal, D. D., *Eur. J. Med. Chem.*, **2013**, *64*, 579–588. <https://doi.org/10.1016/j.ejmech.2013.03.012>.
 9. Bano, S.; Javed, K.; Ahmad, S.; Rathish, I. G.; Singh, S.; Alam, M. S., *Eur. J. Med. Chem.*, **2011**, *46*, 5763–5768. <https://doi.org/10.1016/j.ejmech.2011.08.015>.
 10. Ning, X.; Guo, Y.; Ma, X.; Zhu, R.; Tian, C.; Zhang, Z.; Wang, X.; Ma, Z.; Liu, J., *Bioorg. Med. Chem.*, **2013**, *21*, 5589–5597. <https://doi.org/10.1016/j.bmc.2013.05.043>.
 11. Allen, H. B.; Lee, D. A., *Curr. Med. Res. Opin.*, **1973**, *1*, 547–553. <https://doi.org/10.1185/03007997309111720>.
 12. Ghorab, M. M.; Alsaïd, M. S.; El-Gaby, M. S. A.; Safwat, N. A.; Elaasser, M. M.; Soliman, A. M., *Eur. J. Med. Chem.*, **2016**, *124*, 299–310. <https://doi.org/10.1016/j.ejmech.2016.08.060>.
 13. Angeli, A.; Kartsev, V.; Petrou, A.; Lichitsky, B.; Komogortsev, A.; Pinteala, M.; Geronikaki, A.; Supuran, C. T., *Pharmaceuticals*, **2022**, *15*, 316–339. <https://doi.org/10.3390/ph15030316>.
 14. Akurathi, V.; Dubois, L.; Celen, S.; Lieuwes, N. G.; Chitneni, S. K.; Cleynhens, B. J.; Innocenti, A.; Supuran, C. T.; Verbruggen, A. M.; Lambin, P.; Bormans, G. M., *Eur. J. Med. Chem.*, **2014**, *71*, 374–384. <https://doi.org/10.1016/j.ejmech.2013.10.027>.
 15. Al Matarneh, C. M.; Ciobanu, C. I.; Apostu, M. O.; Mangalagiu, I. I.; Danac, R., *Comptes. Rendus Chim.*, **2018**, *21*, 1–8. <https://doi.org/10.1016/j.crci.2017.11.003>.
 16. Al-Matarneh, C. M.; Nicolescu, A.; Marinaș, I. C.; Chifiriuc, M. C.; Shova, S.; Sillion, M.; Pinteala, M., *Future Med. Chem.*, **2023**, *15*, 1369–1391. <https://doi.org/10.4155/fmc-2023-0121>.
 17. Al Matarneh, C. M.; Sardaru, M. C.; Apostu, M. O.; Rosca, I.; Ciobanu, C. I.; Mangalagiu, I. I.; Danac, R., *Stud. Univ. Babeș-Bolyai Chem.*, **2019**, *64*, 67–80. <https://doi.org/10.24193/subbchem.2019.3.06>.
 18. Al Matarneh, C.; Ciobanu, C. I.; Mangalagiu, V.; Zbancioc, G.; Danac, R., *Rev. Chim. (Bucharest)*, **2020**, *71*, 287–293. <https://doi.org/10.37358/RC.20.3.7999>.
 19. Al-Matarneh, C.; Rosca, I.; Shova, S.; Danac, R., *J. Serbian Chem. Soc.*, **2021**, *86*, 901–915. <https://doi.org/10.2298/jsc200819057a>.
 20. Sardaru, M.-C.; Al Matarneh, C.-M.; Simionescu, N.; Mangalagiu, I. I.; Pinteala, M.; Danac, R., *Rev. Roum. Chim.*, **2024**, *69*, 63–74. <https://doi.org/10.33224/rrch.2024.69.1-2.08>.
 21. Al-Matarneh, C. M.; Nicolescu, A.; Marinaș, I. C.; Găboreanu, M. D.; Shova, S.; Dascălu, A.; Sillion, M.; Pinteală, M., *Molecules*, **2024**, *29*, 772. <https://doi.org/10.3390/molecules29040772>.
 22. Al-Matarneh, C. M.; Pinteala, M.; Nicolescu, A.; Sillion, M.; Mocchi, F.; Puf, R.; Angeli, A.; Ferraroni, M.; Supuran, C. T.; Zara, S.; Carradori, S.; Paoletti, N.; Bonardi, A.; Gratteri, P., *J. Med. Chem.*, **2024**, *67*, 3018–3038. <https://doi.org/10.1021/acs.jmedchem.3c02190>.
 23. Al-Matarneh, C. M.; Simionescu, N.; Nicolescu, A.; Sillion, M.; Angeli, A.; Paoletti, N.; Bonardi, A.; Gratteri, P.; Pinteala, M.; Supuran, C. T., *J. Med. Chem.*, **2025**, *68*, 1863–1882. <https://doi.org/10.1021/acs.jmedchem.4c02586>.
 24. Al-Matarneh, C. M.; Nicolescu, A., *Molbank*, **2024**, *2024*, M1841. <https://doi.org/10.3390/m1841>.
 25. Georgescu, E.; Nicolescu, A.; Georgescu, F.; Shova, S.; Teodorescu, F.; Macsim, A.-M.; Deleanu, C., *Synthesis (Stuttg)*, **2015**, *47*, 1643–1655. <https://doi.org/10.1055/s-0034-1380185>.