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Synthesis and Reactions of Bis Amino Pyrroles Based Benzoin

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تحضير وتفاعلات مركبات ثنائي أمينو بيرول اعتمادا على البنزوين

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Abstract:
A series of diamines, including ethane-1,2-diamine, hydrazine hydrate, and isomeric phenylenediamines (o-, m-, p-) as well as benzidine, were reacted with benzoin in the presence of malononitrile and pyridine catalyst. The reactions primarily yielded bis-pyrrole derivatives (I, III, IV, and VI), except for ethane-1,2-diamine, which predominantly formed a furan derivative (II). In contrast, hydrazine hydrate and o-phenylenediamine did not produce bis-pyrroles, instead yielding a hydrazone derivative (V) and a quinoxaline derivative (VII), respectively. Further derivatization of selected bis-pyrroles (I, IV) and the furan compound (II) with acetic anhydride afforded the corresponding amide derivatives (VIII, IX, and X). All syntheses were performed under mild conditions using straightforward procedures, yielding moderate product quantities. The synthesized compounds (I–X) were thoroughly characterized by melting point analysis, TLC, IR, ^{1}H NMR (including D_2O exchange), ^{13}C NMR, and APT techniques.

Keywords: Pyrrole, Benzoin, Malononitrile, Nucleophilic Addition, Diamines, Bis-Pyrroles, Furan Derivatives.

الملخص
تم تفاعل سلسله من ثنائيات الامين الإيثان-1,2-ثنائي الامين، هيدرات الهيدرازين، 2,1- فينلين ثنائي الامين، 1,3- فينلين ثنائي الامين، 1,4- فينلين ثنائي الامين والبنزيدين مع البنزوين فى وجود مركب مالونونيتريل وحفاز البيريدين. أسفر التفاعل بشكل اساسي عن مشتقات ثنائي البيرول(*I, III, IV*) و (*VI*)ومع ذلك ، نتج عن تفاعل الايثان-2,1-ثنائي الأمين ايضا المركب (*II*) كناتج أساسي .على النقيض من ذلك، لم نتنج تفاعلات هيدرات الهيدرازين و2,1- فينلين ثنائي الامين مركبات ثنائي البيرول بل تكون مشتق الهيدرازون (*V*) والكينوكسالين (*VII*) على التوالي .بعد ذلك تم تفاعل مركبات ثنائي البيرول (*I*، *IV*) والمركب (*II*) مع أنهيدريد حمض الخليك للحصول على مشتقات الأميد المقابلة (*VIII*، *IX*، *X*). تم تنفيذ جميع عمليات التخليق تحت ظروف معتدلة باستخدام طرق مباشرة، وأعطت نتائج متوسطة النتائج. تم توصيف المركبات المُخلَّقة (*I-X*) باستخدام نقاط الانصهار، وكروماتوغرافيا الطبقة الرقيقة (*TLC*)، ومطياف والأشعة تحت الحمراء (*IR*)، والرنين المغناطيسي النووي للبروتون (*H-NMR*1)بما في ذلك تبادل (*D2O*) والرنين المغناطيسي النووي للكربون (*C-NMR*13)، وتقنية *APT*.

الكلمات المفتاحية: بيرول، بنزوين، مالونتريل، إضافة نيكلوفيلية، أمينات ثنائية، ثنائي البيرول، مشتقات الفوران.

Introduction

Pyrroles are among the most significant heterocyclic compounds due to their prevalence in numerous natural and synthetic molecules with remarkable pharmacological and material science applications [1]. These five-membered nitrogen-containing rings exhibit diverse biological activities, including antifungal, antibacterial, anticonvulsant, anti-inflammatory, antihypertensive, antioxidant, antitumor, and immunosuppressant properties [2].

Notable natural pyrrole-containing compounds include heme derivatives, chlorophyll (comprising four pyrrole units linked by methine bridges), bile pigments, vitamin B12, and marine-derived pyrrole alkaloids. Given the broad utility of pyrrole derivatives and their well-documented biological significance [3–6], the design of novel heterocyclic systems based on this scaffold presents a compelling research direction. A synthetic approach utilizing cost-effective and readily available laboratory chemicals, such as benzoin, under optimized reaction conditions ensures straightforward workup procedures and high yields. Such a strategy facilitates the efficient production of new pyrrole-based compounds with potential applications in medicinal and industrial chemistry.

Material and methods

Materials

All chemicals were purchased from Sigma Aldrich (St. Louis, Mo, USA) and were used as received. Reactions were monitored on TLC (Chloroform /methanol). 1H NMR spectra were carried out in the Centre for drug discovery research & development at ain shams university on Bruker 400 MHz with chemical shift (δ) expressed in ppm downfield from tetramethylsilane as an internal stander (δ TMS = 0) using CDCl3 and DMSO-d6 as a solvent. The multiplicity of the signal is as following: s (Singlet), d (Doublet), t (Triplet), q (Quartet), m (Multiplet).13C-NMR were measured in the Centre for drug discovery research & development at ain shams university on Bruker 100 MHz with internal reference TMS δ = 0. Infrared spectra were recorded in the National Research Centre (NRC) at Giza using a Perkin Elmer 2000 FT-IR system spectrometer, where the positions of absorptions have been expressed in wave number units (cm-1). Melting points (m.p) of the synthesized compounds were measured in capillary tubes using Stuart scientific apparatus and are uncorrected.

Methods

a) Reaction of benzoin with diamines (I-VII)

In a 100 ml round-bottom vial with a capacitor and a magnetic drive, a mixture of benzoin (0.02 mol), suitable diamine (0.01 mol), concentrated hydrochloric acid (10-14 drops) in ethanol (30 ml) were heated under reflux for eight minutes, Malononitrile (0.66 ml, 0.02 mol), followed by drops (1 ml) of pyridine were added as a catalyst and left to reflux until a solid formed. the resulting solid was filtered, dried and purified by recrystallization from ethanol to afford compounds (I-VII).

b) Reaction of acetic anhydride with bis amino pyrroles (VIII-X)

(0.01 mol) of bis-amino pyrrole (I, IV) and compound (II) was dissolved in excess acetic anhydride and stirred at room temperature for 24 hours until precipitation occurred. The resulting precipitate was filtered under vacuum thoroughly washed and dried then recrystallized from an appropriate solvent to afford pure Compound VIII, IX. and X.

Results and Discussion

Results

1,1'-(ethane-1,2-diyl)bis(2-amino-4,5-diphenyl-1H-pyrrole-3-carbonitrile) (I): yield 39.25% as a white solid, p.m., 299- 300°C. IR (KBr): vmax (Cm-1) = 1234.00 (C-N), 2187.47 (CN), 3215.37 – 3366.87 (NH2). 1H-NMR (DMSO-d6): δ = 2.80 (t, 2H, CH2), 3.96 (t, 2H, CH2), 6.34 (s, 2H, NH2), 7.08 –7.39 (m, 20H, Ar-H), 8.04 (s, 2H, NH2). 13C-NMR (DMSO-d6): δ = 37.79 (2C), 71.33 (2C), 118.34 (2C), 120.53 (2C), 123.65 (2C), 126.61 (2C), 128. 54 (4C), 128.70 (4C), 128.81 (4C), 129.21 (4C), 131.22 (2C), 131.84 (2C), 133.92 (2C), 148.65 (2C).

2-amino-4,5-diphenylfuran-3-carbonitrile (II): yield 44.11% as a white solid, p.m., 201- 203.5°C. FT-IR: v (cm-1) = 2213.68 (CN), 3061.05 (Ar-CH), 3311.02 – 3464.24 (NH2). 1H-NMR (DMSO-d6): δ = 7.15 – 7.47 (m, 10H, Ar-H), 7.73 (s, 2H, NH2). 13C-NMR (DMSO-d6): δ = 69.79 (1C), 116.02 (1C), 122.28 (1C), 124.75 (2C), 127.36 (1C), 128.78 (4C), 129.03 (1C), 129.33 (1C), 129.42 (1C), 129.89 (1C), 131.71 (1C), 137.20 (1C), 164.04 (1C).

1,1'-([1,1'-biphenyl]-4,4'-diyl)bis(2-amino-4,5-diphenyl-1H-pyrrole-3-carbonitrile) (III): yield 14.2% as an orange solid, m.p.,188-190 ºC. FT-IR: v (cm-1) = 1204.86 (C-N), 2214.18 (CN), 3061.84 (Ar-CH), 3311.70 – 3439.14 (NH2). 1H-NMR (CDCl3): δ = 5.05 (s, 4H, NH2), 7.21-7.28 (m, 14H, Ar-H), 7.36-7.47 (m, 14H, Ar-H). 13C-NMR (CDCl3) = δ = 73.13 (2C), 115.15 (2C), 121.66 (4C), 125.30 (4C),

125.48 (2C), 126.11 (2C), 127.40 (2C), 128.34 (4C), 128.46 (4C), 128.94 (2C), 128.99 (2C), 129.05 (2C), 129.41 (2C), 129.51 (2C), 129.93 (2C), 131.02 (2C), 134.94 (2C), 139.52 (2C), 161.91 (2C).

1,1'-(1,4-phenylene)bis(2-amino-4,5-diphenyl-1H-pyrrole-3-carbonitrile) (IV): yield 8.5 % as a gray solid, p.m., 191- 193 ºC. FT-IR: v (cm-1) = 1205.31 (C-N), 2214.68 (CN), 3061.70 (Ar-CH), 3312.94-3440.19 (NH2). 1H-NMR (CDCl3): δ = 4.91 (s, 4H, NH2), 7.20 – 7.28 (m, 12H, Ar-H), 7.36-7.47 (m, 12H, Ar-H). 13C-NMR (CDCl3): δ = 115.12 (2C), 121.67(2C), 125.30 (2C), 125.45 (2C), 127.41 (4C) ,128.35 (4C), 128.46 (2C), 128.95 (4C), 129.00 (4C), 129.51 (4C), 131.02 (2C), 132.50 (2C), 139.55 (4C), 161.86 (2C).

2,2'-(hydrazine-1,2-diylidene)bis(1,2-diphenylethan-1-one) (V): yield 18.6% as a yellow solid, p.m., 202.2-203.7 ºC. FT-IR: v (cm-1) = 1593.26 (C=N), 1677.22 (C=O), 3064.44 (Ar- CH). 1H-NMR (CDCl3): δ = 7.25-7.40 (m, 6H, Ar-H), 7.51 – 7.64 (m, 10H, Ar-H), 7.97 – 7.99 (m, 4H, Ar-H). 13C-NMR (CDCl3): δ = 197.42 (2C), 167.08 (2C), 135.56 (2C), 134.13 (2C), 132.26 (2C), 131.75 (4C), 129.24 (2C), 129.06 (4C), 128.72 (4C), 128.14 (4C).

1,1'-(1,3-phenylene)bis(2-amino-4,5-diphenyl-1H-pyrrole-3-carbonitrile) (VI): yield 14.4% as a gray solid, p.m., 189.5- 190.5 ºC. 1H-NMR (CDCl3): δ = 4.96 (s, 4H, NH), 7.22–7.28 (m, 12H, Ar-H), 7.36-7.45 (m, 12H, Ar-H). 13C-NMR (CDCl3): δ = 90.19 (2C) ,113.11 (3C), 125.47(1C), 125.76 (1C), 125.87 (1C) ,128.25 (2C), 128.35 (2C) ,128. 50 (4C), 128.71 (2C), 128.98 (2C), 129.03 (1C), 129.21 (1C), 129.30 (1C), 129.48 (1C), 129.53 (1C), 129.64 (1C) ,130.14 (4C), 132.68 (2C), 132.82 (2C) ,134.35 (2C) ,137.32 (2C), 169.96 (2C).

2,3-diphenylquinoxaline (VII): yield 25.3 % as a white solid, p.m., 123.5-125.5 ºC. 1H-NMR (CDCl3): δ = 7.28 –7.44 (m, 6H, Ar-H), 7.54 –7.56 (m, 4H, Ar-H), 7.81–7.83 (m, 2H, Ar-H), 8.26–8.27 (m, 2H, Ar-H) .13C-NMR (CDCl3): δ = 128.33 (4C), 129.00 (2C), 129.04 (2C), 129.93 (2C), 130.27 (4C), 138.57 (2C), 140.92 (2C), 153.35 (2C).

N,N'-(ethane-1,2-diylbis(3-cyano-4,5-diphenyl-1H-pyrrole-1,2-diyl))diacetamide (VIII): yield15.2 % as a white solid, p.m., 272 – 274 ºC. 1H-NMR (CDCl3): δ = 1.68 (s, 3H, CH3), 2.15 (s, 3H, CH3), 3.00 – 3.01 (d, d, 2H, CH2), 3.78 (t, 2H, CH2), 7.11 – 7.42 (m, 20H, Ar-H), 7.86 (t, 1H, NH), 10.10 (s, 1H, NH). 13C-NMR (CDCl3): δ = 22.90 (1C), 23.04 (1C), 43.42 (2C), 89.01 (2C), 116.10 (2C), 122.60 (2C), 127.19 (4C), 128.77 (4C), 129.02 (4C), 129.24 (4C), 130.59 (4C) ,131.60 (2C), 133.02 (2C), 134.41 (4C), 170.15 (1C), 170.61 (1C).

N-(3-cyano-4,5-diphenylfuran-2-yl)acetamide (IX): yield15.8% as a white solid, p.m., 193.5–195 ºC. IR (KBr): vmax (Cm-1) = 1694.16 (C=O), 2223.52 (CN), 3057.58 (Ar-CH), 3223.43-3443.28 (NH). 1H-NMR (CDCl3): δ = 2.29 (s, 3H, CH3), 7.3 –7.43 (m, 10H, Ar-H), 8.39 (s, 1H, NH). 13C-NMR (CDCl3): δ = 23.39 (1C), 112.80 (1C), 122.29 (1C), 126.06 (2C), 128.57 (2C), 128.61 (2C), 128.68 (2C), 128.74 (2C), 129.07 (2C), 129.21 (2C), 129.99 (1C), 150.14 (1C).

N,N'-(1,4-phenylenebis(3-cyano-4,5-diphenyl-1H-pyrrole-1,2-diyl))diacetamide (X): yield 9.5 % as a white solid, p.m., 192– 194 ºC. 1H-NMR (CDCl3): δ = 2.28 (s, 6H, CH3) , 7.27–7.34 (m, 24H, Ar-H) , 8.38 (s, 2H, HN). 13C-NMR (CDCl3): δ = 23.09 (2C), 112.81 (2C), 122.27 (2C), 126.05 (2C), 128.55 (8C), 128.60 (6C), 128.69 (6C), 128.74 (4C), 129.07 (2C), 129.20 (2C), 129.99 (4C), 150.10 (2C), 182.98 (2C).

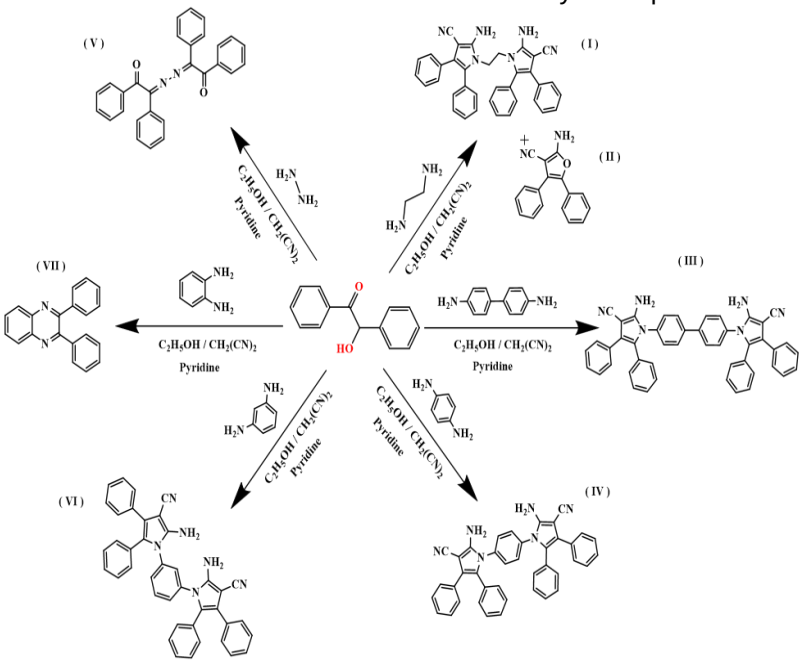
Discussion

The synthesis of 1H-pyrrole derivatives has garnered considerable attention due to their broad biological and medicinal applications. In this study, benzoin served as an electrophilic center, reacting with various aromatic diamines (e.g., ethane-1,2-diamine, benzidine, p-phenylenediamine, m-phenylenediamine) and malononitrile as a nucleophile under optimized conditions (ethanol/pyridine) to afford novel heterocyclic compounds incorporating the 1H-pyrrole core (I, III, IV, and VI) as shown in scheme 1.

The synthesis of I, III, IV, and VI proceeds via nucleophilic attack of the diamine on benzoin's carbonyl group, generating an α-amino ketone intermediate, which undergoes in situ condensation with malononitrile to afford moderate yields of the target bis(1H-pyrrole) compounds. The use of pyridine as a base in ethanol likely facilitates enolization and subsequent cyclization. However, deviations from this pathway were observed with ethylenediamine, hydrazine, and o-phenylenediamine, emphasizing the role of reactant geometry and electronic effects. This study demonstrates the divergent reactivity of benzoin with diamines, where steric and electronic factors critically govern the formation of heterocyclic products. When ethylenediamine was employed, both the expected bis-pyrrole (I) and an unexpected furan derivative (II) formed. The latter likely arises via a Knoevenagel condensation between benzoin and malononitrile, followed by intramolecular cyclization.

This side reaction highlights the competitive pathways accessible under the given conditions, where the nucleophilicity of the amine and the electrophilicity of the carbonyl group direct product distribution. In contrast, the reaction with hydrazine proceeded exclusively to form 2,2'-(hydrazine-1,2-diylidene) bis(1,2-diphenylethan-1-one) (V), bypassing pyrrole formation entirely. This transformation, which

occurs even in the absence of malononitrile, underscores the unique reactivity of hydrazine as a bifunctional nucleophile. The mechanism involves initial attack on the carbonyl carbon, followed by dehydration and intramolecular cyclization. The absence of competing pathways here suggests that the rigidity of the hydrazine-derived intermediate favors this thermodynamic product.



Scheme 1: Reaction of benzoin with diamines.

Notably, o-phenylenediamine exclusively yielded 2,3-diphenylquinoxaline (VII), with no evidence of pyrrole formation. This selectivity is attributed to the proximity of the amino groups, which facilitates imine formation and subsequent cyclization into a quinoxaline framework. The aromatic conjugation and high thermodynamic stability of the quinoxaline ring further drive this preference, overriding potential alternative pathways. These observations underscore the delicate balance between kinetic and thermodynamic control in heterocyclic synthesis. The unexpected formation of VII emphasizes how intramolecular cyclization dominates when using ortho-substituted diamines due to geometric constraints.

The contrasting outcomes between aliphatic and aromatic diamines highlight the importance of rigidity in directing cyclization. Aromatic diamines with para- or meta-substitution favor pyrrole formation due to their ability to stabilize the intermediate without imposing excessive steric strain. In contrast, ethylenediamine's flexibility and o-phenylenediamine's constrained geometry led to alternative pathways. The reaction of benzoin with ethylene diamine yielded two distinct products, with Compound (II) being the major product (44% yield) and Compound (I) forming as a minor product (39% yield). Comprehensive spectroscopic analyses, including IR, ^{1}H NMR, and ^{13}C NMR, were employed to confirm the structures of these compounds, providing insight into their formation and the reaction pathway. The IR spectrum of Compound (I) exhibited characteristic absorption bands corresponding to primary amine (NH_2) and nitrile (C≡N) functional groups.

The presence of two distinct NH_2 stretching vibrations (3215.37 cm^{-1} and 3366.87 cm^{-1}) and a sharp nitrile absorption (2187.47 cm^{-1}) confirmed the expected functional groups. The ^{1}H NMR spectrum further supported the proposed structure, displaying signals for CH_2 protons (2.80 and 3.96 ppm), NH_2 protons (6.34 and 8.04 ppm), and aromatic protons (7.08–7.39 ppm). Notably, the spectrum suggested an asymmetric structure, likely due to restricted rotation around a C–σ bond, leading to non-equivalent proton environments. The ^{13}C NMR spectrum showing fewer signals than expected (14 distinct peaks for 36 carbon atoms), indicated symmetry or overlapping chemical shifts, consistent with the proposed structure.

In contrast, Compound (II) was identified as the major product, with spectroscopic evidence strongly supporting its formation. The ^{1}H NMR spectrum revealed the absence of CH_2 protons, suggesting their involvement in ring formation, while the aromatic region (7.15–7.47 ppm) displayed 10 protons, consistent with a symmetrically substituted furan ring. A singlet at 7.73 ppm was assigned to an NH proton, confirming the presence of a single amine group. The IR spectrum further corroborated the

structure, with absorptions corresponding to NH2 (3311.02–3464.24 cm^{-1}), C≡N (2213.68 cm^{-1}), and aromatic C–H (3061.05 cm^{-1}) stretches.

The disappearance of CH_2 signals and the retention of aromatic protons strongly indicate intramolecular cyclization leading to a furan ring. The preferential formation of Compound (II) (44% yield) over Compound (I) (39%) suggests that the reaction pathway favors furan ring formation under the given conditions. This selectivity may arise from its greater stability due to aromaticity or lower activation energy for cyclization. The absence of CH_2 protons in Compound (II) supports an intramolecular cyclization process, whereas Compound (I) retains the CH_2 groups, indicating an alternative pathway without ring closure. The spectroscopic data conclusively confirm the structures of both products, with Compound (II) being the dominant product due to favorable cyclization.

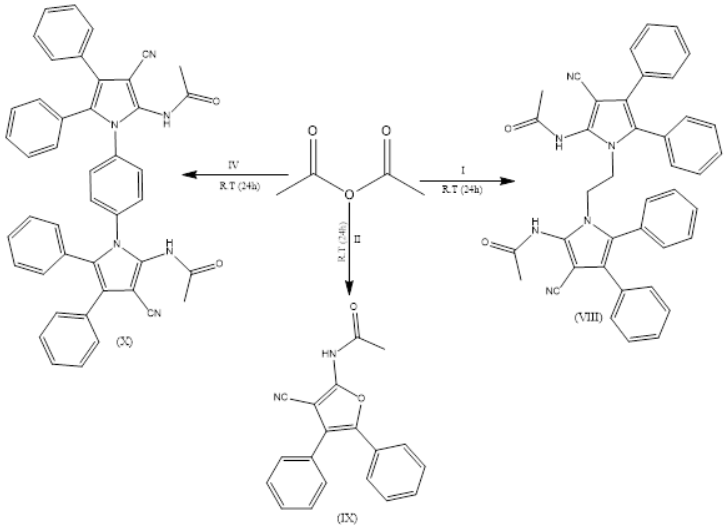
The aromatic regions of the spectra exhibit complex multiplet patterns, with proton counts matching the expected aromatic systems for each compound. The slight variations in chemical shifts among III, IV, and VI likely arise from subtle differences in electronic environments introduced by their respective substituents. Further confirmation is derived from the ^{13}C NMR spectra, where the number of observed signals corresponds precisely to the predicted carbon counts for each structure. The absence of extraneous peaks suggests high purity in the synthesized compounds, with no detectable impurities or by products. Collectively, the IR, ^{1}H NMR, and ^{13}C NMR data provide a coherent and convincing argument for the structural integrity of III, IV, and VI. The consistency across all spectroscopic methods underscores the reliability of the synthetic approach and the accuracy of the proposed molecular frameworks.

On the other hand, the analytical results for compounds V and VII revealed a distinct divergence from the previously studied compounds (I, III, IV, and VI). The initial objective of the reaction between benzoin with hydrazine and ortho-phenylenediamine was the synthesis of a bis-pyrrole derivative. However, this target compound was not successfully obtained; instead, compounds V and VII were formed. Compound V was characterized by IR spectroscopy, which exhibited a carbonyl (C=O) absorption band at 1677.22 cm^{-1} and a C=N stretching frequency at 1593.26 cm^{-1}. The absence of NH_2 protons in the ^{1}H NMR spectrum, along with the presence of only one type of aromatic proton with matching integration values, further supported the proposed structure to compound (V) and (VII). The ^{13}C NMR analysis confirmed the structure of compound V, revealing two distinct carbonyl carbons at 197.42 ppm (ketonic C=O) and two imine carbons (C=N) at 167.08 ppm. The observed carbon count aligned with the proposed structure, corroborating the successful formation of compound V. Similarly, the structural elucidation of compound VII was consistent with the analytical data, demonstrating the formation of an alternative product rather than the intended bispyrrole.

The second step of this research involves the successful acylation of the primary amine groups in compounds I, II and IV to form the corresponding amide derivatives VIII, IX, and X demonstrates the efficiency of acetic anhydride as an acylating agent under mild conditions as illustrated in scheme 2. The reaction proceeded smoothly at room temperature over 24 hours, suggesting that the nucleophilic acyl substitution mechanism is highly favorable for these substrates. The absence of harsh conditions or additional catalysts highlights the practicality of this approach for modifying amine-containing compounds, particularly in the context of bis-pyrrole derivatives.

Spectroscopic analyses provided conclusive evidence for the formation of the amide linkages. The disappearance of primary amine signals in the ^{1}H NMR spectra coupled with the appearance of new singlets corresponding to the methyl protons of the acetyl groups and the amide NH protons, strongly supports the proposed structural changes. Notably, the chemical shifts of the amide NH protons (ranging from 7.86 to 10.10 ppm) are consistent with hydrogen bonding and the deshielding effects typical of amide functionalities. The distinct methyl singlets observed in each derivative further confirm the incorporation of the acetyl groups, with variations in chemical shifts likely arising from differences in the electronic environments of the parent compounds.

The IR spectra further corroborated the acylation, with the appearance of a characteristic amide carbonyl stretch at 1694 cm^{-1} for compound IX. This value aligns with the expected range for amide C=O vibrations, though the slight variations compared to typical amide absorptions (usually around 1650–1680 cm^{-1}) may reflect conformational constraints or hydrogen bonding interactions within the molecular framework. The ^{13}C NMR data provided additional confirmation, with the amide carbonyl carbons appearing between 150–183 ppm. The significant downfield shift observed for compound X (182.98 ppm) suggests a highly deshielded carbonyl environment, possibly due to adjacent electron-withdrawing effects or intramolecular interactions. The consistency between the spectroscopic data and the expected structural modifications underscores the reliability of this acylation method.



Scheme 2: Reaction of bis-pyrroles (I, IV) and compound II with acetic anhydride

The clean conversion, absence of side products, and high specificity for the amine groups indicate that the reaction is both selective and efficient. These findings are particularly relevant for the design of functionalized bispyrole derivatives, as the introduced amide groups may enhance solubility, stability, or further reactivity for subsequent transformations. Moreover, the successful application of this acylation strategy opens avenues for diversifying the structural modifications of similar amine-containing scaffolds. The robustness of this method, combined with its simplicity, makes it a valuable tool in synthetic organic chemistry, particularly in the development of novel heterocyclic compounds with potential applications in medicinal chemistry.

Conclusion

This study highlights the controlled divergent reactivity of benzoin with different diamines and malononitrile, leading to the selective formation of bis-pyrrole derivatives (I, III, IV, and VI) under optimized ethanol/pyridine conditions. The reaction pathway was governed by steric and electronic factors, with ethylenediamine yielding both pyrrole (I) and furan (II) products, where the latter dominated (44%) due to favorable intramolecular cyclization. In contrast, hydrazine exclusively produced the hydrazone-linked (V) bypassing pyrrole formation entirely, while o-phenylenediamine favored quinoxaline (VII) due to geometric constraints promoting intramolecular cyclization. Spectroscopic characterization (IR, ^{1}H NMR, ^{13}C NMR) confirmed the structural identities of all synthesized compounds, with distinct functional group signatures supporting the proposed mechanisms. The acylation of primary amines (I, II, and IV) with acetic anhydride successfully generated amide derivatives (VIII, IX, and X), demonstrating an efficient and mild functionalization strategy. These findings underscore the critical influence of reactant geometry, rigidity, and electronic effects on product distribution, providing key insights for designing heterocyclic frameworks. This research establishes a foundation for heterocycle synthesis, with implications for medicinal chemistry and materials science.

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