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RESUMEN

El benzoilacetato de etilo 1 reacciona con antranilonitrilo 2a, rindiendo el derivado de quinolina 3 junto con el derivado de pirido[3,2-c]quinolina 5. Los compuestos 3 y 5 se hacen reaccionar con malononitrilo 6a, y con cianacetato de etilo 6b, rindiendo los derivados de piridopiridoquinolina 10 y 11, respectivamente. La reacción de 1 con 1,2-fenilendiamina 2b, 2-aminofenol 2c y 2-aminothiophenol 2d, rinde el nuevo derivado de diazepinona 12b y los productos de N-alkilación 14a y 14b, respectivamente.


SUMMARY

Ethyl benzoylacetate 1 reacts with anthranilonitrile 2a to afford the quinoline derivative 3 along with the pyrido[3,2-c]quinoline derivative 5. Compounds 3 and 5 were allowed to react with malononitrile 6a and with ethyl cyanoacetate 6b to afford the pyridoquinoline derivatives 8 and 9 and the pyranopyridoquinoline derivatives 10 and 11 respectively. The reaction of 1 with 1,2-phenylenediamine 2b, 2-amino phenol 2c and 2-amino thiophenol 2d afforded the novel diazepinone derivative 12b and the N-alkylation products 14a and 14b respectively.

Key words: Ethyl benzoylacetate. Anthranilonitrile. Pyridoquinolines. Diazepinones.

INTRODUCTION

In the last few years we have been involved in a program aiming to develop new synthetic routes to heterocyclic systems of anticipated biological activity\(^1\). In the context of this program some pyran-fused quinoline derivatives were required to be tested as potential biodegradable agrochemicals. A quinoline with a structure like 3 (Scheme 1) having o-hydroxy ketone moiety that enables cyclization to the desired compounds seemed suitable to fulfill our objective. Quinoline 3 was thought to be obtained possibly from the reaction of ethyl benzoylacetate 1 with anthranilonitrile 2a. Anthranilonitrile 2a has been frequently used

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for the preparation of quinolines through its reaction with different reagents\(^{12a}\). However, the reaction of ethyl benzoyleacetate 1 with 2a, to our knowledge, hasn’t been investigated.

Thus ethyl benzoyleacetate 1 reacts with 2a in dimethylformamide to afford a mixture of two solid products (1:1 ratio with 70% overall yield, TLC). Fractional crystallization of this mixture afforded a canary yellow product of mp. 213 °C, for which the mass spectrum showed m/z = 264. This product showed absorption bands in the IR spectrum at 3460, 3248, 1665 and 1619 cm\(^{-1}\) corresponding to OH, NH, C = O and C = N respectively. The \(^{1}H\) NMR spectrum revealed signals at δ ppm 7.1-8.3 (m, 9H, aromatic protons); 8.15 (s, 2H, D.O exchangeable, NH); and another D.O exchangeable singlet (1H) at 10.4 attributable to the OH. Structure 3 is thus assigned to this product.

Along with 3, another pale yellow product of mp. >360 °C was separated, for which the mass spectrum showed m/z = 392. It was thought that this product is the pyranooquinoline 4 which is assumed to be formed via the cyclo-condensation of 3 with another molecule of 1. However, the IR spectrum this product showed absorption bands at \(\nu\) 3464, 1666 and 1620 cm\(^{-1}\) corresponding to OH, benzoyl C = O, and C = N functions. The \(^{1}H\) NMR spectrum of this product revealed an aromatic multiplet at δ 7-8.35 ppm (14H); two D.O exchangeable singlets at δ 10.4 (1H) and 10.65 (1H) ppm attributable to two OH groups. If the correct structure was 4, a lactone C = O absorption band at \(\nu\) >1725 cm\(^{-1}\) would have appeared in its IR spectrum\(^{10}\).

Furthermore, NH2 proton signal in its \(^{1}H\) NMR spectrum would have been observed. Based on these spectral data structure 4 was ruled, and structure 5 was established for this product.

The formation of 5 is assumed to proceed via the cyclo-condensation of the active methylene of 1 with the carboxyl group in 3 followed by cyclization with loss of ethanol. The cyclization apparently took place on the NH2 rather than our planned cyclization on the OH.

To confirm our assumption compound 3 was allowed to react with 1 under the same reaction conditions to afford a product, which was found to be identical with 5 as inferred from the TLC, melting point and IR spectra.

It seems that a competition between the OH and the NH2 takes place in favor of the NH2 whenever they are present in the reaction of 4 with 1, which is not the case in 3. The IR spectrum this product showed absorption bands corresponding to OH, benzoyl C = O and C = N functions. The \(^{1}H\) NMR spectrum of this product revealed only one D2O exchangeable singlet (1H) at 10.35 ppm attributable to the OH. Structure 6 is thus assigned to this product.

The reaction of 5 with 6b afforded a yellowish crystalline solid of mp 345 °C. The IR spectrum of this product revealed a pattern similar to that of 10 except having a carbonyl absorption band \(\nu\) ~ 1735 cm\(^{-1}\) instead of the NH bands in that of 10. The \(^{1}H\) NMR spectrum showed only one D.O exchangeable singlet (1H) at δ 10.35 ppm. On the basis of these data structure 11 was given to this product.

Compound 10 could be transformed into 11 upon reflux in ethanolic HCl. The identity was inferred from melting points, TLC and IR spectra.

The reaction of ethyl benzoyleacetate 1 with 1,2-phenylenediamine 2b affords a grey solid product of mp. 205 °C readily soluble in acid medium. Analytical data showed that it is a 1:1 adduct after elimination of ethanol and water, its IR spectrum  showed absorption bands at \(\nu\) 3380, 2220 cm\(^{-1}\) corresponding to OH, NH and CN functions respectively. The \(^{1}H\) NMR spectrum revealed two D.O exchangeable signals at δ 10.3 and 11.15 ppm attributable to OH and NH respectively beside an aromatic multiplet at δ 6.9-8.0 ppm (14H). Structure 10 was thus assigned to this product.

In an attempt to explore the presence of the OH group ortho to the benzoyl group in compounds 5 (where is no competitive NH) to construct a pyrano-fused ring system, it was allowed to react with malononitrile 6a and with ethyl cyanoacetate 6b.

The reaction of 5 with 6a afforded a yellowish white crystalline solid of mp >370 °C. The IR spectrum of this product showed absorption bands at \(\nu\) 3460, 3210 & 3180 and 2218 cm\(^{-1}\) corresponding to OH, NH and CN functions respectively. The \(^{1}H\) NMR spectrum revealed two D.O exchangeable signals at δ 10.3 and 11.15 ppm attributable to OH and NH respectively beside an aromatic multiplet at δ 6.9-8.0 ppm (14H). Structure 10 was thus assigned to this product.

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**EXPERIMENTAL PART**

Melting points were determined on an electrothermal (9100) apparatus and are uncorrected. The IR spectra were recorded as KBr pellets on a Perkin Elmer 1430 spectrophotometer. The \textsuperscript{1}HNMR spectra were taken on a Varian Gemini 300MHz spectrometer in DMSO-$d_6$ using TMS as internal standard. Mass spectra were taken on a Shimadzu GCMS-GB 1000 PX (70 eV). Elemental analyses were carried out by the microanalytical centre at Cairo University.

The reaction of ethyl benzoylacetate 1 with anthranilonitrile 2a, phenylene-1,2-diamine 2b, 2-aminophenol 2c and 2-aminothiophenol 2d

(General procedure)

To a mixture of 1 (0.01 mole) and each of 2a, 2b, 2c or 2d (0.01 mole) in 30 ml of DMF was added few drops of piperidine as catalyst. The reaction mixture was refluxed for 2-3h (TLC control), left to cool overnight, poured on cold water and neutralized with HCl. The precipita-

![Scheme 1](image-url)
ted solid products were filtered off and recrystallized to afford the respective products. The reaction of 1 with 2a afforded a 1:1 mixture of two compounds with an overall yield of 70%. One of these two compounds was recrystallized from ethanol (compound 3, 35%), while the other was recrystallized from DMF (compound 5, 35%):  

4-Amino-3-benzoyl-2-hydroxyquinoline 3  
Canary yellow crystalline product (35%), mp. 213 °C (EtOH). IR ν cm⁻¹ 3464, 1666 and 1620 (OH, C = O and C = N respectively). ¹H NMR: δ ppm 7.1-8.3 (m, 9H, Ar), 8.15 (s, 2H, D₂O exchangeable, NH); 10.4 (s, 1H, OH). Found C₇₆.₂₁, H₅.₁₂, N₉.₂₀. C₂₈H₁₅N₃O₃ (4₄₁.₄₅) requires C₇₆.₁₈, H₃.₅₂, N₉.₂₀.  

3-Benzoyl-1,5-dihydroxy-4-phenylpyrido[3,2-c]quinoline 5  
Pale yellow crystals (35%), mp. 205 °C (EtOH). IR ν cm⁻¹ 3₂₄₈, 1₆₇₄ and 1₆₁₉ (OH, NH₂, C = O and C = N). ¹H NMR: δ ppm 8.2-8.7 (m, 9H, Ar), 9.75 (s, 1H, NH), 6.9-8.1 (m, 9H, Ar). Found C₇₆.₂₁, H₅.₁₂, N₉.₂₀. C₂₈H₁₅N₃O₃ (4₄₁.₄₅) requires C₇₆.₁₈, H₃.₅₂, N₉.₂₀.  

Transformation of 10 into 11  
To a solution of 10 (0.01 mole) in 25 ml of ethanol was added 3 ml of conc. HCl and the reaction mixture was refluxed for 2h, then left to cool to room temperature. It was then poured on cold water and neutralized with ammonia solution where a precipitate appeared which was filtered off and recrystallized. This product was found identical in all respects with compound 11 (mp., TLC and IR spectrum).  

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