

Reaction 2-Carboxybenzaldehyde with Aniline and its derivatives. Part III

Dr. Abdul hakem. R. Betrow

Dr. Khairi. M. Hamza

Dr. Ramadan. M. Tarhoun

*Chemistry Department,
Faculty of Education
Zawia University*

*Chemistry Department,
Faculty of Science
Tripoli University*

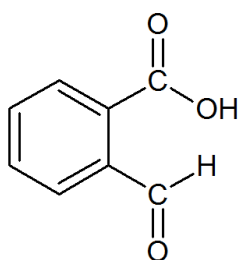
Abstract:

In this study, an investigation was made on the condensation between 2-Carboxybenzaldehyde and aniline and its derivatives 4-bromoaniline, N-methylaniline, N-ethylaniline, and N-phenylaniline. The reaction occurred selectivity at carbon-3 of the lactol form of the 2-Carboxybenzaldehyde, affording in all cases studied 3-arylaminothalides (**B-1– B-5**) in high yield. None of the products of type (**D**) and (**C**) have been formed. The structures of the isolated products were confirmed from their spectral data NMR and IR.

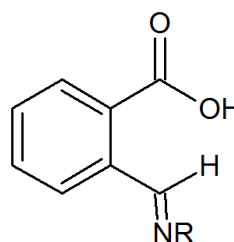
For Part I and II- See references No.1,2.

Introduction:

It was previously reported ^(1, 2) that the reaction of 2-carboxybenzaldehyde (**A**) with hetero aromatic amines gave N-(3-Phthalidyl) amines (**B**) while with aliphatic primary and secondary amines also afforded N-(3-Phthalidyl) amines except in case with a strong nucleophile secondary aliphatic amines such as (diisopropylamine) afforded aminated products *o*-formylbenzamide derivative(**C**). None of the Schiff bases of type (**D**) have been formed in all cases studied.

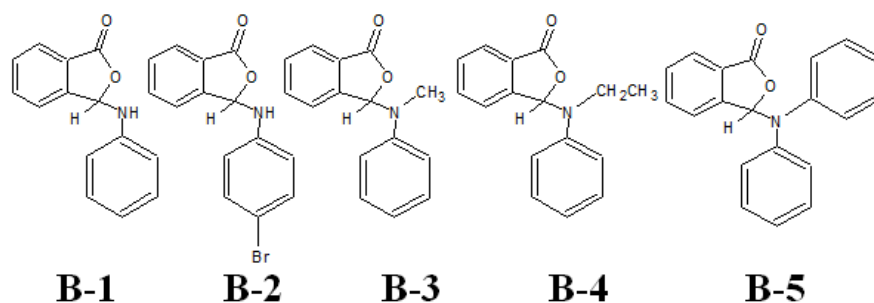
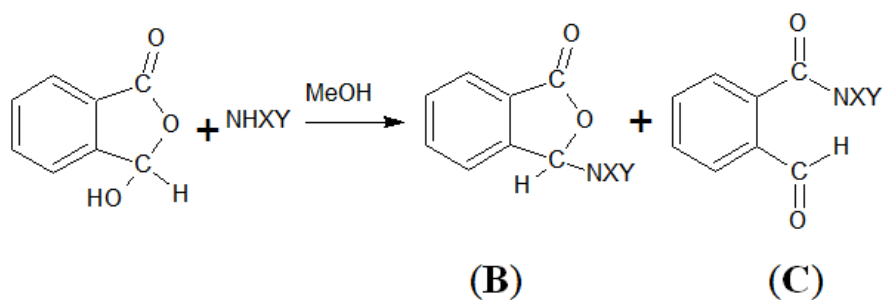


(A)



(D)

3-arylphthalide were known to be used as herbicides and for the growth and germination of seeds⁽³⁾, and also used as a blood viscosity reducing agent⁽⁴⁾ others were used as precursors in the synthesis of biological active compounds such as adrimaycin and daunomycin as anti-tumor compounds⁽⁵⁾ and chlorothiadone a known drug for the treatment of hypertension⁽⁶⁾. For these reasons, the researchers were interested in the synthesis of these compounds. In a similar reaction, it is thought of reacting 2-carboxybenzaldehyde with secondary amines, as strong base but with pronounced steric effect. Thus, the reactions of aniline and its derivatives 4-bromoaniline, N-methylaniline, N-ethylaniline, and N-phenylaniline were conducted as the following scheme shows.



B-1, N-(anilino) phthalide (X = H, Y= Ph)

B-2, N-(4-bromo anilino) phthalide (X = H, Y= C₆H₅Br)

B-3, N-(methyl anilino) phthalide (X = CH₃, Y= Ph)

B-4, N-(ethyl anilino) phthalide (X = CH₂CH₃, Y= Ph)

B-5, N-(diphenyl anilino) phthalide (X =Ph, Y= Ph)

Experimental:

All melting points were measured on electrothermal melting point and were uncorrected, infrared (IR) spectra were measured using Pye- Unicam SP- 300 spectrophotometer as a potassium bromide disc and FTIR. Spectrophotometer. ¹H-NMR were measured using a Bruker operating at 300 MHz spectrometer.

Reaction of 2-carboxybenzaldehyde with Aniline and its derivatives. (General method)

To a solution of 2-carboxybenzaldehyde (1.5g, 0.01mole) in methanol (20ml) was added aromatic amines (0.01mole). The mixture was refluxed for about (40 min) depends on the amines. After cooling,

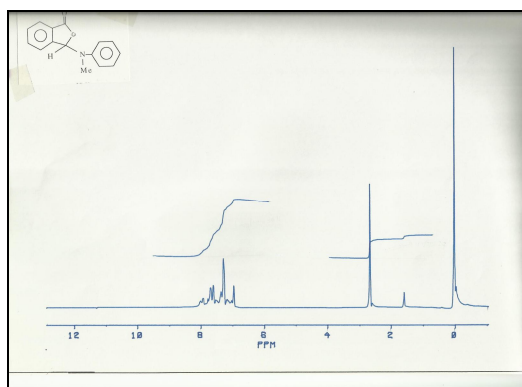
the separated crystals were collected. Recrystallization from methanol gave desired product.

Results and discussion:

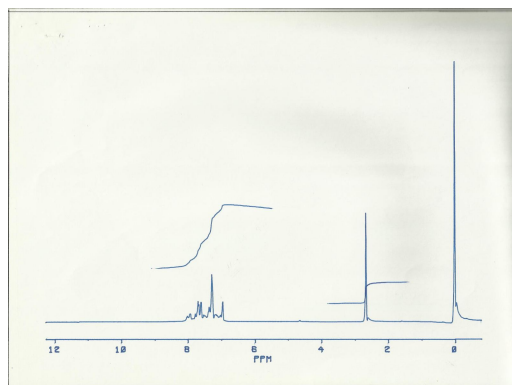
Increasing the size of the substituent attached to the nitrogen and decreasing of the basicity of the amines can be achieved with secondary amines carrying a phenyl group as a substituent such as aniline derivatives. Thus, the secondary amines used in this study were in different classes, those pure aromatic secondary amine, e.g., aniline, 4-bromoaniline and N-phenylaniline and a mixed secondary amine e.g., N-methylaniline, N-ethylaniline.

The reaction of 2-carboxybenzaldehyde with aniline, 4-bromoaniline, N-methylaniline, and N-ethyl aniline in refluxing methanol it afforded in each a solid product. The IR (KBr) spectrum of the products(Fig.3), shows a strong absorption at about 1754 -1730 cm^{-1} indicating the product to have a lactonic moiety and not open structure as that in the previous experiment. The analytical data of isolated phthalides are given in table-1. On the other hand. The $^1\text{H-NMR}$ (CDCl_3) spectra of all products, (Fig. 1 and 2), show a one proton singlet at δ 6.67, δ 6.65, δ 6.94 and δ 6.86 respectively assigned for the phthalidyl proton H-3, there was no sign of any aldehydic proton. These data confirmed that the structures of the products will be in parallel, N-(anilino) phthalide (B-1), N-(4-bromoanilino) phthalide (B-2), N-(methyl anilino) phthalide (B-3) and N-(ethyl anilino) phthalide (B-4). The reaction of N-phenylaniline; as more steric effect and a weaker base, afforded a solid product. Whose IR (KBr) show a strong absorption at 1750 cm^{-1} due the lactonic group. Its $^1\text{H-NMR}$ (CDCl_3) spectra show H-3 at δ 7.27 plus the possible aromatic protons. The highly deshielding (0.36 ppm) compared with

those in compound (B-2) and (B-3) can be attributed to the presence of a second phenyl group which through space cause a strong anisotropic effect leading to lower chemical shift of this protons. These data confirmed that the structure of the product will be N-(diphenylamino)phthalide (B-5). The formation of five products (B-1 – B-5) can be explained as a result from the attack of these amines, weaker than pure aliphatic secondary amines, at C-3 of 2-carboxybenzaldehyde giving rise to the desired products.



(A)



(B)

Reaction 2-Carboxybenzaldehyde with Aniline and its derivatives. Part III—

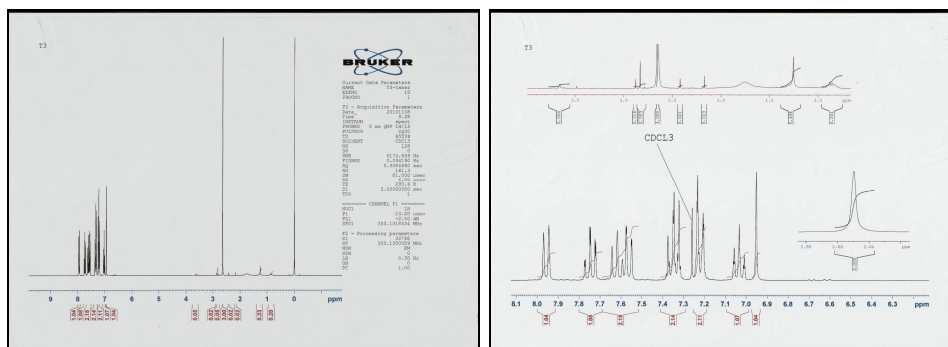


Fig.1. ¹H-NMR spectrum of N-(methylanilino) phthalide (B-3) in CDCl₃.
A) Without D₂O. B) D₂O added.

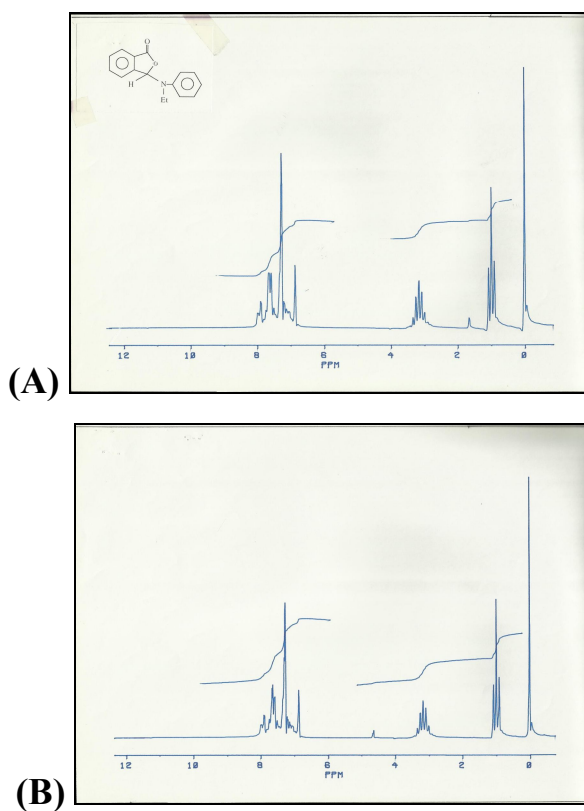
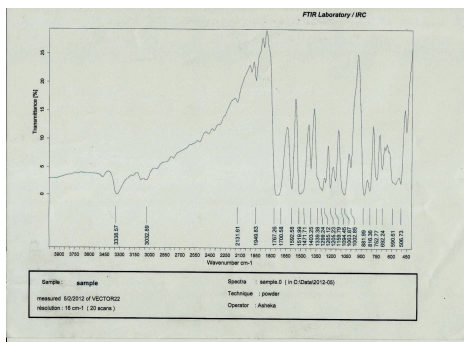
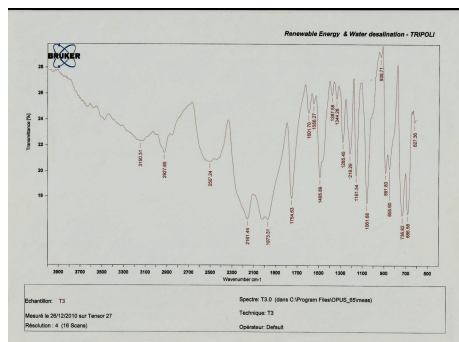


Fig.2. ¹H-NMR spectrum of N-(ethylanilino) phthalide (B-4) in CDCl₃.

A) Without D₂O. B) D₂O added.



(B-2)



(B-3)

Fig.3. I.R of N-(4-bromoanilino) phthalide (B-2) and N-(methylanilino) phthalide (B-3).

Table (1)
Analytical data of phthalides b (b-1- b-5)

Phthalide	Molecular Formula	Melting Point (°C)	Yield (%)	Solvent for Crystallization
N-(anilino) phthalide (B-1)	C ₁₄ H ₁₁ NO ₂	179-180	95	Methanol
N-(4-bromoanilino) phthalide (B-2)	C ₁₄ H ₁₀ BrNO ₂	180-181	92	Methanol
N-(methyl anilino) phthalide (B-3)	C ₁₅ H ₁₃ NO ₂	135-137	90	Methanol
N-(ethyl anilino) phthalide (B-4)	C ₁₆ H ₁₅ NO ₂	80-82	70	Methanol
N-(diphenyl anilino) phthalide (B-5)	C ₂₀ H ₁₅ NO ₂	137-138	55	Methanol

Table(2)

Spectral data of phthalides b (b-1- b-5)

Phthalide	IR(KBr, cm-1) C = O	H-3	NMR (CDCl ₃ ,TMS,ppm) Aromatic Protons
N-(anilino) phthalide (B-1)	1750 (C = O), 1600 (C=C), 3320 (N-H)	6.67 (s, 1H)	7.4- 8.14 (m, 9H+NH)
N-(4-bromoanilino) phthalide (B-2)	1733 (C = O), 1592 (C=C), 3338 (N-H)	6.65 (s, 1H)	7.5 - 8.20 (m, 9H+NH)
N-(methyl anilino) phthalide (B-3)	1750 (C = O), 1600 (C=C)	6.94 (s,1H)	7 0-7.3 (m , 5H) , 7.54- 7.94 (m ,4 H)
N-(ethyl anilino) phthalide (B-4)	1750 (C = O), 1600 (C=C)	6.86 (s,1H)	7.26 (m, 5H), 7.45 - 7.99(m,4H)
N-(diphenyl anilino) phthalide (B-5)	1750 (C = O), 1600 (C=C)	7.27 (s , 1H)	7.06 - 7.68 (m, 14)

References:

- 1-K. M. Hamza and A. R. Betrow, *Zawia, University Bulletin, ISSUE No.13-2011.*
- 2- A. R. Betrow, R. M. Tarhoun and K. M. Hamza,, *Zawia, University Bulletin, ISSUE No.14-2012 .*
- 3-D. D. Wheeler, D .C. Yong; *To Do Chemical Co.U.S.945.865 (1960)., Chem, Abst. 55, 2577f, (1961).*
- 4 - Ogawa, Yoshimitu, *Chin. J P.6383, 13 Apc. (1988) , C . A. 109 . 128818 J. (1988).*
- 5- K. Kobayasi , *Tetrahydron Lett . 3369, (1987) .*
- 6- *J.P.Broom, G.Sammes, J. C. S; Perkin I, 1-3, 466, (1981).*