A FACILE ROUTE FOR THE SYNTHESIS OF SOME NEW SPIRO[INDOLINE-3,3'-INDAN]-2,1'-DIONE DERIVATIVES

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Abstract- Indole-2,3-dione (**1**) was treated with malonic acid in a mixture of ethanol/pyridine to afford 1-[3-(2-oxoindolinylidene]acetic acid (**5**). Compound (**5**) reacted with arenes in the presence of aluminium chloride as catalyst to yield spiro[indoline-3,3'-indan]-2,1'-dione derivatives (**6a-e**).

The synthesis and photochromism of indolinospirochromenes containing condensed fragments in the indoline part of the molecule was achieved.[1] Photochromic spiro[2*H*-1,4-benzoxazine-2,2'-inoline] derivatives and photochromic spiro[indolinenaphthoxazine] derivatives with reddish purple colors and durability were prepared.[2-4]

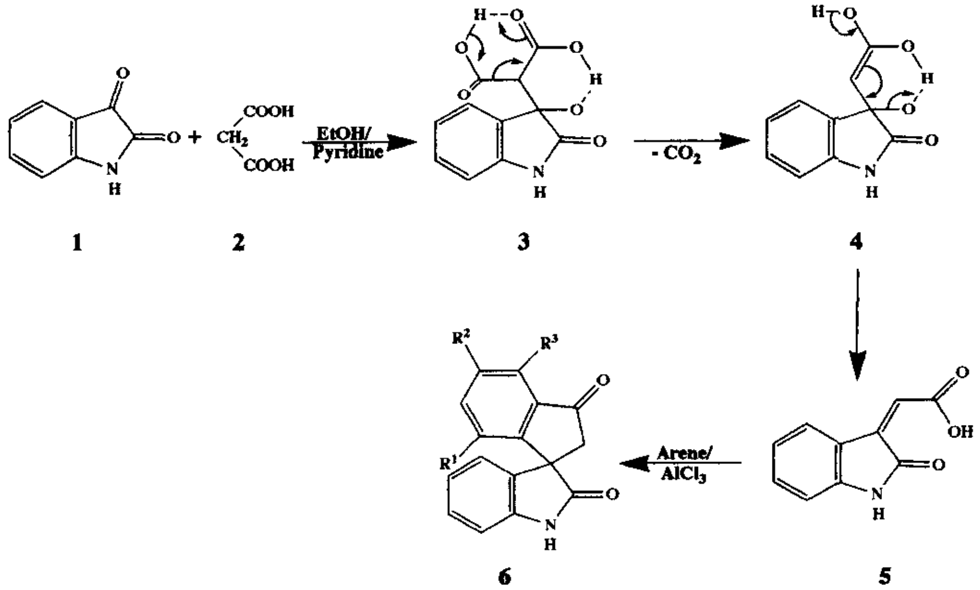
As an extension of our previous works,[5-10] the synthesis of spiro[indoline-3,3'-indan]-2,1'-dione derivatives is reported.

The synthesis was carried out by the reaction of indole-2,3-dione (**1**) with malonic acid in an ethanol/pyridine mixture to yield (Z)-1-[3-(2-oxoindolinylidene]acetic acid (**5**). The formation of compound **5** was based on the reactivity of the carbonyl group at C_3 of indole ring which underwent the condensation reactions in preferable manner than the amidic carbonyl at C_2 of indole moiety.[11]

The reaction of acid (**5**) with arenes in the presence of aluminium chloride gave the spiro[indoline-3,3'-

indan]-2,1'-dione derivatives (**6a-e**) (Scheme 1).

In a typical run, 1-[3-(2-oxoindolinylidene)]acetic acid (**5**) was added portionwise over 1 h to a mixture of aluminium chloride in dry arene. Thus, benzene afforded spiro[indoline-3,3'-indan]-2,1'-dione (**6a**) in 60% yield; similarly toluene gave 6'-methyspiro[indoline-3,3'-indan]-2,1'-dione (**6b**) in 67% yield. Anisole and bromobenzene yielded 6'-methoxyspiro[indoline-3,3'-indan]-2,1'-dione (**6c**) and 6'-bromospiro[indoline-3,3'-indan]-2,1'-dione (**6d**) in 55% and 50% yield respectively. *p*-Xylene gave 4',7'-dimethylspiro-[indoline-3,3'-indan]-2,1'-dione (**6e**) in 69% yield.



a: $R^1 = R^2 = R^3 = H$
b: $R^1 = R^3 = H$ $R^2 = CH_3$
c: $R^1 = R^3 = H$ $R^2 = OCH_3$
d: $R^1 = R^3 = H$ $R^2 = Br$
e: $R^1 = R^3 = CH_3$ $R^2 = H$

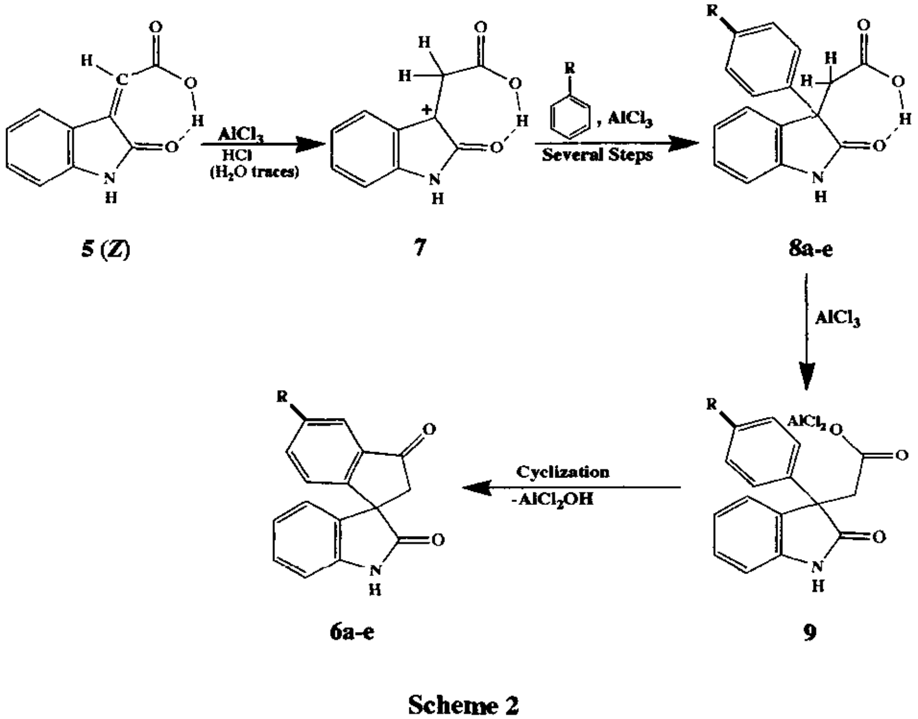
Arenes; Benzene, Toluene, Anisole, Bromobenzene and *p*-Xylene

Scheme 1

The structure of compound (**5**) was established from its elemental analysis and spectroscopic data. The ir (υ, cm^{-1}) spectrum of compound (**5**) showed a characteristic broad absorption band at 2600- 3400 corresponding to the stretching vibrations for hydroxyl group of the carboxyl group, 3150 for NH group of indoline moiety and a broad absorption at 1705-1725 for the carbonyl group of indole ring and the carbonyl group of carboxylic acid residue.[12] Literature survey revealed that ethyl 2-oxo-3-indolinylidenecyanoacetates were formed in *E*/*Z* mixture.[13] In our case the *Z* form is favored and its formation could be explained as shown in Scheme 1 through the intermediates (**3**) and (**4**) which included intramolecular hydrogen bonding.[14]

The formation of **6a-e** can be rationalized as shown in Scheme 2.

Reaction of **5** (***Z***) with the $AlCl_3$ catalyst in the presence of traces of water gives the carbocation (**7**) which can alkylate the *para* position of the arenes used or the position 2 in the case of *p*-xylene[15] to afford compounds (**8a-e**). Compounds (**8a-e**) cyclize under the reaction conditions to yield mixture (**6a-e**).



Scheme 2

The structures of compounds (**6a-e**) were elaborated on the basis of their elemental analyses and spectroscopic data. The ir (υ, cm^{-1}) spectrum of compound (**6a**) showed a characteristic strong absorption band at 3170 corresponding to the stretching vibrations of the NH group of indole ring, 1740 for the carbonyl group of the indanone moiety and 1705 for the carbonyl group of the indole ring. The nmr (δ, ppm) spectrum of **6a** ($CDCl_3$) showed the following signals: 3.90 (2H, s), the methylene protons of the indanone ring, 7.00- 7.50 (8H, m) the aromatic protons of indanone and indole ring and 10.00 (1H, s) for the NH proton in indole moiety.

EXPERIMENTAL

The time required for completion of reaction was monitored by thin layer chromatography (tlc). Melting points are uncorrected. Nmr (δ, ppm) spectra were measured on EM-360 90-MHz spectrometer using TMS as internal standard. Ir (υ, cm^{-1}) spectra were recorded as KBr pellets on a Pye-Unicam Sp200-G spectrophotometer. Elemental analyses were determined on a Perkin-Elmer 240C microanalyser.

Synthesis of 1-[3-(2-oxoindolinylidene)]acetic acid (5)

A mixture of isatin (14.7 g, 0.1 mol) and malonic acid (10.4 g, 0.1 mol) in ethanol-pyridine mixture (150 ml, 4:1) was refluxed for 48 h. The reaction mixture was cooled to room temperature and the solvents were removed by distillation to afford the crude product. The crude product was recrystallized from water to give 14.7 g (78% yield) of the pure compound (**5**), mp 262-264 °C. Anal. Calcd for $C_{10}H_7NO_3$: C, 63.49; H, 3.70; N, 7.40. Found: C, 63.32; H, 3.52; N, 7.20. Ir (υ, cm^{-1}) (KBr), 2600- 3400 (OH), 3150 (NH), and 1705- 1725 (C=O); nmr (δ, ppm) (DMSO-d_6): 6.65 (1H, s), 7.00- 7.50 (4H, m), 9.60 (1H, s), 10.20 (1H, s).

Reaction of 1-[3-(2-oxoindolinylidene)]acetic acid (5) with arenes in the presence of aluminium chloride catalyst; Synthesis of spiro[indoline-3,3'-indan]-2,1'-dione derivatives (6a-e)

General procedure:

A mixture of compound (**3**) (0.01 mol) and aluminium chloride (7.92 g, 0.06 mol) in the appropriate arene (25 ml) was stirred under reflux for 6 h. The reaction mixture was cooled to room temperature, decomposed with 10% hydrochloric acid, and extracted with chloroform. The extract was washed with water, 10% sodium carbonate solution, and again with water and then dried over anhydrous magnesium sulfate. The solvent and the unreacted arene were removed by distillation to afford the title crude products (**6a-e**).

Spiro[indoline-3,3'-indan]-2,1'-dione (**6a**):

This compound was prepared (60% yield) according to the above general procedure and it was purified by recrystallization from CH_2Cl_2/petroleum ether (bp: 80-100 °C; 1:3), mp 110-112 °C. Anal. Calcd for $C_{16}H_{11}NO_2$: C, 77.10; H, 4.41; N, 5.62. Found: C, 77.00; H, 4.32; N, 5.30. Ir (υ, cm^{-1}) (KBr): 3170 (NH), 1740, 1705 (C=O); nmr (δ, ppm) ($CDCl_3$/TMS): 3.85 (2H, s), 6.85-8.00 (8H, m), 10.00 (1H, s).

6'-Methylspiro[indoline-3,3'-indan]-2,1'-dione (**6b**):

It was purified by the recrystallization from CH_2Cl_2/petroleum ether (bp: 80-100 °C 1:3), mp 115-117 °C (67% yield). Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.56; H, 4.94; N, 5.32. Found: C, 77.56; H, 4.72; N, 5.20. Ir (υ, cm^{-1}) (KBr): 3150 (NH), 1705, 1740 (C=O); nmr (δ, ppm) ($CDCl_3$/TMS): 2.30 (3H, s), 3.85 (2H, s), 6.85-8.00 (7H, m), 10.00 (1H, s).

6'-Methoxyspiro[indoline-3,3'-indan]-2,1'-dione (**6c**):

It was recrystallized from $CHCl_3$/hexane (1:3), mp 225-227 °C (55% yield). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.65; N, 5.01. Found: C, 73.00; H, 4.42; N, 5.00. Ir (υ, cm^{-1}) (KBr): 3160 (NH), 1705, 1740 (C=O); nmr (δ, ppm) ($CDCl_3$/TMS): 3.20 (3H, s), 3.90 (2H, s), 6.90-8.10 (7H, m), 10.10 (1H, s).

6'-Bromospiro[indoline-3,3'-indan]-2,1'-dione (**6d**):

It was purified by recrystallization from $CHCl_3$/hexane (1:3), mp 160-162 °C (50% yield). Anal. Calcd for $C_{16}H_{10}NO_2Br$: C, 58.71; H, 3.05; N, 4.28. Found C, 58.65; H, 3.00; N, 4.10. Ir (υ, cm^{-1}) (KBr): 3150 (NH), 1705, 1740 (C=O); nmr (δ, ppm) (DMSO-d_6): 3.90 (2H, s), 7.00-7.90 (7H, m), 10.10 (1H, s).

4',7'-Dimethylspiro[indoline-3,3'-indan]-2,1'-dione (**6e**):

It was recrystallized from CH_2Cl_2/hexane (1:3), mp 170-172 °C (69% yield). Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.97; H, 5.41; N, 5.05. Found: C, 77.80; H, 5.20; N, 5.00. Ir (υ, cm^{-1}) (KBr): 3160 (NH), 1705, 1740 (C=O); nmr (δ, ppm) (DMSO-d_6): 2.30 (6H, s), 3.95 (2H, s), 7.00-8.10 (6H, m), 10.10 (1H, s).

REFERENCES

1. I. V. Manakova, M. A. Gal'bershtam, G. K. Bobyleva, N. M. Przhiyalgovshaya, and L. N. Kurkovskaya, *Khi. Geterotsikl. Soedin*, 1980, **1**, 104 (*Chem. Abstr.*, 1989, **110**, 23707q).
2. K. W. Suk and C. C. Wen, *PCT Int. Appl. WO* 88 02,371 (Cl. C07D498/10), 07 Apr. 1988, US Appl. 912,718, 26 Sep. 1986; 33 pp., (*Chem. Abstr.*, 1989, **110**, 156108s).
3. Y. Shinichi and T. Takashi, *Jpn. Kokai Tokkyo Koho* JP 63,275,587 [88,275,587] (Cl. C07D498/10), 14 Nov. 1988, Appl. 87/106,311, 01 May 1987; 6 pp., *(Chem. Abstr.*, 1989, **110**, 222675c).
4. N. Mikito, I. Takeaki, and M. Takao, *Jpn. Kokai Tokkyo Koho* JP 63,316,783 [88,316,783] (Cl. C07D498/10), 26 Dec. 1988, Appl. 87/152,691, 19 Jun 1987; 5 pp., (*Chem. Abstr.*, 1989, **110**, 222677e).
5. M. F. El-Zohry, *Org. Prep. Procedures, Inter.*, 1992, **24**, 81.
6. M. F. El-Zohry, I. M. A. Awad, Z. A. Hozien, and A. A. Abdel-Hafez, *Indian J. of Chem.*, 1993, **32b**, 1109.
7. M. F El-Zohry, I. M. A. Awad, and A. A. Abdel-Hafez , *Arch. Pharm.*, 1993, **326**, 115.
8. M. S. Al-Thebeiti and M. F. El-Zohry, *Phosphorus, Sulfur and Silicon,* 1994, **88**, 251.
9. M. F. El-Zohry and A. M. El-Khawaga, *J. Org. Chem.*, 1990, **55**, 4036.
10. M. F. El-Zohry, *Phosphorus, Sulfur and Silicon,* 1992, **66**, 311.
11. G. S. Singh, N. Siddiqui, and S. N. Pandeya, *Arch. Pharmacal Res.*, 1991, **15(3)**, 272.
12. P. C. S. Simon, *Tables of Spectral Data for Structure Determination of Organic Compounds,* Springer-Verlag, Berlin, Heidelberg, New York, Tokyo, 1983. (Translation).
13. M. S. Morales-Rios, Y. Mora-Perez, and P. Joseph-Nathan, *Magn. Reson. Chem.*, 1992, **30**, 1153.
14. M. I. Younes, M. F. El-Zohry, and S. A. Metwally, *Z. Naturforsch.*, 1986, **41b**, 134.
15. R. M. Roberts and A. A. Khalaf, *Friedel-Crafts Alkylation Chemistry*, Marcel Dekker, New York, 1984, pages 228, 249 and 260.

Received, 8th May, 1995