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Enaminones in Heterocyclic Synthesis part 2: One-Pot Synthesis of Some New Indeno [3,2-b] pyridines

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Six new indeno[3,2-b]pyridine derivatives were synthesized via reactions of 1-phenyla-mino-3-indenone with cyano olefins.

Key words : 1-Phenylamino-3-indenone, cyano olefins, indeno [3,2-b] pyridines

INTRODUCTION

Some indan-1,3-dione derivatives were reported to exhibit biological activity as, e.g., antiinflammatory (Varache-Beranger *et al.*, 1991; Rovert-Piessard *et al.*, 1990), anticoagulant and psychopharmacological (Arens *et al.*, 1976) properties. On the other hand, very recently, our laboratory (Hammouda *et al.*, 1994) reported on the reaction of 5,5-dimethyl-3-phenylamino-2-cyclohexen-1-one -as an enaminone- with activated cyano olefins as a new simple synthetic route for quinolines. In the light of these considerations, and in continuation of the work on enaminones (Hammouda *et al.*, 1994; Hammouda *et al.*, 1987; Hamama *et al.*, 1988a) and indan-1,3-dione and its derivatives (Hammama *et al.*, 1988b, Hammouda *et al.*, 1988; Afsah *et al.*, 1990, Mashaly, 1993), the present work deals with the synthesis of some new functionalized indeno [3,2-b] pyridines **3a-c** and **5a-c** of potential biological activity. Compounds **3a-c** and **5a-c** were synthesized via reactions of the enaminone 1-phenylamino-3-indenone **1** with the cyano olefins **2a-c** and **4a-c**, respectively.

MATERIALS AND METHODS

Melting points were determined on a Griffin Melting Point Apparatus and were uncorrected. The IR spectra were recorded on a Unicam SP2000 Spectrophotometer as KBr disc (ν, in cm^{-1}). ^1H NMR spectra were on Varian EM-390 (90 MHz) using TMS as an internal standard (chemical shift in δ, ppm) and $CDCl_3$ or DMSO-d_6 as solvents. Elemental analysis were performed at the Microanalytical Data Unit at Mansoura and Cairo Universities.

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Synthesis of the indeno [3,2-b] pyridines 3-c and 5a-c

Method A: A solution of **1** (0.003 mol) and the 0.003 mol) of each of the appropriate aldehyde ArCHO and cyanomethylene $CH_2(CN)X$ (X=CN for **3a-c**; CO_2 Et for **5a-c**) in absolute ethanol (25 ml) and piperidine (0.1 ml) was proceeded as in Method A and afforded the same products **3a-c** and **5a-c** (m.p. and mixed m. p., cf. Table I).

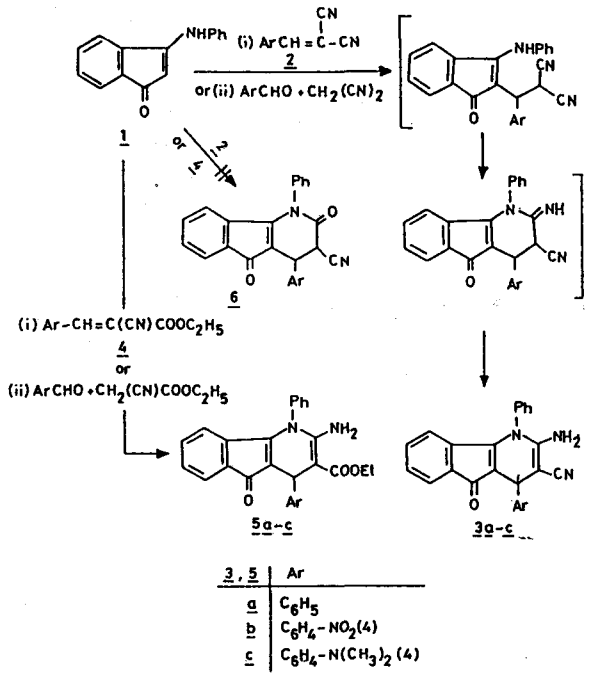
IR(cm^{-1}) **3a**: 3450, 3420 (NH_2), 2190 (conjugated C≡N), 1700 (C=O); **3b**: 3445, 3360 (NH_2), 2195 (conjugated C≡N), 1690 (C=O), 1515, 1345 (NO_2); **3c**; 3480, 3400 (NH_2), 2200 (conjugated C≡N), 1690 (C=O); **5a**: 3470, 3280 (NH_2), 1715 (C=O, ester), 1690 (C=O); **5b**: 3470, 3255 (NH_2), 1720 (C=O, ester), 1690 (C=O) and **5c**: 3470, 3410 (NH_2), 1735 (C=O, ester), 1690 (C=O). ^1H NMR (δ, ppm): **3b**: 4.85 (s, 1H, H-4), 6.85-8.25 (m, 15H, Ar-H and NH_2) and **5a:** 1.15 (t, 3H, CH_3), 4.0 (q, 2H, CH_2), 5.0 (s, 1H, H-4), 6.55 (s, 2H, NH_2), 7.0-7.7 (m, 14H, Ar-H).

RESULTS AND DISCUSSION

Refluxing **1** and **2a-c** in a (1:1) molar ratio in an ethanolic piperidine solution afforded red solid products assigned **3a-c**. Under the same reaction conditions, **1** and **4a-c** afforded, also, red solid products assigned **5a-c**. Structure 4 was excluded as the possible reaction product of either **1** and **2a-c** or **1** and **4a-c** based on previous comparable work (Hammouda *et al.*, 1994) and elemental and spectral analyses (cf. Materials and Methods and Table I). The IR spectra of compounds **3a-c** revealed the presence of an NH_2 and C≡N groups at 3480-3360 cm^{-1} and 2200-2190 cm^{-1}, respectively. Compounds **5a-c** showed an NH_2 and C=O (ester) hands at 3470-3255 cm^{-1} and 1725-1715 cm^{-1}, respectively. The ^1H NMR spectra offered further evidences for the proposed structures, where

Table I. Characterization data of the new indeno [3, 2-b] pyridines

No. (col.)	m.p. (°C)	Yield (%)	Molecular formula (Mwt)	Found (Calc.)		
				C %	H %	N %
3a (red)	236-7	73	$C_{25}H_{17}N_3O$ (375.4)	79.94 (79.84)	4.52 (4.57)	11.14 (11.19)
3b (red)	228-30	70	$C_{25}H_{16}N_4O_3$ (420.4)	71.38 (71.42)	3.81 (3.84)	13.30 (13.33)
3c (red)	237-9	75	$C_{27}H_{22}N_4O$ (418.5)	77.45 (77.49)	5.27 (5.30)	13.31 (13.39)
5a (red)	223-4	68	$C_{27}H_{22}N_2O_3$ (422.5)	76.74 (76.76)	5.26 (5.25)	6.60 (6.63)
5b (red)	224-5	77	$C_{27}H_{21}N_3O_5$ (467.5)	69.35 (69.37)	4.55 (4.53)	8.98 (9.00)
5c (red)	224-5	71	$C_{29}H_{27}N_3O_3$ (465.5)	74.80 (74.82)	5.84 (5.85)	9.00 (9.03)



Scheme 1

for compound **3b** the H-4 appeared at δ 4.85 ppm and the NH_2 appeared at δ 6.85-8.25 ppm in a multiplet with the aromatic protons. While for compound 5a the δ valuess were 1.15 and 4.0; 5.0 and 6.55 ppm for the ethyl ester; H-4 and NH_2 groups, respectively (cf. Materials and Methods). Furthermore, compounds **3a-c** and **5a-c** were unambiguously synthesized by another route involving one-pot condensation of **1**, the appropriate aldehyde ArCHO and cyanomethylene CH_2 (CN)X -(X=CN; CO_2Et for **3a-c** and **5a-c**, respectively)- in a molar ratio of (1:1:1) in refluxing ethanolic piperidine (cf. Shceme 1).

Formation of **3** (or **5**) via route (i) (Scheme 1) involves initial Michael addition of **1** to the ylidenic bond in **2** (or **4**) forming an acyclic intermediate which cyclized by the nucleophilic attack of the NH group on the cyano carbon, followed by tautomerisation to the final product **3** (; or **5**). While in route (ii) (Scheme 1), formation of **3** (; or **5**) involved initial condensation of the aldehyde with the cyanomethylene affording the activated cyano olefin **2** (; or **4**), followed by addition of **1** to **2** (; or **4**) as above.

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