A Study on the Mannich Reaction with 1-Phenylamino-3-indenone

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Mannich Reaction. 1-Phenylamino-3-indenone

Mannich reaction of the title compound 1 with formaldehyde and morpholine, piperidine or piperazine afforded the Mannich bases 3–5 respectively, whereas the indeno[1,2-d]pyrimidines (6–7) were obtained where primary amines were used. Treatment of 2 with formaldehyde gave benz[b]indeno-diazepine (8). The reaction of formaldehyde with 1 was also investigated.

Very few cases were reported for the aminomethylation of 1,3-indandiones [1] and no Mannich reaction of enaminoes derived from 1,3-indandione has been described. In continuation of our studies [2–5] on 1,3-indandiones and in view of the synthetic importance of enaminoes [6], the title compound 1 was subjected to Mannich reactions with morpholine, piperidine or piperazine and formalin to afford 2-(N-morpholino- or piperidino- methyl)-1-phenylamino-3-indenone (3, 4) and N,N'-bis(1-phenylamino-3-inden-2-ylmethy)piperazine (5). Compounds 3–5 exist as mixtures of tautomeric phenylamino and phenylimino forms. The IR spectra of all compounds showed bands at 1670 (CO enamino) and a single weak band at 3440 cm⁻¹ (NH). The phenylimino form may be responsible for two bands at 1620 (C=N) and 1735 cm⁻¹ (CO of indanone moiety).

On the other hand, treatment of 1 with primary amines and formalin in a molar ratio of (1:1:2) gave 2,4-dihydro[indeno[1,2-d]pyrimidine-5-ones (6, 7). That the phenylamino group and the 2-position of the indenone moiety are involved in the formation of pyrimidine ring system is in line with the work of Roth [7] on dimedone enamino.
The synthesis of indeno-diazepines via intramolecular Mannich type cyclization has been accomplished through treatment of 1-(o-aminoanilino)-3-indenone (2) with formaldehyde to afford 5,10-dihydrobenz[b]indeno[1,2-e][1,4]diazepine-12-one (8). This Mannich type cyclization is similar to that reported [8] for the synthesis of some dibenzo[b,e][1,4]diazepines.

In connection with the present work and in view of the work of Greenhill [9] on the reaction of enaminones with aldehydes. Compound 1 was treated with formaldehyde in acetic acid to give a product which was identified as 2-hydroxymethyl derivative (9); the IR spectrum showes bands at 1670 (CO enaminone), a broad band at 3440 (NH) and 3610 cm\(^{-1}\) (OH).

The reaction of 1 with two equivalents of formaldehyde in ethanol containing acetic acid gave 3-phenyl-indeno[1,2-d]oxazine-8-one (10). The structure of 10 was established through its analytical and IR spectral data which showed peaks at 1110 (C-O-C stretch.), a broad band at 1300-1285 (C-N stretch.) and 1715 cm\(^{-1}\) (CO of indenone).

### Experimental

Melting points (uncorrected) were taken in open capillary tubes by the use of Gallenkamp electric melting point apparatus. Infrared spectra were performed on Pye Unicam Infracord Spectrophotometer Model SP 2000 using KBr.

2-(N-Morpholinomethyl)-1-phenylamino-3-indenone (3), 2-(N-piperidinomethyl)-1-phenylamino-3-indenone (4) and N,N'-bis(1-phenylamino-3-indenon-2-ylmethyl)piperazine (5)

**General procedure:** A solution of the enaminone (1) (0.5 g; 2.3 mmol), formalin (40%) (0.15 g (0.37 ml), 5 mmol) and amm. acetate or methylamine (2.3 mmol) in ethanol (50 ml) and few drops of acetic acid (0.5 ml) was heated for 3 h on a steam bath, kept overnight at room temperature. The reaction mixture was worked up as in case of 3-5. The resulting solid products were crystallized from ethanol.

**Compound 3:**
M.p. 195 °C (73% yield).

**Analysis for C\(_{20}\)H\(_{20}\)N\(_2\)O\(_2\)** (320.38)
Calcd C 74.97 H 6.29 N 8.75,
Found C 74.62 H 6.12 N 8.53.

**Compound 4:**
M.p. 197 °C (79% yield).

**Analysis for C\(_{21}\)H\(_{22}\)N\(_2\)O** (318.41)
Calcd C 79.21 H 6.97 N 8.80,
Found C 79.06 H 6.80 N 8.53.

**Compound 5:**
M.p. 140 °C (77% yield).

**Analysis for C\(_{18}\)H\(_{18}\)N\(_2\)O** (276.33)
Calcd C 78.11 H 5.72 N 10.05.

1-(o-Aminoanilino)-3-indenone (2)

Compound 2 was prepared as described in earlier report [10]. M.p. 138 °C (77% yield).

**Analysis for C\(_{15}\)H\(_{13}\)N\(_2\)O** (236.27)
Calcd C 76.25 H 5.12 N 11.86,
Found C 76.12 H 5.02 N 11.71.
5,10-Dihydrobenz[b]indenon-
[1,2-e][1,4]diazepine-12-one (8)

A solution of the enaminone (2) (0.5 g, 2.12 mmol), formalin (40%) (0.07 g (0.18 ml), 2.3 mmol) in ethanol (50 ml) and few drops of acetic acid (0.5 ml) was heated for 3 h on a steam bath, kept overnight at room temperature. The reaction mixture was worked up as in case of 3–5. The precipitated product was filtered off and crystallized from ethanol to give 8 as a grey powder, m.p. 206 °C (47% yield).

IR: a very weak broad band at 3400–3340 (N–H stretch.), 1350 (C–N stretch.) and 1715 cm⁻¹ (CO of indenone).

Analysis for C₁₆H₁₂N₂O (248.28)
Calcd C 77.40 H 4.87 N 11.29,
Found C 77.28 H 4.81 N 11.11.

2-Hydroxymethyl-1-phenylamino-3-indenone (9)

A solution of the enaminone (1) (0.5 g; 2.3 mmol), paraformaldehyde (0.07 g; 2.3 mmol) in glacial acetic acid (30 ml), was heated for 2 h on a steam bath, kept overnight at room temperature. The reaction mixture was worked up as above. The precipitated product was filtered off and crystallized from ethanol to give 9 as a pale yellow powder, m.p. 130 °C (62% yield).

Analysis for C₁₆H₁₃NO₂ (251.27)
Calcd C 76.48 H 5.21 N 5.57,
Found C 76.31 H 5.07 N 5.49.

3-Phenyl-indeno[1,2-d]oxazine-8-one (10)

A solution of the enaminone (1) (0.5 g; 2.3 mmol), formalin (40%) (0.15 g (0.37 ml), 5 mmol) in ethanol (50 ml) and few drops of acetic acid (0.5 ml) was heated for 2 h on a steam bath, kept overnight at room temperature. The reaction mixture was worked up as above. The precipitated product was filtered off and crystallized from ethanol to give 10 as a yellow powder, m.p. 119 °C (57% yield).

Analysis for C₁₇H₁₃NO₂ (263.28)
Calcd C 77.55 H 4.98 N 5.32,
Found C 77.68 H 4.86 N 5.40.