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Note

Synthesis of some novel 5, 6-dihydro-6-[4'-substituted phenyl]-12*H*- indeno [2, 1-*c*]-1, 5-benzodiazepin-7-ones

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Synthesis of hitherto unknown 5, 6-dihydro-6-phenyl-12*H*-indeno[2, 1-*c*]-1, 5-benzodiazepin-7-ones **2** through Michael type addition of *o*-phenylenediamine to 2-benzylideneindane-1, 3-diones is reported.

Keywords: Benzodiazepin-7-ones, Michael type addition of *o*-phenylenediamine

IPC: **Int.Cl[8] C 07 D**

Although a number of [1, 5] diazepines fused to a variety of carbocyclic[1-2] and heterocyclic[3-5] ring systems have been synthesized in the past and screened for their various biological properties such as anticonvulsant[6], antivasopressin[7], sedative[8], anticholecytokinin[9] and anti-HIV activity[10], but the literature does not record any attempts made towards the synthesis of indenobenzodiazepines. In view of these biological properties and in continuation of our interest in utilizing 2-benzylideneindane-1, 3-diones for the synthesis of novel multicyclic heterocyclic ring systems, we report in this paper one pot synthesis of some hitherto unknown 5, 6-dihydro-6-[4'-substituted phenyl]-12*H*-indeno[2, 1-*c*]-1, 5-benzodiazepin-7-ones **2**.

Michael addition of *o*-phenylenediamine to 2-benzylideneindane-1, 3-dione **1** (ref. 11-12) in refluxing ethanol afforded the corresponding 5, 6-dihydro-6-phenyl-12*H*-indeno [2, 1-*c*]-1, 5-benzodiazepin-7-ones **2** (**Scheme I**) in excellent yields.

The structures of all the indenobenzodiazepinones **2** have been corroborated through their IR, ^{1}H NMR and mass spectral analysis. The IR spectra of **2** showed a broad band of medium intensity in the region 3228-3306 cm^{-1} due to N-H stretching along with a strong band in the region 1663-1690 cm^{-1} due to C=O (stretching) in an α, β-unsaturated five-membered ketone. A shift of about 30-60 cm^{-1} of this peak to lower wavenumber as compared to C=O (1720 cm^{-1}) in the starting 2-benzylideneindane -1, 3-diones **1** is probably partly due to endocyclic double bond and partly due to further increase in conjugation of the C=O group with the *n*-electrons of the β-imino group.

The ^{1}H NMR spectra of **2** in the aliphatic region exhibited a one-proton singlet at δ 5.60 assignable to the benzylic C_6-H. A noteworthy feature of the aromatic region of ^{1}H NMR spectra of compounds **2** was the appearance of two one proton doublet of doublet (J=7.3 and 1.15 Hz) in the region δ 7.35-7.40 and 6.50-6.60 due to C_8-H and C_4-H, respectively. The deshielding of the former proton is due to anisotropic effect of the adjacent C_7-keto group while the shielding of the later proton (*i.e.*C_4-H) is due to +R effect of C_5-NH group.

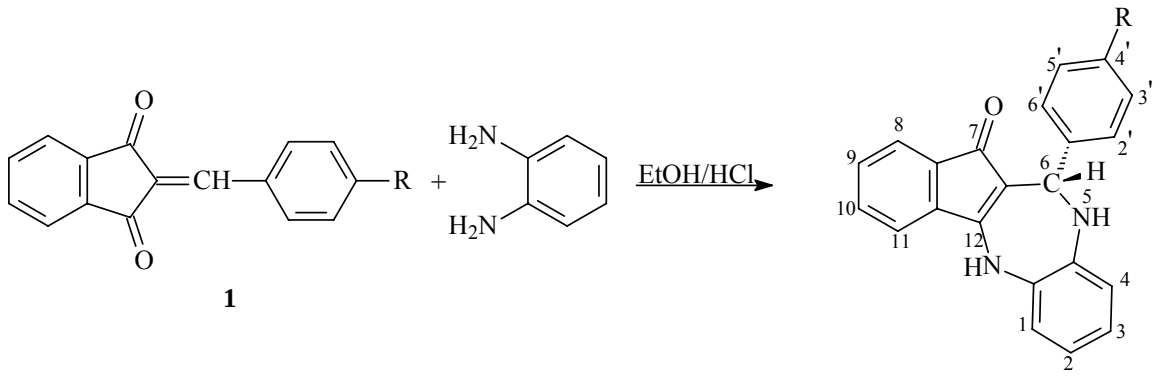
The structure of these indenobenzodiazepinones **2** have been further supported by their mass spectra which besides their respective molecular peaks showed two common prominent ion peaks *i.e.* m/z 247 and 219 whereas the former peak must have arisen due to the elimination of 6-phenyl or substituted phenyl group from their respective molecular ions, the later peak is derived from the peak at m/z 247 by loss of 28 mass units *i.e.* CH=NH moiety.

Biological activity

All the indenodiazepinones **2** prepared in the present investigation were screened for their antibacterial activity against *S. aureus* (gram-positive) and *P. aeruginosa* (gram-negative) species by the Filter Paper Disk method with Muller-Hinton agar as medium using 100μg / mL of the compound. Against these bacteria, the zone of inhibition of the various controls were ampicillin (14-22 mm), chloramphenicol (15-18 mm), penicillin G (14-22 mm) while the indenobenzodiazepinones **2** showed an inhibition zone of only (2-5 mm) thereby suggesting that these compounds do not have any significant antibacterial activity.

Experimental Section

Melting points reported are uncorrected. IR spectra were recorded in KBr on a Buck scientific M500 IR



Scheme I

spectrophotometer and ^{1}H NMR spectra in DMSO + $CDCl_3$ on a 300 MHz Bruker spectrometer, the chemical shifts are recorded on a δ scale using TMS as the internal standard.

5, 6-Dihydro-6-[4′-substituted pheny1]-12*H*-indeno[2, 1-*c*][1, 5] benzodiazepin-7-one: General procedure. A solution of a suitable 2-benzylidene-indane-1, 3-dione (5 mmoles) and *o*-phenylene-diamine (7.5 mmoles) in ethanol (50 mL) containing HCI (6-7 drops) was refluxed for 4 hr, progress of reaction being monitored by TLC. Thereafter the reaction mixture was cooled to room temperature and poured into aqueous $NaHCO_3$ and extracted with $CHCI_3$ (2 × 50 mL). The organic layer was washed with water (2 ×50 mL), dried over anhydrous $MgSO_4$ and distilled. The crude mass so obtained was passed through a column of silica gel using benzene-ethyl acetate (9:1) mixture as eluent to obtain shining orange crystals of 5, 6-dihydro-6-substituted phenyl-12*H*-indeno[2, 1-*c*][1, 5] benzodiazepin -7-one **2**.

5, 6-Dihydro-6-pheny1-12*H*-indeno[2, 1-*c*][1, 5]-benzodiazepin-7-one 2a. m.p.197-99°; Yield (80.2%); IR (KBr, cm^{-1}): 3306 (m, N-H stretch), 1690 (s, C=O stretch); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.56 (s, 1H, C_6-H), 6.50-6.60 (dd, 1H, C_4-H, *J*=7.30 and 1.26 Hz), 6.80-6.90 (m 2H, C_2-H and C_3-H), 7.02-7.12 (m, 6H, C_1-H, $C_{2'}$-H, $C_{3'}$-H, $C_{4'}$-H, $C_{5'}$-H, $C_{6'}$-H), 7.20-7.42 (m, 4H, C_8-H, C_9-H, C_{10}-H, C_{11}-H), 7.80 (brs, IH, N-H exchangeable with D_2O); MS: (m/z, % relative intensity), M^+ (324, 54.7), (296, 17.8), (295, 38.8), (247, 56.4), (219, 100), (193, 17.8), (44, 34.8).

5, 6 Dihydro-6-(4'-methylphenyl)-12*H*-indeno [2, 1-*c*][1, 5] benzodiazepin-7-one 2b. m.p.205-206°; Yield (75%); IR (KBr, cm^{-1}): 3275 (m, N-H stretch), 1690 (s, C=O stretch); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.15 (s, 3H, $C_{4'}$-CH_3), 5.52 (s, 1H, C_6-H), 6.50-6.60 (dd, IH, C_4-H, *J* = 7.30 and 1.26 Hz), 6.84-6.88 (m 2H, C_2-H and C_3-H), 6.89 (d, 2H, $C_{2'}$ -H, C_6 -H, *J* = 8.10 Hz), 6.98-7.05 (m, 3H, C_1-H, C_3 -H, C_5 -H), 7.29-7.35 (m, 3H, C_9-H, C_{10}-H, C_{11}-H), 7.42-7.48 (dd, IH, C_8-H, *J* = 8.80 and 1.70 Hz), 7.80 (brs, IH, N-H exchangeable with D_2O); MS: (m/z % relative intensity), M^+ (338, 62.6), (309, 34.4), (247, 59.4), (219, 100), (91, 21.4), (77, 26.3).

5, 6-Dihydro-6-(4′-methoxyphenyl)-12*H*-indeno-[2, 1-*c*][1, 5] benzodiazepin-7-one 2c. m.p. 210-11°; Yield (71%); IR (KBr, cm^{-1}): 3293 (s, N-H stretch), 1670 (s, C=O stretch); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.68 (s, 3H, C_4-OCH_3), 5.51 (s, 1H, C_6-H), 6.50-6.60 (dd, IH, C_4-H, *J*=7.30 and 1.26 Hz), 6.66-6.70 (d, 2H, $C_{3'}$-H and $C_{5'}$-H, *J*=6.73 Hz), 6.86-6.89 (m, 2H, C_2-H & C_3-H), 6.98-7.00 (d, 2H, $C_{2'}$-H and $C_{6'}$-H, *J* = 8.7 Hz), 7.05-7.10 (dd, IH, C_1-H, *J*=7.72 and 1.36 Hz), 7.30-7.38 (m, 4H, C_9-H, C_{10}-H, C_{11}-H, N-H), 7.45-7.50 (dd, IH, C_8-H, *J*=8.25 and 1.56 Hz); MS: (m/z, % relative intensity), M^+ (354, 64.8), (339, 7.6), (325, 27.5), (247, 38.5).

5,6-Dihydro-6-(4′-nitrophenyl)-12*H*-indeno [2, 1-*c*][1, 5] benzodiazepin-7-one 2d. m.p. 259-60°; Yield (69%); IR (KBr, cm^{-1}): 3228 (s, N-H stretch), 1664 (s, C=O stretch), 1520 (s, asymmetric NO_2 stretch), 1320 (s, symmetric NO_2 stretch); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.56 (s, IH, C_6–H), 6.55-6.58 (dd, IH, C_4-H, *J*=7.75 and 1.47 Hz), 6.88-6.98 (m, 2H, C_2-H & C_3-H), 7.08 (dd, IH, C_1-H, *J* = 7.72 and 1.38 Hz), 7.32-7.34 (d, 2H, $C_{2'}$-H & $C_{6'}$-H, *J* = 8.1 Hz), 7.34-7.46 (m, 4H, C_9-H, C_{10}-H, C_{11}-H, N-H), 7.48 (dd, IH, C_8-H, *J*= 8.26 and

1.36 Hz), 8.05 (d, 2H, $C_{3'}$-H and $C_{5'}$-H, *J*= 6.73 Hz); MS: (m/z, % relative intensity), M^+ (369, 99.8), (341, 109), (247, 66.1), (221, 100), (219, 88.6), (194, 62), (102, 24.5), (77, 29.9).

5, 6 -Dihydro-6-(4′-chlorophenyl)-12*H*-indeno[2, 1-*c*][1, 5] benzodiazepin-7-one 2e. m.p. 237-38°; Yield (82%); IR (KBr, cm^{-1}): 3306 (s, N-H stretch), 1668 (s, C=O stretch); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.56 (s, 1H, C_6- H), 6.54-6.60 (dd, IH, C_4-H, *J*=7.10 and 1.85 Hz), 6.60-6.80 (m, 2H, C_2-H and C_3-H), 7.02 (dd, IH, C_1-H, *J*=7.28 and 1.29 Hz), 7.12-7.15 (m, 4H, $C_{2'}$-H, C_3- H, $C_{5'}$-H, $C_{6'}$-H), 7.30-7.40 (m, 4H, C_9-H, C_{10}-H, C_{11}-H, N-H), 7.45-7.50 (dd, IH, C_8-H, *J*= 8.15 and 1.42 Hz); MS: (m/z, % relative intensity), M^{+1}(358, 89.5), (329, 39.5), (247, 60), (219, 100) (193, 14.6), (102, 11.6).

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