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NOTE

Analgesic Activity of Isatin Derivatives

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Schiff bases of isatin are prepared and characterized on the basis of IR and NMR spectral data. The final compounds are evaluated for analgesic activity.

Key Words: Isatin derivatives, Analgesic activity.

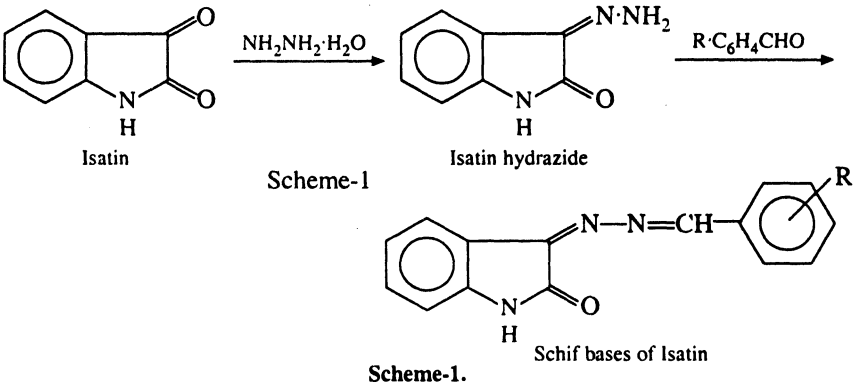
Isatin derivatives were reported to possess wide range of CNS activity *e.g.*, analgesic[1], CNS stimulant[2], potentiation of phenobarbitone induced narcosis[3], antidepressant[4, 5], anticonvulsant[6] and anti-inflammatory activity[7, 8]. Schiff bases of isatin and its derivatives with trimethoprim were synthesized and tested for anti-HIV activity[9]. In the present communication, Schiff bases of isatin are prepared and evaluated for analgesic activity.

Derivatization includes the following two steps:

(i) Synthesis of Isatin Hydrazides: Equimolar quantities of isatin (E. Merck) and hydrazine hydrate in alcohol are refluxed for 2 h. The product which separated out on cooling, is filtered and recrystallised with alcohol, 85%, 220°C.

Characterization of Isatin Hydrazide: IR (cm^{-1}) 3300 $\nu(NH_2)$, 1685 $\nu(C{=}O)$; ^{1}H-NMR (δ) 2.8 (6H, s, $2XCH_3$), 6.4 (1H m, =CH), 6.85 (2H, d, Ar—H), 6.96 (1H, d, Ar—H), 7.13 (2H, d, Ar—H), 7.20 (1H, d, Ar—H), 9.5 (1H, s, NH).

(ii) Synthesis of Schiff bases: Equimolar quantities of isatin hydrazide and aromatic aldehyde (Table-1) in alcohol are refluxed for 3 h. The contents are concentrated and cooled down. The product which separated out on cooling is filtered and recrystallised with alcohol **(Scheme-1)**.

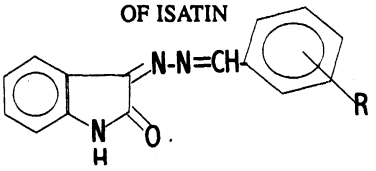


Isatin — Isatin hydrazide — Schif bases of Isatin

Scheme-1

Scheme-1.

TABLE-1
PHYSICAL CHARACTERISTICS AND ANALGESIC ACTIVITY OF SCHIFF BASES OF ISATIN



Compd.	m.f.	R	Yield (%), m.p. (°C)	Mean basal reaction time
1a	$C_{18}H_{11}N_3O_4$	3,4,5-trimethoxy	70, 190	7.53
1b	$C_{17}H_{16}N_4O$	*p*-dimethylamino	70, 216	8.00
1c	$C_{15}H_{11}N_3O$	H	70, 250	8.50
1d	$C_{16}H_{13}N_3O_2$	*p*-methoxy	70, 180	7.25
1e	$C_{15}H_9N_3OCl_2$	2,4-dichloro	60, 230	6.25
1f	$C_{15}H_{10}N_3OCl$	*o*-chloro	60, 226	6.50
1g	$C_{15}H_{11}N_3O_2$	*o*-hydroxy	60, 220	5.75
1h	$C_{16}H_{14}N_3O$	4-hydroxy 3-methyl	60, 255	7.75

Characterization of 3-[2′-(4″-dimethyl amino) benzyl hydrazine] indole-2-one (1b): IR (cm^{-1}): 1686 ν(C=O), 1657 ν(C=C), 1466 (C=N); ^{1}H-NMR (δ): 6.4 (1H, m, =CH), 6.8 (2H, d, Ar—H), 6.96 (1H, d, Ar—H), 7.10 (1H, d, Ar—H), 7.13 (2H, d, Ar—H), 7.34 (2H, d, Ar—H), 9.8 (1H, s, NH).

Characterization of 3-(2′- benzyl hydrazine) indole-2-one (1c): IR (cm^{-1}) 1700 ν(C=O), 1615 ν(C=C), 1462 ν(C=N), 1332, 1200, 751, 666; ^{1}H NMR (δ): 6.8 (3H, d, Ar—H), 6.96 (2H, d, Ar—H), 7.15 (1H, d, Ar—H), 7.15 (1H, d, Ar—H), 7.20 (2H, d, Ar—H), 9.8 (1H, s, NH).

Analgesic activity: The activity is carried out on albino mice by Eddy's hot plate method. The albino mice were kept under standard condition at ambient temperature at 25 ± 2°C. The suspension of standard drug aspirin and test compounds were prepared in 0.5% CMC. The aspirin (25 mg/kg) and test compound (30 mg/kg) were injected by peritoneal route. The results in terms of basal reaction time (BRT) are recorded in Table-1, which shows that compounds were found to possess analgesic activity but comparatively less than aspirin.

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