Synthesis of 1-*H*-inden-1-one derivatives via the reaction of Shiff bases with carbon suboxide

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1-oxo-*N*-phenyl-1*H*-inden-2-carbamide were obtained by reaction of Schiff bases with carbon suboxide (C_3O_2) in presence of $AlCl_3$.

Keywords: Shiff bases, carbon suboxide, 1-*H*-inden-1-one derivatives

In recent years many works have been published on 1*H*-Inden-1-one derivatives have different pharmacological activities including: antimicrobial,[1-3] fungicidal,[3] anti-HIV,[4] anti-tumor,[5] herbicidal,[6] and anti-inflammatory activity.[7-10] It is known that the presence of an aromatic or aliphatic chain at position 2 or 3 of the 1-H-inden-1-one containing double bonds conjugated with the ring increases antimicrobial and herbicidal activity.[4-6] However, absence of conjugation increase the anti-inflammatory activity.[8-10]

Continuing our research on the reactivity of carbon suboxide with Schiff bases[11-13], we synthesised various 2-carboxy-anilide-1H-inden-1-one derivatives (**3a–e**) by reaction of carbon suboxide (C_3O_2)[18] (**2**) with azomethine (**1a–e**) (molar ratio 1:1) (Scheme 1).

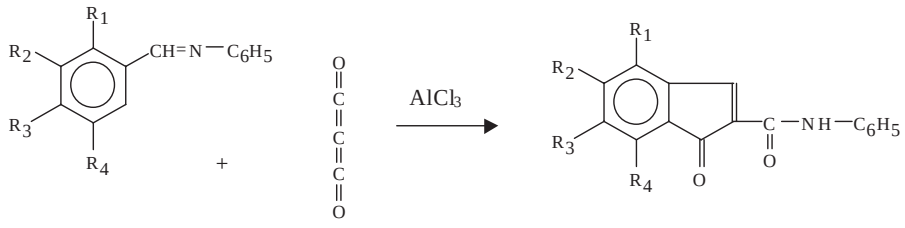
Schiff bases (**1a–e**) were prepared by the method according to the literature.[14]

Catalytic amounts of aluminium chloride were added to avoid the formation of malonic acid and to increase the electrophilic attack of C_3O_2 on the aromatic ring. A viscous gum was obtained at the end of the reaction. It was then washed with 10% aqueous $NaHCO_3$ and extracted with $CHCl_3$. After concentration under reduced pressure, the organic solution gave a crude residue that showed two spots on TLC. Two major compounds were isolated from the crude residue by column chromatography (Silica gel) using benzene-ethylacetate (in various molar ratios) as eluents. The structures of compounds **3a–e** were confirmed by their analytical and spectral data (FTIR, MS, ^{1}H NMR and ^{13}C NMR see Tables 1 and 2).

Compounds **3a–e** probably were derived from an initial attack of the carbonyl carbon on azomethinic nitrogen, providing an ionic, seven-membered-ring intermediate (I), which gives **3a–e** derivatives through the intermediate (II) (Scheme 2). The proposed mechanism has precedent from previous work on similar reactions.[15,16]

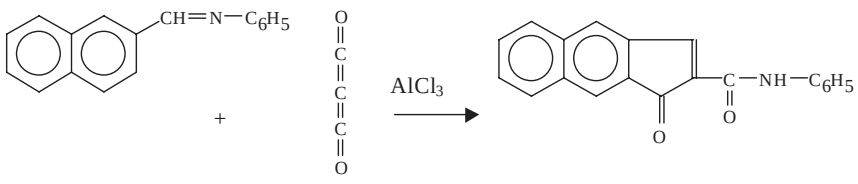
Experimental

Melting points were determined on a Kőfler apparatus and are uncorrected. The FTIR spectra were recorded on a Perkin Elmer System 2000 spectrophotometer using nujul mulls. ^{13}C and ^{1}H NMR spectra were recorded on a Varian Unity 330 using TMS as an internal standard. Mss spectra were taken with a QMD 1000 instrument (Fisons instrument) at 70 eV using a direct inlet system. Elemental analyses were carried out on a Carlo Erba Model 1106 Elemental analyser. Commercially available reagent-grade reagents and solvents were used. All compounds were purchased from Aldrich Chemical Co. and the solvents were dried rigorously before use according to standard methods. Carbon suboxide was prepared by pyrolysis of di-*O*-acetyltartaric anhydride.[18] Silica gel 60, 230–400 mesh (Merck) was used for column chromatography.



1a-d **2** **3a-d**

1a R_1=H; R_2=H; R_3=H; R_4=H
1b R_1=OCH_3; R_2=H; R_3=OCH_3; R_4=OCH_3
1c R_1=Cl; R_2=H; R_3=H; R_4=H
1d R_1=H; R_2=NO_2; R_3=H; R_4=H



1e **2** **3e**

Scheme 1 Reaction of Schiff bases with C_3O_2 in presence of $AlCl_3$.

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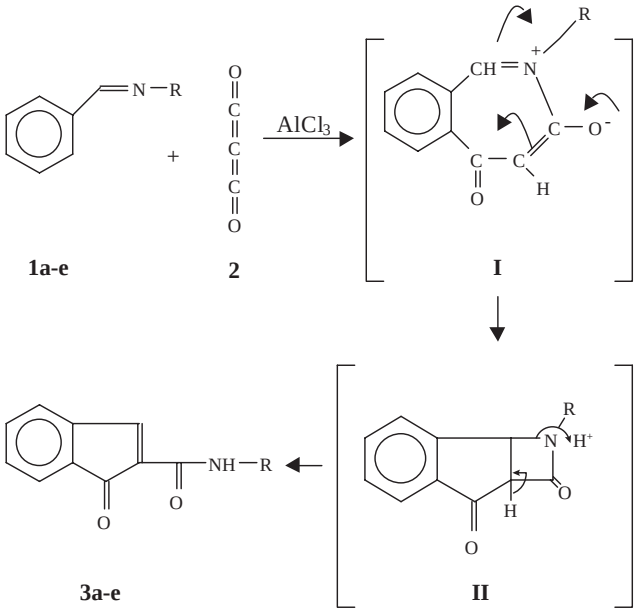
Table 1 Analytical and spectral data for compounds **3a-e**

Compd.	Yield/%	M.p./°C	IR (ν_{max} cm^{-1}) nujol	Elemental Analysis Calc./% (Found) C	H	N	Molecular Formula M^+ (*m/z*)
3a	60	120–121	3350, 1720, 1695, 1620, 1590, 1250, 1200, 1020, 750	77.10 77.13	4.42 4.81	5.69 5.34	$C_{16}H_{11}NO_2$ 249
3b	47	114–116	3360,1740, 1650, 1600, 1580, 1200, 1040, 1000, 810	67.20 67.24	5.0 5.21	4.12 4.00	$C_{19}H_{17}NO_5$ 339
3c	56	131–133	3400, 1710, 1690, 1580, 1190, 1050, 800	65.30 65.28	3.40 3.30	9.52 9.47	$C_{16}H_{10}NO_2Cl$ 283
3d	52	96–98	3600, 1720, 1680, 1620, 1590, 1210, 920, 760	80.26 80.59	4.35 4.97	4.68 4.50	$C_{20}H_{13}NO_2$ 299
3e	38	105–107	3380, 1720, 1680, 1620, 1590, 1060 860, 750	67.72 68.00	3.52 3.79	4.93 4.91	$C_{16}H_{10}N_2O_4$



Scheme 2 Proposed mechanism from compounds 3a–e

General procedure for synthesis of **3a–e**: Carbon suboxide (**2**) (1.10 g, 16.0 mmol) was slowly added at –70°C to stirred solutions of **1a–e** (16 mmol) in 400 ml of anhydrous chloroform. When the addition was completed, a catalytic amount of $AlCl_3$ was added and the mixture was kept under stirring at 0°C for 4 h and RT for 48 h. At completion of the reaction, the solvent was evaporated and the residue extracted with $CHCl_3$. The organic layer was evaporated under reduced pressure to give a solid. The solid was chromatographed on silica gel with benzene: ethyl acetate (different ratio) to give **3a–e**. The analytical and spectral data for compounds **3a–e** are reported in Tables 1 and 2.

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Table 2 ^{1}H and ^{13}C NMR data for compounds **3a-e**.

Compd.	^{1}H NMR (δ, ppm) DMSO-d_6	^{13}C NMR (δ, ppm) DMSO-d_6
3a	10.02 (s, 1H, NH, D_2Oexch), 8.30 (s, 1H, CH=), 7.82–7.00 (m, 9H, arom)	189.7, 159.3, 158.9, 144.8, 138.1, 133.8, 129.4, 123.2, 120.4, 120.0
3b	10.20 (s, 1H, NH, D_2O exch), 8.40 (s, 1H, CH=), 7.40–7.10 (m, 5H, arom), 6.75 (s, 1H, arom), 4.00–3.80 (m, 9H, OCH_3)	188.1, 159.4, 159.2, 152.4, 150.3, 140.7, 138.0, 134.6, 130.6, 126.5, 121.3, 120.2, 120.0, 105.8, 60.5, 55.9, 55.6
3c	10.05 (s, 1H, NH, D_2O exch), 8.65 (s, 1H, CH=), 7.70–7.02 (m, 8H, arom)	190.2, 160.1, 159.1, 150.9, 141.5, 140.2, 138.3, 134.5, 130.6, 122.1, 120.4, 120.1, 117.4
3d	10.17 (s, 1H, NH, D_2O exch), 8.63 (s, 1H, CH=), 8.40–7.25 (m, 11H, arom)	190.1, 158.8, 158.2, 143.5, 140.8, 138.3, 136.3, 134.4, 132.2, 129.9, 127.7, 128.9, 120.8, 120.2, 108.1
3e	10.50 (s, 1H, NH, D_2O exch), 8.93(s, 1H, CH=), 7.50–7.20 (m, 8H, arom)	190.4, 158.9, 152.2, 138.1, 137.3, 136.21, 135.9, 130.5, 128.8, 120.9, 120.7, 120.1

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