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Imino Diels-Alder Reactions Catalyzed by Indium Trichloride ($InCl_3$). Facile Synthesis of Quinoline and Phenanthridinone Derivatives.

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Abstract: Anhydrous indium trichloride ($InCl_3$) is found to catalyze the imino Diels-Alder reactions and results in facile synthesis of quinoline derivatives. A previously unreported series of phenanthridinones was obtained by the treatment of cyclohexenones with Schiff bases.

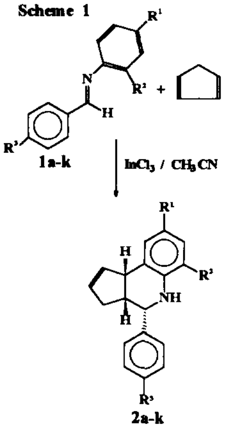
The imino Diels-Alder reaction is one of the powerful synthetic methods for the synthesis of pyridine and quinoline derivatives.[1] Lewis acids such as BF_3. Et_2O and TFA have been found to catalyze the Diels-Alder reaction of keto-imines[2] and Schiff bases[3]. Although Lewis acids promote the reaction, more than stoichiometric amounts of the acids are required due to the strong coordination of the acids to nitrogen atoms[1]. Recently Kobayashi[4] reported that lanthanide triflates catalyze Diels-Alder reactions and Mukaiyama aldol reactions in water[5] due to its high coordination number and a fast coordination - dissociation equilibrium in aqueous solutions. This paper describes the anhydrous indium trichloride catalyzed imino Diels-Alder reaction of Schiff bases with cyclopentadiene and cyclohexenone.

In the presence of 20mol% anhydrous indium trichloride ($InCl_3$), N-benzilideneaniline (**1a**) was treated with cyclopentadiene (CPD) in acetonitrile at room temperature. The imine acted as a heterodiene and the reaction proceeded smoothly to give the corresponding tetrahydroquinoline derivative in 30 min (Scheme 1).

Although, Schiff bases act as heterodienes in the presence of Lewis acids with cyclopentadiene, cyclohexadiene and other dienophiles, reaction of Schiff bases as heterodienes with cycloalkenones is unprecedented. Therefore, in the present work we treated cyclohexenone with N-benzylidene-p-nitroaniline (**3b**) in acetonitrile using 20 mol% indium trichloride and stirred at room temperature for 24h. We obtained very good yields of phenanthridone derivatives[6] **4b** and **5b** in a ratio of 67:33 in a overall yield of 70%. (Scheme 2). The wide spectrum of biological activities[7] of phenanthridinones underscores the need to find new synthetic methods.

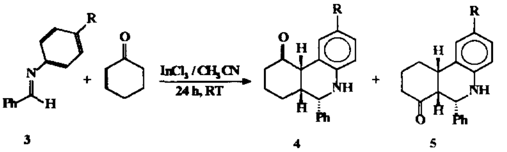
In conclusion, we have shown that in the presence of anhydrous indium trichloride, Schiff bases act as heterodiene and reacts well with cyclopentadiene and cyclohexenone and results in novel synthesis of quinoline and phenanthridinone derivatives.

Scheme 1



Product^a	R^1	R^2	R^3	Time (min.)	Yield (%)^b
2a	H	H	H	30	75
2b	NO_2	H	H	30	95
2c	OCH_3	H	H	45	58
2d	Cl	H	H	30	84
2e	Cl	CH_3	H	30	90
2f	H	COOH	H	45	78
2g	H	C_2H_5	H	45	82
2h	H	NO_2	H	30	75
2i	H	H	CH_3	45	65
2j	H	H	Cl	30	77
2k	Cl	H	Cl	30	80

Scheme 2



Schiff base	R	Product^{a,c} Ratio of 4:5	Overall yield (%)
3a	H	69 : 31	65
3b	NO_2	67 : 33	70
3c	OCH_3	68 : 32	60
3d	Cl	73 : 27	68

a. All reactions were conducted at room temperature by addition of 20mol% $InCl_3$ to a mixture of Schiff base and cyclopentadiene or cyclohexenone in acetonitrile and products were characterised by Mass, IR, ^1H NMR and ^{13}C NMR.
b Isolated yield. c. The reactions were completed in 24h. Product ratio is based on isolation by column chromatography.

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6. Representative spectral data: Compound **4b** : ^1H NMR (300 MHz, $CDCl_3$) δ 7.99(m, 2H), 7.29(m, 4H), 6.54(m, 2H), 4.88(d, J=2.3Hz, 1H), 4.68(d, J=2.0Hz, 1H), 2.76(m, 1H), 2.65(m, 1H), 2.52(m, 1H), 2.32(m, 1H), 2.06(m, 1H), 1.70(m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.06, 152.48, 139.24, 138.16, 129.12, 127.98, 126.27, 125.92, 125.72, 113.06, 111.74, 61.90, 50.64, 49.08, 43.06, 25.16, 16.54; MS(m/e): 322(M^+); IR (KBr) : 3368, 2960, 1731, 1599, 1319, 1119 cm^{-1}. Compound **5b** : ^1H NMR (300 MHz, $CDCl_3$) δ 7.95(m, 2H), 7.24(m, 4H), 6.55(m,2H), 4.79(d, J=2.3Hz, 1H), 4.66(m, 1H), 2.86(m, 1H), 2.71(m, 1H), 2.49(m, 1H), 2.16(m, 2H), 1.78(m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.75, 152.56, 139.30, 138.10, 129.23, 129.15, 128.07, 125.91, 125.76, 125.29, 111.98, 111.77, 65.37, 51.96, 49.23, 45.01, 23.77, 22.18; MS(m/e): 322(M^+); IR (KBr) : 3368, 2927, 1729, 1597, 1320, 1116 cm^{-1}.
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