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Convenient Synthesis of Pyrano[*3,2-c*]quinolines and Indeno[*2,1-c*] quinolines by Imino Diels-Alder Reactions

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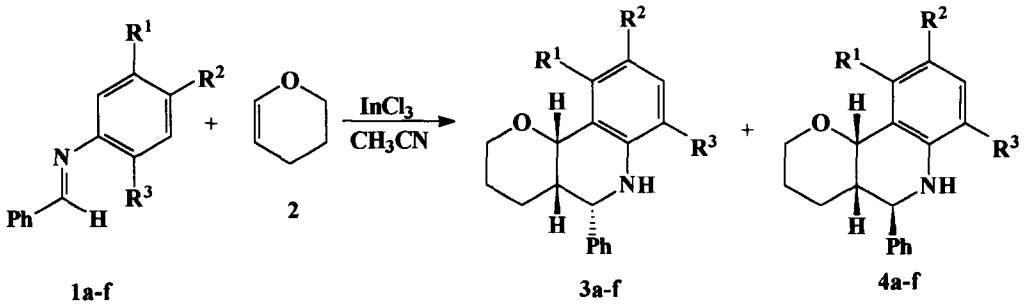
Abstract: Anhydrous indium trichloride ($InCl_3$) is found to catalyze the imino Diels-Alder reaction of 3,4-dihydro-2*H*-pyran and indene with Schiff's bases to afford pyrano[*3,2-c*]quinolines and indeno[*2,1-c*] quinolines. Imino Diels-Alder reactions of *N*-benzylidene 1-naphthylamine with 3,4-dihydro-2*H*-pyran and indene results in efficient synthesis of phenanthridine derivatives.

Pyrano quinoline moiety is present in many alkaloids.[1] Pyrano quinoline derivatives possess wide range of biological activities such as psychotropic activity,[2] antiallergic activity,[3] antiinflammatory activity,[4] estronegic activity[5] and are used as a potential pharmaceuticals.[6] Indeno quinoline derivatives also possess wide range of biological activities such as 5-HT-receptor binding activity,[7] antiinflammatory activity,[8] and also act as antitumor agents[9] and inhibitor for steroid reductase.[10] Imino Diels-Alder reactions provide an easy entry into quinoline derivatives.[11] Recently, we have shown that indium trichloride activates the imines[12] in the imino Diels-Alder reaction of Schiff's bases with cyclopentadiene and cycloalkenones.

Few reports are available for the synthesis of pyrano- and indeno quinolines by imino Diels-Alder reactions.[13] Herein, we wish to report the synthesis of pyrano- and indeno quinolines by imino Diels-Alder reactions of 3,4-dihydro-2*H*-pyran and indene with Schiff's bases catalyzed by indium trichloride ($InCl_3$).

In the presence of 20 mol % anhydrous indium trichloride ($InCl_3$), *N*-benzylidene aniline **1a** was treated with 3,4-dihydro-2*H*-pyran **2** in acetonitrile at room temperature. After 30 minutes we obtained pyrano quinolines **3a** and **4a** in a ratio of 41:59 in an overall yield of 80 % (Scheme 1).

Scheme 1



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Pyrano quinolines **3** and **4** were obtained in varying ratios for imines derived from *p*-substituted anilines. In the case of imines derived from 2,4- and 2,5-disubstituted anilines, pyrano quinoline derivative **4** was obtained as major compound. The results are summarized in Table 1.

Table 1. Reaction of Schiff's bases with 3,4-dihydro-2*H*-pyran (2) employing 20 mol% $InCl_3$.[a]

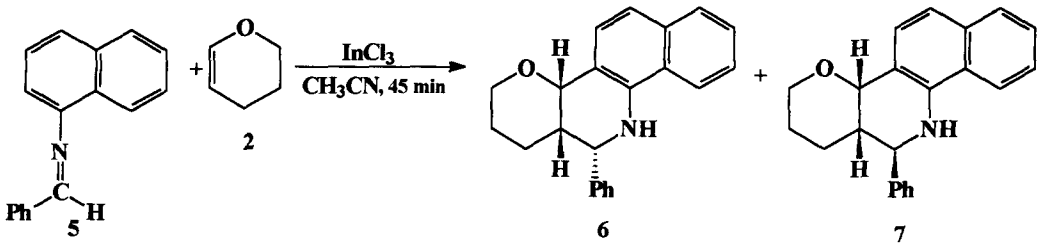
Schiff's base	Substituents			Time, min.	Product[b] ratio of 3:4	Overall yield (%)
	R^1	R^2	R^3			
1a	H	H	H	30	41:59	80
1b	H	Cl	H	30	34:66	50
1c	H	OCH_3	H	240	58:42	70
1d	H	CH_3	H	120	68:32	70
1e	H	Cl	CH_3	40	5:95	46
1f	CH_3	H	CH_3	180	5:95	45

a: All reactions were conducted at room temperature by addition of 20 mol % $InCl_3$ to a mixture of Schiff's base and 3,4-dihydro-2*H*-pyran in acetonitrile.

b: Products were characterized by Mass, IR, ^1H NMR and ^{13}C NMR. The ratio based on isolation by chromatography.

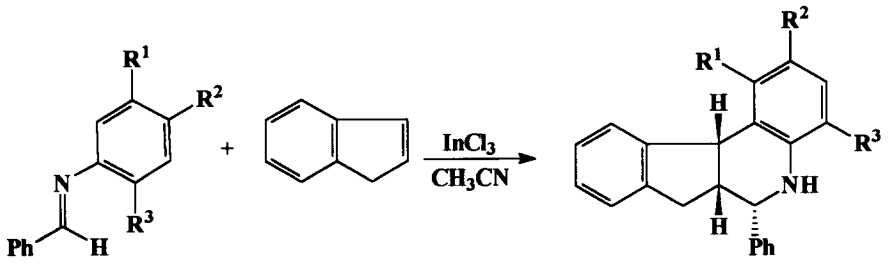
Indium trichloride also catalyzes effectively the imino Diels-Alder reaction of 3,4-dihydro-2*H*-pyran with *N*-benzylidene 1-naphthylamine **5** and resulted in phenanthridine derivatives **6** and **7** in a ratio of 32:68 in an overall yield of 53 % (Scheme 2).

Scheme 2



Next, *N*-benzylidene aniline **1a** in acetonitrile was stirred at room temperature with indene **8** in the presence of 20 mol % indium trichloride. After 6 h, indenoquinoline **9a** was obtained in moderate yield (Scheme 3). Only one isomer was obtained in the reaction of Schiff's bases with indene and the results are summarized in Table 2.

Scheme 3



1a-f 8 9a-f

Table 2 : Reaction of Schiff's bases with indene (8) employing 20 mol % $InCl_3$.[a]

Shiff's base	Product[b]	Substituents			Time, h	Yield (%)[c]
		R^1	R^2	R^3		
1a	**9a**	H	H	H	6	40
1b	**9b**	H	Cl	H	6	48
1c	**9c**	H	OCH_3	H	24	30
1e	**9e**	H	Cl	CH_3	12	48
1f	**9f**	CH_3	H	CH_3	9, reflux	65

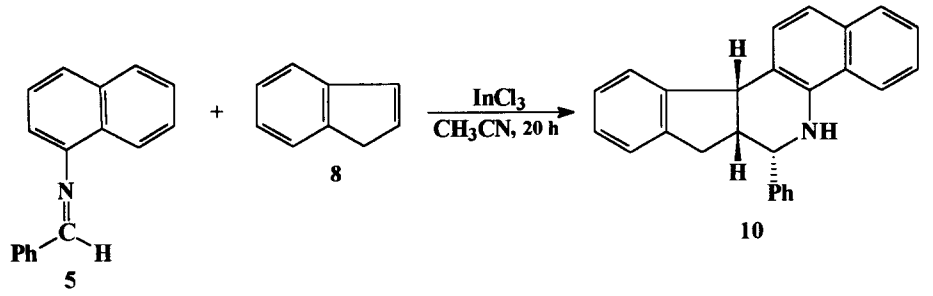
a : All reactions were conducted at room temperature by addition of 20 mol % $InCl_3$ to a mixture of schiff's bases and indene in acetonitrile.

b : Products were characterized by Mass, IR, ^1H NMR and ^{13}C NMR.

c : Isolated yield.

When *N*-benzylidene 1-naphthylamine **5** in acetronitrile was treated with indene **8** in the presence of 20 mol % $InCl_3$, indeno phenanthridine[14] **10** was obtained in 50 % yield (Scheme 4).

Scheme 4



5 8 10

In conclusion, we have shown that indium trichloride catalyzes the imino Diels-Alder reaction of Schiff's bases with 3,4-dihydro-2*H*-pyran and indene which provides a convenient synthesis of pyrano

[*3,2-c*]quinolines and indeno[*2,1-c*]quinolines. Application of imino Diels-Alder reaction to *N*-benzylidine 1-naphthylamine results in novel synthesis of phenanthridine derivatives.

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14. Selected spectral data for compound **10** : ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80-7.08(m, 15H), 4.85(br s, 1H), 4.75(d, 1H, J = 7.2Hz), 4.71(br s, 1H, NH), 3.47(m, 2H), 2.50(m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.2, 142.9, 142.7, 139.4, 132.6, 128.6, 128.5, 127.5, 127.3, 126.9, 126.7, 126.1, 125.2, 125.1, 125.0, 124.9, 119.6, 118.5, 117.6, 57.7, 48.1, 46.8, 30.9; MS(m/e): 347(M^+); IR (KBr) : 3414, 3065, 1577 cm^{-1}.