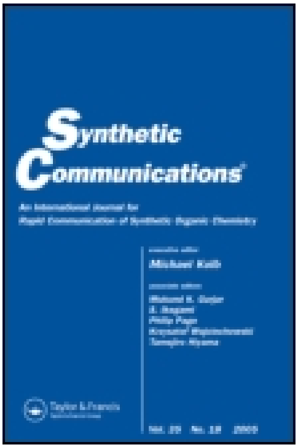

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IMINO DIELS-ALDER REACTIONS CATALYZED BY OXALIC ACID DIHYDRATE. SYNTHESIS OF TETRAHYDROQUINOLINE DERIVATIVES

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IMINO DIELS–ALDER REACTIONS CATALYZED BY OXALIC ACID DIHYDRATE. SYNTHESIS OF TETRAHYDROQUINOLINE DERIVATIVES

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ABSTRACT

Oxalic acid dihydrate is found to catalyze the Imino Diels–Alder reaction of schiff bases derived from substituted anilines with cyclopentadiene, results in the formation of Tetrahydroquinoline derivatives in moderate yields.

Tetrahydroquinoline derivatives are an important class of Natural products which exhibit biological activities such as psychotropic,[1] anti-allergenic,[2] antiinflammatory[3] and estronegic[4] activities. Lewis acids like $BF_3.Et_2O$,[5] $InCl_3$,[6] Lanthanide triflates[7] and protic acids such as TFA,[8] p-TsOH[9] have been found to catalyze the reaction of aldimines with electron rich dienophiles. The reaction of N-benzylidene aniline with 3,4-dihydropyran calatysed bt BF_3 Et_2O takes 12 h and yields only 25% of pyranoquinoline.[5] Since oxalic acid dihydrate is an inexpensive and commercially available acid, explored its ability to catalyze the imino Diels–Alder Reactions effectively.

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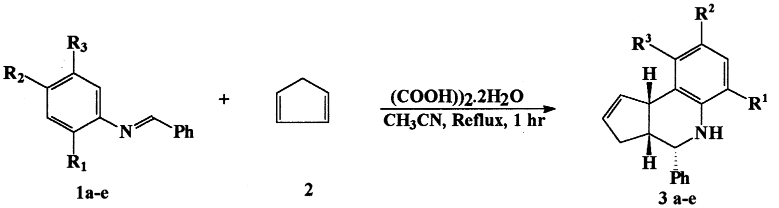
N-benzylideneaniline (**1a**) was refluxed with cyclopentadiene (**2**) in the presence of oxalic acid in acetonitrile for 1 h. The imine acted as a heterodiene and the reaction proceeded smoothly to give the corresponding tetrahydroquinoline (**3a**) in 58% yield. This is the first report for the imino Diels–Alder reaction catalyzed by oxalic acid dihydrate.



Scheme 1.

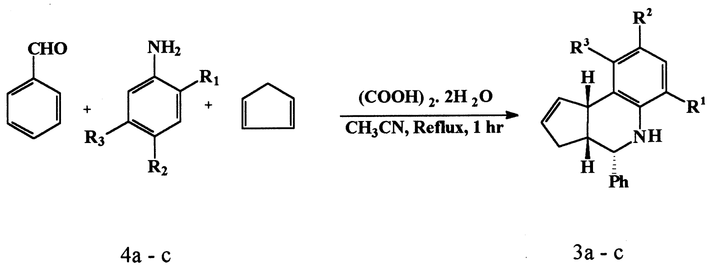
Table 1. Synthesis of Cyclopentaquinolines

Entry	Imines	Substituents R^1	R^2	R^3	Yield (%)
1	1a	H	H	H	58
2	1b	H	Cl	H	49
3	1c	H	COOH	H	75
4	1d	CH_2CH_3	H	H	77
5	1e	CH_3	H	CH_3	67

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

Imines generated *insitu* from aldehydes and amines, immediately reacts with cyclopentadiene to afford cyclopentaquinolines in an one pot way without the need of pre-formation of the imines. It was found that the reaction of benzaldehyde, aniline and cyclopentadiene in acetonitrile was refluxed in the presence of oxalic acid dihydrate to yield the product **3a** in 51% yield in 1 h.

The reaction of bezaldehyde, aniline with cyclopentadiene catalyzed by oxalic acid was also conducted in aqueous medium (CH_3CN-H_2O) to give the product **3a** in 45% yield. The reaction of morpholine enamine with N-benzylidene aniline catalysed by PTSA takes 12 h,[10] where as oxalic acid catalysed reaction of N-benzylidene aniline with cyclopentadiene goes to completion within one hour. Lewis acids like $InCl_3$, BF_3, Et_2O require anhydrous conditions, but commercial sample of oxalic acid can be used



4a - c

3a - c

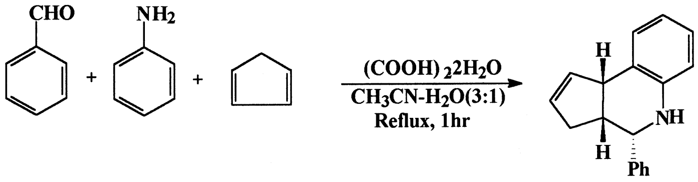
$R^1 = H, R^2 = H, R^3 = H$; 51%

$R^1 = CH_2CH_3, R^2 = H, R^3 = H$; 42%

$R^1 = CH_3, R^2 = H, R^3 = CH_3$; 69%

Scheme 2.

for imino Diels–Alder reaction. BF_3 Et_2O gets hydrolysed to the hydroxide in aqueous medium where as in the case of oxalic acid the reaction can be conducted in aqueous medium with out any decomposition.



3 a

In conclusion, this paper describes a simple method for obtaining tetrahydroquinolines using commercially available, an inexpensive oxalic acid dihydrate as a catalyst.

EXPERIMENTAL

To a stirred solution of schiff base 1b (2.5 mmol) and cyclopentadiene (0.330 g, 5 mmol) in acetonitrile (10 ml) was added oxalic acid dihydrate (0.315 g, 2.5 mmol) and refluxed for 1 h. The reaction mixture poured over an ice water and extracted with chloroform (3 × 10 ml). The combined organic layer was washed with saturated $NaHCO_3$ (10 ml) and brine (10 ml), dried over anhydrous Na_2SO_4, then concentrated under reduced pressure. The residue was purified by column chromatography using silicagel (60–120 mesh) and eluted with petroleum ether: Ethyl acetate (95:5) to afford 3b as pale yellow crystalline solid in 49% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44 (m, 5H), 7.04 (d, 1H, J = 2.1 Hz), 6.93 (dd, 1H, J = 2.2 Hz, J = 8.6 Hz), 6.55 (d, 1H, J = 8.5 Hz), 5.82 (m, 1H), 5.69 (m, 1H), 4.61 (d, 1H, J = 2.9 Hz), 4.09 (d, 1H, J = 8.6 Hz), 3.76 (br s, 1H), 3.05 (m, 1H), 2.67 (m, 1H), 1.86 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.1, 142.3, 133.4, 130.8, 128.6, 128.4, 127.6, 127.3, 126.4, 123.4, 116.9, 57.9, 46.2, 45.7, 31.4; MS (m/z): 281 (M^+), 283 ($M^+ + 2$); IR (KBr): 3363, 1470 cm^{-1}.

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