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Mild and efficient method for oxidation of alcohol to carboxylic acid followed by synthesis of amide analogues of Corey's lactone

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ABSTRACT

A mild, safe and efficient method for the oxidation of Corey's lactone to carboxylic acid under modified Anelli's oxidation condition has been developed. The oxidation reaction proceeded at room temperature under biphasic reaction in DCM/water with high yield. Further, treatment of carboxylic acid with various amines was studied for the first time, resulting in the formation of amides in good to excellent yields.

Keywords: Oxidation; Alcohol; Carboxylic acid; Amines; Amide.

INTRODUCTION

Corey's lactone is precursor for the synthesis of prostaglandin analogues[1a] which have a diverse range of biological activity. Members of the prostaglandin $F_{2\alpha}$[1b] family are generally highly potent compounds for the treatment of glaucoma and ocular hypertension[1c]. In this paper, we report the Oxidation of Corey lactone to corresponding carboxylic acid with sodiumperiodate/sodiumchloride/water [2] in presence of TEMPO catalyst under biphasic reaction. The acid is further reacted with different amines in presence of *p*-toluenesulfonyl chloride/DMAP gives corresponding amide analogues. The synthetic scheme of these compounds is shown in Scheme-2.

MATERIALS AND METHODS

All the reagents used for reactions are of L.R. Grade.IR spectra were recorded as KBr pellets on Thermo Nicolet Avatar 330 FT-IR spectrometer.^{1}H NMR spectra were recorded on Bruker Avance-300 spectrometer operating at 200 MHz using TMS as internal standard. Mass spectra (EI, 70 eV) were recorded on an HP5989B mass spectrometer.

Synthesis of (3aR,4R,5R,6aS)-5-(([1,1'-biphenyl]-4-carbonyl)oxy)-2-oxohexa hydro-2H-cyclopenta [b]furan-4-carboxylic acid. 2.

Corey's lactone (1.0 gm, 2.84 mmol) and TEMPO (0.0284 mmol) in DCM(10 mL) in 50 ml round bottom flask and stirred for 10-15 min, a solution of sodium periodate (1.4 gm, 5.68 mmol), sodium chloride (33 mg, 0.568 mmol) in water (10 mL) were added in to reaction mass and stirred vigorously for 10-12 h at 25-30^{o}C. Separated bottom organic layer and aqueous layer extracted with DCM (5 mL). Organic layer was washed with 5% $Na_2S_2O_3$ solution (10 mL). Organic layer dried over sodium sulphate and concentrated under reduced pressure solid was obtained. The crude product was recrystalliation in di isopropyl ether (15 mL) gives pure Corey's lactone acid 2 was obtained wt: 0.95 gm Yield: 95% A white solid; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ=2.45-2.53(t, 2H), 2.58-2.74(d, 1H), 2.98-3.09(m, 1H), 3.16(s, 1H), 3.45(s, 1H), 5.20(s, 1H), 5.77(s, 1H), 6.72-6.91(s, 1H), 7.39-7.49(m, 3H), 7.61-7.71(dd, 4H), 8.05-8.09(d, 2H); IR (KBr): 2523 , 1776 ,1706 cm^{-1}; found: m/z 383.10 [M+18]

Synthesis of amide analogues of Corey's lactone

To a mixture of Corey's acid 1 (250 mg, 0.68 mmol) in DCM (10 mL) solution and cooled to 0-5^{o}C. Added PTsCl (134 mg, 0.70 mmol),stirred for 15-20min, followed by addition of DMAP(83 mg, 0.68 mmol),stir for 15-20 min and amine (0.68 mmol) was added to the reaction, then the reaction mass temperature raised to 23-25^{o}C and stirred for 1-2h.The reaction was monitored by thin-layer chromatography(TLC). After completion, the reaction mixture was washed with citric acid solution (10%) 25mL and water (25 mL) . The organic layer was washed with brine solution.The organic layer was concentrated, and the residue was subjected to column chromatograph (15% Acetone and Cyclohexane mixture) to obtain pure Corey's amide.

The specific compounds 3-8 have been synthesized according to the above general procedure; yield and reaction cycle time have been reported in below examples and Table-3.

(3aR,4R,5R,6aS)-4-(diethylcarbamoyl)-2-oxohexahydro-2H-cyclopenta[b]furan-5-yl [1,1'-biphenyl] -4-carboxylate 3.

Colourless residue : ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ=1.12-1.25(t, 6H), 2.42-2.47(m, 2H), 2.48-2.59(m, 2H), 2.93-3.00(m, 1H), 3.25-3.38(q, J= ,3H), 3.47-3.56(d, 2H), 5.33-5.37(q, J= ,1H), 5.49(q, J= ,1H), 7.61-7.62(d, 2H) 7.67-7.69(d, 2H), 8.05-8.07(d, 2H); IR(KBr): 3304, 1770, 1713, 1632 cm^{-1}; found: m/z 422.20[M+1].

(3aR,4R,5R,6aS)-4- (benzylcarbamoyl)-2-oxohexahydro-2H-cyclopenta[b]furan-5-yl[1,1'-biphenyl]-4-carboxylate 4.

A white solid; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ=2.33-2.42(m, 2H), 2.53-2.57(d, 1H), 2.92-2.99(m, 2H), 3.67-3.71(t, 1H), 4.46-4.51(d, 2H), 5.24-5.27(q, 1H), 5.42(t, J= ,1H), 7.26-7.33(m, 6H), 7.44-7.48(t, 2H), 7.59-7.61(d, 2H), 7.65-7.67(d, 2H), 8.03-8.06(d, 2H); IR(KBr): 3304 , 1769 , 1725 , 1633 cm^{-1}; found: m/z 456.25 [M+1].

(3aR,4R,5R,6aS)-4- (hexylcarbamoyl)-2-oxohexahydro-2H-cyclopenta[b]furan-5-yl[1,1'-biphenyl]-4-carboxylate 5.

A white solid; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ= 0.89(t, 3H), 1.30(s, 6H), 1.51-1.56(m, 2H), 2.30-2.41(m, 2H), 2.52-2.56(d, 1H), 2.86-2.98(m, 2H), 3.26-3.31(q, 2H), 3.66(s, 1H), 5.23-5.25(q, 1H), 5.39(q, 1H), 7.38-7.48(m, 3H), 7.60-7.69(m, 4H), 8.06-8.08(d, 2H); IR(KBr): 3308, 1769 , 1726 , 1644 cm^{-1}; found: m/z 450.35 [M+1].

(3aR,4R,5R,6aS)-2-oxo-4-(4,5,6,7-tetrahydrothieno[3,2-c]pyridine-5-carbonyl) hexahydro-2H-cyclopenta[b]furan-5-yl[1, 1'-biphenyl]-4-carboxylate 6.

A white solid; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ=2.44-2.50(m, 3H), 2.88-3.02(m, 3H), 3.61-3.67(t, 2H), 4.02-4.10(m, 2H), 4.61-4.75(m, 2H), 5.35-5.39(q, 1H), 5.40-5.54(q, 1H), 6.81-6.89(d, 1H), 7.16(d, 1H), 7.38-7.48(m, 3H), 7.61-7.71(m , 4H), 8.04-8.09(d, 2H); IR(KBr): 3504 , 1774 , 1710 , 1638 cm^{-1}; found: m/z 488.25[M+1].

(3aR,4R,5R,6aS)- 4-(morpholine-4-carbonyl)-2-oxohexahydro-2H-cyclopenta [b]furan-5-yl[1,1'-biphenyl]-4-carboxylate 7.

A white solid; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ=2.40-2.51(m, 3H), 2.93-3.00(m, 1H), 3.36(s, 1H), 3.44-3.49(m, 1H), 3.63-3.67(t, 3H), 3.77-3.86(t, 4H), 3.97-4.00(d, 1H), 5.37-5.40(t, 1H), 5.48(s, 1H), 7.39-7.50(m, 3H), 7.62-7.71(d, 4H), 8.06-8.08(d, 2H); IR(KBr): 1772 , 1709 ,1645 cm^{-1} ; found: m/z 436.25 [M+1].

(3aR,4R,5R,6aS)-2-oxo-4-(piperidine-1-carbonyl)hexahydro-2H-cyclopenta [b]furan-5-yl [1,1'-biphenyl]-4-carboxylate 8.

A white solid; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ=1.59-1.71(m, 6H), 2.46-2.54(m, 3H), 2.94-3.02(q, 1H), 3.38(s, 1H), 3.59-3.75(m, 5H), 5.35-5.38(q, 1H), 5.54(s, 1H), 7.39-7.50(m, 3H), 7.62-7.71(d, 4H), 8.07-8.09(d, 2H); IR(KBr): 1767 , 1708 , 1642 cm^{-1} ; found: m/z 434.6 [M+1].

RESULTS AND DISCUSSION

From the synthetic point of view, oxidation of alcohol to carboxylic acid is a gateway to new kinds of organic molecules. But, traditional methods for oxidation of Corey's lactone involve strong basic/acidic conditions viz. Dess martin periodinane,[3] TEMPO/TCCA,[4] TEMPO/NCS,[5]. We modified TEMPO catalyzed Anelli's oxidation by using $NaIO_4$ as the terminal oxidant and NaCl as co-catalyst; the present system could work at room temperature gives carboxylic acids and produces good yields.

We have worked on different reaction conditions for oxidation Corey's lactone.The oxidation of Corey's lactone with TCCA/sodium acetate in presence of TEMPO catalyst at 0-5^{o}C produced very poor yield that was as low as 45%. Furthermore, the the by-products formed in this reaction was not able to remove completely from reaction mass.In Anellis oxidation (TEMPO/NaOCl) condition, the observed yield was merely 10%. The poor yield is because of high basic condition (pH around 8.5 to 9.5), which lead to deprotection of ester with biphenyl group.We modified Anellis oxidation with TEMPO catalyst by using $NaIO_4$/NaCl under bi phasic reaction in DCM and water at ambient temperature. The reaction condition is mild acidic, and the observed yields are excellent, as high as 95%. This method is applicable when the alcohols are sensitive to basic condition.

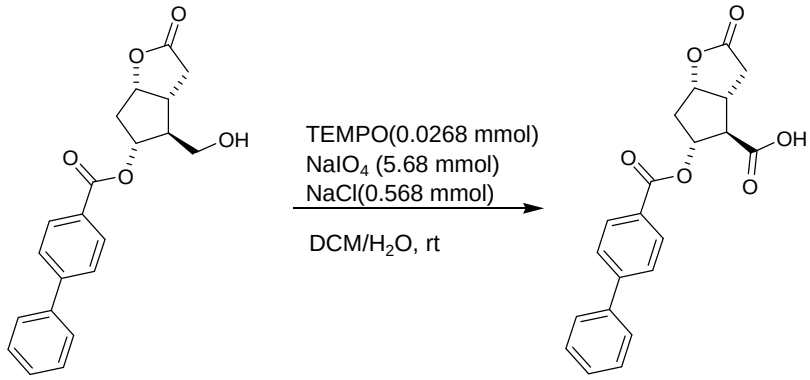
To optimize the reaction conditions, we examined the oxidation of (1S,5R,6R,7R)-6-formyl-7-[(4-phenylbenzoyl)oxy]-2-oxabicycl-[3.3.0]octan-3-one to corresponding acid with different oxidizing agents such as $NaIO_4$/NaCl/H_2O, TCCA/CH_3COONa and NaOCl/$NaHCO_3$ in presence of TEMPO catalyst at different reaction conditions and temperatures and the results are shown in Table 1.

We report here a green, practical, and efficient methodology for the oxidation of alcohol to carboxylic acid using $NaIO_4$/NaCl in presence of TEMPO catalyst under biphasic condition in

DCM/Water at room temperature .To the best of our knowledge, this is the fist time that $NaIO_4$/NaCl is used in an Anellis type oxidation reaction.(Scheme 1)

Table 1. Effect of different conditions for oxidation of primary alcohol to carboxylic acid.

Entry	Reagents	Temperature (^oC)	Time(h)	Yield(%)
1.	$TCCA/CH_3COONa$	0-5	4	30
2.	$NaOCl/NaHCO_3$	0-5	2	10
3.	$NaIO_4/NaCl/H_2O$	25-30	8	95



1 **2**

Scheme 1: Oxidation of alcohol to carboxylic acid

Several synthetic methods have been reported for the direct conversion of carboxylic acid to amides in the prior art. Herein, we present the study of synthesis of amides by the reaction of Corey's carboxylic acid with different amines under neutral condition. Initially, the reaction of carboxylic acid with amines was tested at different reaction conditions DCC/HOBt,[6-10] DCC/DMAP [8] this required long reaction time and tedious work-up. Ph_3P/TCCA,[11] condition triethyl amine used as a base. Under these reactions condition yields are very low and the carboxylic acid has been degraded. In CDI/DBU,[12] method involve two to three sequential synthetic steps, harsh reaction conditions that give low yields. In some cases, hazardous or expensive reagents are employed.

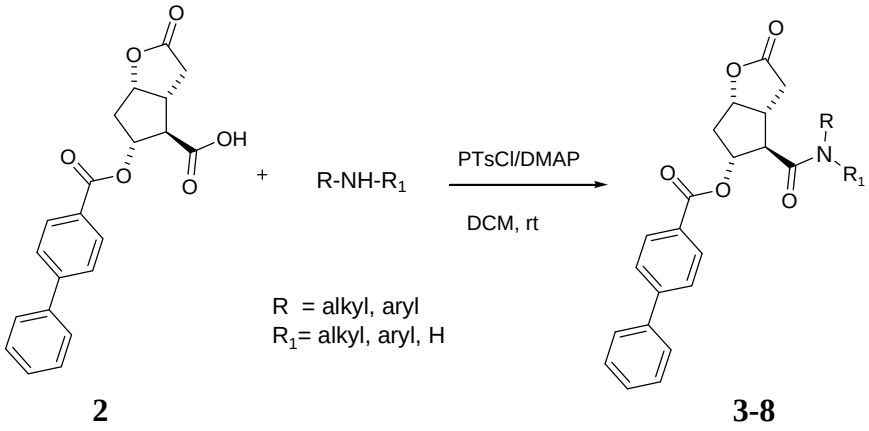
As part of our continuing efforts on the development for the preparation of amide compounds, we have introduced in this account a simple, mild and an efficient method for amide formation by using PTsCl and DMAP (4-dimethyl amino pyridine).

Herein, we describe a straight forward approach for the synthesis of amides from carboxylic acid. Our initial experiments were conducted with different reagents and each reagent their own braw backs, then we identified the reaction of carboxylic acid with amines in presence of PTsCl/DMAP. Optimization of reaction by using different bases such as triethyl amine, pyridine, N,N'-dimethyl aminopyridine (DMAP),DBU and K_2CO_3 in dichloromethane as solvent at room temperature. The results showed that N,N-dimethyl aminopyridine (DMAP) is the most preferred base (Table 2).

Table 2. Effect of base on the amide formation

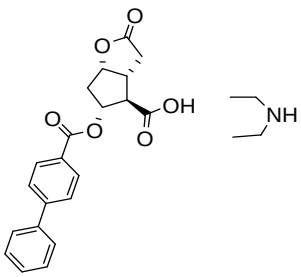
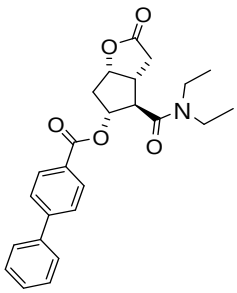
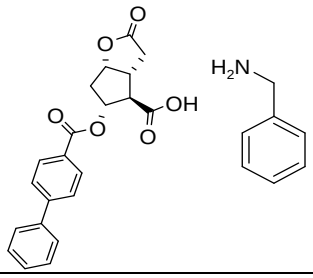
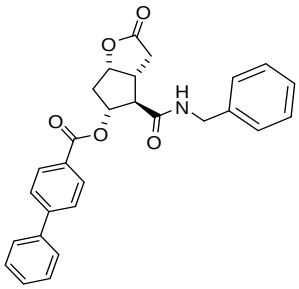
Entry	Base	Temperature (^oC)	Time(h)	Yield(%)
1.	Et_3N	25-30	1.0	60
2.	Pyridine	25-30	4.0	70
3.	DBU	25-30	1.0	40
4.	DMAP	25-30	0.5	95
5.	K_2CO_3	25-30	7.5	10

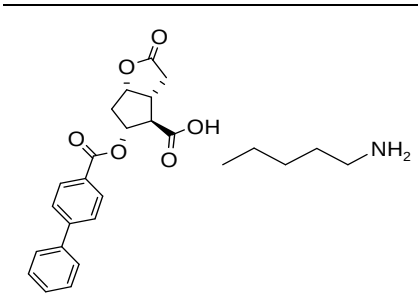
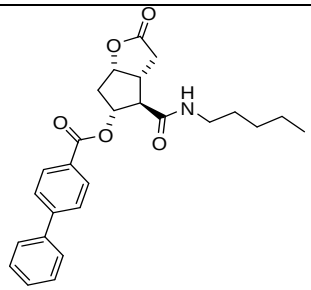
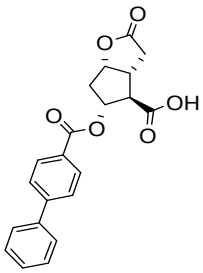
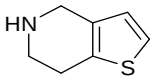
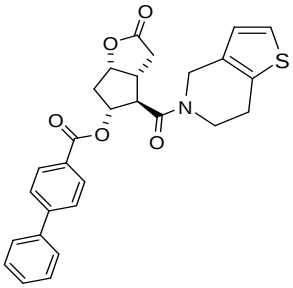
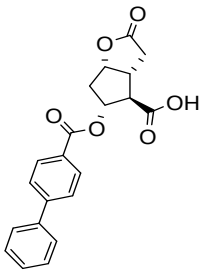
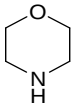
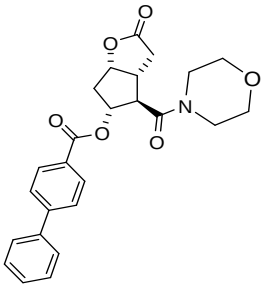
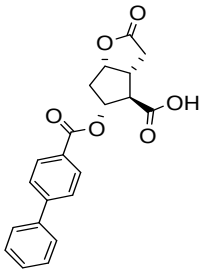
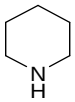
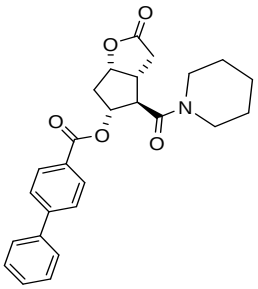
An efficient method for Amide formation of the carboxylic acid with different amines by using PTsCl/DMAP (Scheme 2).



Scheme 2: Synthesis of amides

Table 3. Synthesis of various amides (3-8) by using PTsCl/DMAP

Reagents	Products	Time(h)	Yield (%)
		1.5	85
		1.5	92

			2.5	94
			2.0	90
			1.5	95
			2.5	92

The carboxylic acid **2** (1.0 mmol) was treated with PTsCl (1.0 mmol) and DMAP(0.5 mmol) at 0-5^{o}C followed by addition of amine(1.0 mmol), reaction was slow and resulted in very poor yield. When using DMAP (1.0 mmol with respected to acid), significant improvement was observed. Accordingly, the carboxylic acid was dissolved in dichloromethane, cooled to 0-5^{o}C and added PTsCl, DMAP in to the reaction mixture followed by amine and the resulting suspension was allowed to warm to room temperature. The reaction mixture was stirred for 1-2h.

We synthesized some amide analogues by this method. Each compound was fully characterized on the basis of its spectroscopic properties viz IR, ^{1}H NMR and MS.

As shown in Table 3, this methodology affords the expected products in good to excellent yield.

CONCLUSION

In summary, we have developed an efficient method for oxidation of basic sensitive alcohol of Corey's lactone **1** to carboxylic acid with $NaIO_4/NaCl/H_2O$ in presence of TEMPO catalyst. The reaction could be performed at room temperature under bi phasic condition. The formed carboxylic acid **2** was further reacted with different amines in presence of PTsCl/DMAP to produce corresponding amides. This procedure provides an alternative method for the amide formation of carboxylic acids, which are sensitive to basic conditions.

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