A Review on Reactions and Applications of Oxazolones

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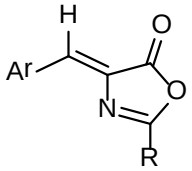
Abstract- 2-Oxazolin-5-Ones(azlactones) are multifunctional compounds and are known to react at C=C,C=N,C=O bonds. These participate in a number of replacement reactions, cycloadditions, other type of reactions as well as dimerisation react ions leading to formation of a variety of heterocyclic compounds. This review attempts to present the prolific development in recent years exclusively in the chemistry of 2-Oxazolin-5-Ones and gives a critical and unified account of these in the heterocyclic Chemistry.

Index Terms- Azlactone, acetylcholine receptors, Photoswitches, Hydrolases, diazocarbonyls, reactive polymers.

I. INTRODUCTION

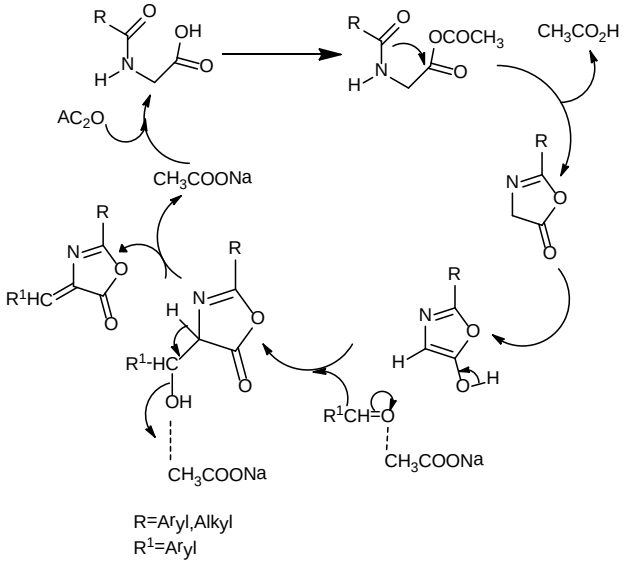
Azlactone provides a basic skeleton structure and also is a part of great importance for its drug characteristics.The basic nucleus imidazole emerges from the drug intermediate Azlactone. First Plochl [1] reported its formation by the acetic anhydride mediated condensation of hippuric acid with benzaldehyde. Erlenmeyer established the structure and named it as 'azlactone'.



These compounds exhibit important biological activities such as antimicrobial[2], antibacterial[3], analgesic[4], antifungal[5],anticancer[6,7], anti-inflammatory[8],neuroleptic[9], sedative[10], antidiabetic[11] and antiobesity[12]. Azlactones are important intermediates in the preparation of several chemicals including Aminoacids[13],peptides[14], some heterocyclic precursors[15]as well as coupling and photosensitive devices for proteins[16].They exhibit promising photophysical and photochemical activities [17,1,8,19] and as P^H sensors[20].

During the past few decades,Many research papers have been published in the area of Erlenmeyer synthesis by using different methods such as usage of catalysts like Al_2O_3,organic bases, supported heteropolyacids, $Yb(oTf)_3Ca(OAc)_2$,$Bi(OAc)_3$,$H_3PW_{12}O_{40}$ [21,22,23,24,25,26]. The Erlenmeyer azlactones are 5 membered heterocyclic compounds containing N and O as heteroatoms.The C-2 and C-4 positions of azlactones are crucial for their various biological activities[27].

Proposed Mechanism for Erlenmeyer plochl reaction

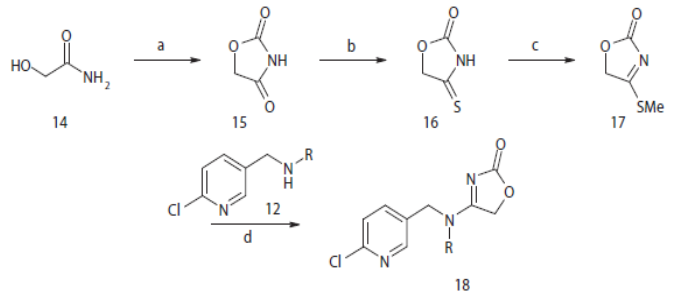


Scheme 1

Discovery,Synthesis and evaluation of N-substituted amino-2[5H]-oxazolones as novel insecticides activating nicotinic acetylcholine receptors

There has been a renewed interest in searching for novel neonicotinoid insecticides to overcome resistance while maintaining attractive physical properties and biological profiles[28,29].Inspired by N-substitued enaminolactones which as potent insecticides[30],W.Zhang etal prepared N-substituted amino-2(5H)-oxazolones a novel class of insecticides acting as nicotinic acetylcholine receptor(nAchR) agonists which show potent activity against hemipteran insect species[31].

4-Amino-2(5)H-oxazolones were prepared by cyclization of**14** glycolamide with **a**diethyl carbonate in the presence of potassium tert-butoxide in methanol at 80^{o}Cgenerated **15**oxazolidinedione.The amide carbonyl group of dione was then selectively converted into a thiocarbonyl group when treated with**b** Lawesson reagent toluene,110^{o}C giving the product **16** 4-thio-oxazolidine-2-one.This thioamide was further converted into **17** 4-methylsulfanyl-5H-oxazol-2-one in presence of **c** MeI, NaOAc,dichloromethane and subsequent displacement with required **d** secondary amines and chloroform at 61^{o}C gave desired product 4-amino-2(5H)-oxazolones.



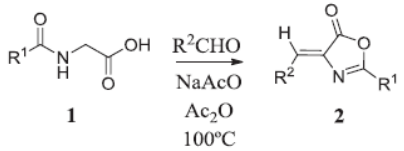
Scheme 2:

Oxazolones as photoswitches

The synthesis and applications of molecular photoswitches, their use to modify the properties of complex systems has been extensively studied[32]. Molecular switches could be classified based on the stimulus used to induce the nuclear motion involving light, chemical or electrochemical energy or the reaction that takes place like ring closing/opening or bond isomerisation in most cases. Light activated switches that perform a c=c photoisomerisation[33], azobenzene[34], overcrowded alkenes[35] and retinal-based switches[36] have been applied in many different technological applications.

I.Funes-Ardoiz et al reported[37] a new family of switches inspired in the green florescent protein(GFP), obtained from aequorea Victoria jelly fish and its optical properties are determined by a photoexcitable green light emitter chromophore[38]

Benzylidene-Oxazolones have been used as precursor for the synthesis of GFP derivatives and their photoisomerisation is already known[39,40]. The recent results on the photophysics and photochemistry of Benzylidene-Oxazolones are presented[41]



R^1= Me, Ar
R^2=Ar

Benzylidene-Oxazolones **2** are good moeities for efficient photoswitches as they are easily synthesised, feature good photoisomerisation quantum yields and are thermally stable[36].

A 0.01M solutions of different photoswitches**2** in acetonitrile and irradiated with wavelength 350nm until the PSS(Photo Stationary state) is reached.

Photostationary state for molecular photoswitches **2** irradiated at 350 nm

Entry	R^1	R^2	Compound	Ratio at PSS	
				%Z	%E
1	Me	*p*-BrPh	**2a**	54	46
2	Me	*p*-Tol	**2b**	75	25
3	Me	*p*-MeOPh	**2c**	42	58
4	Me	*o*-MeOPh	**2d**	41	59
5	Me	*p*-NO_2Ph	**2e**	76	24
6	Me	*p*-CNPh	**2f**	62	38
7	Me	Ph	**2g**	70	30
8	Ph	*p*-BrPh	**2h**	36	64
9	Me	*o*-Br	**2i**	40	60
10	Ph	*p*-NO_2Ph	**2j**	80	20
11	Ph	*p*-CN	**2k**	55	45

If the substituent of phenyl group in R^2 is an electron donor group, such as methoxy, the percentage of E-isomer at the PSS increases. When and electron withdrawing group such as nitro, there is no significance change in the isomers ratio compared with 2b if substituent R^1 is modified from Me to Ph and R^2 remains the same, the percentage of E-isomer at the PSS significantly increases.

The two isomers(Z and E) of compounds 2g(R^1=Me, R^2=Ph) and the compound 2a(R^1=Me, R^2=P-BrPh) in deoxygenated acetonitrile and trans-stillbene in deoxygenated hexane was used to measure the fluorescence lifetime, which showed low quantum yield(0.005). This shows that isomerisation process is not affected. Although structurally similar to the GFP chromophore, the modifications introduced in the compounds under study turned them into efficient photoswitches.

The substantial conformational changes associated with E/Z isomerisation have attracted attention to 4-Benzylidene-Oxazolones as potential molecular switches in biomolecular photo control[42].

Scheme 3

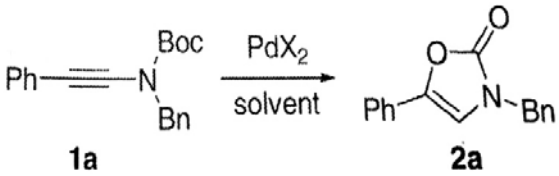
Pd-catalyzed cyclization of N-alkynyl tert-butyloxycarbamates with oxazolones

The development of general and practical procedures for the synthesis of oxazolones is highly desirable as they are important class of heterocyclic compounds occurring in many natural products and pharmacological active molecules.

The traditional method utilises Lewis acid or base catalyzed condensation of 1,2-aminoketones with carbonyl compounds[43].A promising method for the synthesis of oxazolones came from the groups of Hashmi and Gagosz[44] where they reported an approach of 3,5-disubstituted oxazolones via Au-Catalyzed transformation of N-alkynyl tert-butyloxycarbamates. More recently Lautenes and co-workers described an elegant synthesis 3,5-disubstituted oxazolones by the Pd-catalyzed reaction of β,β-dibromoenamides[7]. Z.Lu et al(Zenghui Lu, Xiaowei Xu, Zhaozhen Yang, Lichun Kong, Gangguo Zhu. Tetrahedron lett.2012,53,3433-3436) reported simple and efficient method for the synthesis of highly functionalized oxazolones including 3,5-disubstituited and 3,4,5-trisubstituted oxazolones[45].

Synthesis of 3,5-disubsitituted Oxazolones

Screening of the reaction conditions[a]



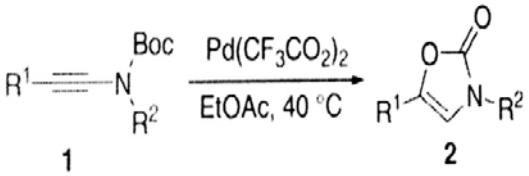
Entry	Catalyst	Solvent	Yield[b] (%)
1	$Pd(OAc)_2$	THF	70
2	/	THF	NR
3	$Pd(MeCN)_2Cl_2$	THF	77
4	$Pd(PhCN)_2Cl_2$	THF	75
5	$PdCl_2$	THF	72
6	$PdBr_2$	THF	69
7	$Pd(CF_3CO_2)_2$	THF	79
8	$Pd(CF_3CO_2)_2$	Dioxane	54
9	$Pd(CF_3CO_2)_2$	CH_3CN	48
10	$Pd(CF_3CO_2)_2$	CH_2Cl_2	47
11	$Pd(CF_3CO_2)_2$	CH_3OH	38
12	$Pd(CF_3CO_2)_2$	Toluene	50
13	$Pd(CF_3CO_2)_2$	HOAc	35
14	$Pd(CF_3CO_2)_2$	EtOAc	84

[a] Reaction conditions: **1a** (0.25 mmol) and Pd catalyst (0.013 mmol) in 1 mL of solvent at 40 °C for 5–8 h.
[b] Isolated yields.

2a=3,5-disubstituted Oxazolones

The oxazolone product **2a** was isolated in 70% yield by treating **1a** 5 mol % of $Pd(OAc)_2$ in THF at 40^0 C for 8 hrs. It is found that 5 mol % of $Pd(CF_3\ CO_2)_2$ as catalyst and with use of EtOAc as the solvent at 40^0 C produced 3,5-disubstituted oxazolones in 84% yield.

Table 2
Synthesis of 3,5-disubstituted oxazolones **2**[a]

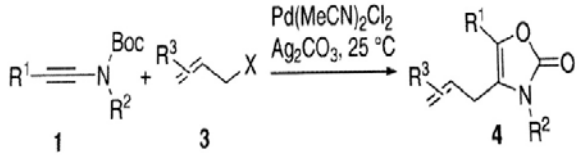


Entry	1	R^1	R^2	Yield[b] (%)
1	**1a**	Ph	Bn	84 (**2a**)
2	**1b**	4-F-C_6H_4	Bn	72 (**2b**)
3	**1c**	4-Cl-C_6H_4	Bn	80 (**2c**)
4	**1d**	2-Cl-C_6H_4	Bn	78 (**2d**)
5	**1e**	4-Br-C_6H_4	Bn	83 (**2e**)
6	**1f**	3-Br-C_6H_4	Bn	88 (**2f**)
7	**1g**	4-Me-C_6H_4	Bn	78 (**2g**)
8	**1h**	4-*t*-Bu-C_6H_4	Bn	83 (**2h**)
9	**1i**	4-MeO-C_6H_4	Bn	80 (**2i**)
10	**1j**	3,4-MeO_2-C_6H_3	Bn	82 (**2j**)
11	**1k**	2-Naphthyl	Bn	75 (**2k**)
12	**1l**	*n*-C_8H_{17}	Bn	63 (**2l**)
13	**1m**	$TBSO(CH_2)_2$	Bn	70 (**2m**)
14	**1n**	TES	Bn	NR
15	**1o**	Ph	Ph	77 (**2o**)
16	**1p**	Ph	*n*-Bu	71 (**2p**)
17	**1q**	Ph	Cy	72 (**2q**)

[a] Under the optimal conditions.
[b] Isolated yields.

Ynamide **1a** was treated with 3 equiv of allyl chloride **3a** as well as 1.5 equiv of K_2CO_3 and 5 mol % of $Pd(MeCN)_2Cl_2$ in EtOAc the desired 3,4,5-trisubstituted oxazolone **4a** was generated in 45% yield, together with the formation of 27% of **2a** when substrate **1a** was treated with 20 equiv of allyl chloride **3a** and 5 mol % of $Pd(MeCN)_2Cl_2$ using K_2CO_3 as a proton scavenger, the yield of 3,4,5-tyisbustituted oxazolone **4a** was obtained 72% yield. When 1.5 equiv of Ag_2CO_3 the yield was enhanced by 87%.

Table 3
Synthesis of 3,4,5-trisubstituted oxazolones **4**[a]

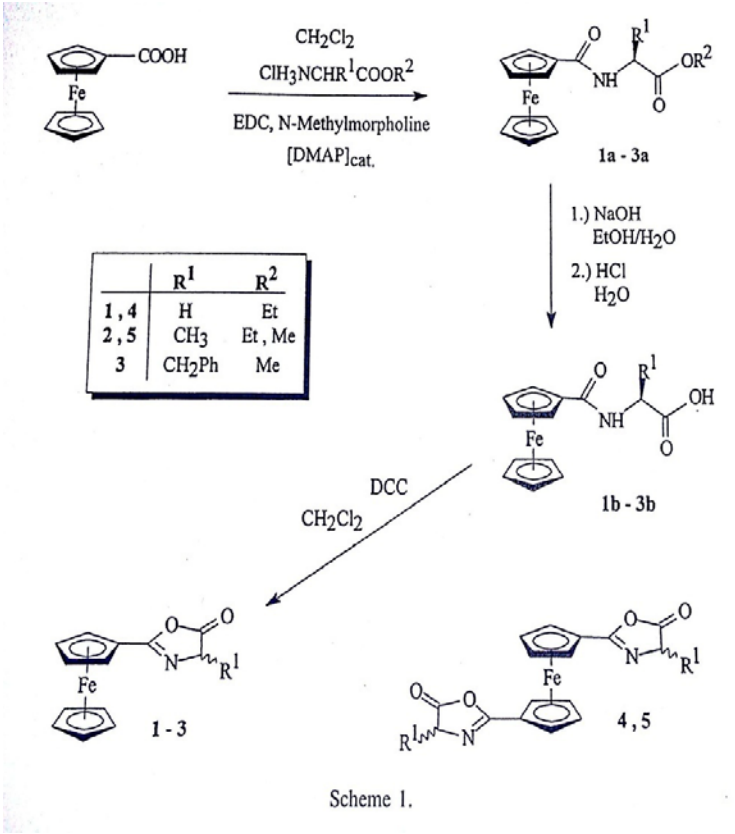


Scheme 4:

Ferrocenyl-Oxazolones as N and C donors in Pd(II),Pt(II) and Ir(III) complexes and ferrocenoyl dipeptides.

Metal complexes of Oxazolones can provide information on the coordination chemistry of N-heterocycles .Morever ring opening[46]of organo metallic oxazolones gives rise to peptides attached to a metal.In continuation of studies on oxazolone metal complexes[47]the synthesis and reaction of 2-ferrocenyl substituted 5(4H)oxazolones are reported[48].These are starting materials for the synthesis of racemic[49] or optically active[50]ferrocenyl alanine which was incorporated into peptides to follow their redox properties[51].The 1,1'-ferrocenyl bis(alanine)is available from 1,1'-diiodo-ferrocene[52]

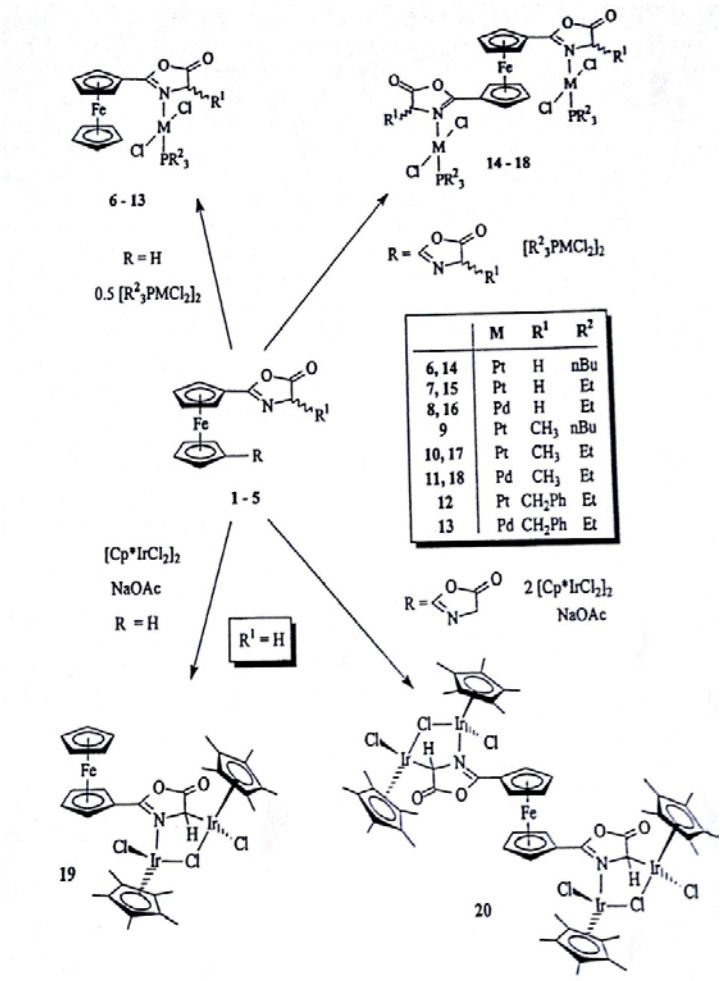
Ferrocenyl-α-amino acid esters **1a-3a** were synthesized from ferrocene carboxylic acid and α-amino acid esters,according to published procedures (scheme1)[53].The first compounds of this type were reported by Schlogl[54]



Scheme 1.

The synthesis of a new series of N-coordinated oxazolone complexes **6-18** was achieved by W.Bauer et al[55] atom as donors.The reaction of **1** and **4** with the chloro bridged halfsandwich iridium complex $[Cp^*IrCl_2]_2$ leads to α-metallation

of the oxazolone ring to give the C,N and chloro bridged trinuclear and pentanuclear complexes **19** and **20.**



	M	R¹	R²
6, 14	Pt	H	nBu
7, 15	Pt	H	Et
8, 16	Pd	H	Et
9	Pt	CH_3	nBu
10, 17	Pt	CH_3	Et
11, 18	Pd	CH_3	Et
12	Pt	CH_2Ph	Et
13	Pd	CH_2Ph	Et

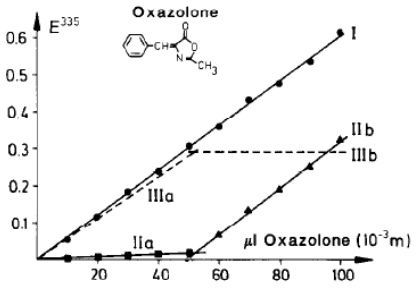
A solution of the appropriate chlorobridged tri-alkylphosphine complex in CH_2Cl_2 was treated with a slight excess of the corresponding 2-ferrocenyl-5(4H)-oxazolone **1-5.** After 3-4 hr stirring at room temperature, the solution was concentrated in vacuo and an excess of diethyl ether was added. The precipitate was centrifuged off and solution was evaporated. The residue was taken up in CH_2Cl_2 and added dropwise to an excess pentane. The product was centrifuged off ,washed twice with pentane and dried in vacuo for 50^0C for several hours.

Scheme 5:

Active site titrations of Hydrolases using Oxazolones as substrates

Oxazolones are used as substrates for enzymes[56-60].The stability of the acyl enzymes formed by the oxazolones is sufficient for active site titrations and the spectral changes upon the hydrolysis of the oxazolones to dehydroamino acids are large enough for precise measurements. The Oxazolones greatly differ in solubility.Some of them are soluble in water and others in organic solvents like dimethyl sulfoxide. Baese and Havsteen[61]tested a variety of oxazolones in various solvents in active site titrations of α-chymotrypsin,tyrpsin, carboxypepetidase and aminopeptidase. The results were obtained with a single enzyme in solution which are equivalent from those gained when a related enzyme also was present in the reaction mixture and the analytical precision,also with enzyme mixtures,equalled that offered by classical substrates.

Titration of the active site of α-chymotrypsin with MBO(2-methyl-4-benzylidine-oxazolone)at pH 5.0 and 19°C is demonstrated below.The theory of active site titrations is described by Schonbaum et al[62].The effect of deacylation was eliminated by extrapolation to zero time.



Titration of the active site of α-chymotrypsin with MBO at pH 5.0 and 19°C. Symbols: ●, I; ■, IIa; ▲, IIb. I, Concentration dependence of the extinction of the oxazolone in the absence of the enzyme. II, Steady-state extinction after addition of the enzyme. The intersection between the segments a and b defines the equivalence point. III, Lines derived by difference measurements.

From the titration curve it is observed that the active site normality using oxazolones was within the experimental error independent of the method employed. The pH dependence was tested in the range from 5.0 to 8.0.It was less than 2.2%.Since many biological samples contain several related hydrolases, some of which are only present as impurities, the extent of the interference due to cross reactivity was investigated. This potential source of error remained for the oxazolones below an acceptable level of 1-2%,Even when the hydrolases were present in equimolar concentrations as evidenced from the following table.

Active Site Titrations of Chymotrypsin (CT) in the Presence of Trypsin (T) at pH 5.0 and 19°C

Substrate	λ (nm)	ΔE	n_{CT} (μM)	E_{280}^{CT+T}	E_{280}^{CT}	m_{CT} (μM)	m_T (μM)	Purity of CT (%)
MBO	335	0.271	13.4	1.416	0.724	14.6	19.7	91.7
MBO	335	0.265	13.1	1.590	0.704	14.3	25.5	91.6
MNBO	380	0.247	13.1	1.418	0.731	14.7	19.7	89.1
MNBO	380	0.244	12.9	1.400	0.719	14.5	19.6	89.0

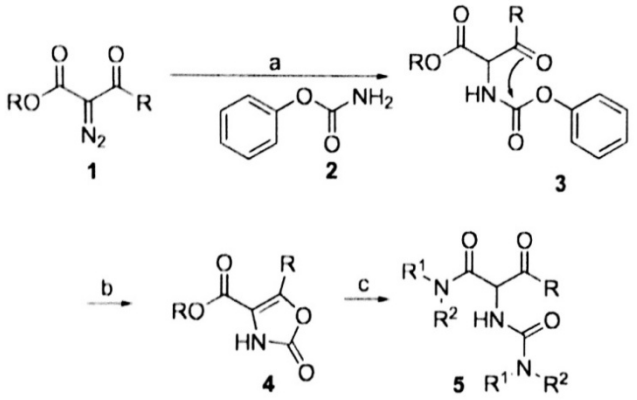
MBO=2-methyl-4-benzylidine-oxazolone
MNBO=2-methyl-4-(4'-nitrobenzylidine)-oxazolone

Scheme 6:

Solid phase synthesis of oxazolones via Wang resin bound diazocarbonyls

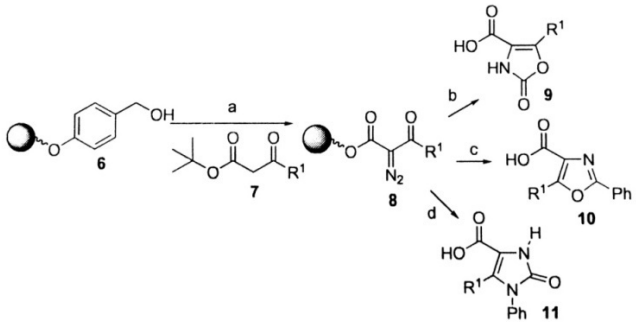
The solid phase organic synthesis (SPOS)plays a vital role in conveniently handling large number of synthetic intermediates[63]**.**M.Yamashita et al harnessed the synthetic utility of diazocarbonyl compounds[64] in order to prepare a set of biologically privileged 'lead-like' scaffolds.The author focused on application of polymer-bound α-diazo-β-ketoesters[65]as key building blocks for the diversity-oriented synthesis(DOS)[66]of a series of heterocycle libraries,including Oxazoles[67]indoles[68],imidazolones and imidazoles[69], and pyrazinones and pyrazines[70].

A Novel and efficient N-H insertion strategy for the synthesis of oxazolones from diazocarbonyls has been devised by M.Yamashita et al .Additionally,in order to synthesize oxazolone arrays using solid-phase synthetic methodology,an alternative TFA (trifluoro acetic)labile linker strategy was developed;the Wang resin bound diazocarbonyl substrates were also shown to be of great utility in the preparation of oxazoles and imidazolones[71]M.Yamashita et al found that phenyl carbamate **2** is an excellent coupling partner when reacted with diazocarbonyls(scheme1).Moreover treatment of this intermediate **3** withmild base afforded the ring closed oxazolone products **4.**However,when this chemistry was applied to a solid phase approach,the aluminium amide cleavage conditions gave ring-opened urea products **5.**



1.a)Rh_2Oct_4 (2mol%),2(3equiv),toluene-dichloroethane 1:1,80^{0}C(b)^{i}Pr$_2$EtN(3equiv) ,toluene,reflux,6h; (c)R^1R^2NH (3equiv), $AlMe_3$(3equiv),toluene,100^{0}C,16h

Wang resin bound substrates were investigated and found to be ideal substrates for oxazolone synthesis.The Wang bound β-ketoesters were synthesized using a transesterification reaction. A mixture of Wang resin **6** and ^{t}Bu- β-ketoesters **7** was heated to reflux in toluene, after washing, standard diazotransfer conditions provided the corresponding Wang resin-bound α-diazo-β-ketoesters **8**.This building block **8** is treated with phenyl carbamate **2** in the presence of rhodium octanoate catalyst to give the N-H insertion products that were treated sequentially with ^{i}Pr$_2$EtN and TFA to provide oxazolones **9**.Key building blocks **8** were also used to synthesize a series of oxazoles **10** and imidazolones **11** using an N-H insertion/cyclodehydration strategy. For the oxazole synthesis,a primary amide was used as the insertion component,the heterocycle ring was closed using Burgess reagent,and the oxazoles **10** were obtained by cleavage with TFA.In the case of the imidazolones,a primary urea was used as the insertion component, the product from this reaction was treated with TFA to achieve both cyclization to the imidazole and cleavage from the resin in one pot.Each of the oxazolones **9**,oxazoles **10**,and imidazolones **11** cleavage products were assessed by HPLC.



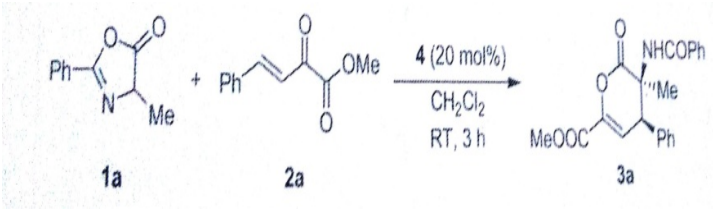
(a)(i)7(3equiv),toluene,reflux,16h;(ii)dodecylbenzenesulfonylazide(3equiv),Et_3N(3equiv),toluene,24h;(b)(i)Rh_2Oct_4(2mol%),**2**(3equiv),toluene,70^{0}C,1h;(ii)^{i}Pr$_2$EtN(3equiv),toluene,reflux,6h;(iii)TFA,rt,3h;(c)(i) Rh_2Oct_4(2mol %),$PhCONH_2$(3equiv),toluene-dichloroethane 1:1,80^{0}C,1h,70^{0}C,1h;(ii)Burgess reagent (3 equiv), THF,μW, 100^{0}C,10 min;(iii)TFA,rt,3h;(d)(i) $PhNHCONH_2$ (3equiv)toluene-dichloroethane 1:1;80^{0}C, 1h; (ii)TFA,rt,3h.

Scheme 7:

Asymmetric cycloaddition reaction of oxazolones with β,ϒ-unsaturated α-keto esters by using cinchona alkaloids as catalysts.

Y.Ying et al reported the cycloaddition of β,ϒ-unsaturated α-keto esters with oxazolones[72]

With commercially available cinchona alkaloid catalysts,the reaction is completed within several hours at room temperature to provide highly functionalized δ-lactones with adjacent α-quarternary-β-tertiary stereocenters in highly yields and enantioselectivities.The reaction of 4-methyl-2-phenyloxazol-5(4H)-one **1a** with (E)-methyl-2-oxo-4-phenylbut-3-enoate **2a** was selected. commercially available quinine **4a** was used as catalyst which gave the desired product **3a** with 82% yield and 70% ee with exclusive diastereoselectivity[73].



This reaction provides an easy access to highly functionalized chiral δ-lactones with adjacent α-quaternary –β-tertiary stereocenters.

Scheme 8:

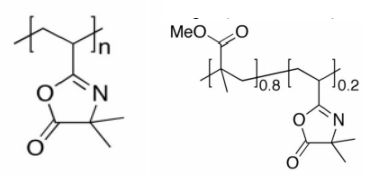
Nano-Imprinted Thin Films of Reactive, Azlactone-Containing Polymers

Fredin et al reported an approach to the introduction of nanoscale and microscale topographic features into thin films of reactive, azlactone-containing polymers. They demonstrated that (i) Nano-imprint lithography (NIL) can be used to imprint films of reactive polymers **1** and **2** using methods developed for the imprinting of nanoscale and microscale topographic features into conventional, non-reactive polymers, (ii) the azlactone groups in these materials do not degrade or react substantially during the imprinting process, and (iii)the resulting topographically

patterned films can be chemically functionalized post-fabrication by treatment with either small molecules or polymers containing primary amine groups[74]Methods for the chemical functionalization of surfaces have led to significant progress toward the design of functional biomaterials and provide useful tools for understanding the chemical interactions between cells and surfaces that drive or guide cellular response[75-88]. The work reported was based upon the results of numerous past studies describing the influence of surface topography on cell behaviour[89-92]**.**Advances in the field of lithography have yielded methods for the transfer of nanometer-scale features to polymers and other soft materials that could prove useful for addressing and investigating several of the goals outlined[93-95].

The methods that have been developed for the transfer of nanometer-scale features into soft materials are by using nano-imprint lithography (NIL)[96-99].NIL is a process in which a master (e.g., silicon, typically prepared *via* conventional lithographic techniques) is pressed into a thermoplastic material heated above its glass transition temperature (*Tg*). When the thermoplastic is cooled below *Tg*, the master is removed, leaving the negative relief of the master in the imprinted material.

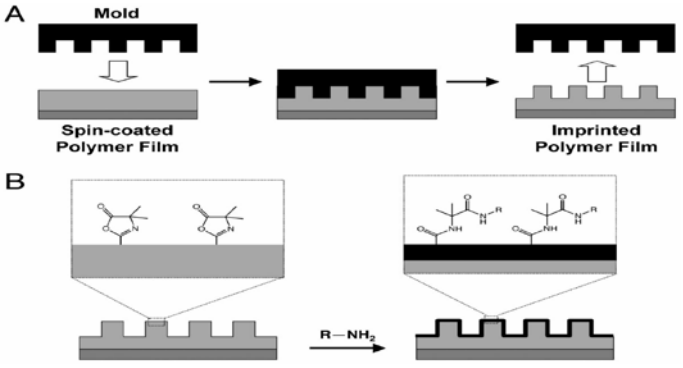
Fredin et al conducted an initial set of experiments to determine whether thin films of polymers **1** and **2** could be imprinted with features having micrometer- and nanometer-scale dimensions. Thin films of polymers **1** and **2** (e.g., ~200 nm thick) were spin-coated from solutions in ethyl acetate onto planar silicon and glass substrates and imprinted using methods for NIL.



Polymer **1** Polymer **2**

Polymers **1** and **2** can be cast as thin films and have glass transition temperatures of approximately 101 °C and 96 °C, respectively, which are in the range of temperatures commonly used for NIL.

vTo determine whether the azlactone groups of imprinted films were available for reaction at the surface after imprinting, films of polymers **1** and **2** were imprinted with the pattern of lines 2 μm wide described above and were subsequently exposed to a small molecule fluorophore functionalized with a primary amine group showed fluorescence micrographs of imprinted films of polymers **1** and **2**, respectively, that were treated with a drop of an aqueous solution of tetramethylrhodamine (TMR) cadaverine for one minute and then soaked in deionized water for three hours to remove unreacted fluorophore. Fredin et al observed that the fluorescence associated with the film of polymer **1** appears brighter than the fluorescence associated with the film of polymer **2**.This result is consistent with the large difference in the amount of azlactone groups in the homopolymer (polymer **1**) relative to the copolymer (polymer **2**), and suggests that it may be possible to tune the amount or density of reactive functional groups at the surfaces of these films for particular applications by control over the structures and compositions of the polymers used to form the films.

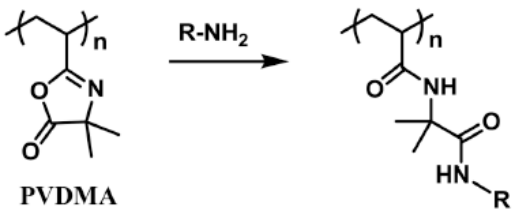


Scheme 9:
Functionalization of Fibers Using Azlactone-Containing Polymers

Buck and Lynn reported an approach to the functionalization of fibers and fiber-based materials that is based on the deposition of reactive azlactone-functionalized polymers and the 'reactive' layer-by-layer assembly of azlactone-containing thin films. They demonstrated (i) that the azlactone-functionalized polymer poly(2-vinyl-4,4-dimethylazlactone) (PVDMA) can be used to modify the surfaces of a model protein-based fiber (horsehair) and cellulose-based materials (e.g., cotton and paper), and (ii) that fibers functionalized in this manner can be used to support the fabrication of covalently crosslinked and reactive polymer multilayers assembled using PVDMA and poly(ethyleneimine) (PEI). The growth, chemical reactivity, and uniformity of films deposited on these substrates were characterized using fluorescence microscopy, confocal microscopy, and scanning electron microscopy (SEM)[100].

The azlactone-functionalized polymer poly(2-vinyl-4,4-dimethylazlactone) (PVDMA; Eq. 1) can be used to fabricate covalently crosslinked polymer multilayers by reactive layer-by-layer assembly with olyethyleneimine (PEI), a hyperbranched polymer that contains primary amine-functionalized end groups[101-103]. The approach to layer-by-layer assembly reported here exploits the reactivity of polymers containing azlactone functionality. Azlactone-functionalized polymers react rapidly with a range of different amine-functionalized nucleophiles (Eq. 1) and can be used to synthesize a broad range of functional materials; the broader reactivity and general characterization of azlactone-functionalized polymers has been reviewed comprehensively[104]. several recent studies have demonstrated the use of azlactone-functionalized polymers to design reactive interfaces and tailor the physicochemical properties of surfaces[105-112].

Azlactone-functionalized polymers have been used in polymer layers[111,112]**,**bulk thin films[113], and reactive polymer multilayers[101-103]useful for the immobilization of proteins[102,106-109] and other molecules[101-103,105,110-113].

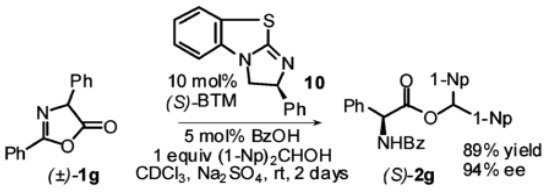


Eq.1
PVDMA= poly(2-vinyl-4,4-dimethyl azlactone)

Scheme 10:
Dynamic Kinetic Resolution of Azlactones

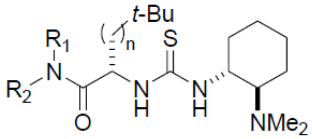
Yang et al proposed a new highly enantioselective method for the DKR(Dynamic Kinetic Resolution) of azlactones. It is especially suited for the C4-aryl-substituted substrates, thus complementing the previously available enzymatic and non enzymatic protocols.Dynamic kinetic resolution (DKR)[114] of azlactones[115] by way of their enantioselective alcoholysis provides an attractive approach to the asymmetric synthesis of α-amino acid derivatives.

Enantioselective acyl transfer catalyst benzotetramisole (BTM) has been found to promote dynamic kinetic resolution of azlactones providing di(1-naphthyl)methyl esters of α-amino acids with up to 96% ee[116].



1g =2,4-diphenylazlactone
2g=di(1-naphthyl)methyl esters of α-amino acids

A highly efficient alcoholytic ring opening of azlactones was effected with the bifunctional Organocatalyst given below.



R_1 = Me, R_2 = Bn

The level of enantioselectivity of the product esters obtained is the highest ever achieved in the chemically catalyzed DKR of azlactones[117]**.** A fairly broad range of azlactones containing both aliphatic and aromatic substituents was employed in the DKR.

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