Oxonium ylide formation

Oxonium ylides generated by cyclisation of O-allyloxy or O-benzyloxyarylcarbenes on the ether oxygen atom are known to undergo [2,3]- or [1,2]-sigmatropic rearrangements, as well. From: Advances in heterocyclic chemistry, 1996Michael P. Doyle, in Extensive Organometallic Chemistry II, 1995Using reactions of oxonium yliders falls into three classes: [2,3]-sigmatropic rearrangements, [1,2]-Stevens rearrangements, and oxygen-hydrogen joining reactions. In addition, oxygen transfer processes, which are generally associated with epoxides, and 1,4 elimination reactions, not unlike those already described for sulfonium, (Equations (29) and (36)), and ammonium ylides (Equation (44)), are present with oxonium ylider.15The availability of Rh2(OAc)4 as a catalyst for diazode composition allowed the generation of metal carbons at temperatures higher than 25 °C is .104 so the introduction of Rh2(OAc)4 as a catalyst that is effective for oxonium ylide generation gave new opportunities for catalytic method development.A.F. Khlebnikov, ... R.R. Kostikov, in Advance in heterocyclic chemistry, 1996The generation of oxonium ylides by degradation of malonat 616 followed by a [2,3]-sigmatropic shift ger dioxane 617 (86JA6060). Similarly, the rearrangement of oxonium ylide derived from 618 (R = H or Me) provides 68% of the dioxane 619 (R = H) and 16% of 1,4-dioxacyclococtane 620 or dioxane 619 (R = Me) as a single diastereomer (86JA6062). Photolysis or thermolysis of 621 results in dioxin 622 (51 and 31%), respectively, the product of migration of one of the acetal oxygen moieties in the carbien intermediate 623 (82JOC4226). The formation of stable cyclic six-membered O- and S-containing ylides in carben reactions is uncommon. Intramolecular reaction to 624 produces the solsolable ylide intermediate 625, the structure of which was determined by X-ray analysis (87JA3010). (Butenyoxy)diazoacetic ester 626 (R = H2C=CHCH2) undergoes intramolecular cyclopropanation to form 627 (28-58%) when decomposed photochemically, thermochemically, or by transition-metal catalysis (CuOSO2CF3). (Alkynyloxi)diazoacetic ester 626 (R = C≡CMe) under photolytic and catalytic conditions produces 628 derived from tandem intramolecular cyclopropenation and cyclopropene-vinylcarbene isomerization (94MI1). Flash vacuum pyrolysis of 629 yields 630 in 15% yield along with other products [85JA(107)8297]. The reaction of trithiapentalenes with diphenylcarbene produces sulfonium ylides undergoing rearrangement followed by formation of 1,3-dithiins 631 (83CJC1161). The carbide, generated by catalytic degradation of diphenyldiazephene, reacts with cyclic disulfides, giving 1.3-dithianes 632. Under the same conditions, ethyl diazoacetate with 3,3,5,5-dithiolan-4-one also gives the equivalent of dithiane as the product of a formal S-S insertion (85TL5187).J. Wang, Y. in Reference Module in Chemistry, Molecular Sciences and Chemical Engineering, 2013The second major pathway for oxonium ylide is [1,2] shift (Stevens rearrangement). Compared to the [2,3]-sigmatropic rearrangement, which is an orbital symmetry-permitted concerted process, the [1,2] shift has a higher activation barrier. [1,2]-Shift is generally considered as a step-by-step process with radical pairs as possible intermediates.18Formation of cyclic oxonium ylide followed by [1,2]-shift may be a useful approach for medium-sized or bridged cyclic compounds.8.19West and collaborators have recently reported the synthesis of cyclooctanoid systems based on such an approach.16 α-Diazo ketones 49a and 49b, when treated with 10 mol% Cu(hfacac)2 in CH2Cl2 at reflux, generate a five-member oxoniumylide which then undergoes [1,2] shifts to yield 52a and 52b in good returns, respectively. 52b can be converted into 53, which can be used in the synthesis of natural products with molten 5-8 bicyclic skeletons (eqn [7]). For metal carbene intermediate 50a or 50b, obviously there are other possible reaction routes. When Rh2(OAc)4 or rhodium (II) tripeny acetate [Rh2(O2CCPh3)4] is used as a catalyst, the reaction primarily produces intramolecular C-H insertion products. Treatment of 49a or 49b with Cu(tfacac)2 in CH2Cl2 at reflux, conditions of ylide formation/[2,3]-sigmatropic rearrangement,8 resulted in only low yields of several unidentified products. [7] An interesting feature of this reaction is that [1,2]-displacement of ylides 51a and 51b revenues mostly with a high degree of retention of configuration. Such high stereospecificity is unusual because the [1,2]shift is believed to be a stepwise process with radical pair intermediates. The results can be rationalized by adopting a very rapid radical recombination compared to bond rotation. As discussed above, cumulative data show that the catalyst, substrate structure and other competing metallocarbene pathways significantly affect ylide formation and the subsequent reorganization process. West and collaborators have recently studied selectivity in rearrangement via five- or six-member oxonium ylides through intramolecular competitive formation and rearrangement of two different oxonium yliders via the same metallocarbene (Schedule 7).20 The study shows that five-membered ylide formation is generally favored. However, the properties of the migrant group in the subsequent residor can override the preference of the five-member ring. In the reaction with α-diazo ketone 54 with Cu(tfacac)2, pyranone 58 is formed predominantly since allylic [2,3]-sigmatropic rearrangement is more feasible than [1,2]-shift. The results strongly suggest that five-membered ylide 55 is in equilibrium with its six-member counterpart 56. It is also observed that the catalyst can dramatically affect the reaction se selectivity. When Rh2(OAc)4 or Rh2(O2CCPh3)4 is employed as a catalyst, the reaction gives five-membered ylide shift product consideration. In addition, even a relatively small change in the ligand of the copper catalyst [from Cu(tfacac)2 to Cu(hfacac)2] significantly alters the selectivity. Catalyst-dependent selectivity strongly suggests metal associated ylide in the old-image step. Catalyst can thus change the properties of ylide. It can also affect the equilibrium of different ylide species such as 55 and 56.Schedule 7. Selectivity in [1,2] shifts via five or six-membered oxonium ylide. Doyle et al. recently reported that the axial-equatorial conformation alcove distribution of reactant diazoacetoacetate or its metal carbide intermediate is reflected in Rh(II) catalyzed oxonium ylide forming reactions.21 For example, reactions from 3-(trans-styryl)tetrahydropyranone-5-diazoacetoacetate and its para-substituted derivatives 59 provide a mixture of diastereoisomeric products 61-62 through [2,3]-sigmatropic and [1,2]-Stevens rearrangement (Schedule 8). Competition between [2,3] and [1,2]-oxonium ylide rearrangements is relatively common, especially with diazoketones. This competition is generally thought to be due to steric influences in structurally rigid systems. It was observed that an increase in the size of the stearie group was an advantage for [1,2]-oxoniumylide rearrangement. Schedule 8. The competition for [2.3]-sigmatropic reorganization and [1,2]-Steven reorganization. Asymmetric induction in the formation of ylide/[1,2] shifts has also been studied with chiral metal complexes. Katsuki and coworkers examined the reaction of (±)-2-phenyloxethane with 0.5 equiv. tert-butyl diazoacetate in the presence of Cu(I) catalyst. Chiral bipyridine ligand 65 provides trans- and cis-tetrahydrofurans 66 and 67 with 75 and 81 % ee, (eqn [8]).22 This asymmetric ring expansion was applied by the same group to their enantioselective synthesis of trans-Whisky lactone.23[8]Desymmetization strategy in enantioselective oxonium 23[8]Des Yemetisation strategy in enantioselective oxonium 2 formation/[1,2] shift reaction has been reported by Doyle and co-workers.24 With Rh2(4S-MPPIM)4 as catalyst, up to 88% ee (eqn [9]) is obtained. [9] Patrick J. Murphy, in Comprehensive Organic Functional Group Transformations, 1995The 2.3-rearrangement of oxonium ylides effects a similar transformation as that found in [2,3]-Wittig reaction. Various methods exist for generation of ylide <91CRV263>; these include metal-catalyzed degradation of α-diazo ketones <86JA6060, 86ja6062,= 88tl5119,= 92tl6193=>with intramolecular 2.3-rearrangement and similar intermolecular versions using α-diazomalonate <72JA3870>and α-diazoacetate-based <71JOC1732>rearrangements of allylic ethers. Trimethylsilyloxonium ylider can also be generated in situ by the treatment of α-allyloxyacetic esters with TMSO-Tf and trietylamin <86TL4511>. Representative examples are given in Scheme 51.T. Graening, F. Thrun, in Comprehensive Heterocyclic Chemistry III, 2008I the rhodium-catalysed formation of av</86TL4511> </71JOC1732> </72JA3870> </86JA6060,> </91CRV263> </91CRV263> 63, an asymmetric [2,3] reorganization has been achieved. When N-phthaloyl-(S)-tert-leucine was used as ligand, an ee of up to 60% (Schedule 100) <1997TL4705>was obtained. Dihydrobenzofurans can be obtained via dienone-phenol rearrangement of spirooxeans prepared by photo preparation of quinones with electrons-sensitive alkenes (Schedule 101) <1996H(43)619>. Either benzo or dihydrobenzofurans can be obtained in the [3,3]-sigmatropic rearrangement of N-trifluoroacetyl-enehydroxylamines, depending upon the choice of the reagent (Schedule 102) <2006SL3415>. Flavons have been shown to suffer from a stereospecific ring contraction to provide trans-2-aryl-2,3-dihydrobenzo[b]furan-3 carboxoxylates in treatment with phenyliodonium acetate, trimethyltoforte and sulfuric acid (Equation 151) <2002T4261>. (151) P.H. Ducrot, in Comprehensive Organic Functional Group Transformations II, 2005The [2,3]-rearrangement of enantiomerically pure oxonium ylides has <1997CRV2341, 1996crv223,= 2001csr50=>reviewed and a monograph has recently been published on the chemistry of oxonium yliderna , which brings together the <B-2002MI001>different methods of their preparation. Reorganization of allyl oxoniums has benefited from the development of diazo-derived carbene chemistry <1998CRV911, 2001csr50,= 1995joc53,= 1999t6577=>. Many chiral catalysts have been studied (Schedule 34) <1996TL107, 2001tl6361,= 1998ja7653,= b-1998mi001,= 1995jcs(p1)1373,= 1997tl4705,= 2001ta877=>and allows for good enantiocontrol of the rearranged products. The main problem to be addressed in this catalytic process is to avoid a competitive cyclopropanation reaction of allyl moiety <1997TL5265, 2000tl6265=>. The main use of this methodology deals with the synthesis of substituted tetrahydrofurans (Equation (79)) <1998TL8813, 1996tl5605=>. Other examples of application in the field of synthesis of natural products have been reported <1999CC749, 1998tl97,= 2001cc459,= 1996tl5053,= 1997joc3902,= 1998tl1691,= 2002ij283,= 2000tl6265,= 2001ja5144=>. (79) R. Bach, ... J. Lacour, in extensive organic synthesis II (second edition), 2014Stevens and related rearrangements are reactions involving the formation of ammonium, sulfonium, and oxoniumylide intermediates and then migrations of activated alkyl groups from onium heteroatoms to nucleofilaylide carbon. For this review and in the future with the previous Comprehensive Organic Synthesis report,1 only reactions involving ammonium and sulfonium intermediates will be detailed. This choice is dictated by the abundant synthetic and mechanistic similarities that occur between the nitrogen- and sulphur-based reorganizations. In fact, these transformations have been studied in parallel since the 1928 and 1932 reports by Stevens of the treatment of phenacylbenzyl dimethylammonium 1 and methyl sulfonium 3 bromides with sodium hydroxide or meoxide to form amine 2 and sulphide 4 in good yield (equations 1 and Dessa migration av benzylgrupper från N</1999CC749,> </1998TL8813,> </1997TL5265,> </1996TL107,> </1998CRV911,> </B-2002MI001> </1997CRV2341,> </B-2002MI001> </1997CRV2341,> </B-2002MI001> </1997CRV2341,> </B-2002MI001> </1997CRV2341,> </2002T4261> </2006SL3415> </1996H(43)619> </1997TL4705> </1997TL4705> S atoms to the adjacent coal centers are typical examples of so-called [1,2]-Stevens rearrangements. Transformations of this type are often synthetically useful and they will be highly detailed in this review. [2,3]-Stevens rearrangements where substrates carry allyl or propargyl substitutes on onium atoms were historically reported later (5 to 6, equation 3).4.5 They are also the focus of many studies that will be covered extensively. In these reactions, to the migration of the unsaturated side chains to the nucleofilaylid ekolet, the C-C bondage is usually formed at the γ-carbon of the migrating side chains and important mechanistic differences arise that will be described. If the onium ion carries a benzy-like substitute, a related reorganization often occurs which involves, in an elementary step, an attack of the cellular ylid echo in the aromatic nucleus of the benzyl group (7 to 8, equation 4). This reactivity, which will also be detailed, was first reported by the Sommelet and its mechanism investigated by Hauser and thus its Sommelet-Hauser denomination.6,7The fields of [1,2]-Stevens, [2,3]-Stevens, and Sommelet-Hauser rearrangements of ammonium and sulfonium ylides were previously reviewed; the previous comprehensive organic synthesis report dated 1991.1,8–13 After a section detailing the mechanisms taken into account for these reactions, this chapter will chart the latest progress made over the last 20 years or so and show how wide and active the field is (over 200 references).N.J. Thumar, ... W.H. Hu, in Advances in Organometallic Chemistry, 2016News, Davies group reported rhodium-catalysed reactions of tertiary propargylic alcohols with methyl and styrdiazoacetates resulting in tandemoxonium ylide/[2,3]-sigmatropic reorganization, instead of the expected O-Hion. The 2.3-sigmatropic rearrangement proceeds through cleavage of the O-H bond to generate a diradic intermediate that favors 2.3-sigmatropic reorganization with donor/acceptor carbenese and more well-functioned propargylic alcohols. Allenes are produced with high enantioselectivity (88-98% ee) using dirhodium tetraprolineate complex, Rh2(S-DOSP)4. The main feature is the presence of a two-point mount during the ylide formation and the diradic nature of [2,3] sigmatropic reorganization (Schedule 85).121Scheme 85. Asymmetric tooth emylide formation/[2,3]-sigmatropic reorganization of diazoketones with propargylic alcohols. Donor/acceptor-substituted rhodium carbenese are useful for synthesis of medium-sized carbocycles. A range of vinyl diazoacetates and allyl alcohols were found to be suitable partners for the synthesis of cyclopentans in exceptional yield and stereocontrol by Davies' group. Rhodium-catalysed reactions of vinyl diazoacetates with (E)-1,3-disubstituted 2-butenols generate cyclopentanes, with four stereogenic centers with very high levels of stereoselectivity (99% ee, dr). The reaction proceeds through a carben-initiated domino sequence consisting of five distinct steps: rhodium-bound oxonium ylide formation, [2,3]-sigmatropic reorganization, oxy-cope rearrangement, enol-keto tautomerization, and finally an intramolecular carbonyl ene reaction. The low catalyst loads, readily available starting materials and in-depth understanding of the mechanistic details make this an important method for accessing cyclopen nuclei to common prostaglandinanta antiglaucoma agents (Schedule 86).122Scheme 86. One-pot domino sequence for the synthesis of a cyclopentane. Similarly, cyclohexane are also formed as single stereoisomers in good yield by a one-pot reaction of vinyl diazoacetates and allyl alcohols by a rhodium-carbene initiated domino reaction. The reaction-injury mechanism includes a tooth emylide formation/[2,3]-sigmatropic reorganization, oxy-Cope reorganization and type II carbonylene ylene, in an overall process that occurs with a high degree of stereo control. The products are formed with excellent stereo control (> 97:3 dr, 99% ee) (Schedule 87).123Scheme 87. One-pot domino sequence for synthesis of a cyclohexane. The pyrrolidine alkaloid (±)-Preussin, an antifungal, antiviral, and antibacterial agent that also induces apoptosis in several human cancer cell lines, can be synthesized from decanal and diethyl 3-diazo-2-oxopropylphosphonate in three stages in total yield of 40%. The most important step is the highly stereo-selecting Cu-catalyzed ylide formation and then a [1,2]-Stevens rearrangement. This approach is applicable to Prussian analogues, for the rapid construction of all-cis-substituted pyrrolidines alkaloids. This stereowell roller sequence may be useful for asymmetric synthesis of prussian, employing chiral amines in aza-michael reaction (Scheme 88).124Scheme 88. Three-stage synthesis of (±)-Preussin.Polycyclic ring systems that have multiple stereogenic centers into the target skeleton are an effective approach to increasing the complexity of chemically generated molecules. In addition, fused O-heterocyclic compounds such as hydroepoxyisochromare are commonly found in drugs and natural products. Applying multicomponent cascade reactions is powerful and effective for constructing these complex molecules from simple starting materials in an operational step-economy way. Very recently, Hu's group report an enantioselective three-component/Diels-Alder process to make the functionalized hydroepoxyisandromen scaffold with the moltenpolycyclic system containing six chiral carbon centers. Subsequent one-pot epoxidation of the product allows to make more complex molecule with up to a total of eight chiral centers (Schedule 89).125Scheme 89. One-pot three-component cascade/subsequent epoxidation to eight stereogenic centers. This method demonstrates an atom and step-economic approach to the rapid construction of poly ring-fused O-heterocyclic compounds with high molecular complexity from simple starting materials.R. Alan Graziella-Ioana Dragomir, underway in heterocyclic chemistry, 2015 Aminocarben Pri2N(Men)C: reacts with benzaldehyde to give dioxolan 1 in 72% yield (14JA5023) and a chiral gadolinium complex has developed for to achieve generation and highly stereodiva life cyclobaddition of oxonium yliders derived from epoxides 2 with an added aldehyde to give dioxolaner 3 (14CC2161). A multi-stage route is involved in gold-N heterocyclic carbide catalyzed addition of acetoxydiynes such as 4 with two equivalents of an aldehyde to give de cyclohexadienyldioxolanes 5 (14CEJ713). The multifunctional compound 6 has been introduced as a key intermediate in the synthesis of fluorinated amino sweeteners (14SL1253). Desymmetrization of quinols 7 of an acetalization-Michael supplement mediated by acids difenylphosphate gives the dioxolane products 8 with high diastereoselectivity (14SL713). The reaction of epoxides with CO2 to provide 1,3-dioxolan-2-as has been further investigated and new effective catalysts include metal organic frames (14AGE2615) and aluminum heteroscorpionate complex (14MI674). Detailed mechanistic and kinetic studies on the bimetallic aluminum hall catalyzed version of this process have emerged (14CEJ8182, 14CEJ15005). This process has also been used as a means of converting bicyclic epoxides into cyclic 1.2 diols by formation and base hydrolysis of the cyclic carbonates (14AGE10416). A new one-pot conversion of aldehydes to 4-substituted 1.3-dioxolan-2-ones 9 involves treatment with a sulfonium or sulfoxoniumylide in an atmosphere of CO2 (14SL97). In this process, the sodium iodide found from the ylide generation plays a key role in opening the originally formed epoxide to provide a 2-iodoal gase, which then reacts with CO2. A new method uses a base like DBU and a silver salt to catalyze the reaction of propargylic alcohols 10 with CO2 to give dioxolones 11 (14SL1178). Bromocyclization of the allylic carbamates 12 occurs with complete selectivity depending on the choice of reagent, with N-dibromo-p-toluenesulfonamide giving the oxazolidinones 13 while N-dibromo-p-benz nitroenesulfonamide provides 2-imino-1,3-dioxolanes 14 (14SL1921). Experimental IR and Raman spectroscopic data have been compared to those predicted from density functional theory for the simple bromomethyldioxolones 15 and 16 (14JST(1056-7)38), and the X-ray structure of benzodioxole 17 has been reported (14CEJ2529). Dioxolanone protection of methyl vinyl ketone as 19 is crucial to the success of a new ruthenium-catalyzed α-alkylation of piperidine 18 to afford 20 (14ASC 1610), and organocatalytic enanthive aryylation of isatins 21 with sesamol 22 provides 3-hydroxyoxindoles 23 (14CAJ1305). Intermediate 24 derived from cyclohexylideneglyceraldehyde have been used in the synthesis of (R)-proline, 3,4-dihydroxyproline and related compounds (14S2481). Bis(dioxolane) 25 reacts in an effective Petasis boronic Mannich reaction to synthetic intermediate 26 (14S2672). Good diastereoselectivity is observed in Michael's addition of chiral lithium amides to cis dioxolanes 27 (14TA534). Palladium-mediated decarboxylative cyclocyofdioxyls 28 with formaldehyde is controlled by the chiral ligand to provide either enantiomer 29 or 30 of vinyl dioxolane (14AGE6439), and the corresponding cycloadditionloon to substituted acrylonitles produces chiral tetrahydrofurans 31 (14AGE11257). A new natural product isolated from Clerodendrum bungei has been identified by spectroscopic and X-ray methods as an unequal mixture of the tricyclic dioxolane enantiomers 32 and 33 (14TL2277). The new cytotoxic natural product citrinoviric acid from the marine fungus Trichoderma citrinoviride has dioxolanonekarboxylen structure 34 (14H(89)189). The racemic dioxolanon 35 was prepared as an analogue of the natural product antrodioxolanon, which has the isomeric meso structure (14OBC1100). Stereoregular isotactic poly(mandelic acid), a biodegradable polyester analogue of polystyrene, can be obtained by ring-opening polymerization of dioxolanione 36 (14AGE13858), and the benzodioxole-containing monomer 37 has been used to prepare polymer films with useful electrochromatic properties (14MI245). Taddol-derived guanidine 38 has been used as an effective catalyst for asymmetric fluorination of 1,3-dicocarbon compounds (14AJC1115). Potent in vitro antitumor activity has been reported for the thiazofurine analogue 39 (14T2343). Many new drug agents contain an important benzodioxole unit including neuropilin-1 receptor antagonists 40 with potential antitumor applications (14BML4254), anti-inflammatory agent 41 (14MI60), DPP -IV inhibitors as 42 for the treatment of type 2 diabetes (14BML1918), and monoacylglycerol lipase inhibitors as 43 for the treatment of multiple sclerosis (14AGE13765). (14AGE13765).