Pergamon

Tetrahedron, Vol. 53, No. 24, pp. 7999-8065, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00264-0

TETRAHEDRON REPORT NUMBER 422

Organic Reactions on Alumina

George W. Kabalka* and Richard M. Pagni*

Department of Chemistry
The University of Tennessee
Knoxville, Tennessee 37996-1600

Contents

1. Introduction 7999
2. Nature of Alumina and Modified Alumina 8000
3. Reactions 8005
    - 3.1. Deuterium exchange 8005
    - 3.2. Epoxide ring opening 8006
    - 3.3. Elimination and dehydrative condensation reactions 8008
    - 3.4. Addition reactions 8012
    - 3.5. Aromatic and vinyl substitution 8015
    - 3.6. Nucleophilic substitution and solvolysis 8018
    - 3.7. Condensation reactions and conjugate additions 8022
    - 3.8. Reactions of carboxylic acids and derivatives 8025
    - 3.9. Isomerizations, rearrangements, and pericyclic reactions 8028
    - 3.10. Protection and deprotection 8037
    - 3.11. Oxidation and reduction reactions 8039
    - 3.12. Photochemical reactions 8044
    - 3.13. Miscellaneous reactions 8045

INTRODUCTION

Although it may seem normal, particularly in the light of the sophistication of modern organic synthesis, the practice of carrying out reactions in solution may reflect tradition rather than actually being advantageous. As described in a recent commentary[1] concerning the selective binding and removal of guest molecules from a microporous metal-organic framework,[2] the reluctance of organic chemists to examine reactions in other environments may be short-sighted. Consider, for example, the case of reactions run on the surfaces of solids. Even though this field is relatively new, it is already apparent to practitioners that one can carry out many synthetically useful reactions on solids, often going faster and/or generating higher yields than via the solution

---

**E-mail: Kabalka@utk.edu* and *RPagni@utk.edu* FAX: *(423)974-2997*

counterparts. There is also every expectation that new reactions, not attainable in solution, will be discovered as new solid reaction media are developed.

Organic reactions have been carried out on the surfaces of many solids,[3-10] notably zeolites,[11-17] clays,[18-26] silica gel,[3-10, 27] alumina,[3-10, 28] and polymers,[3,4,29] all of which have distinctive surface characteristics. Zeolites, both naturally occurring and synthetic, are aluminosilicates which possess three-dimensional structures with interconnecting channels and cavities. Reactions may take place in the channels and in the cavities if the substrate is small enough or on the exterior of the surface if it is not. Zeolites, which also have exchangeable metal cations, have found wide use in the manufacture of gasoline. Clays are aluminosilicate minerals with exchangeable cations but, unlike zeolites, they possess lamellar or layered structures with the interiors available to reactants. By contrast, silica gel and alumina, which are widely used in chromatography, do not contain accessible channels or cavities. Instead, these materials have large surface areas and highly porous exteriors which are available to substrates.

Of the metal oxides described above, alumina is particularly interesting. It has been used industrially as filler, adsorbent, drying agent, catalyst, catalytic support, precursor to aluminum metal, and as a reagent in the synthesis of other aluminum-containing compounds such as aluminum sulfate and fluoride.[30] What is especially interesting to the organic chemist is that alumina can be used as catalyst, support and reagent. Because the surface of alumina can also be modified in a variety of ways, the number of potential environments available for organic reactions is very large.

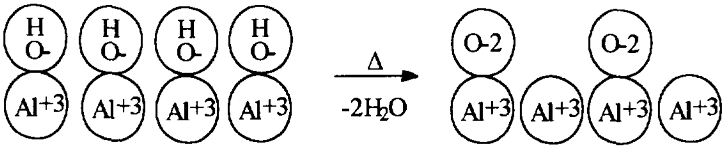
This article will review what is currently known about synthetically useful organic reactions which occur on the surface of alumina and modified alumina. Just as it is important to understand how solvents influence solution-phase chemistry,[31] it is equally important to understand the surface of alumina. An overview of what is known about the surface of alumina is presented in the next section.

NATURE OF ALUMINA AND MODIFIED ALUMINA

The term alumina refers to a series of ionic solids which have the formula $Al_2O_3 \cdot (H_2O)_n$, where n = 0 to 3, although none of them actually contains H_2O.[30] They are derived by heating naturally occurring or synthetic, crystalline and amorphous $Al(OH)_3$ $[Al_2O_3 \cdot (H_2O)_3]$ and $AlO(OH)$ $[Al_2O_3 \cdot (H_2O)]$. Gibbsite and boehmite, for example, are crystalline $Al(OH)_3$ (monoclinic) and $AlO(OH)$ (ortho-rhombic), respectively. The endpoint in the synthesis, which occurs by heating the materials above 1100 °C, is corundum, one of the hardest substances known and the thermodynamically most stable form of Al_2O_3. This material is not widely used in organic chemistry.[32] At temperatures below 1100 °C, a series of transition aluminas can be generated whose structures are dependent on the precursor, final temperature and mode of heating. During the course of thermolysis, hydroxyl groups combine to generate H_2O which is driven from the solids. Heating to 600 °C, for example, yields the γ series of aluminas which contain ρ, χ, η and γ types; these materials, have the formula $Al_2O_3 \cdot (H_2O)_n$, with $n<0.6$. Higher temperatures, 800 - 1000 °C, yield the δ series of aluminas which contain very few OH groups (n ~ 0), and includes κ, θ and δ varieties, all of which are more highly crystalline than the γ varieties. Although outwardly these transition aluminas are much alike, they possess different physical properties including densities, surface areas, pore volumes and diameters. When exposed to water, the surfaces of the transition aluminas are hydrated, yielding a surface layer of hydroxyl groups.[33]

γ-Alumina, typically formed by heating boehmite between 400° and 500 °C, is widely used to separate compounds by column chromatography and is the transition alumina most commonly used to carry out surface organic chemistry.[28,34] It possesses a defect spinel structure[35] and generally has a surface area of 100-300 m^2/gx or greater. The large surface area implies that the alumina particles are small. The surface area contained in 1 g of solid is equivalent to the area of a square room 10-17 m on a side. A monolayer coverage on the surface will contain several mmols of a typical organic compound. This belies the widely held belief that one cannot run surface reactions on a large scale. Unlike a smooth surface which has a fractal dimension of 2, γ-alumina has a fractal dimension close to 3,[36] implying a very rough, irregular surface. The roughness can be attributed in part to the presence of pores on the surface, which also contributes to the large surface area.

If one looks at the ideal surface of hydrated γ-alumina from the side, as proposed by Peri,[33] one observes that the surface is terminated by hydroxyl groups, each of which is directly above an aluminum ion in the next layer of the crystallite. Since there are 12.5 hydroxyl groups on the surface per 100 $Å^2$, this corresponds to 3.2 mmol of hydroxyl groups per gram of solid for an alumina with a surface area of 155 m^2/g. Water may also be hydrogen bonded to the surface hydroxyl groups. When the solid is heated, physisorbed H_2O is lost initially and then adjacent hydroxyl groups react with one another by proton transfer to generate oxide (O^{-2}) and H_2O, which is driven from the surface. Higher activation temperatures result in the production of greater quantities of water. At 400 °C, for example, about 50% of the hydroxyl groups are lost; at 600 °C, 80% are lost and, at 800°, close to 100% are removed. Furthermore, when H_2O is driven from the surface, one Al^{+3} ion is exposed for every O^{-2} that is generated.

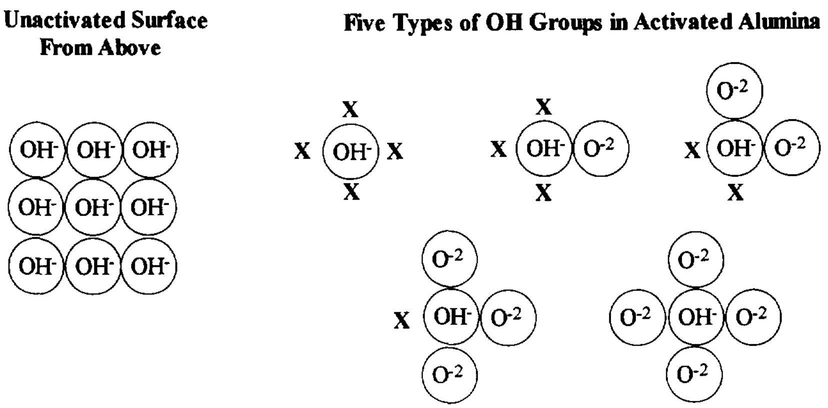


Thus, there are three species on the surface, OH^-, O^{-2} and Al^{+3}, whose concentrations are interdependent and controlled by the activation temperature. Based on this model, the surface can exhibit a variety of properties; OH^- will act as a very weak Brønsted acid,[35] as well as a base and possibly a nucleophile, O^{-2} should be a strong base and nucleophile, and Al^{+3} is a Lewis acid. Because the ions are immobile at the temperatures used to carry out organic reactions, an activated solid will have strongly basic and acidic sites adjacent to each other which is not possible to achieve in fluid solution. These adjoining sites may act cooperatively, analogous to what occurs at the active sites of enzymes. In addition to serving catalytic roles, the surface components may also serve as reagents, donating species such as hydrogen, hydroxyl, oxide and water.

Unactivated γ-alumina is basic.[37] When contacted with H_2O, for example, it yields a basic solution. γ-Alumina can be "neutralized" by reaction with ethyl acetate, HCl or acetic acid to provide neutral and then acidic alumina. Basic, neutral and acidic aluminas, available commercially from several sources, are the types most commonly used in organic synthesis. As noted by Posner,[28,34] it is important to report the type (and activity) of the alumina used in a synthetic procedure because each type influences an organic reaction differently. Alumina is also amphoteric. When the solid is brought into contact with a sufficiently basic solution (pH greater than the solid's isoelectric point which normally occurs at pH = 7.2-9), the surface hydroxyl groups are deprotonated and cations are placed onto the surface under reversible conditions. This represents a simple method for introducing cations onto the alumina surface. On the other hand, when the solid is contacted with a sufficiently acidic aqueous solution, the surface hydroxyl groups are protonated which puts anions on the surface.

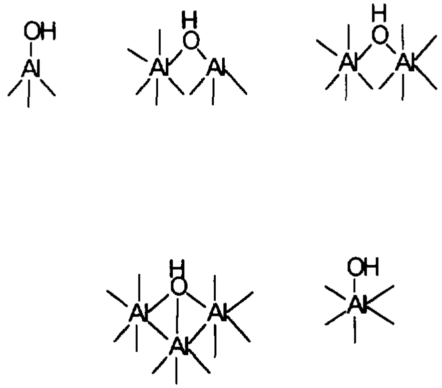
Studies in which activated aluminas are placed in contact with a series of indicator dyes of varying basicity[37,38,39] suggest that the surface has modest acidity. The nature, number and strength of the acidic sites vary with the activating temperature. Infrared studies of pyridine[38] chemisorbed onto alumina reveal that the surface acids sites are entirely Lewis in character. On the other hand, ^{13}C NMR studies of *n*-butylamine, which is considerably more basic than pyridine, adsorbed on γ-alumina which had been activated at 350 °C *in vacuo* ($350°$-Al_2O_3) demonstrate that both Lewis and Brønsted acid sites co-exist on the surface.[40] The weakly basic substrates appear to preferentially interact with the Lewis sites, while more basic substrates interact with both. As described later, the strongly basic sites are able to deprotonate weakly acidic substrates.

Not all the hydroxyl groups on the surface are in structurally identical environments. IR studies have revealed up to five OH stretching frequencies, depending on how the alumina is treated.[33] Peri's model, which assumes that a single phase (100) of the alumina crystallite terminates at the surface, was generated to explain the IR data.[33] In this model, the unactivated surface contains a layer of structurally and chemically equivalent hydroxyl groups, each of which resides above an octahedral Al^{+3} ion in the second layer. After activation by heating, a series of five types of hydroxyl groups are created which differ in the number and arrangement of O^{-2} and Al^{+3} ions surrounding them. Whether the five types of hydroxyl groups are chemically different is not known.

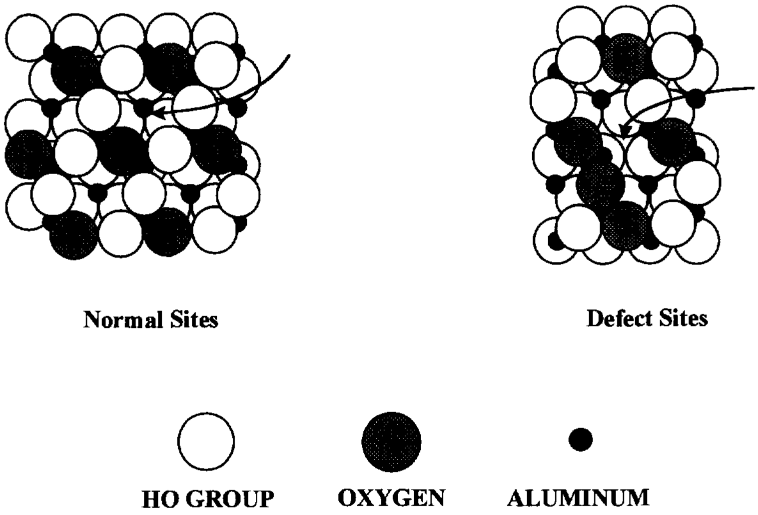


X represents a vacancy below which lies an aluminum ion

Knözinger and Ratnasamy (K-R) proposed an alternate theory[41] which not only rationalizes the IR spectra but also other spectroscopic and chemical data. In the K-R theory, three planes (100, 110 and 111) terminate the crystallite. This places different types of hydroxyl groups on the surface and octahedral and tetrahedral aluminum ions in the second layer. Unlike the Peri model, in which the types of hydroxyl groups are determined by the number of neighboring oxide anions, the K-R theory generates five distinct hydroxyl groups by the way in which OH is bonded to tetrahedral and octahedral aluminum ions, as shown below. Varying acidities and basicities are assigned to the five kinds of OH groups. For the 111 plane, which plays a prominent role in the K-R theory, there are 75% basic OH's and 25% acidic OH's, with the basic ones lying in one row and alternating with acidic ones in the adjacent row. It is then possible to readily dehydroxylate until the 25% of acidic OH's are used up. Aluminum ions are exposed in this fashion. Beyond this total of 50% dehydroxylation, which occurs on activation between 300 °C and 400 °C, dehydroxylation becomes abnormal in that adjacent basic OH's must react with one another to produce water. Defect sites or holes are created in this process. Other, still different sites are generated at still



higher temperatures. Although this is an idealized reaction scheme, it has considerable merit because catalytic activity, including that for the Diels-Alder reaction, occurs at the point that theory predicts the presence of defect sites on the surface.



Many solid state NMR studies of alumina have been reported, [40,42-53] a few of which are relevant in the present context. Of particular note is a recent ^{1}H NMR study of the surface hydroxyl groups[51] which revealed five resonances for γ-alumina activated at 700 °C in air, a result consistent with the IR results and the K-R model; physisorbed water was also detected on a less activated alumina. NMR studies of molecules adsorbed on the surface (ammonia, pyridine and tricyclohexylphosphine) show that there are at least two Lewis acid sites on the surface.[45,48-50] Fripiat has assigned the Lewis acidic sites to aluminum ions in tetrahedral and metastable pentacoordinate environments.[44-46,50] Interestingly, the surface pentacoordinate aluminum ions are in some way associated with one-electron acceptor sites on the surface which were detected indirectly by ESR using easily oxidized probe molecules.[44] One-electron donor sites also exist on the surface of alumina.[55] The one-election donor and acceptor sites, which exist predominantly on more activated aluminas, have yet to be exploited in synthetic organic chemistry.

In conclusion, it is clear that the surface of alumina provides a polar environment,[56,57] favorable to many ionic and heterolytic reactions. Organic substrates have a variety of mechanisms by which they can interact with the surface including hydrogen bond formation and acid-base reactions. In addition to these two-electron phenomena, easily oxidized or reduced molecules can participate in one-electron transfers with the surface, especially on highly activated surfaces. Subtle differences, of course, may exist because not all surface hydroxyls, oxides, or aluminum ions are equivalent although this fact has not proven to be important in understanding the majority of reactions. In some chemistry, these differences in surface characteristics do have an impact. It is also clear that the surface can play a role in many organic reactions and that substrates may interact with the surface anisotropically, a result not possible in most solutions. In addition a large number of surface-modified aluminas have been created and utilized in organic synthesis. These new materials have been prepared in a number of ways. As noted earlier, one can add cations and anions to the solid by equilibration at pH's above and below the solid's isoelectric point. Salts are most often added to the surface, however, by evaporation of an aqueous salt solution in contact with the solid, yielding what is generally known as a supported reagent.[3-5] Scores of salts, and other reagents, have been added to alumina in this fashion. One advantage of using the evaporation method for the introduction of an adsorbate is that the surface concentration can be readily controlled. One must be cautious in using excess adsorbate because crystallites, or islands, may form on the surface under those circumstances. One must also be aware of the fact that the adsorbates may not retain their identity on the surface. Evaporation of KF in water onto alumina yields a widely used, very basic solid containing no free F^-.[5] The chemistry of KF on alumina will be described in more detail later in this article. Even in cases where the added material does not undergo an apparent chemical reaction with the surface components, one cannot assume that free ions exist there. Anions and other bases, for example, have a propensity to bind to the Lewis acid sites on the surface.

Modified surfaces have also been prepared by chemical reactions which take into account the likely chemical characteristics of the surface components.[3-5] One can, for example, alkylate the OH groups by reaction with CH_2N_2 or the oxide ions by reaction with alkyl halides such as benzyl chloride. Both surface hydroxyls and oxides also react with inorganic and organic acid halides. Numerous reactions of this type have been carried out.

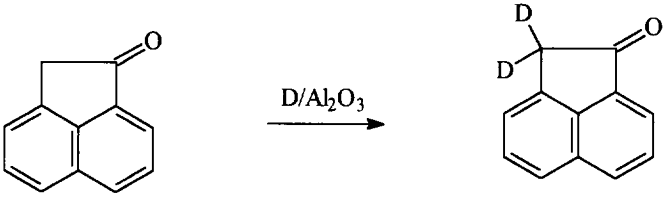
REACTIONS

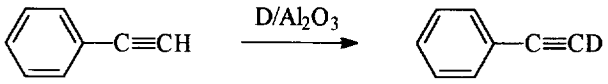
With knowledge of the nature of the alumina surface, one can begin to understand the organic chemistry carried out on alumina. As there have been substantive discussions of the organic chemistry of alumina in the literature, primarily in the late 1970's, this article will report on work published primarily between 1980 and 1996.

DEUTERIUM EXCHANGE

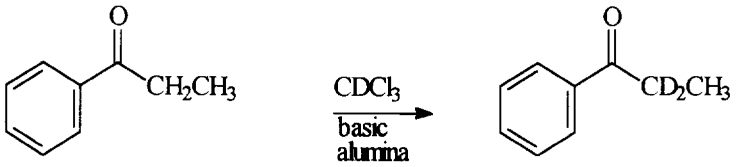
Modified alumina can be used to deuterate acidic organic molecules because the solid is basic. The surface hydrogens must first be replaced with deuterium. D_2 has been used for this purpose,[58] but this source of deuterium is not particularly convenient. Pagni and Kabalka described a procedure to deuterate alumina (D/Al_2O_3)[59] in which small amounts of D_2O (6% by weight) and activated solid are equilibrated at 350 °C, then cooled, and the solid activated again, if necessary. Several such cycles yield a solid whose surface is nearly 100% deuterated, with minimal wastage of D_2O.

D/Al_2O_3 has been used to deuterate a variety of hydrocarbons and ketones.[59,60] Phenylacetylene, acenaphthenone, acetophenone and diethyl malonate, for example, were readily and extensively deuterated at room temperature in a pentane or pentane-ether slurry. The diethyl malonate reaction was complete in less than five minutes. Fluorene and indene, whose pK_as are comparable to that of phenylacetylene, underwent exchange more slowly which suggests the operation of a steric effect. Similarly, 2-norbornanone underwent exchange at the 3-exo position under conditions which the sterically more hindered camphor did not. Triphenylmethane, pK_a >30, also underwent exchange, demonstrating that the surface contains very basic sites. Ethyl acetoacetate behaved oddly, with its methylene hydrogens exchanging rapidly, but only to the extent of 70% deuteration, while the much less acidic methyl group yielded 100% deuterium exchange after an extended period of time.





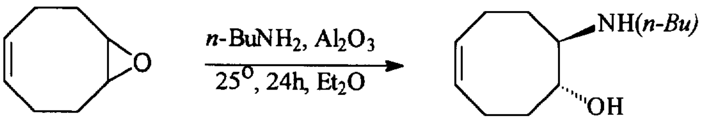
Kunick and Messinger developed an alternative method of deuteration[61] in which basic alumina is used to catalyze the exchange and $CDCl_3$, an acidic molecule, is the source of deuterium. The $CDCl_3$ was used in great excess and a very high, but not 100%, exchange was observed in the five substrates examined.

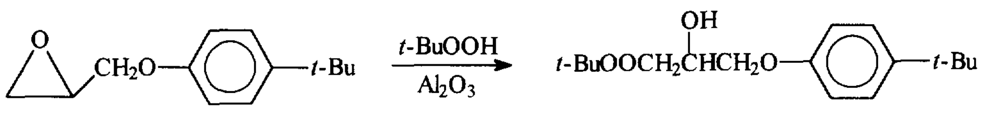


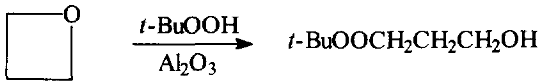
(93% deuterated)

EPOXIDE RING OPENING

Epoxides are versatile compounds in organic synthesis. They are readily prepared from alkenes, ketones and aldehydes and, owing to their ring strain (27 kcal/mol) and oxygen lone pairs, the rings cleave regioselectively under acid and base conditions to give vicinally disubstituted products of defined stereochemistry. In pioneering work, Posner showed that the nucleophilic ring opening of epoxides by alcohols, thiols, benzeneselenol, amines and acetic acid occurs readily on neutral and basic alumina, normally yielding a single product uncontaminated by

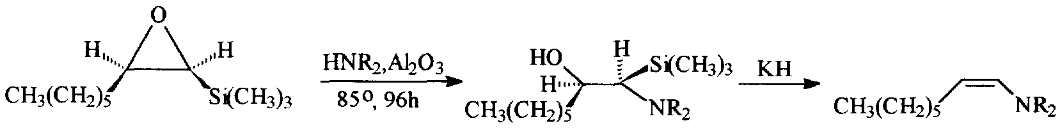




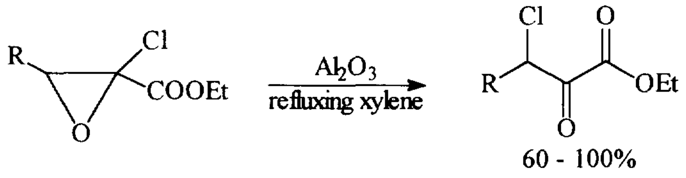


impurities which often plague these reactions in solution.[28,34,62] More recently, Kropf and coworkers have extended these epoxide scissions using *t*-BuOOH on activated alumina as nucleophile[63,64] Oxetanes (ring strain = 26 kcal/mol) also undergo ring scission with *t*-BuOOH. For the more than twenty examples reported, the nucleophile (*t*-BuOO$^-$) preferentially attacks the less hindered site of the epoxide or oxetane.

In another interesting application of this methodology, Hudrlik demonstrated that a *cis*-silylsubstituted epoxide (below) reacts with pyrrolidine and morpholine on neutral alumina to give an hydroxylamine stereoselectively which, on treatment with KH, eliminates Me$_3$SiOH to form an (*E*)-enamine[65] These reactions are sluggish in the absence of alumina. Surprisingly, the *trans* epoxide is inert to the alumina-catalyzed reaction.

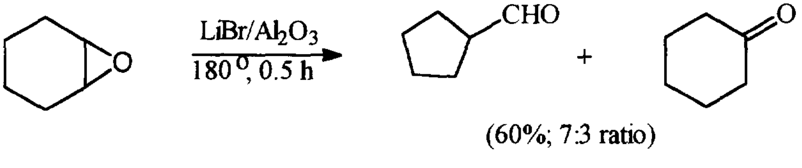


Epoxides react on activated alumina in the absence of nucleophiles to yield complex mixtures of isomerized and rearranged products.[66-71] These reactions appear to be initiated by the Lewis acid-catalyzed ring opening of the epoxides by acid sites on the alumina. On the other hand, chloroepoxyesters, formed in the Darzens condensation, isomerize in high yield to single products on alumina in refluxing xylene.[72] No reaction occurs in the absence of alumina.



R = Et, *n*-Pr, *i*-Pr, *n*-Bu, *t*-Bu, *n*-Pentyl

The supported reagent, LiBr adsorbed on Al_2O_3 ($LiBr/Al_2O_3$), also catalyzes the isomerization of epoxides to aldehydes and ketones, either in refluxing toluene or in the gas phase at 180°.[73] $LiCl/Al_2O_3$, $MgBr_2/Al_2O_3$ and $LiBr/SiO_2$ were less effective catalysts for these reactions. A mixture of LiBr and Al_2O_3 also was not as effective. Clearly, the Lewis acidic cation, its counterion, and the support influence these reactions. Unfortunately, nothing is presently known about how inorganic salts interact with the alumina surface.

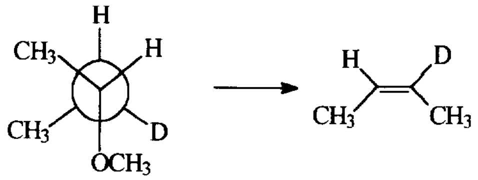


ELIMINATION AND DEHYDRATIVE CONDENSATION REACTIONS

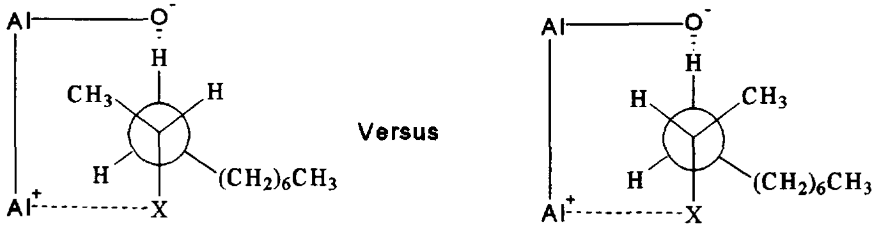
Elimination reactions are among the most studied of all solution reactions and they proceed via multiple mechanisms.[74] Concerted reactions including the base-induced E2 reaction, the pericyclic Cope elimination and the stepwise El and ElcB reactions (which proceed via both carbocation and carbanion intermediates) all yield olefins by overall β elimination. Solution dehydration reactions are also common and their mechanisms varied.[74] Classic examples of these include Fischer esterification and imine formation by the reaction of an aldehyde or ketone with ammonia or an amine derivative.

Because activated alumina is polar, contains potentially catalytic acid and base sites on its surface, and is itself dehydrated, it is not surprising that elimination and dehydration reactions occur readily on alumina.[6] Many early reactions were carried out in the gas phase at elevated temperatures; gas-solid reactions are of particular interest to catalytic scientists and chemical engineers. Two recently reported elimination reactions, one occurring with a gaseous reactant at high temperatures and the other with the same reactant in solution at room temperature, demonstrate the utility of the reaction.

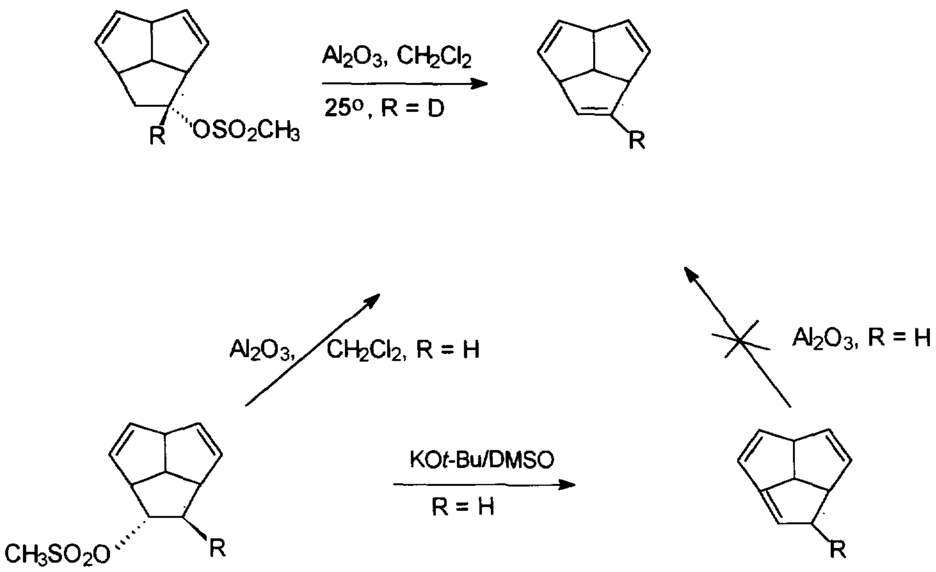
Bauer and Thomke studied the elimination of methanol from 2-methoxy-, 2-methoxy-2-deutero-, and *d, l-erthyro*-2-methoxy-3-deuterobutane in the gas phase at 183-332 °C in the presence of γ alumina.[75] The reaction occurred largely by concerted (E2) *anti* elimination of methanol to give predominately *cis*-2-butene. Saytzev elimination to give *cis*- and *trans*-2-butene dominated over Hofmann elimination to give 1-butene at all temperatures. *Syn* E2 elimination also occurred and became more important as the reaction temperatures increased. Small percentages of E1 elimination were also detected at higher reaction temperatures. The predominant reaction pathway involved an *anti* elimination from a staggered conformation in which the two methyl groups are close to one another.



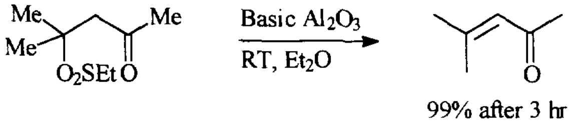
Závada and Pánková examined the elimination of HX from a series of 2-substituted decanes containing OTs, Cl, Br and I in ether at 25 °C in the presence of Woelm alumina which had been previously activated at 400 °C for 6 hr.[76] Similar to what was observed by Bauer and Thomke, 2-decene was formed in greater amounts than 1-decene in all cases and *cis*-2-decene was the major geometric isomer. The selectivities are higher than those observed in KO*t*-Bu/benzene. There was also a large leaving group effect. These results are consistent with the reaction occurring by the concerted *anti* elimination of HX. Steric effects may be invoked to explain the preponderance of *cis*-2-butene in the product mixture.

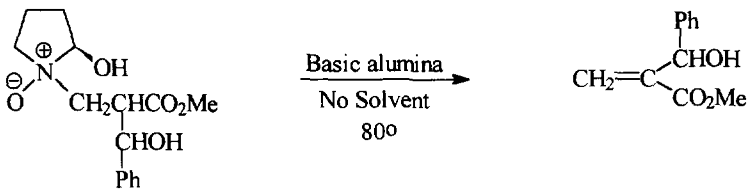


Posner was the first to study surface catalyzed elimination reactions from a synthetic perspective.[77] He and his coworkers found that tosylates often underwent elimination on Woelm alumina more cleanly than in solution. Competing displacement of the tosylate by hydroxyl to form an alcohol was also observed in several cases. More recently, Paquette prepared triquinacene[78] and optically active deuterotriquinancene[79] by elimination of CH_3SO_3H from the corresponding mesylates using alumina. Interestingly, isotriquinacene, which does not isomerize to triquinacene on alumina, is instead formed in solution.

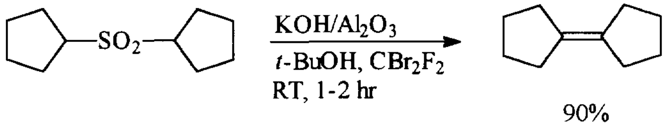


β-Eliminations of sulfinic acids from sulfones[80] and the conjugate bases of hydroxylamines from a series of amine oxides[81] have also been carried out successfully on basic alumina. This latter reaction is particularly interesting because the thermally induced Cope elimination of the same substrates was not as efficient. Elimination of HBr from alkyl bromides using the very basic KF/Al_2O_3 has also been reported.[82] Alumina-catalyzed β-elimination of HCl[83] and HOAc[84] to form conjugated enones and HF from 1,1-difluoroindene to yield 1-fluoroindene[85] are also known.

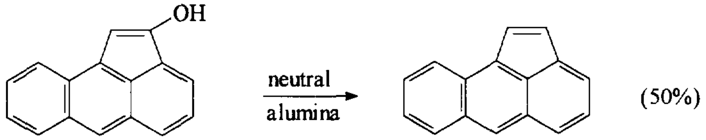


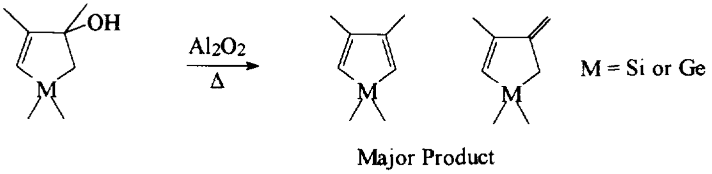


Alumina was used in a novel, synthetically useful version of the Ramburg-Bäckland reaction.[86] In this procedure, the sulfone is treated with KOH supported on alumina, and CBr_2F_2. The function of the KOH/Al_2O_3, is two fold: (1) to induce bromination of the carbon α to the SO_2 group via the sulfone's conjugate base, and (2) to induce 1,3 elimination of HBr from the α-bromosulfone. Excellent yields were reported for the seventeen examples reported in the two papers.

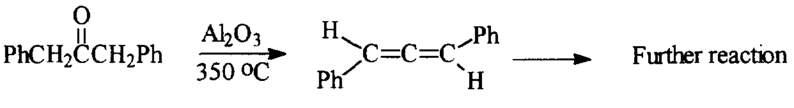


β-Elimination of H_2O from alcohols is often used to generate alkenes. Dehydration of 2-aceanthrynol in refluxing benzene in the presence of alumina afforded aceanthrylene, for example.[87] Other methods of dehydration were far less effective. Vapor phase dehydration of allylic alcohols over hot Al_2O_3 (230-300 °C) has been used to generate isomeric heterocycles.[88]

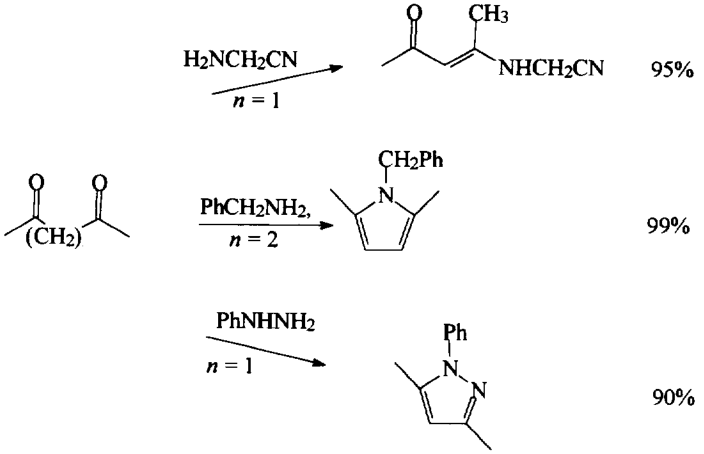




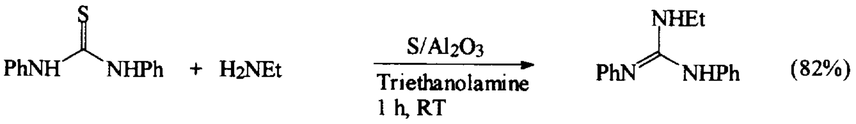
Other dehydrations using hot alumina have been reported. Dibenzyl ketone, for example, affords 1,3-diphenyl-1,2-propadiene at 350°C which in turn isomerizes to phenylindenes at higher temperatures;[89] while 2-*N*-phenylaminobenzyl alcohol yields acridine and dihydroacridine at 350 °C via an azaxylylene intermediate.[90] *p*-Menthenols generated mixtures of conjugated and non-conjugated dienes on alumina at 240 °C in the injection port of a GC.[91] None of the above reactions occurred at the indicated temperatures in the absence of alumina.



Synthetically useful reactions of amines with aldehydes and ketones to form imines on alumina are known. Texier-Boullet has demonstrated, for example, that these reactants generate imines on alumina in the absence of solvent in good to excellent yields.[92] Aminoalcohols react similarly with aldehydes.[93] On the other hand, amines, diamines and hydrazines react with 1,3- and 1,4-diones, usually at 20 °C in the absence of solvent, to yield enamines and aromatic heterocycles.[94] Procedures to convert aldehydes into nitriles on KF/Al_2O_3,[95] and into α-aminonitriles, on alumina,[96] have been published.



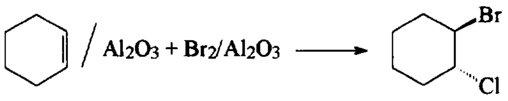
Thioureas react with amines in the presence of triethanolamine and lac (precipated) sulfur on alumina to yield guanidines.[97] The function of the sulfur is to facilitate the removal of H_2S by reaction with triethanolamine.



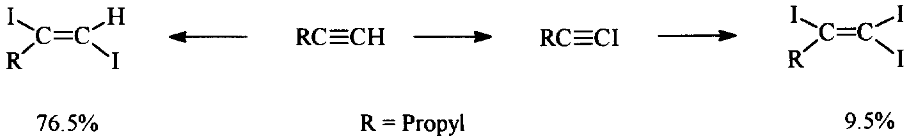
ADDITION REACTIONS

The polar addition of halogens and strong acids to carbon-carbon double and triple bonds has been studied extensively in solution.[98] Polar additions of species such as water, alcohols and acids to carbon-carbon multiple bonds have also been achieved on alumina and other solids. The earlier studies were often carried out at elevated temperatures,[6] but more recent studies have focused on reaction conditions of interest to organic chemists.

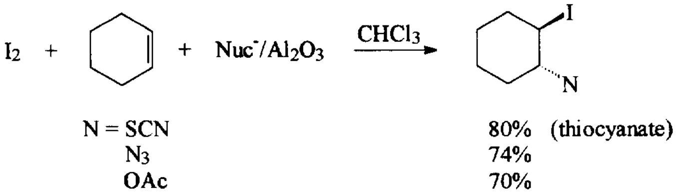
Reaction of Br_2 with cyclohexene on neutral alumina at room temperature in the absence of solvent surprisingly affords *trans*-1-bromo-2-chlorocyclohexane.[99,100] The *trans*-1,2-dibromocyclohexane also obtained in the reaction does not form on the surface of the alumina but during workup when unreacted Br_2 and cyclohexene are extracted from the solid into solution. The chlorine in the product arises from two sources: (1) Cl^- impurity on the alumina and (2) CCl_4 which was used to adsorb Br_2 onto the surface. CCl_4 is known to react with surface oxide to generated Cl^-.[101]



Alkynes react with I_2 in petroleum ether in the presence of activated (400°) and unactivated alumina to form vicinally substituted (*E*)-diiodoalkenes.[99,100,102,103] No reaction occurs in the absence of the solid. Terminal alkynes also afford 1,1,2-triiodoalkenes on unactivated alumina through an intermediate 1-iodo-1-alkyne.[103]

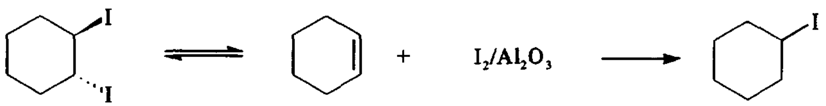


I_2 reacts readily with alkenes and nucleophiles supported on alumina (Merck) and other solids to form stereo- and regioselectively substituted iodoalkanes.[104] The reported yields are superior to those achieved in the absence of the supports. Based on these results, it is easy to imagine the addition of numerous other halogen/nucleophile combinations to alkenes on alumina.



The reaction of alkenes with I_2 on alumina in the absence of an added nucleophile takes a different, but synthetically useful, pathway than the reactions described above. For example, when cyclohexene is treated with I_2 in petroleum ether at 35° in the presence of activated (400°) neutral alumina, iodocyclohexane is produced in 85% yield after 2 hours.[99, 100,105] HI, but not I_2, has added to the double bond. HI is apparently generated *in situ* by the reaction of I_2 with surface hydroxyl groups which then undergoes an irreversible two-step ionic reaction with the alkene in the polar environment. I_2 also adds to the double bond but this product regenerates the starting alkene.

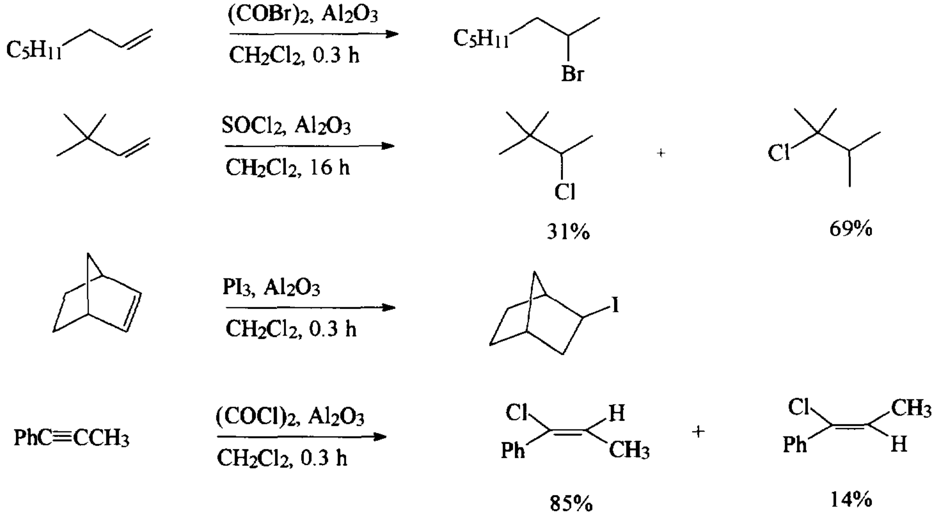
This procedure is a convenient method to generate and add HI to alkenes, a reaction often difficult to carry out in solution.



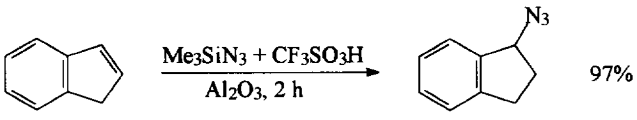
Kropp[106-109] and Laszlo[110] have expanded on the concept of reacting an *in situ* generated hydrogen halide with alkenes and alkynes. This chemistry, described below, has developed into a powerful methodology for adding HX to carbon-carbon multiple bonds. The formation of HX requires the reaction of an appropriate acid anhydride with the surface hydroxyl groups of alumina or silica gel. Alumina works best when activated at 120° prior to use. Listed below are common precursors to HX.

HCl: $(COCl)_2$, $SOCl_2$, AcCl
HBr: $(COBr)_2$, PBr_3, Me_3SiBr, AcBr
HI: PI_3, AcI, Me_3SiI, (I_2)

The additions occur by ionic pathways involving carbocations and are much faster on Al_2O_3 than they are in solution. The initial additions of HX are largely *syn* but the products often equilibrate with more stable isomers. Notably, the reactions of HBr on the solids are not prone to competing free-radical, *anti*-Markovnikov additions which plague these reactions in solution. Several examples are shown below.

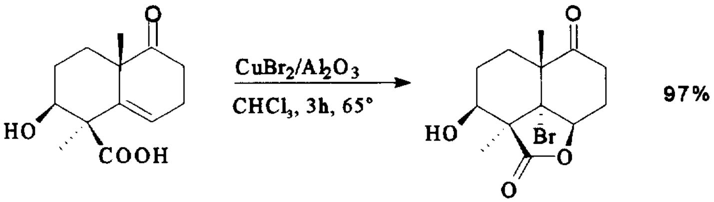


Kropp and coworkers also developed a procedure to generate and add HN_3 to alkenes.[107]



Two protocols suitable for use in the undergraduate laboratory have been published concerning the addition of HCl to 1-propynylbenzene[111] and (*R*)-carvone[112] on alumina.

An alternative to the traditional halolactonization procedure was recently reported[113] in which $CuBr_2$ adsorbed on alumina served as the source of Br_2. Since the reaction illustrated below proceeds poorly with Br_2 in $CHCl_3$, the lactonization in the presence of $CuBr_2/Al_2O_3$ undoubtedly occurred on the surface of the solid.

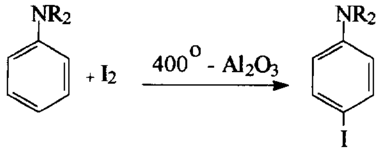


AROMATIC AND VINYL SUBSTITUTION

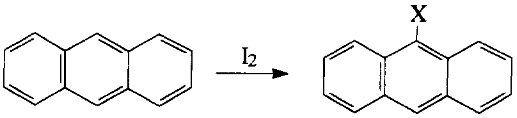
Alumina provides an almost ideal environment for electrophilic aromatic substitution reactions. Not only is its surface polar but its surface constituents, e.g. the partially exposed aluminum ions, are capable of catalyzing the formation of electrophiles. The older literature describes many examples of this chemistry[6,114] but the reactions were most often carried out at elevated temperatures, either because the substrates were deactivated or the electrophiles were difficult to generate or were unreactive. Although electrophilic aromatic substitution has been studied extensively using other solids,[3-5] there are surprisingly few studies involving alumina. Examples of synthetic interest are described below. Examples relevant to environmental chemistry are also known.[115]

Halogenation of aromatic substrates on alumina is well documented. Iodinations have been carried out using I_2 on neutral alumina[99,100,116] and $CuCl_2/Al_2O_3$, a Lewis acid.[117] Brominations have been carried out using Br_2 on neutral alumina[118] or with $CuBr_2$ adsorbed on alumina,[119-122] which yields Br_2 *in situ*; chlorinations have been carried out using $CuCl_2/Al_2O_3$.[119-121,123] Several of these reactions are distinctive.

The reaction of Br_2 on alumina with alkylbenzenes is surprisingly fast ($\tau_{1/2} <$ 1 minute)[118] and the normally unreactive I_2 reacts efficiently with a variety of aromatic substrates on activated (400°) alumina at room temperature.[99,100,116] Interestingly, *N*,*N*-dimethylaniline yields *p*-iodo-*N*,*N*-dimethylaniline at room temperature whereas aniline is unreactive even at 100°.[116] Aniline, but not *N*, *N*-dimethylaniline, is undoubtedly rendered unreactive by complexation to aluminum ions on the surface. Iodine is also activated toward reaction by the Lewis acidic $CuCl_2$ and $CuSO_4$ adsorbed on alumina.[117] In most cases, the aromatic compounds are iodinated readily using $CuCl_2/Al_2O_3$. Anthracene, on the other hand, is chlorinated. In this case, Cl_2, which is generated in the reaction $2\ CuCl_2 \rightarrow 2CuCl + Cl_2$, serves as the electrophile. Iodination of anthracene is achieved using I_2 on $CuSO_4/Al_2O_3$.

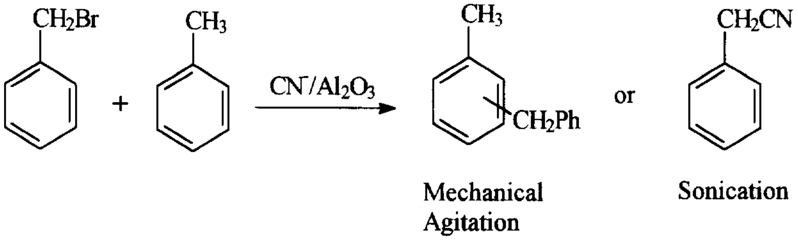


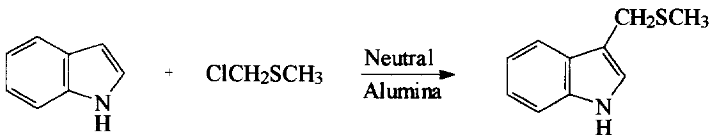
R = H 0% at 100°
= CH_3 45% at RT



$CuCl_2/Al_2O_3$ X = Cl (90%)
$CuSO_4/Al_2O_3$ X = I (73%)

Several Friedel-Crafts alkylation reactions on alumina are known.[124-134] In an attempt to convert an alkyl bromide into a nitrile, benzyl bromide was treated with CN^- on Al_2O_3 in an aromatic solvent. Inexplicably, mechanical agitation of the mixture afforded the Friedel-Crafts products, whereas sonication[135] of the mixture yielded the expected benzyl nitrile.[124,125] The reaction of substituted benzenes with allyl chlorides[127] is interesting because two solids were used in the reaction, one ($ZnCl_2/SiO_2$) to catalyze the reaction and other (K_2CO_3/Al_2O_3) to remove the HCl as it was generated. Indoles react very rapidly with α-chloromethylthiomethyl ethers on neutral alumina at room temperatue.[129,130] An intramolecular alkylation on the very acidic $SOCl_2$ chemisorbed on alumina has also been described.[133-136]





Nucleophilic aromatic substitution reactions also occur on alumina (Table 1). Dalton and Regen demonstrated that bromo- and iodobenzenes are converted to the corresponding nitriles when treated with NaCN and $(Ph_3P)_4Pd$ on alumina under mild conditions.[137] The substitution reactions did not proceed as well in the absence of alumina or in the absence of $(Ph_3P)_4Pd$. Clark has demonstrated [138-142] that it is possible to displace the halogen on haloaromatic compounds using Cu(I) salts on alumina in which the counterion is also the nucleophile. These reactions work well although they usually require elevated temperatures and a high boiling, aprotic, dipolar solvent. In addition Clark has carried out extensive spectroscopic studies in order to characterize these reagents. IR studies of CuCN on alumina, for example, show the species to be $Cu^+Cu(CN)_2^-$.[141] A recent example of nucleophilic aromatic substitution used alumina to arylate indole at nitrogen using $KF-Al_2O_3$, a reagent to be described in detail in a later section of this article, and a crown ether in DMSO.[144] Dinitrobenzenes form Meisenheimer complexes in solution when contacted with a slurry of $KF-Al_2O_3$ or $CsF-Al_2O_3$ and DMSO.[144] Examples are also known in which alumina is an ineffective medium for nucleophilic aromatic substitutions.[145,146]

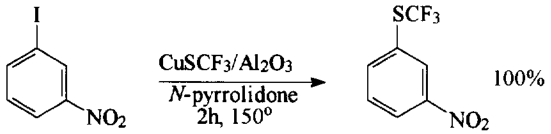
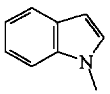
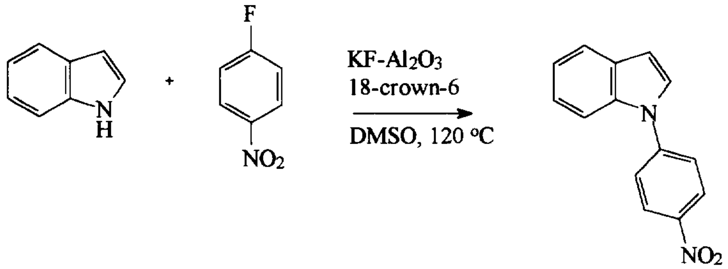
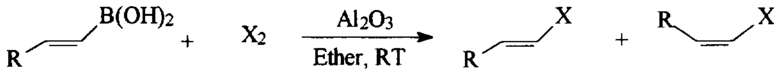


Table 1. Nucleophilic Aromatic Substitution on Alumina

ArX ⟶ ArNuc		Reagent	Substrates
X	*Nuc*		
Br, I	CN	NaCN on Al_2O_3 + $(Ph_3P)_4Pd$.[137]	bromo- and iodoaromatics
Cl, Br	I	CuI on Al_2O_3.[138]	bromo- and chlorobenzene and toluenes
Br	I	$KCuI_2$ on Al_2O_3.[139]	aryl bromides
I, Br	SCF_3	$CuSCF_3$ on Al_2O_3.[140]	bromo- and iodobenzenes, most with activating substituents
Br	CN	CuCN on Al_2O_3.[141]	bromobenzene
I	-SCN, -NCS, CN, -S-, -S-S-	CuSCN + Al_2O_3, CuSCN on Al_2O_3.[142]	2-iodonitrobenzene
F	ArX (X=O, S, NMe, NH)	ArX on $KF-Al_2O_3$ (X=OH,SH,NHMe, NH_2).[147]	2- and 4-fluorobenzonitriles
F,Cl,Br,I, NO_2, CN, OMe		Indole on $KF-Al_2O_3$.[143]	substituted benzenes with activating substituents
Cl	Alkoxy	Alcohols on KF or CsF on neutral alumina.[148]	chloroquinones



Vinylboronic acids react with Br_2 and I_2 in the presence of base to yield vinyl halides. When alumina is the base, terminal (*E*)-vinylboronic acids react with I_2[149] and Br_2[150] to yield mixtures of (*E*)- and (*Z*)-1-haloalkenes. The (*E*) product arises by attack of X_2 on the complexed boronic acid and the (*Z*) product arises by *anti* addition of X_2 to the double bond of the boronic acid followed by *anti* elimination of $B(OH)_3$ and X^- from the complexed adduct.



R = $Cl(CH_2)_3$, X = I 74 : 26 (82%)
R = $Cl(CH_2)_3$, X = Br 20 : 80 (56%)

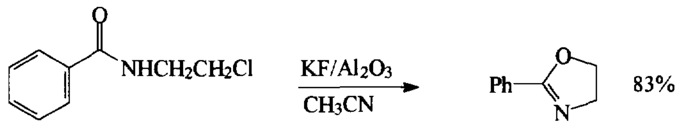
NUCLEOPHILIC SUBSTITUTION AND SOLVOLYSIS

Nucleophilic substitution reactions readily occur on alumina and many examples using halogen, oxygen, sulfur and carbon nucleophiles have been reported in the literature. S_N1 reactions are favorable owing to the polar nature of, and the presence of nucleophiles (O^{-2}, OH^-) on, the surface. S_N2 reactions are often rendered favorable because an unreactive, uncharged nucleophile can be converted into its more nucleophilic conjugate base when it contacts the basic solid. Although there is some evidence that charged nucleophiles such as CN^- [151,152] and I^-[153] have comparable or better reactivity on alumina than in other environments, there are not enough data available to state that this is a general phenomenon. One explanation for the seemingly high reactivity of certain nucleophiles is the high surface area of the reagent when dispersed over the surface of the solid.[152,154]

S_N2 reactions in which alkyl halides, tosylates, and sulfates react with carboxylates,[155-157] alkoxides,[158-161] aryloxides,[159-161] hydroxide,[162-164] oxide,[164] and the conjugate base of an amide[165] on alumina have been described in recent years. KF/Al_2O_3, a strong base, has been used in some of these cases to activate the nucleophile.[158-159,161-162] Microwave activation has also proved helpful.[155-157]

Several of these reactions are noteworthy. Diols are monomethylated with CH_2N_2 on alumina; 1,10-decanediol afforded the monomethyl ether in 86%, for example.[160] Mitchell and Benicewicz have shown that chloroamides are converted into heterocycles on KF/Al_2O_3;[165] this material is clearly sufficiently basic to deprotonate amides which have pK_as ~25. The hydroxide and oxide on the surface of alumina also serve as nucleophiles.[162-164] Benzyl chloride and bromide yield dibenzyl ether in two-step processes which uses nucleophilic OH^- on unactivated alumina and oxide on activated alumina.[164] Liquid CCl_4 reacts with oxide, but not hydroxide, on the surface of alumina at room temperature.[164] It has been shown that this reaction represents a simple, indirect method to measure the oxide concentration of alumina.[164]

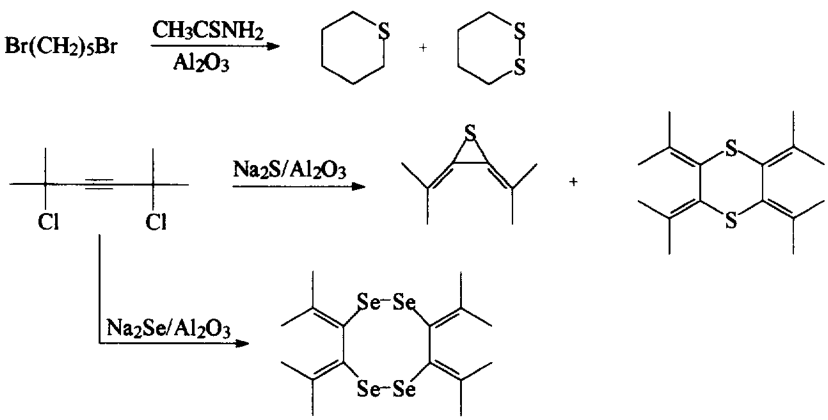
$$HOCH_2(CH_2)_8CH_2OH \xrightarrow[Al_2O_3]{CH_2N_2} HOCH_2(CH_2)_8CH_2OCH_3$$



$$PhCH_2Cl + O^{-2} \longrightarrow Cl^- + PhCH_2O^- \xrightarrow{PhCH_2Cl} (PhCH_2)_2O + Cl^-$$

Aliphatic nucleophilic substitution reactions involving adsorbed S^{-2},[166-172] HS^-,[167] alkyl S^-,[166] SCN^-,[173] the thioenolate of methyl dithiopropanoate,[174] phenylsulfinate,[175] and thioethers[176] occur on alumina and on the more basic KF/Al_2O_3[174] and KOH/Al_2O_3.[166] Microwaves and ultrasound accelerate the reaction of phenylsulfinate with alkyl halides, reactions which work better on alumina than on other solids.[175] H_2S, a source of nucleophilic HS^-, can be generated *in situ* by the hydrolysis of $CH_3C(S)NH_2$ on the surface of unactivated alumina.[167]

Ever since Regen's initial report on the use of S^{-2}/Al_2O_3 to prepare thioethers,[166] this reagent has found wide use in synthesis,as evidenced by the preparation of cyclic ethers.[167,169-171] Pagni and Kabalka have shown, for example, that S^{-2}/Al_2O_3 is an effective alternative to the high dilution method currently used to prepare macrocyclic thioethers.[167] HS^-/Al_2O_3 is also an effective nucleophile for the preparation of cyclic sulfides and disulfides, the latter of which result from the oxidative coupling of thiols by O_2[167] which is a reaction known to occur on alumina.[177] Gleiter has reported methods to prepare sulfur- and selenium-containing radialenes using S^{-2}/Al_2O[169a] and Se^{-2}/Al_2O_3,[178] respectively.



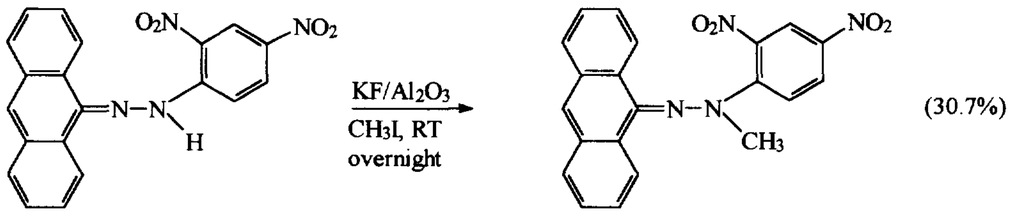
The behavior of SCN^- on alumina is interesting in that substrates reacting via the S_N2 mechanism yield thiocyanates exclusively while those reacting by the S_N1 mechanism yield mixtures of thio- and isothiocyantes.[173] The amount of KSCN on the alumina has an effect on yield and distribution of products.

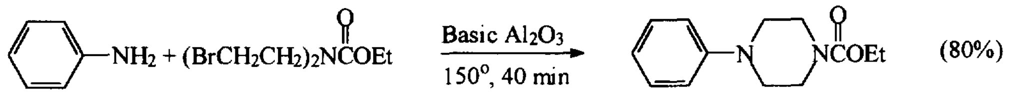
$$n\text{-BuBr} \xrightarrow{SCN^-/Al_2O_3} n\text{-BuSCN} \quad (100\%)$$

$$t\text{-BuBr} \xrightarrow{SCN^-/Al_2O_3} \underset{90}{t\text{-BuBr}} \; + \; \underset{10}{t\text{-BuNCS}} \quad (80\%)$$

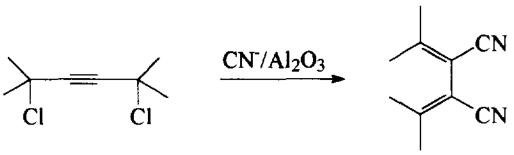
The use of halide nucleophiles on alumina is rare. Clark has shown that I^- on Al_2O_3 is a very effective agent for the iodination of alkyl chlorides and bromides.[179] Tundo described a procedure for iodinating alkyl bromides using modified aluminas as phase transfer catalysts.[180]

Amines[181-183] and amides[184-187] undergo S_N2 reactions with alkyl halides when activated for reaction by adsorption on alumina, as well as the very basic KF/Al_2O_3, KOH/Al_2O_3 and K_2CO_3/Al_2O_3. Alkylation of weakly acidic amides required the highly basic solids. Recent examples of this chemistry include the alkylation of hydrazines on KF/Al_2O_3[186] and of arylamines on basic alumina;[187] neutral alumina was not as effective in this latter reaction.

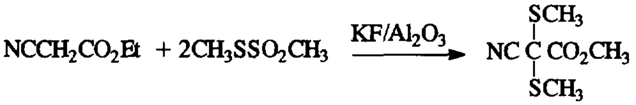




Alumina-assisted S_N2 reactions involving carbon-centered nucleophiles are also known. Several studies have described, for example, the utility of CN^-/Al_2O_3 for the conversion of alkyl halides to nitriles.[124,125,151,152,169a,188-190] Furthermore, Regen[151] and Clark[152] have reported kinetics studies of several of these reactions. Clark has also described IR spectra of KCN/Al_2O_3 and KCN on KF/Al_2O_3.[152] On KCN/Al_2O_3 at low loading, the ν (C≡N) band is broad but only slightly perturbed from the normal value; at loadings >5 molecules of KCN/nm^2, ν (C≡N) due to microcrystals of KCN is apparent. Recently Gleiter reported the use of CN^-/Al_2O_3 in an interesting S_N2' reaction.[169]

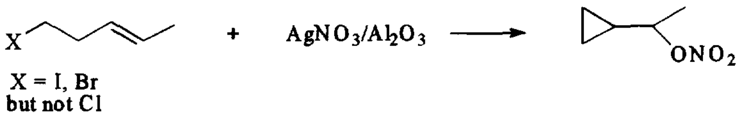


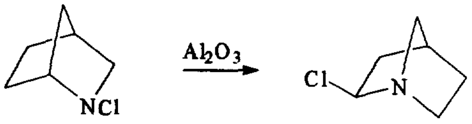
Enolates[191] and carbanions derived from doubly activated methylene compounds such as malononitrile, acetoacetate esters, malonate, cyanoacetate, and phenylacetate esters also function as nucleophiles on alumina.[189,192-198] The reactions of the acidic methylene compounds occur most readily on basic solids such as KF/Al_2O_3, $NaOEt/Al_2O_3$, $NaOMe/Al_2O_3$ and KO*t*-Bu/Al_2O_3. The selectivities are very impressive. Ethyl acetoacetate, diethyl malonate and 2,4-pentanedione afford monoalkylated products in high yields when treated with 1 equivalent of NaOEt on Al_2O_3 and high yields of dialkylated products when treated with 2 equivalents of $NaOEt/Al_2O_3$.[197] Malononitrile is monobenzylated exclusively on basic alumina and KF/Al_2O_3.[195] Chiral acetoacetates react with optically inactive 2-octyl bromide and 1-phenylethyl bromide on KO*t*-Bu/Al_2O_3 to give products with higher optical purities than those obtained for the same reactions carried out in K_2CO_3/DMSO.[196] An ad hoc argument in which steric effects between the reactants and the surface are minimized was used to explain the observed selectivities. Little unfortunately is known about how organic compounds interact with solid surfaces. Dithioacetals may also be prepared by this enolate methodology.[198]



$$NCCH_2CO_2Et + 2CH_3SSO_2CH_3 \xrightarrow{KF/Al_2O_3} NC\overset{SCH_3}{\underset{SCH_3}{C}}CO_2CH_3$$

There are surprisingly few examples of nucleophilic substitution reactions which clearly proceed through carbocations. Some of the previously noted reactions of SCN^-/Al_2O_3 with alkyl halides involve carbocations.[173] The reactions of (*E*)-5-bromo- and (*E*)-5-iodo-2-pentene with $AgNO_3$ adsorbed on Al_2O_3 apparently also do.[199] The clean isomerizations of strained *N*-chloroamines to *C*-chloroamines on alumina may also proceed through carbocations or intimate ion pairs, although dyotropic shifts not involving carbocations offer another possibility.[200]





CONDENSATION REACTIONS AND CONJUGATE ADDITIONS

The areas in which alumina and modified aluminas, particularly KF/Al_2O_3,, have found their greatest use in organic synthesis are the base catalyzed and base induced condensation reactions, conjugate additions and ylide reactions. A summary of the reactions which appeared since 1980 is found in Table 2.[201] Prior to describing these reactions, a short discussion of KF/Al_2O_3, which is essential to the success of many of these reactions, will be presented.

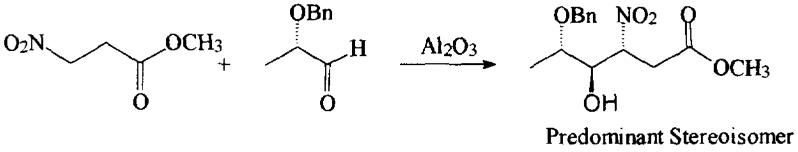
Fluoride is a weak base in water where it is highly solvated. On the other hand in aprotic dipolar solvents, where anions are poorly solvated, F^- is a strong base.[202] In attempts to prepare solid base analogs of

F^- in aprotic dipolar solvents, fluoride salts have been adsorbed to the surfaces of numerous solids from aqueous solution. One of these, KF on alumina, is a particularly effective base for the alkylation of alcohols.[203] Several investigators have reported the characterization of KF/Al_2O_3 using a variety of spectroscopies and physical organic methods.[204-209] It is clear from these studies that KF reacts with Al_2O_3 to generate base:

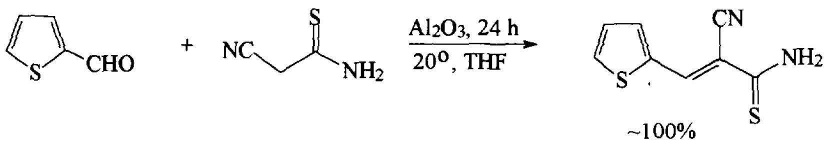
$$12KF + Al_2O_3 + 3H_2O \rightarrow 2K_3AlF_6 + 6KOH.$$

However, the activity of KF/Al_2O_3 is not entirely due to the KOH generated because catalytic activity is greater than one can ascribe to KOH alone. Coordinatedly unsaturated F^-, i.e. unsolvated, and the cooperative interaction of F^- with the hydrated surface may also contribute to the basicity.[209]

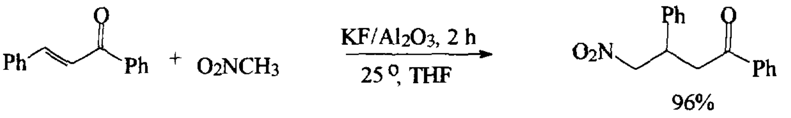
Space limitations preclude a detailed discussion of these heterogeneous base catalyzed reactions. Suffice it to say that the heterogeneous reactions compare favorably (reaction time, temperature, ease of workup, yield, selectivity, etc.) to analogous reactions carried out in solution. When deciding which solid medium to use, alumina is the catalyst of choice when an acidic substrate is the source of the nucleophile while KF/Al_2O_3 is the solid of choice when weakly acidic compounds are used to generate the nucleophile. Several representative reactions are shown below.



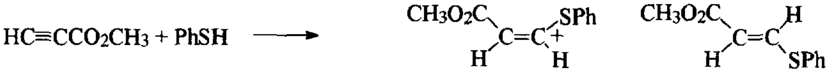
(Ref 210)



(Ref 211)

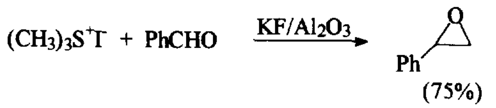


(Ref 212)

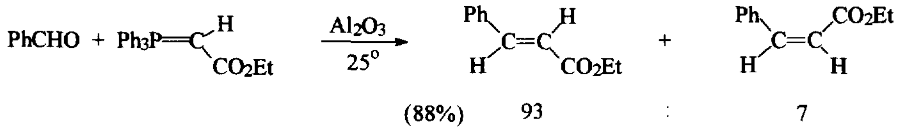


Al2O3, ether, 10°, 1 h (97%)	87	:	13
No Al2O3 (79%)	63	:	37

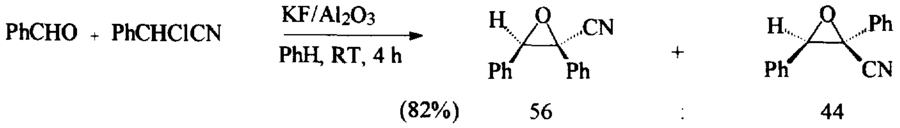
(Ref 213)



(Ref 214)



(Ref 215)



(Ref 216)

Table 2. Base Catalyzed Condensation, Conjugate Addition, and Ylid Reactions

Reaction Type	Bond Formation	Solid Catalysist	References
Aldol, Knoevenagel, Henry and Related Condensations	C-C	Al_2O_3	210,211, 217-237
	C-C	KF/Al_2O_3	238-253
	C-P	Al_2O_3	254
	C-P	KF/Al_2O_3	240, 255,256
Michael and Conjugate Addition	C-C	Al_2O_3	232, 257-262
	C-C	KF/Al_2O_3	212, 216, 263-272
	C-O	Al_2O_3	273-275
	C-S	Al_2O_3	213
	C-S	KF/Al_2O_3	269
	C-N	Al_2O_3	276, 277
	C-P	KF/Al_2O_3	240, 255
Darzens	C-C and O-C	KF/Al_2O_3	216, 240
Tishchenko	C-O	Na/Al_2O_3; $BuLi/Al_2O_3$	278
Wittig and Wittig-Horner	C-C	Al_2O_3	214, 215
	C-C	KF/Al_2O_3	214
Sulfonium Ylide + Aldehyde	C-C and O-C	KF/Al_2O_3	214
Sulfoxonium Ylide + Enone	C-C and C-C	KF/Al_2O_3	214

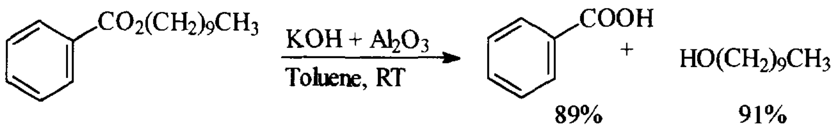
REACTIONS OF CARBOXYLIC ACIDS AND DERIVATIVES.

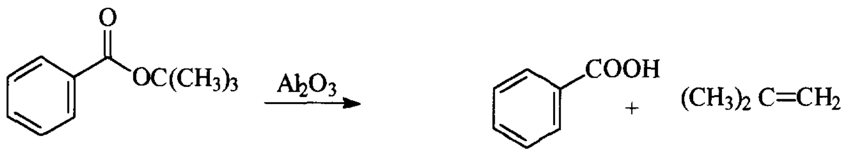
Alumina has been extensively used as a catalyst and medium for the interconversion of carboxylic acids and their derivatives. As many of these transformations involve the loss or addition of H_2O, the use of alumina should not be surprising because it is both a dehydrating agent, especially when activated, and a source of H_2O in the form of its surface OH groups.

The esterification of acids over solid catalysts has been observed for a long time[6, 279] and several synthetically useful examples occurring on alumina have been reported in recent years. Since conversion of carboxylate anions into esters has already been discussed, the focus here will be on the conversion of acids into esters. Loupy *et al.* described a simple procedure for the Fischer esterification reaction using *p*-toluenesulfonic acid adsorbed on alumina, a reaction activated by microwaves.[157] Chihara demonstrated that one can selectively monomethylate dicarboxylic acids on alumina with CH_2N_2,[280] a selectivity not available in solution. This selective monomethylation (using CH_2N_2 or $(CH_3)_2SO_4$) on alumina has been widely studied in Japan[160,281-283] and represents a significant contribution to organic synthesis. IR studies have revealed, in the case of terephthalic acid, why this selectivity occurs:[284] the diacid reacts with the surface to form a monocarboxylate anion lying normal to the surface leaving the unreacted COOH free to be alkylated.

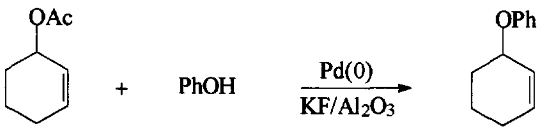
$$\mathrm{HOOC(CH_2)_{10}COOH} \xrightarrow[\mathrm{Al_2O_3}]{\mathrm{Me_2SO_4}} \underset{(97\%)}{\mathrm{CH_3OOC(CH_2)_{10}COOH}} + \underset{3\%}{\mathrm{CH_3OOC(CH_2)_{10}COOCH_3}}$$

Esters can also be converted into carboxylic acids. Treatment of esters with a mixture of crushed KOH and neutral Al_2O_3 yields carboxylic acids and alcohols in high yield.[285] Spectroscopic studies have shown that alkyl benzoates are hydrolyzed on alumina films.[286,287] *tert*-Butyl benzoate also undergoes acid-catalyzed hydrolysis on alumina films.[287]

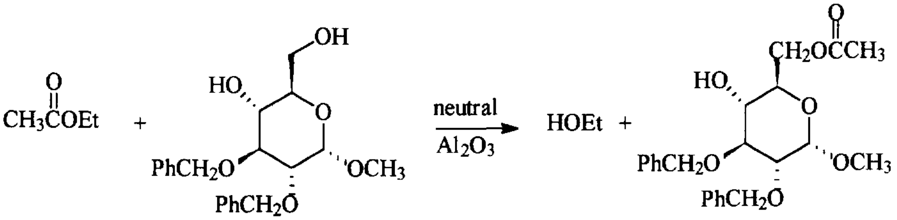




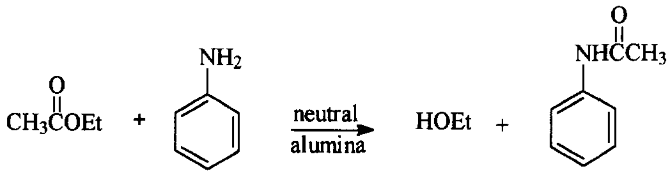
Allyl acetates react with phenol in the presence of catalytic amounts of Pd(0) and KF/Al_2O_3 to yield allyl phenyl ethers in good to excellent yields.[288] These reactions likely occur by reaction of π-allyl palladium complexes with phenoxide anion.



Synthetically useful transesterification reactions also occur on alumina. Primary alcohols, for example, are acetylated in high yield in a slurry of ethyl acetate (solvent and reactant) and neutral alumina.[289] For diols and triols, primary sites are acetylated in preference to secondary sites.[290] Aniline and *p*-bromoaniline, but not aliphatic amines, are likewise acetylated in a slurry of ethyl acetate and alumina.[290]

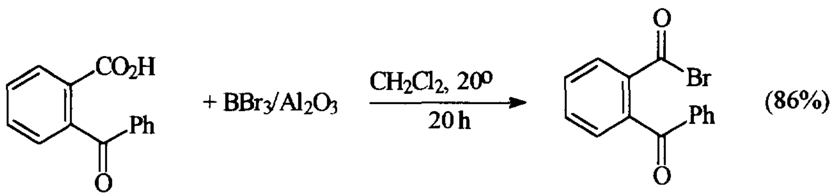


97% (based on recovered reactant)

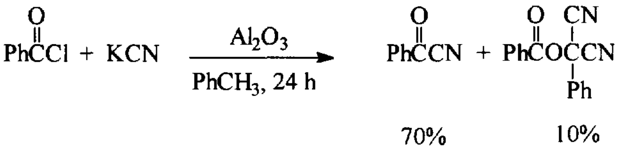


80%

Modified Al_2O_3 in which BBr_3 is chemisorbed to the surface of Al_2O_3 can be used for the synthesis of acyl bromides.[291] Treatment of carboxylic acids with BBr_3/Al_2O_3 which contains BBr bonds yields acyl bromides in high yields. Interestingly, the reaction of carboxylic acids with BBr_3 in solution does not yield acyl bromides.

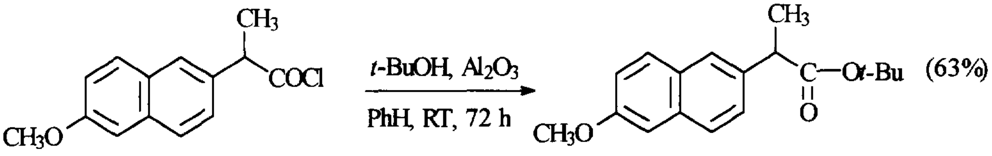


Acyl halides react with nucleophiles on alumina. Acyl, for example, react considerably faster with H_2O and CH_3OH in the presence of Al_2O_3 than in homogeneous solution.[292] Dimethylthiocarbamoyl chloride reacts with phenols on KF/Al_2O_3 to yield *S*-aryl *N*,*N*-dimethylthiocarbamates in very good yield;[293] these esters isomerize by a formal 1,3 sigmatropic shift to *O*-aryl *N*,*N*-dimethylcarbamates when heated (microwave) on a variety of supports including alumina. Benzoyl chloride undergoes an interesting reaction with KCN on Al_2O_3 to yield not only benzoyl nitrile but also a dimer.[294]

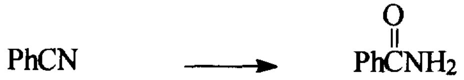


$$\mathrm{Ph\overset{\overset{O}{\|}}{C}Cl} + \mathrm{KCN} \xrightarrow[\mathrm{PhCH_3,\ 24\ h}]{\mathrm{Al_2O_3}} \underset{70\%}{\mathrm{Ph\overset{\overset{O}{\|}}{C}CN}} + \underset{10\%}{\mathrm{Ph\overset{\overset{O}{\|}}{C}O\overset{\overset{CN}{|}}{\underset{\underset{Ph}{|}}{C}}CN}}$$

Acyl chlorides yield *t*-butyl esters when treated with *t*-butyl alcohol and activated alumina.[295] The acid chloride of optically active naproxen yields the *t*-butyl ester with retention of configuration, thus ruling out a ketene as an intermediate in the reaction. Acyl bromides yield *t*-butyl esters in good to excellent yield when treated with *t*-butyl alcohol and activated basic alumina.[296]



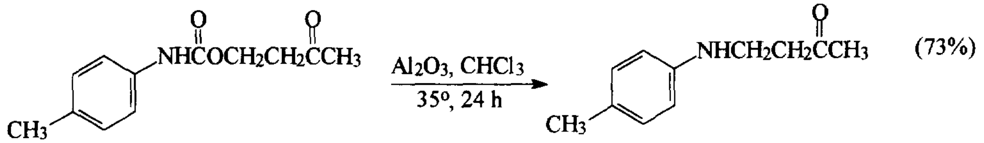
There are two excellent procedures in the literature for the conversion of nitriles into amides using alumina. This transformation in solution is, of course, often plagued by the competing hydrolysis of the amide. In the first procedure, the nitrile in refluxing *t*-butyl alcohol is treated with KF/Al_2O_3 in which a significant amount of water is retained on the surface.[297] In the second method, the nitrile is treated directly with unactivated neutral alumina; in this case the surface hydroxyl groups serve as the source of water.[298]



$$PhCN \longrightarrow Ph\overset{O}{\overset{\|}{C}}NH_2$$

KF/Al_2O_3, refluxing *t*-BuOH	74%
Al_2O_3 (N), no solvent, 60°	83%

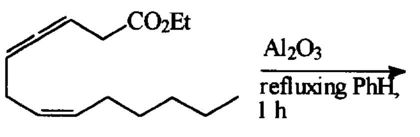
Trichloroacetyl carbamates are rapidly cleaved to the corresponding carbonates on neutral alumina[299] Carbamates with β-acetyl groups are converted into amines when contacted with neutral alumina.[300] These transformations undoubtedly occur by a sequence of reactions involving elimination (E1cB), loss of CO_2, and conjugate addition to the vinyl ketone generated *in situ*.



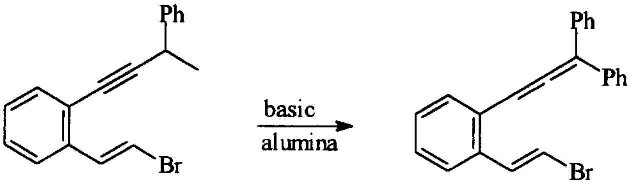
ISOMERIZATIONS, REARRANGEMENTS, AND PERICYCLIC REACTIONS

Because of the importance of alkene isomerization in heterogeneous catalysis, the mechanisms by which model alkenes, 1-butene and (*E*)- and (*Z*)-2-butene, interconvert have been extensively studied.[38] On acidic solids, the isomerizations usually occur by a protonation-deprotonation mechanism involving the 2-butyl cation whereas, on basic solids, the reactions occur by a deprotonation-protonation mechanism involving allyl anions. Alumina generally functions as a solid base in these isomerizations. The even more basic $NaOH/Al_2O_3$,[301] Na/Al_2O_3,[301] K/Al_2O_3,[302] and KF/Al_2O_3,[303] function as superbasic catalysts in the isomerization of alkenes.

Several of these prototropic reactions have proven useful in synthesis, two of which are shown below. The driving force for these reactions is the formation of more conjugated, and thus more stable, products. An interesting example of a prototropic isomerization in which conjugation is not

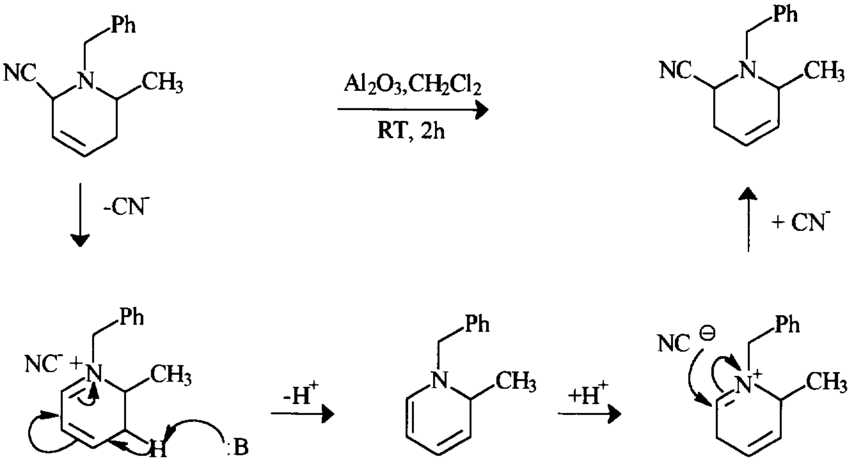


(Ref. 307)



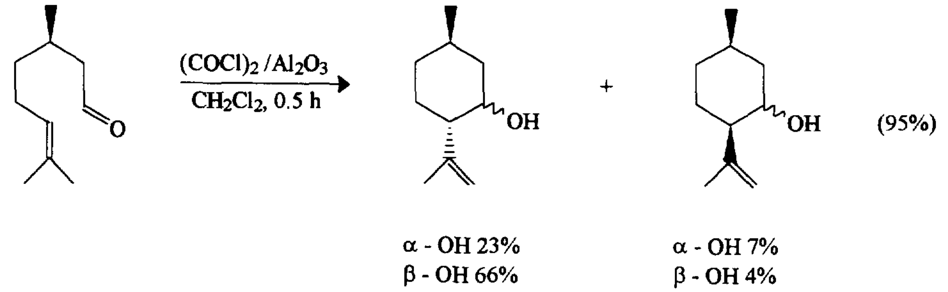
(Ref. 310)

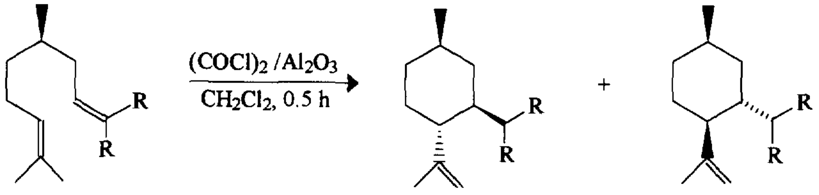
the driving force of the reaction was reported by Bonin *et al.*[311] In this case the substrate undergoes 1,4-elimination of HCN (E1) followed by 1,2 addition of HCN to the intermediate.



(90%)

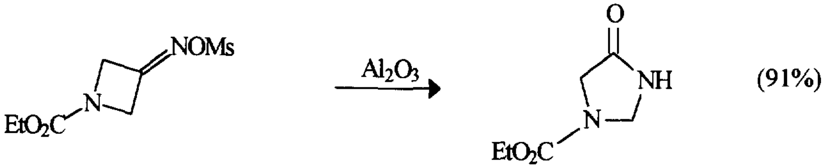
Other isomerization reactions are also known to occur on alumina including the ring opening of epoxides[312,313] and the mutarotation of glucose.[314,315] On basic alumina, the terpene (R)-citronellal undergoes the Cannizzaro reaction.[133] On acidic alumina, on the other hand, the terpene isomerizes to a cyclic alcohol.[316] On alumina acidified with CH_3SO_3H, HCl and oxalyl chloride, the terpene yields four cyclized products.[133] A diester related to citronellal also cyclizes when treated with $(COCl)_2/Al_2O_3$.[133] The Lewis acid $FeCl_3$ on Al_2O_3 also catalyzes this and related ene reactions.[317-319]



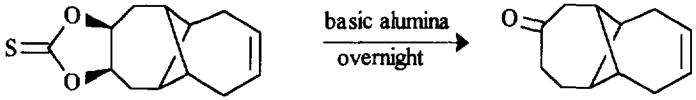


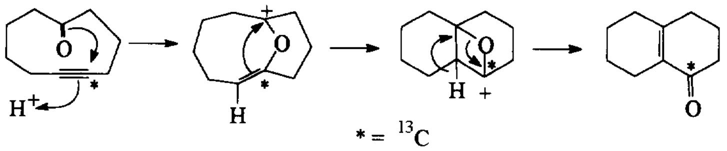
R = CO_2CH_3			
	$(COCl_2)/Al_2O_3$, 0.5 h	62%	5 %
	$(FeCl_3)/Al_2O_3$, CH_2Cl_2, -78 oC ⟶ RT	90.9%	1.1%

Several rearrangements have been examined on alumina[320-322] including the Beckmann rearrangment.[323] This latter reaction has been studied extensively on solid acids because of the industrial importance of the conversion of cyclohexanone oxime into caprolactam.[38] An example of a Beckmann rearrangement occurring on alumina is shown below;[324] this rearrangement also proceeds using more traditional catalysts.



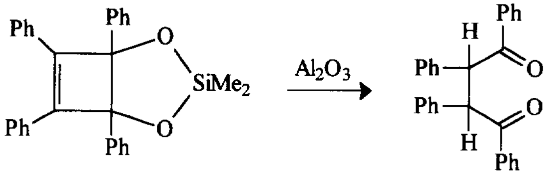
Recently a cyclic thiocarbonate has been shown to undergo a pinacol-like rearrangement on basic alumina.[325] 5-Cyclodecynone, on the other hand, undergoes an acid-catalyzed transannular rearrangement on neutral alumina and in methanol containing HCl or H_2SO_4 to give an isomeric conjugated ketone.[326]



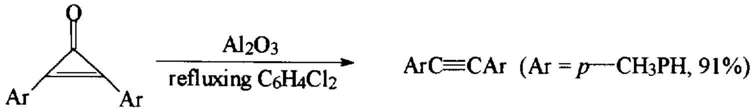


Pericyclic reactions have been studied extensively on alumina and other solids. As will be apparent in the following discussion, however, some of these transformations occur by alternate mechanisms. Nevertheless, regardless of how these reactions occur, many of them are synthetically useful.

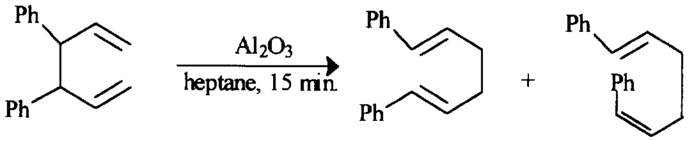
Treatment of the cyclic dialkoxylsilane, shown below, with Al_2O_3 on a TLC plate afforded a mixture of meso and *d,l* 1,2,3,4-tetraphenyl-1,4-butanedione. A plausible mechanism for this reaction involves initial hydrolysis of the silane to form a dihydroxycyclobutene followed by electrocyclic ring opening to form a dienediol which tautomerizes to yield the observed products.[327]



Thermolysis of diarylcyclopropenones on Al_2O_3 in refluxing 1,2-dichlorobenzene generated diarylacetylenes in 80-95% yield. [328] These cheletropic reactions gave higher yields of alkynes than the comparable homogeneous reactions.

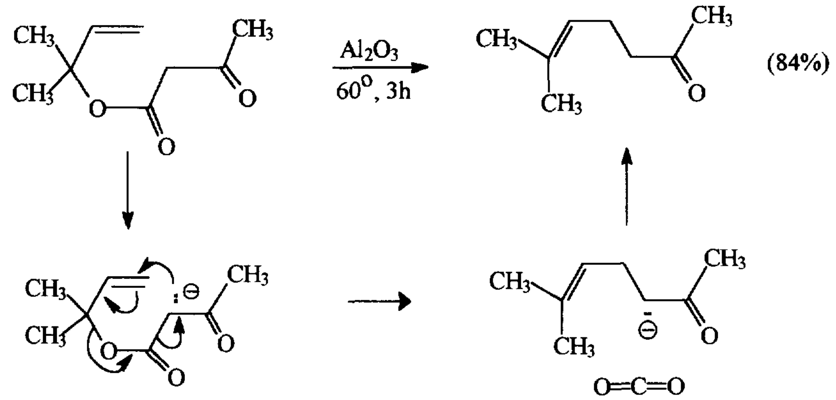


Numerous sigmatropic reactions occur on alumina. A remarkable example is the 3,3 sigmatropic reaction (Cope rearrangement) of *meso-* and *d,l*-3,4-diphenyl-1,5-hexadiene.[329] The *d,l* isomer yielded (*E,E*)-1,6-diphenyl-1,5-hexadiene in 15 minutes at room temperature on Al_2O_3 previously activated at 650° - 700°. The *meso* isomer reacted more slowly and yielded (*E,E*)- and (*E,Z*)-1,6-diphenyl-1,5-hexadiene. A reasonable supposition is that these transformations are catalyzed by Lewis acid sites on the surface of the solid.

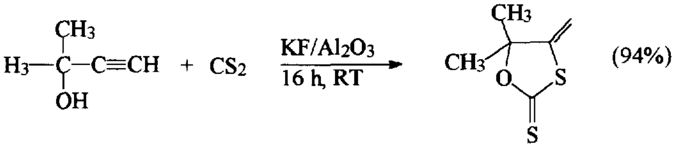


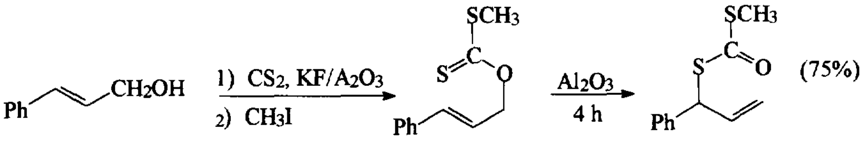
d,l	84%	—
meso	3.5%	7.5%

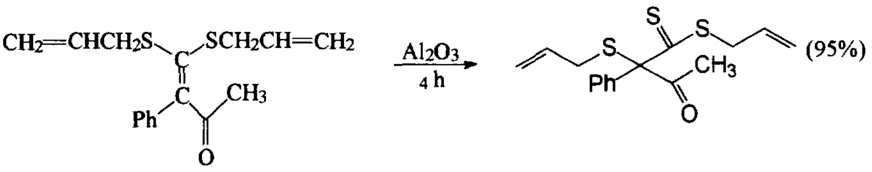
The Carroll rearrangement, which is similar to a 3,3 sigmatropic shift (Claisen rearrangement), also occurs on alumina at temperatures far lower than required in homogeneous solution[330-332] Interestingly, an allyl acetoacetate underwent the Carroll rearrangement on alumina but a 1,3 sigmatropic shift on SiO_2. These results suggest that the Carroll rearrangement occurred from the conjugate base of the allyl ester.



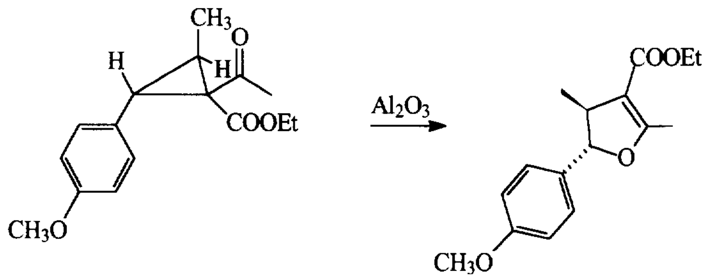
Villemin has shown that propargylic alcohols react with CS_2 on KF/Al_2O_3 to afford dithiocarbonate anions that add intramolecularly to triple bonds.[333,334] Allyl alcohols, on the other hand, yield stable dithiocarbonate anions. However, if these anions are treated with methyl iodide, the resulting xanthate esters undergo the Claisen rearrangement on alumina at room temperature.[335] Bis(allylthio)enones are not only prepared from the reaction of ketones containing α-CH_2 groups with CS_2 and allyl chloride on KF/Al_2O_3 but also undergo the thio Claisen rearrangement on the solid as well.[336]

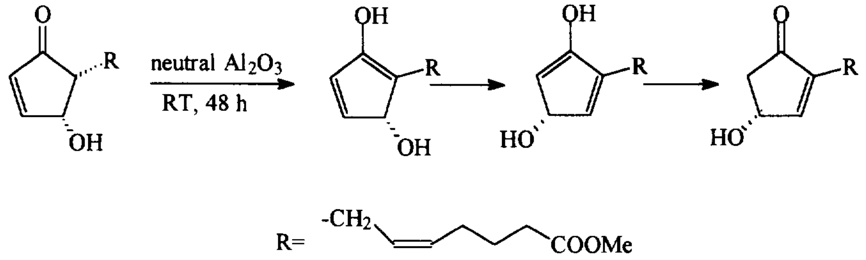


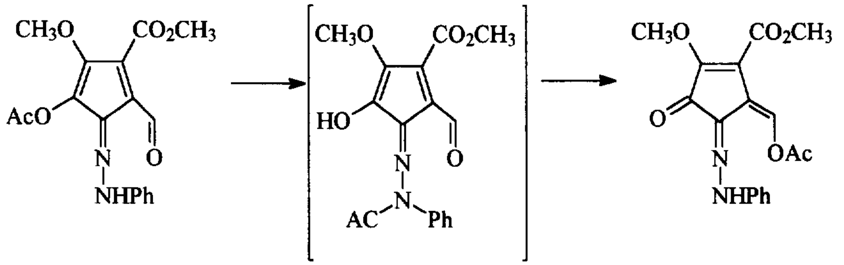




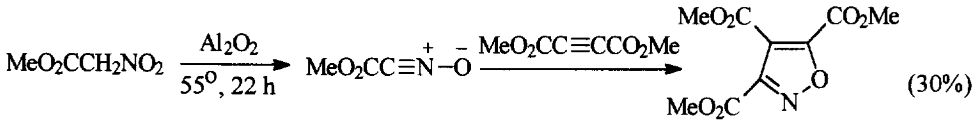
1,3-, 1,5-, 1,6-, And 1,7-sigmatropic shifts have also been observed on alumina. Cyclopropyl ketones, for example, isomerize with retention of cyclopropane stereochemistry on neutral alumina at room temperature via a formal 1,3-sigmatropic shift.[337] 5-Alkyl-4-hydroxycyclopentenone also isomerizes to a 2-alkyl-4-hydroxycyclopentenone on neutral alumina at room temperature.[338] This unusual transformation undoubtedly occurs by a 1,5 sigmatropic shift of OH on the enol of the reactant, a 5-hydroxycyclo-pentadiene. Although the heptamethylcyclohexadienyl cation undergoes a 1,2 (1,5) shift of CH_3 in solution and in the solid state, the isomerization is fastest when the substrate is adsorbed on alumina.[339] A pentafulvene derivative undergoes an intramolecular 1,7 acyl shift on Al_2O_3 and SiO_2.[340] This formal 1,7-sigmatropic shift likely occurs in two steps. In the first, the acyl group is transferred from oxygen to the hydrazone nitrogen and, in the second, the acyl group is transferred to the oxygen atom attached to the other side of the five-membered ring.

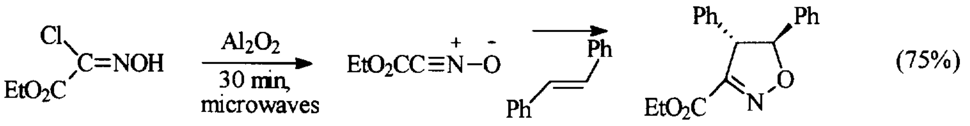




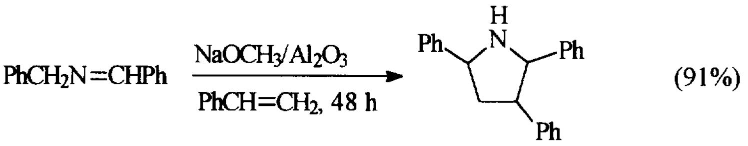


Alumina and several of its derivatives serve a variety of roles in heterogeneous cycloaddition and retrocycloaddition reactions. With methyl nitroacetate, for example, alumina functions as a dehydrating agent to yield the *N*-oxide of methyl cyanoformate which then undergoes a 3 + 2 cycloaddition with dimethyl acetylenedicarboxylate.[341] KF/Al_2O_3 behaves similarly in this reaction.[341] With chloro- (hydroximino)acetate, alumina functions as a dehydrochlorinating agent to yield a similar nitrile oxide which subsequently undergoes 3+2 cycloadditions with numerous alkynes and alkenes.[341]

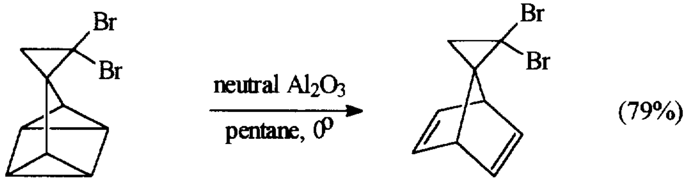




NaOCH$_3$ on alumina, a strong base, deprotonates *N*-benzylidenebenzylamine to yield an allyl-like anion which reacts with styrene to ultimately yield a pyrrolidine derivative.[342] The reaction does not

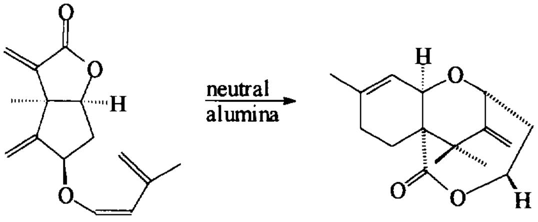


proceed with NaOCH$_3$ alone. On the other hand, alumina[343] and a cobalt complex supported on alumina[344] catalyze the retro 2+2 cycloaddition reaction of quadricyclanes. How these reactions occur is presently not known.



Owing to its importance in mechanistic and synthetic organic chemistry, the Diels-Alder, or 4+2 cycloaddition, reaction has been studied extensively on many solids including alumina. Much of the interest in the heterogeneous Diels-Alder reaction can be attributed to the fact that the catalysts are Lewis acidic and the rate and selectivity of the Diels-Alder reaction are influenced by Lewis acids. Activated alumina is of course a Lewis acid. Due to space limitations, only reactions on alumina will be described.

Parlar and Baumann determined the *endo* to *exo* selectivity of the reaction of cyclopentadiene with acrolein, methyl acrylate and acrylonitrile on neutral alumina and four other solids.[345] The reaction of cyclopentadiene and methyl acrylate, described in detail below, gave in particular high *endo* selectivity. Koreeda *et al.* discovered serendipitously that an acid-sensitive tetraene underwent an intramolecular Diels-Alder reaction when chromatographed on neutral alumina to give a tetracyclic adduct possessing the skeleton of the sesquiterpene verrucarol.[346]



Pagni, Kabaka *et al.* have shown that alumina activity profoundly affects the diastereoselectivities of the heterogeneous Diels-Alder reactions of cyclopentadiene with acrylate,[57, 347-349] maleate,[57, 350] and fumarate[57,349-351] esters (Table 3). For example, the *endo*:*exo* (N:X) selectivity of the methyl acrylate reaction is without precedent (Table 3).[57,347] The relatively low selectivity on unactivated alumina is consistent with an uncatalyzed reaction occurring in a polar environment. The slowly increasing N:X ratio as the alumina activity goes up can be attributed to an increasing fraction of the reaction being catalyzed by exposed surface aluminum ions. The very large N:X ratio of 52 on 400°-Al_2O_3, a value as high as ever achieved in solution, is due to the reaction being catalyzed by the highly active defect sites which were described earlier. Recall that defect sites begin to appear on the surface when alumina is activated above 300°.[41] On highly activated alumina, where new types of Lewis acids are exposed to the surface, the *exo* adduct is slightly preferred. Experiments proved that this effect is due to a very facile epimerization of the adducts via the retro-Diels-Alder reaction.[57,347] The results for the menthyl acrylate reaction, where two selectivities were measured,[350,351] were similar to but not as dramatic as those for the methyl acrylate reaction.

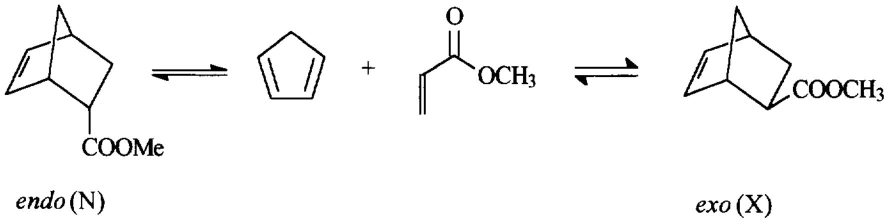
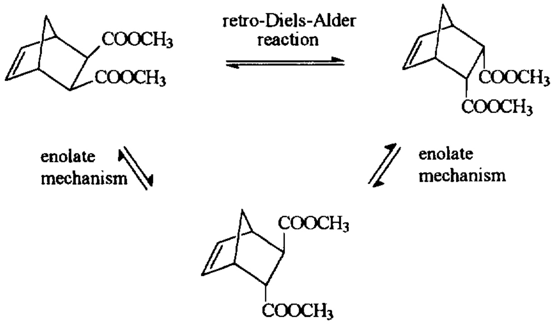


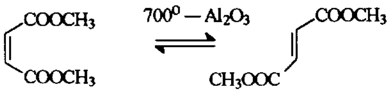
Table 3. **Diastereoselectivities for Diels-Alder Reactions of Cyclopentadiene on Alumina.**

Alumina Activity	Dienophile					
	Methyl Acrylate[a]	Menthyl Acrylate[c]		Dimethyl Maleate[f]	Dimenthyl Fumarate[g]	Menthyl Methyl Fumarate[g,h]
	N:X[b]	N:X	% de[d] of N	N:X	%de[d]	N:X
Unactivated	5.8	4.3	14.9	4.2	14.5	1.56
200°-Al_2O_3	7.0			5.0	16.7	1.94
300°-Al_2O_3	10.3					
400°-Al_2O_3	52	8.1	29.1[e]	7.0	17.7	2.44
600°-Al_2O_3		1.2				
700°-Al_2O_3				15.6	18.7	3.00
800°-Al_2O_3	0.93	1.2	26.0[e]			

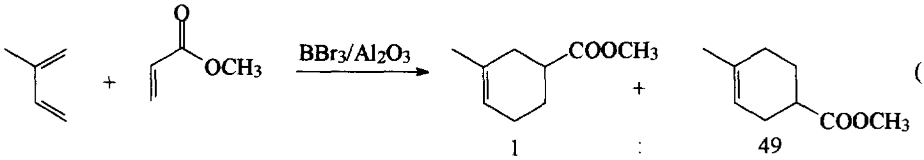
[a]Reactions run at 50°. [b]N=endo, X=exo. [c]Reactions run at 65° unless stated otherwise. [d]de=diastereomeric excess. [e]Reactions run at 0°. [f]Reactions run at room temp. [g]Reactions run at 22°.
[h]% de's for these reactions were all close to 0.

Unlike the previously described results, the N:X selectivities of the dimethyl maleate[57,350] and menthyl methyl fumarate[351] reactions, as well as the diastereomeric excess of the dimenthyl fumarate [349,351] reaction, increased steadily as the activity of the alumina increased. The values were large, even on highly activated alumina, suggesting that the adducts did not epimerize. However, it was found that the adducts did epimerize, but not as rapidly as the methyl acrylate adducts. Detailed experiments demonstrated that the two dimethyl maleate and one dimethyl fumarate adducts interconverted by competing reactions, with epimerization via enolates being faster than epimerization via the retro-Diels-Alder reaction. The dienophiles also interconverted on highly activated alumina.





Highly Lewis acidic solids, prepared by chemisorption of Lewis acids to silica gel,[352-356] alumina,[352-355, 357] and polymers,[358] are also effective catalysts for many Diels-Alder reactions. For example:

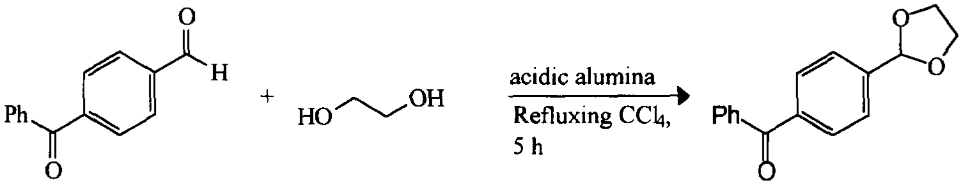


(76%) (Ref. 357)

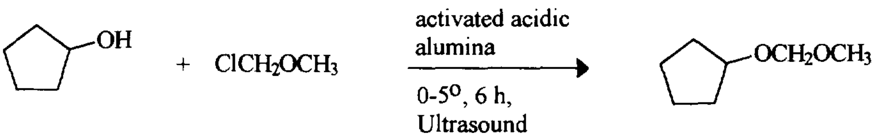
PROTECTION AND DEPROTECTION

Protecting and deprotecting a functional group is a universally used methodology in organic synthesis. Many of the reactions described in this article can be envisioned in this light. This section of the review will deal specifically with studies in which this methodology is explicitly highlighted.

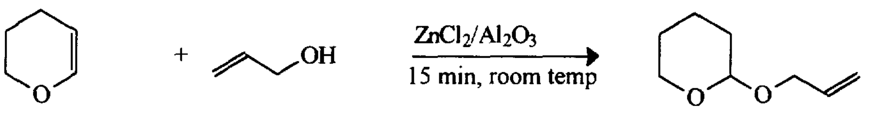
Kamitori *et al.* have shown that acidic alumina is an effective catalyst for the acetalization of aldehydes,[359] with aldehydes being considerably more reactive than ketones in the reaction. Ranu and coworkers described two procedures for the protection of alcohols, one with methoxymethyl chloride on alumina,[360] and the other with dihydropyran on $ZnCl_2/Al_2O_3$.[361]



(100%) (Ref. 359)

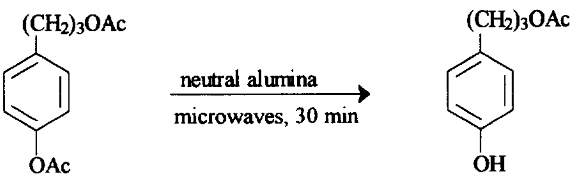


(83%) (Ref. 360)

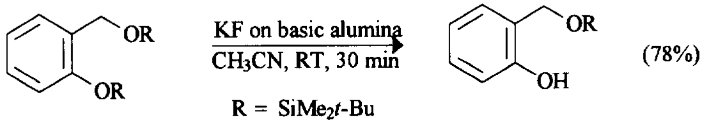


(85%) (Ref. 361)

A modest number of deprotection reactions on alumina are known (Table 4). Some of these reactions are chemoselective.



(Ref. 362)

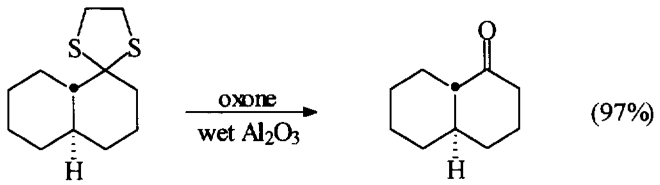


(Ref. 363)

Table 4. Deprotecting Reactions on Alumina and Modified Alumina

Reactant	Product (Yield)	Catalyst	Conditions	Reference
Aryl methyl ethers	Phenols (50-80%)	KF/Al_2O_3	210-215°, 3-5 h	364
Pivaloates and acetates	Alcohols (60-97%)	Neutral Al_2O_3	microwave, variable times	365
Phenol acetates	Phenols (82-96%)	Neutral Al_2O_3	microwave, several minutes	362
Aryl aldehyde diacetates	Aryl aldehydes (88-98%)	Neutral Al_2O_3	microwave, <1 min	366
Benzyl esters	Carboxylic Acids (89-95%)	Neutral Al_2O_3	microwave, <15 min	367
t-Butyldimethylsilyl ethers	Phenols (55-92%)	KF/Al_2O_3	ultrasound, CH_3CN, room temp.	363
t-Butyldimethylsilyl ethers	Alcohols (42-98%)	Alumina + H_2O	room temp, 6-24 h, hexane	368
t-Butyldimethylsilyl ethers	Alcohols, Phenols (68-93%)	Neutral alumina	microwave, 10-15 min	369
1° and 2° silylethers	Alcohols (>80%)	Alumina + H_2O	room temp, variable times, hexane	370

Ceccherelli et al. have described a convenient procedure for converting 1,3-dithianes into the corresponding carbonyl compound using Oxone® and wet alumina.[371]

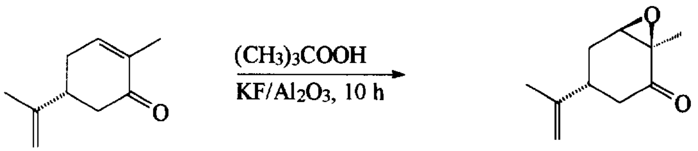


OXIDATION AND REDUCTION REACTIONS

Although alumina itself is not an oxidizing or reducing agent, it often provides a suitable environment for the oxidation and reduction of organic compounds by other reagents. These heterogeneous reactions frequently have desirable characteristics not available to their solution counterparts. The following discussion will focus first on oxidizing and then on reducing agents.

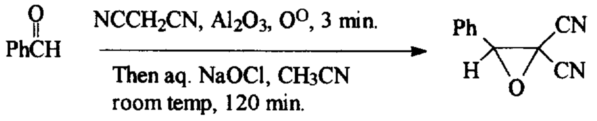
tert-Butylhydroperoxide is widely used for the epoxidation of alkenes including the Sharpless asymmetric epoxidation. On alumina this reagent has been used to convert cyclohexanol into cyclohexanone.[372] On basic alumina, it has been used to oxidize sulfoxides,[373] while on KF/Al_2O_3, it has been used to epoxidize enones.[374] The conjugate base of *tert*-butylhydroperoxide is the likely oxidant on the basic solids.

$$[CH_3(CH_2)_3]_2SO \xrightarrow[\text{basic } Al_2O_3,\ 4\ h]{(CH_3)_3COOH,\ CH_2Cl_2} [CH_3(CH_2)_3]_2SO_2 \qquad (92\%)$$



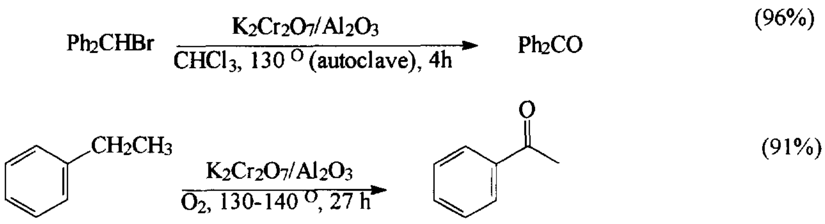
(85%)

A heterogeneous mixture of aqueous NaOCl and alumina has been used to oxidize primary[375] and secondary[376] alcohols to aldehydes and ketones and to epoxidize electron deficient alkenes.[376,377] An innovative, one-flask, tandem Knoevenagel and epoxidation reaction in which alumina plays an essential role has been described by Foucaud and Bakouetila.[377]

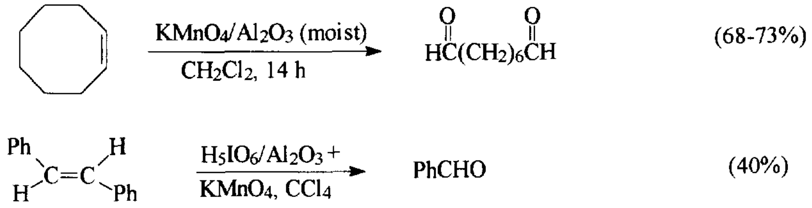


(98%)

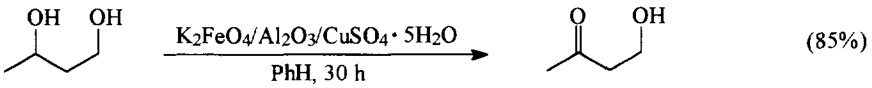
Chromium compounds supported on alumina have also been used as oxidizing agents. The orange-colored pyridine chlorochromate/Al_2O_3, for example, converts primary and secondary alcohols into aldehydes and ketones, often in higher yields than solution counterparts.[378-380] $KClCrO_3/Al_2O_3$[381] and CrO_3/Al_2O_3 (deactivated)[382] likewise convert alcohols into aldehydes and ketones. $K_2Cr_2O_7/Al_2O_3$, on the other hand, oxidizes primary and secondary alkyl halides to aldehydes and ketones.[383] The chromium compound can also be used as a catalyst if the oxidizing reaction is run in the presence of the expendable O_2.[384,385] $KMnO_4/Al_2O_3$ can likewise be rendered catalytic in the presence of O_2.[384]



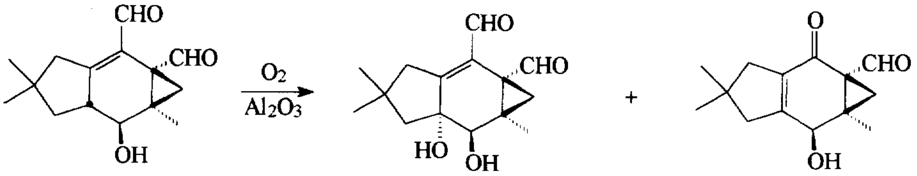
KMnO$_4$ has been used stoichiometrically in several heterogeneous oxidations. Lee and coworkers have shown that carbon-carbon double bonds are cleaved to aldehydes with KMnO$_4$ on moist Al$_2$O$_3$ in good to excellent yields;[386] arenes with benzylic hydrogens, on the other hand, are converted to ketones.[387] Villemin showed that arenes also yield ketones when treated with H$_5$IO$_6$/Al$_2$O$_3$.[388] They demonstrated that, in conjunction with KMnO$_4$, H$_5$IO$_6$/Al$_2$O$_3$ cleaves C-C double bonds.[388,389]

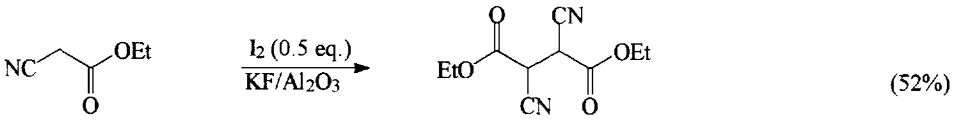


K$_2$FeO$_4$ has not been widely used as an oxidant in organic synthesis because it is insoluble in organic solvents. However, when it is mixed thoroughly with basic alumina and CuSO$_4$•5H$_2$O, however, it selectively oxidizes secondary alcohols to ketones.[390,391]

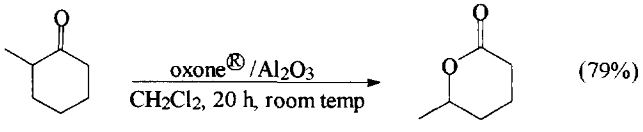


Molecular oxygen serves as an oxidant in the oxidative coupling of 2-naphthols using CuSO$_4$/Al$_2$O$_3$ (catalyst)[392] and the hydroxylation and deformylation of unsaturated sesquiterpene dialdehydes occurs readily on alumina itself.[393] Although the mechanism by which the sesquiterpene reaction occurs is unknown, the reaction may be initiated by deprotonation of the reactant by the alumina followed by addition of O$_2$ to the resultant carbanion. The oxidation of a carbanion is known for reactions of active methylene compounds with I$_2$ (oxidant) on KF/Al$_2$O$_3$ (base).[394]

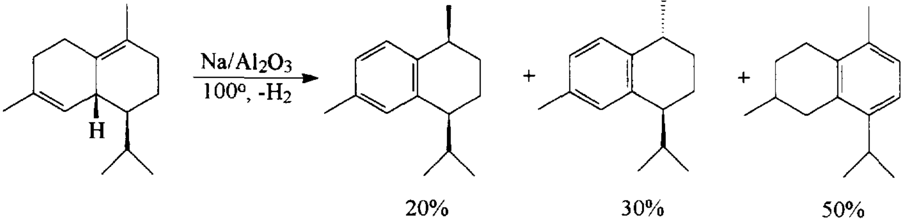




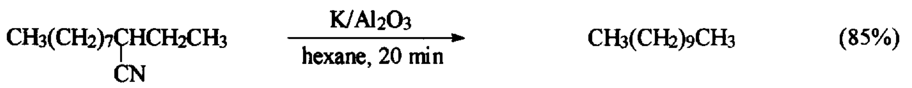
An interesting variant of the Baeyer-Villliger reaction involves the conversion of ketones into lactones in good yields under mild conditions using oxone® ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) on alumina (deactivated by addition of water).[395]



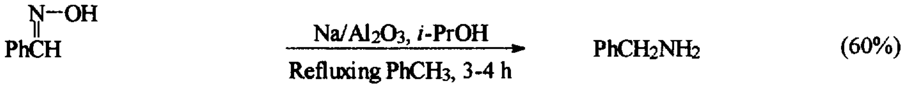
Sodium dispersed on alumina, a bright to dark grey free-flowing powder prepared by the reaction of Na (2-10 wt.%) with basic Al_2O_3 at 200°, normally functions as a base for the isomerization of alkenes and as a reductant. In reactions with the natural product (+)-δ-radinene, however, it functions as a dehydrogenation agent.[396]



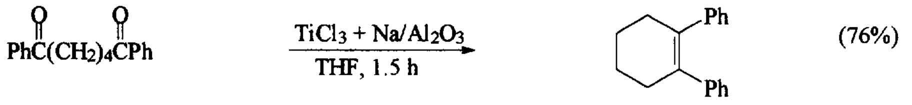
Na/Al_2O_3 and K/Al_2O_3, a blue solid prepared by melting potassium over Al_2O_3 at 150° under argon, normally function as reducing agents. K/Al_2O_3, for example, has been used for the decyanation of nitriles[397] while Na/Al_2O_3 has been used to reduce ketones, esters and oximes.[398] Na/Al_2O_3 has also been used to reduce $TiCl_3$ to a lower valent titanium species, subsequently used in the McMurray coupling of aldehydes and ketones.[399]



$$CH_3(CH_2)_7\underset{CN}{C}HCH_2CH_3 \xrightarrow[\text{hexane, 20 min}]{K/Al_2O_3} CH_3(CH_2)_9CH_3 \quad (85\%)$$



$$Ph\overset{N-OH}{CH} \xrightarrow[\text{Refluxing } PhCH_3\text{, 3-4 h}]{Na/Al_2O_3\text{, } i\text{-PrOH}} PhCH_2NH_2 \quad (60\%)$$



$$Ph\overset{O}{C}(CH_2)_4\overset{O}{C}Ph \xrightarrow[\text{THF, 1.5 h}]{TiCl_3 + Na/Al_2O_3}$$

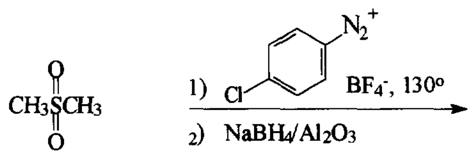
(76%)

Na_2S is a well-known reductant. Na_2S/Al_2O_3, a reagent previously described in this article as a source of nucleophilic S^{-2}, was found to reduce *p*-nitrobenzaldehyde and other aromatic and aliphatic aldehydes to the corresponding alcohols.[400] Ando *et al.* showed, however, that these were really Cannizzaro reactions in which the aldehyde is converted into equal amounts of alcohol and carboxylic acid, with the hydroxyl groups on the surface of the solid serving as the source of hydroxide.[401]

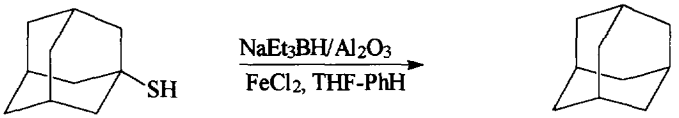
$$PhCHO \xrightarrow{\text{cyclohexane}} PhCH_2OH$$

Na_2S/acidic Al_2O_3	32%	[+ PhCOOH (30%)]
Na_2SO_3/neutral Al_2O_3	38%	
Na_2SO_3/neutral Al_2O_3	48%	
neutral Al_2O_3	44%	

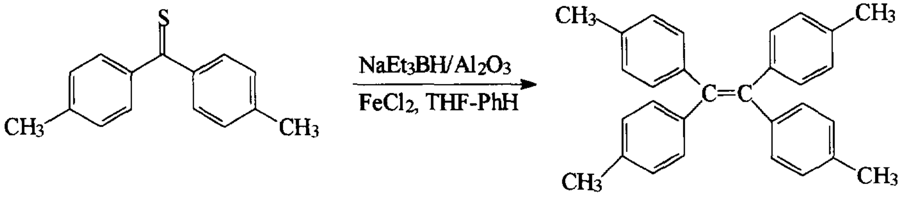
Borohydrides and borane supported on alumina are reducing agents. $NaBH_4/Al_2O_3$, for example, has been used successfully since 1969 to reduce aldehydes, ketones and acyl chlorides to alcohols.[402-404] $NaBD_4/Al_2O_3$ has also been used as a reductant.[405] Furthermore, $NaBH_4/Al_2O_3$, has been used in a two-step process which converts sulfones to sulfoxides.[406] The pyridine borane complex, when adsorbed to alumina, has also been used to reduce aldehydes; under the same conditions ketones were unreactive.[407] $NaEt_3BH/Al_2O_3$, in conjunction with $FeCl_2$ in THF-benzene, has been shown to convert thiols and thiones to hydrocarbons.[408]



(40-60%)

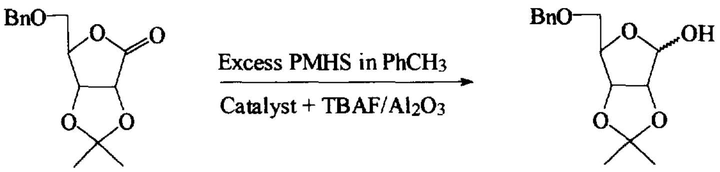


(73%)



(68%)

Two other intriguing uses of alumina in reduction reactions should be mentioned. The first of these involves the burgeoning field of fullerene chemistry. When $C_{60}O$, an epoxide of C_{60}, is passed through a column of neutral alumina, C_{60} is recovered in 91% yield.[409] The mechanism of this deoxygenation reaction is unclear. The other example is in the area of organic synthesis. When lactones are treated with the reducing agent, polymethylhydrosiloxane (PMHS), a catalytic amount of $Cp_2Ti(p\text{-}ClC_6H_4O)_2$ and a subcatalytic amount of tetrabutylammonium fluoride (TBAF) on alumina, lactols are produced in excellent yields.[410] The role of the TBAF/Al_2O_3 seems to be to activate the catalyst.

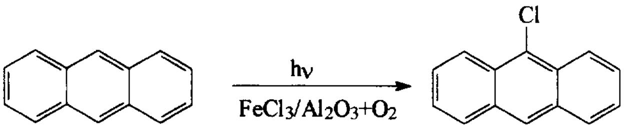


(91%)

PHOTOCHEMICAL REACTIONS

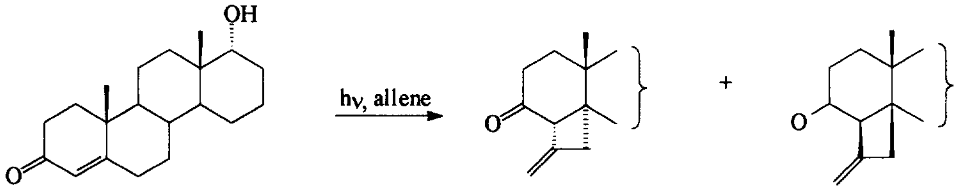
Although there have been many photochemical studies carried out on organic compounds adsorbed on alumina, few are of synthetic interest because the photoproducts have rarely been identified. A few of the photoreactions with potential synthetic applications will be summarized.

de Mayo and coworkers studied the photochlorination of aromatic hydrocarbons on $FeCl_3/Al_2O_3$ in the presence of air.[411] Anthracene, for example, yielded 9-chloroanthracene. The reactions, which were not as effective when carried out either on $FeCl_3/SiO_2$ or in the absence of air, were likely initiated by electron transfer from the arene excited state to Fe (III).



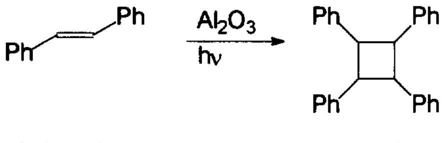
(40%)

de Mayo has also studied the 2+2 photoaddition of alkenes to steroidal enones.[412] The addition of an alkene to one of these steroids on Al_2O_3 demonstrated a reversal of stereochemistry to that observed in solution.



methanol (-70°)	91.5	:	8:5
alumina (20°)	6	:	94

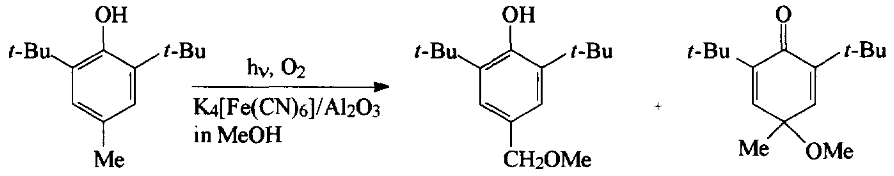
Photolysis of *trans*-stilbene adsorbed on crystalline alumina afforded a 2+2 dimer (stereochemistry not given);[413] no isomerization to *cis*-stilbene occurred. This behavior is unlike that seen in the gas and solution phases where isomerization is dominant.



Photolysis of benzyl alcohol on alumina, surprisingly, afforded dibenzyl ether;[101] this behavior is not observed in solution. A plausible mechanism for the formation of the ether involves the photogeneration of a benzyl cation which subsequently reacts with benzyl alcohol.

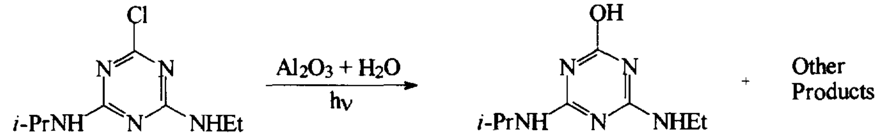
$$PhCH_2OH \xrightarrow[Al_2O_3]{h\nu} PhCH_2OCH_2Ph + H_2O$$

Photolysis of 2,6-di-*tert*-butyl-4-methylphenol in methanol in the presence of $K_4[Fe(CN)_6]$ supported on acid-treated τ-Al_2O_3 afforded two oxidation products.[414] Experiments suggest that illumination of $Fe(CN)_6^{-4}$ in the presence of O_2 afforded $Fe(CN)_6^{-3}$, the catalyst in the reaction. Photolysis of phenyl-substituted ethylenes on alumina in the presence of air also yielded oxidation products.[415]



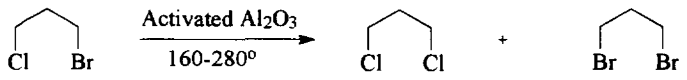
$$2\ Ph_2C{=}CH_2 \xrightarrow[\text{acidic alumina + air}]{h\nu} Ph_2CO \quad (96\%)$$

Several photoreactions on alumina are of environmental, as well as synthetic, interest. Naphthalene[416] and anthracene,[417] for example, afford oxygenated products when photolyzed on alumina in the presence of air. The herbicide atrazine undergoes photohydrolysis in a suspension of H_2O and Al_2O_3 at a rate five times faster than in H_2O alone.[418]

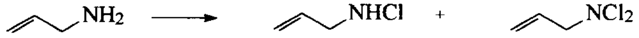


MISCELLANEOUS REACTIONS

Shinoda and Yasuda have described an unusual metathesis reaction in which 1,3-dichloro- and 1,3-dibromopropane are generated by passing 1-bromo-3-chloropropane vapor over hot alumina.[419]

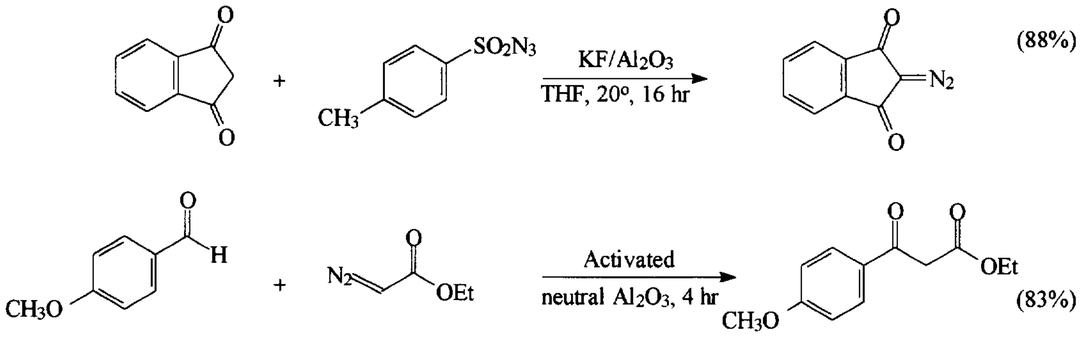


Chlorination of fatty acids adsorbed on alumina with Cl_2 or *tert*-BuOCl occurs selectively at the ω to ω-2 positions.[420] Treatment of the resulting chloroacids with DBU yields marcrocyclic lactones. Chlorination of primary amines with *N*-chlorosuccinimide (NCS) on alumina produces *N*, *N*-dichloroamines in excellent yields.[421] Chlorination using NCS alone affords only *N*-chloramines.



NCS	88%	---
NCS/Al_2O_3	---	82%

One can generate and react diazo compounds on alumina. Active methylene compounds, for example, afford diazo compounds when treated with tosyl azide on KF/Al_2O_3.[422] This is a variation of a well-known procedure for making diazo compounds in solution. Ethyl diazoacetate, on the other hand, reacts with aldehydes on alumina at 30° to yield β-ketoesters in very good yields.[423]



ACKNOWLEDGEMENT

The authors thank Research Corporation, the National Science Foundation and the Department of Energy for support of their research on organic reactions on alumina.

REFERENCES AND NOTES

1. Lee, S. *Nature* **1995**, *378*, 662.
2. Yaghi, O. M.; Li, G.; Li, H. *Nature* **1995**, *378*, 703.
3. *Preparative Chemistry Using Supported Reagents*; Laszlo, P. ed.; Academic Press: San Diego, 1987.

4. *Solid Supports and Catalysis in Organic Synthesis;* Smith, K. ed.; Ellis Horwood: Chichester, 1992.

5. Clark, J. H. *Catalysis of Organic Reactions by Supported Inorganic Reagents;* VCH: New York, 1994.

6. Beránek, L.; Kraus, M. in *Comprehensive Chemical Kinetics*; Bradford, C. H., Tipper, C. F. H. eds; Elsevier: Amsterdam, 1978; Vol. 20, p. 385.

7. (a) McKillop, A.; Young, D. W. *Synthesis* **1979**, 401.
   (b) McKillop, A.; Young, D. W. *Synthesis* **1979**, *481.*

8. Bram, G.; d'Incan, E.; Loupy, A. *Nouv. J. Chim.* **1982**, *6*, 689.

9. Laszlo, P. *Acc. Chem. Res.* **1986**, *19*, 121.

10. Smith, K. *Bull. Soc. Chim. Fr.* **1988**, 272.

11. Dyer, A. *An Introduction to Zeolite Molecular Sieves;* Wiley: NY 1988.

12. Szostak, R. *Molecular Sieves. Principles of Synthesis and Identification*; Van Norstrand Reinhold: NY 1989.

13. Izumi, Y. Vrube, K.; Onaka, M. Zeolite, *Clay and Heteropoly Acid in Organic Reactions*; VCH: Weinheim, 1992.

14. Hőlderich, W.; Hesse, M.; Näumann, F. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 226.

15. van Bekkum, H.; Kouwenhoven, H. W. *Recl. Trav. Chim. Pays-Bas.* **1989**, *108*, 283.

16. Isakov, Y. I.; Isakova, T. A.; Minachev, K. M. *Izv. Akad. Nauk SSSR, Sr. Khim.* **1989**, 608.

17. Perot, G.; Guisnet, M. *J. Mol. Cat.* **1990**, *61*, 173.

18. Balogh, M.; Laszlo, P. *Organic Reactions Using Clay*; Springer-Verlag: Berlin, 1993.

19. *Chemistry of Clay and Clay Minerals*; Newman, A. C. D. ed.; Wiley: NY, 1987.

20. Cornélis, A.; Laszlo, P. *Synthesis* **1985**, 909.

21. Ballantine, J. A. in *Chemical Reactions in Organic and Inorganic Constrained Systems*; Selton, R. ed.; D. Reidel: Dordnecht, Holland, 1986.

22. Cornélis, A.; Laszlo, P. in *Chemical Reactions in Organic and Inorganic Constrained Systems*; Selton, R. ed.; D. Reidel: Dordnecht, Holland, 1986.

23. Laszlo, P. *Science* **1987**, *235*, 1473.

24. Laszlo, P.; Cornélis, A. *Aldrich. Chim. Acta.* **1988**, *21*, 97.

25. Delaude, L.; Laszlo, P.; Smith, K. *Acc. Chem. Res.* **1993**, *26*, 607.

26. (a) Cornélis, A.; Laszlo, P. *Synlett* **1994**, 155.
    (b) Izumi, Y.; Onaka, M. *Adv. Catal.* **1992**, *38*, 245.

27. Basiuk, V. A. *Russ. Chem. Rev.* **1995**, *64*, 1003.

28. Posner, G. H. *Angew. Chem. Int. Ed. Chem.* ***1978***, 17, *487.*

29. Früchtel, J. S.; Jung, G. *Angew Chem. Int. Ed. Engl.* **1996**, *35*, 17.

30. Misra, C. *Industrial Alumina Chemicals;* American Chemical Society: Washington, 1986.

31. Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; VCH:Weinheim, 1988.

32. Tundo, P. *Continuous Flow Methods in Organic Synthesis;* Ellis Horwood, New York, 1991.

33. Peri, J. B. *J. Phys. Chem.* **1965**, *69*, 211, 220, 231.

34. Posner, G. H. In *Preparative Chemistry Using Supported Reagents;* Laszlo, P. ed.: Academic Press: San Diego, 1987; p 287.

35. Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*; 4th ed.; Wiley: NY, 1980.

36. Avnir, D.; Farin, D.; Pfeifer, P. *New J. Chem.* **1992**, *16*, 439.

37. Parks, G. A. *Chem. Rev.* **1965**, *65*, 177.

38. (a) Tanabe, K. *Solid Acids and Bases*; Kodansha: Tokyo, 1970. (b) Tanabe, K.; Misono, M.; OnoY.; Hattori, H. *New Solid Acids and Bases;* Elsevier: Amsterdam, 1989.

39. Olah, G. A.; Surya Prakash, G. K.; Sommer, J. *Superacids*; Wiley: NY, 1985.

40. Dawson, W. H.; Kaiser, S. W.; Ellis, P. D.; Inners, R. R. *J. Am. Chem. Soc.* **1981**, *103*, 6780.

41. Knözinger, H.; Ratnasamy, P. *Catal. Rev. Sci. Eng.* **1978**, *17*, 31.

42. McMillan, M.; Brinen, J. S.; Haller, G. L. *J. Catal.* **1986**, *97*, 243.

43. Ellis, P. D.; Huggins, B. A. *J. Am. Chem. Soc.* **1992**, *114*, 2098.

44. Chen, F. R.; Davis, J. G.; Fripiat, J. J. *J. Catal.* **1992**, *133*, 263.

45. Coster, D.; Blumenfield, A. L.; Fripiat, J. J. *J. Phys. Chem.* **1994**, *98*, 6201.

46. Blumenfeld, A. L.; Coster, D. L.; Fripiat, J. J. *Chem. Phys. Lett.* **1994**, *231*, 491.

47. Dawson, W. H.; Kaiser, S. W.; Ellis, P. D.; Inners, R.R. *J. Phys. Chem.* **1982**, *86*, 867.

48. Majors, P. D.; Ruidy, T. E.; Ellis, P. D. *J. Am. Chem. Soc.* **1986**, *108*, 8123.

49. Majors, P. D.; Ellis, P. D. *J. Am. Chem. Soc.,* **1987**, *109*, 1648.

50. Hu, B.; Gay, I. D. *Langmuir* **1995**, *11*, 3845.

51. DeCanio, E. C.; Edwards, J. C.; Bruno, J. W. *J. Catal.* **1994**, *148*, 76.

52. Schramm, S.; Kirkpatrick, R. J.; Oldfield, E. *J. Am. Chem. Soc.* **1983**, *105*, 2483.

53. Walter, T. H.; Oldfield, E. *J. Phys. Chem.* **1989**, *93*, 6744.

54. See also Gruver, V.; Fripiat, J. J. *J. Phys. Chem.* **1994**, *98*, 8549.

55. Houng-Van, C.; Ghorbel, A.; Teichner, S. J. *Bull. Soc. Chem. Fr.* **1972**, 437.

56. Michels, J. J.; Dorsey, J. G. *Langmuir* **1990**, *6*, 414.

57. Pagni, R. M.; Kabalka, G. W.; Hondrogiannis, G.; Bains, S.; Anosike, P.; Kurt, R. *Tetrahedron* **1993**, *49*, 6743.

58. See Table 1 in reference 41 for citations.

59. Gaetano, K.; Pagni, R. M.; Kabalka, G. W.; Bridwell, P.; Walsh, E.; True, J.; Underwood, M. *J. Org. Chem.* **1985**, *50*, 499.

60. Kabalka, G. W.; Pagni, R. M.; Bridwell, P.; Walsh, E. Hassaneen, H. *J. Org. Chem.* **1981**, *46*, 1513.

61. Kunick, C.; Messinger, P. *Chem. Ber.* **1986**, *119*, 1429.

62. Posner, G. H.; Rogers, D. Z. *J. Am. Chem. Soc.* **1977**, *99*, 8208, 8214.

63. Kropf, H.; Amirabadi, H. M.; Mosebach, M.; Torkler, A.; von Wallis, H. *Synthesis 1983, 587.*

64. Kropf, H.; Torkler, A. *J. Chem Res. (S)* **1985**, 304.

65. Hudrlik, P.; Hudrlik, A. M.; Kulkarni, A. K. *Tetrahedron Lett.* **1985**, *26*, 139.

66. Taran, M.; Delmond, B. *Tetrahedron Lett.* **1982**, *23*, 5535.

67. Serramedan, D.; Marc, F.; Peneyre, M.; Filliatre, C.; Chabardes, P.; Delmond, B. *Tetrahedron Lett.* **1992**, *33*, 4457.

68. French, L. G.; Charlton, R. P. *Heterocycles* **1993**, *35*, 305.

69. Marc, F.; Soulet, B.; Delmond, D.; Serramedan, D. *Tetrahedron* **1994**, *50*, 3381.

70. Arata, K.; Hayano, K.; Shirahama, H. *Bull. Chem. Soc. Jpn.* **1993**, 66, 218.

71. Arata, K.; Nakamura, H.; Nakamura, Y. *Bull, Chem. Soc. Jpn.* **1994**, *67*, 2351.

72. Tsuboi, S.; Furutani, H.; Takeda, A. *Synthesis* **1987**, 292.

73. Suga, H.; Miyake, H. *Synthesis* **1988**, 394.

74. Smith, M. B. *Organic Synthesis*; McGraw-Hill: New York, 1994.

75. Bauer, R.; Thomke, K. *J. Mol. Cat.* **1983**, *73*, 311.

76. Závada, J.; Pánková, M. *Coll. Czech. Chem. Chem. Comm.* **1990**, *55*, 704.

77. (a) Posner, G. H.; Johnson, R. J.; Whalen, M. *J. Chem. Soc., Commun.* **1972**, 218. (b) Posner, G. H.; Gurria, G. M.; Bublak, K. A. *J. Org. Chem.* **1977**, *42*, 3173.

78. Paquette, L. A.; Kramer, J. D. *J. Org. Chem.* **1984**, *49*, 1445.

79. Paquette, L. A.; Kearney, F. R.; Drake, A. F.; Mason, S. F. *J. Am. Chem. Soc.*, **1981**, *103*, 5064.

80. Vidal, J.; Huet, F. *Tetrahedron Lett.* **1986**, *27*, 3733.

81. (a) Brand, M.; Drewes, S. E.; Roos, G. H. P. *Synth. Commun.* **1986**, *16*, 883. (b) Brand, M.; Drewes, S. E. *Synth. Commun.* **1987**, *17*, 795.

82. Yamawaki, J.; Kuwate, T.; Ando, T.; Hanafusu, T. *Bull Chem. Soc. Jpn.* **1983**, *56*, 1885.

83. Inokuchi, T.; Asanuma, G.; Torii, S. *J. Org. Chem.* **1982**, *47*, 4622.

84. Hudlicky, T.; Srnak, T. *Tetrahedron Lett.* **1981**, *22*, 3351.

85. Moss, R. A.; Xue, S.; Sauers, R. R. *J. Am. Chem. Soc.* **1996**, *118*, 10307.

86. (a) Chun, T.-L.; Fong, S.; Li, Y.; Man, T.-O.; Poon, C.-D. *J. Chem. Soc., Chem. Commun.* **1994**, 1771. (B) Cao, X.-P.; Chan, T.-L.; Chun, H.-F.; *Tetrahedron Lett.* **1996**, *37*, 1049.

87. Plummer, B. F.; Al-Saigh, Z. Y.; Arfan, M. *J. Org. Chem.* **1984**, *49*, 2069.

88. Laporterie, A.; Manuel, G.; Iloughman, E. H.; Dubac, J. *Nouv. J. Chim.* **1984**, *8*, 437.

89. Jayami, M.; Pant, N.; Anathan, S.; Narayanan, K.; Pilai, C. N. *Tetrahedron Lett.* **1986**, 42, 4325.

90. Hodgetts, I.; Noyce, S. J.; Starr, R. C. *Tetrahedron Lett.* **1984**, *25*, 5435.

91. Bestmann, H. J.; Kobold, V.; Vostrowsky, O. *Ann.* **1986**, 234.

92. Texier-Boullet, F. *Synthesis* **1985**, 679.

93. Devine, P. N.; Reilly, M.; Oh, T. *Tetrahedron Lett.* **1993**, *34*, 5827.

94. Texier-Boullet, R.; Klein, B.; Hamelin, J. *Synthesis* **1986**, 409.

95. Villemin, D.; Lalaoui, M.; Alloum, A. B. *Chem. Ind.* **1991**, 176.

96. Hanafusa, T.; Ichihara, J.; Ashida, T. *Chem. Lett.* **1987**, 687.

97. Ramadas, K. *Tetrahedron Lett.* **1996**, *37*, 5161.

98. March, J. *Advanced Organic Chemistry*; 3rd ed.; Wiley: New York, 1985; Chapter 15.

99. Pagni, R. M.; Kabalka, G. W.; Boothe, R.; Gaetano, K.; Stewart, L. J. In *Physical Organic Chemistry 1986*; Kobayashi, M. ed.; Elsevier: Amsterdam, 1987; p. 399.

100. Pagni, R. M.; Kabalka, G. W.; Boothe, R.; Gaetano, K.; Stewart, L. J.; Conaway, R.; Dial, C.; Gray, D.; Larson, S.; Luidhardt, T. *J. Org. Chem.* **1988**, *53*, 4477.

101. Hondrogiannis, G.; Lee, L. C.; Kabalka, G. W.; Pagni, R. M. *Tetrahedron Lett.* **1994**, *35*, 6211.

102. Larson, S.; Luidhardt, T.; Kabalka, G. W.; Pagni, R. M. *Tetrahedron Lett.* **1988**, *29*, 35.

103. Hondrogiannis, G.; Lee, L. C.; Kabalka, G. W.; Pagni, R. M. *Tetrahedron Lett.* **1989**, *30*, 2069.

104. Ando, T.; Clark, J. H.; Cork, D. G. Fujita, M.; Kumura, T. *J. Chem. Soc., Chem. Commun.* **1987**, 1301.

105. Stewart, L. J.; Gray, D.; Pagni, R. M.; Kabalka, G. W. *Tetrahedron Lett.* **1987**, *28*, 4497.

106. Kropp, P. J.; Davis, K. A.; Crawford, S. D.; Tubergen, M. W.; Kepler, K. D.; Craig, S. L.; Wilson, V.P. *J. Am. Chem. Soc.* **1990**, *112*, 7433.

107. Breton, G. W.; Daus, K. A.; Kropp, P. J. *J. Org. Chem.* **1992**, *57*, 6646.

108. Kropp, P. J.; Daus, K. A.; Tubergen, M. W.; Kepler, K. D.; Wilson, V. P.; Craig, S. L.; Baillargeon, M. M.; Breton, G. W. *J. Am. Chem. Soc.* **1993**, *115*, 3071.

109. Kropp, P. J.; Crawford, S. D. *J. Org. Chem.* **1994**, *59*, 3102.

110. Laszlo, P.; Delaude, *Tetrahedron Lett.* **1991**, 32, *3705.*

111. Pienta, N. J.; Crawford, S. D.; Kropp, P. J. *J. Chem. Ed.* **1993**, *70*, 682.

112. Miles, W. H.; Nutaitis, C. F.; Berreth, C. L. *J. Chem. Ed.* **1994**, *71*, 1097.

113. Rood, G. A.; DeHann, J. M.; Zibuck, R. *Tetrahedron Lett.* **1996,** *37*, 157.

114. See for, example, Klemm, L. H.; Taylor, D. R. *J. Org. Chem.* **1980**, *45*, 4320, 4326.

115. See, for example, (a) ApSimon, J. W.; Chau, A. S.; Sampson, R.; Tze, H.; Fruchier, A. *Can. J. Chem.* **1982**, *60*, 2002. (b) Ramdahl, T.; Bjørseth, A.; Lokensgard, D. M.; Pitts, J.N. Jr. *Chemosphere* **1984**, *13*, 527. (c) Schoonenboom, M. H.; Smit, P. N.; Olie, K. *Chemosphere* **1992**, *25*, 1897. (d) Schoonenboom, M. H.; Zoetemeijer, H. E.; Olie, K. *Appl. Cat. B.* **1995**, *6*, 11.

116. Boothe, R.; Dial, C.; Conaway, R.; Pagni, R. M.; Kabalka, G. W. *Tetrahedron Lett.* **1986**, *27*, 2207.

117. Kodomari, M.; Amanokura, N.; Takeuchi, K.; Yoshitomi, S. *Bull Chem. Soc. Jpn.* **1992**, *65*, 306.

118. Ranu, B. C.; Sarkar, D. C.; Chakraborty, R. *Synth. Commun.* **1992**, *22*, 1095.

119. Kodomari, M.; Satoh, H.; Yoshitomi, S. *J. Org. Chem.* **1988**, *53*, 2093.

120. Kodomari, M.; Satoh, H.; Yoshitomi, S. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 4149.

121. Thapliyal, P. C.; Singh, P. K.; Khanna, R. N. *Synth. Commun.* **1993**, *23*, 2821.

122. Singh, P. K.; Khanna, R. N. *Synth. Commun.* **1993**, *23*, 2083.

123. Kodomari, M.; Takahashi, S.; Yoshitomi, S. *Chem. Lett.* **1987**, 1901.

124. Ando, T.; Sumi, S.; Kawate, T. Ichihara, J.; Hanafusa, T. *J. Chem. Soc., Chem. Commun.* **1984**, 439.

125. Ando, T.; Kawate, T.; Ichihara, J.; Hanafusa, T. *Chem. Lett.* **1984**, 725.

126. Baek, S. -H.; Srebnik, M.; Mechoulam, R. *Tetrahedron Lett.* **1985**, *26*, 1083.

127. Kodomari, M.; Nawa, S.; Miyoshi, Ti. *J. Chem. Soc., Chem. Commun.* **1995**, 1895.

128. Ishibashi, H.; Mita, N.; Matsuba, N.; Kubo, T.; Nakanishi, M.; Ikeda, M. *J. Chem.Soc., Perkin Trans 1.* **1992**, 2821.

129. Ishibashi, H., Nishida, K.; Ikeda, M. *Synth. Commun.* **1993**, *23*, 2381.

130. Takusaro, H.; Okazaki, S. *Chem. Lett.* **1984**, 885.

131. Clark, J. H.; Martin, K.; Tearsdale, A.; Barlow, S. J.; *J. Chem. Soc. Chem. Commun.* **1995**, 2037.

132. Glusencamp, K. -H.; Büchi, G. *J. Org. Chem.* **1986**, *51*, 4481.

133. Kropp, P. J.; Breton, G. W.; Craign, S. L.; Crawford, S. D.; Durland, W. F. Jr.; Jones, J. E. III; Raleigh, J. S. *J. Org. Chem.*, 1995, ***60*, 4146.**

134. Pozharskii, A.F.; Vistrobskii, N. V. *Russ. Chem. Bull.* **1996**, *45*, 971.

135. Ley, S. V.; Low, C. M. R. *Ultrasound in Synthesis*; Springer-Verlag: Berlin, 1989.

136. For an example of nitration on Al_2O_3 using N_2O_4 see Nagy, S. M.; Zubkov, E. A.; Shubin, V. G.; Pelmenschikov, A. G.; Paukshts, E. A.; Razdobarova, N. L. *Acta Chim. Hung.* **1992**, *129*, 579.

137. Dalton, J. R. Regen, S. L. *J. Org. Chem.* **1979**, *44*, 4443.

138. Clark, J. H.; Jones, C. W. *J. Chem. Soc., Chem. Commun.* **1987**, 1409.

139. Clark, J. H.; Jones, C. W.; Duke, C. V. A.; Miller, J. M. *J. Chem. Res. (S)* **1989,** 238; *J. Chem. Res (M)* **1989**, 1745.

140. Clark, J. H.; Jones, C. W.; Kybett, A. P.; McClinton, M. A. Jr.; Miller, M.; Bishop, D.; Blade, R. J. *J. Fluor. Chem.* **1990**, *48*, 249.

141. Clark, J. H.; Duke, C. V. A.; Miller, J. M.; Brown, S. J. *J. Chem. Soc., Chem. Commun.* **1986**, 877.

142. Clark, J. H.; Jones, C. W. *Inorg. Chim. Acta* **1979**, *179*, 41.

143. Smith, W. J. III; Sawyer, J. S. *Tetrahedron Lett.* **1996**, 299.

144. Clark, J. H.; Robertson, M. S.; Smith, D. C.; Cook, A.; Streich, C. *J. Fluor. Chem.* **1985**, *28*, 161.

145. Fukawa, I.; Tanabe, T.; Dozono, T. *J. Chem. Soc, Perkin Trans 2* **1992**, 377.

146. Bebon-Rampal, C.; Vanhove, D. *Bull. Soc. Chim. Fr.* **1992**, *129*, 501.

147. Schmittling, E. A.; Sawyer, J. S. *J. Org.Chem.* **1993**, *58*, 3229.

148. Anufriev, V. P.; Norikov, V. *Tetrahedron Lett.* **1995**, *36*, 2515.

149. Sponholtz, W. R. III; Pagni, R. M.; Kabalka, G. W.; Green, J. F.; Tan, L. C. *J. Org. Chem.* **1991**, *56*, 5700.

150. Willis, D. A.; McGinnis, M. B.; Kabalka, G. W.; Pagni, R. M. *J. Organomet. Chem.* **1995**, *487*, 35.

151. Regen, S. L.; Quici, S.; Ryan, M. D. *J. Am. Chem. Soc.* **1979**, *101*, 7629.

152. Clark, J. H.; Duke, C. V. A. *J. Org. Chem.* **1985**, *50*, 1330.

153. Clark, J. H.; Jones, C. W. *J. Chem. Res. (S)* **1990**, 39.

154. Villemin, D.; Ben Alloum, A. *Synth. Commun.* **1990**, *20*, 925.

155. Gutierrez, E.; Loupy, A.; Bram, G.; Ruiz-Hitzky, E. *Tetrahedron Lett.* **1989**, *30*, 945.

156. Bram, G.; Loupy, A.; Majdoub, M. Gutierrez, E.; Ruiz-Hitzky, E. *Tetrahedron* **1990**, *46*, 5167.

157. Loupy, A.; Petit, A.; Ramdani, M.; Yvanaeff, C.; Majdoub, M.; Ladiad, B.; Villemin, D. *Can. J. Chem.* **1993**, *71*, 90.

158. Yamawaki, J.; Ando, T. *Chem. Lett.* **1990**, 533.

159. Ando, T.; Yamawaki, J.; Kawate, T.; Sumi, S.; Hanafusa, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 2504.

160. Ogawa, H.; Ichimura, Y.; Chihura, T.; Teratani, S.; Taya, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2481.

161. Patek, M.; Lebl, M.; Budesinky, M. *Tetrahedron Lett.* **1992**, *33*, 4507.

162. Otomatsu, H.; Higashiyama, K.; Honda, T.; Kametani, *J. Chem. Soc., Perkin I* **1982**, 2399.

163. Beebe, T.P. Jr.; Crowell, J. E.; Yates, J. T. Jr. *J. Phys. Chem.* **1988**, *92*, 1296.

164. Hondrogiannis, G.; Tan, L. C. Pagni, R. M.; Kabalka, G. W.; Herold, S.; Ross, E.; Green, J.; McGinnis, M. *Tetrahedron Lett.* **1994**, *35*, 6211.

165. Mitchell, M. A.; Benicewicz, B. C. *Synthesis* **1994**, 675.

166. Czech, B.; Quici, S.; Regen, S. L. *Synthesis* **1980**, 113. See also Singh, A.; Mehrotra, A.; Regen, S. L. *Synth. Commun.* **1981**, *11*, 409.

167. Tan, L. C.; Pagni, R. M.; Kabalka, G. W.; Hilmyer, M.; Woosley, J. *Tetrahedron Lett.* **1992**, *33*, 7709.

168. Pradhan, N. C.; Sharma, M. M. *Ind. Eng. Chem. Res.* **1992**, *31*, 1610.

169. (a) Gleiter, R.; Röckel, H.; Irngartinger, H.; Oeser, T. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1270. (b) Gleiter, R.; Ritten, J.; Irngartinger, H.; Lichtenthäler, J. *Tetrahedron Lett.* **1991**, *32*, 2883. (c) Gleiter, R.; Rittinger, S.; Langer, H. *Chem. Ber.* **1991**, *124*, 357.

170. (a) Nicolaou, K. C.; Zuccarello, G.; Riemer, C.; Estevez, V. A.; Dai, W. -M. *J. Am. Chem. Soc.* **1992**, *114*, 7360. (b) Nicolaou, K. C.; Skokatas, G.; Maligres, P.; Zuccarello, G.; Schweiger, E. J.; Toshima, K.; Wendeborn, S. *Ang. Chem. Int. Ed. Engl.* **1989**, *28*, 1272.

171. Kerwin, S. M. *Tetrahedron Lett.* **1994**, *35*, 1023.

172. Bodwell, G. J.; Houghton, T. J.; Koury, H. E.; Yarlagadda, B. *Synth. Lett.* **1995**, 751.

173. Ando, T.; Clark, J. H.; Cork, D. G.; Fujita, M.; Kimura, T. *J. Org. Chem.* **1987**, *52*, 681.

174. Villemin, D. *J. Chem. Soc., Chem. Commun.* **1985**, 870.

175. Villemin, D.; Ben Alloum, A. *Synth. Commun.* **1990**, *20*, 925.

176. Jigajnni, V. B.; Wightman, R. H.; Campbell, M. M. *J. Chem. Res. (S)* **1983**, 187; *J. Chem. Res. (M)* **1983**, 1801.

177. Liu, K.-T.; Tong, Y. C. *Synthesis* **1979**, 669.

178. Gleiter, R.; Röckel, H.; Nuber, B. *Tetrahedron Lett.* **1994**, *35*, 8779. See also reference 169c for other uses of Se^{-2}/Al_2O_3.

179. Clark, J. H.; Jones, C. N. *J. Chem. Res. (S)* **1990**, 39.
See also Quici, S.; Regen, S. L. *J. Org. Chem.* **1979**, *44*, 3436.

180. Tundo, D.; Venturello, P.; Angeletti, E. *J. Am. Chem. Soc.* **1982**, *104*, 6551.

181. Yamawaki, J.; Ando, T.; Hanafusa, T. *Chem. Lett.* **1981**, 1143.

182. Duc, N. H.; Hiep, N. B.; Hoa, L. T. N.; Son, C. P. N. *C. R. Acad. Sci., Paris, Ser. 2.* **1985**, *300*, 799.

183. Sukata, K. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 838.

184. Galons, H.; Bergerat, I.; Combet-Farnoux, C.; Micoque, M.; Decodts, G.; Bram, G. *J. Chem. Soc., Chem. Commun.* **1985**, 1730.

185. Abdulganeeva, S. A.; Erzhanov, K. B. *Zh. Org. Khim.* **1989**, *25*, 521.

186. Thangaraj, K.; Morgan, L. R. *Synth. Commun.* **1994**, *24*, 2063.

187. Mishani, E.; Dence, C. S.; McCarthy, T. J.; Welch, M. J. *Tetrahedron Lett.* **1996**, *37*, 319.

188. Regen, S. L.; Quici, S.; Liaw, S.-J. *J. Org. Chem.* **1979**, *44*, 2028.

189. Bram, G.; Fillebeen-Khan, T.; Geraghty, N. *Synth. Commun.* **1980**, *10*, 279.

190. Takahashi, K.; Nishizuka, T.; Iida, H. *Tetrahedron Lett.* **1981**, *25*, 2389.

191. Ruppert, J. F.; White, J. D. *J. Am. Chem. Soc.* **1981**, *103*, 1808.

192. Bhattacharjee, G.; Ghutak, O. R.; Charkravarty, A. K. *J. Chem Soc. Perkin 1* **1989**, 1515.

193. (a) Bram, G.; Fillebeen-Khan, T. *J. Chem. Soc., Chem. Commun.* **979**, 522. (b) Bram, G.; Geraghty, N.; Nee, G.; Seyden-Penne, J. *J. Chem. Soc., Chem. Commun.* **1980**, 325.

194. Ferroud, D.; Genet, J. P.; Muzart, I. *Tetrahedron Lett.* **1989**, *25*, 4379.

195. Diez-Barra, E.; de la Hoz, A.; Moreno, A.; Sánchez-Verdú, P. *Synthesis* **1989**, 391.

196. Bram, G.; Cabaret, D.; Welvart, Z.; Geraghty, N. W. A.; Garvey, J. *Tetrahedron Lett.* **1988**, *29*, 4615.

197. Ranu, B. C.; Bhar, S. *J. Chem. Soc. Perkin Trans. 1* **1992**, 365.

198. Villemin, D.; Ben Alloum, A.; Thibault-Starzyk, F. *Synth. Commun.* **1992**, *22*, 1359.

199. Hrubiec, R. T.; Smith, M. B. *J. Chem. Soc. Perkin 1* **1984**, 107.

200. Davies, J. W.; Malpass, J. R.; Walker, M. P. *J. Chem. Soc., Chem. Commun.* **1985**, 686.

201. Retro-aldol condensations also occur on alumina: Campelo J. M.; Garcia, A.; Luna, D.; Marinas, J. M. *Can. J. Chem.* **1984**, *62*, 638.

202. Clark, J. H. *Chem. Rev.* **1980**, *80*, 429.

203. Yamawaki, J.; Ando, T. *Chem. Lett.* **1979**, 755.

204. Weinstock, L. M.; Stevenson, J. M.; Tomellini, S. A.; Pan, S.-H.; Utne, T. *Tetrahedron Lett.* **1986**, *27*, 8345.

205. Ando, T.; Brown, S. J.; Clark, J. H.; Cork, D. G.; Hanafusa, T.; Ichihara, J.; Miller, J. M.; Robertson, M. S. *J. Chem. Soc. Perkin Trans. II* **1986**, 1133.

206. Ando, T.; Clark, J. H.; Cork, D. G. Kimura, T. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3281.

207. Clark, J. H.; Goodman, E. M.; Smith, D. K.; Brown, S. J.; Miller, J. M. *J. Chem. Soc., Chem. Commun.* **1986**, 657.

208. Ando, T.; Clark, J. H.; Cork, D. G.; Hanafusa, T.; Ichihara, J.; Kimura, T. *Tetrahedron Lett.* **1987**, *28*, 1421.

209. Duke, C. V. A.; Miller, J. M.; Clark, J. H.; Kybett, A. P. *J. Mol. Catal.* **1990**, *62*, 233.

210. Hanessian, S.; Kloss, J. *Tetrahedron Lett.* **1985**, *26*, 1261.

211. Villemin, D.; Martin, B. *Synth. Commun.* **1993**, *23*, 2259.

212. Bergbreiter, D. E.; Lalonde, J. J. *J. Org. Chem.* **1987**, *52*, 1661.

213. Kodomari, M.; Saitoh, G.; Yoshitomi, S. *Bull Chem. Soc. Jpn.* **1991**, *64*, 3485.

214. Texier-Boullet, F.; Villemin, D.; Richard M.; Moison, H.; Foucaud, A. *Tetrahedron* **1985**, *41*, 1259.

215. Dhavale, D. D.; Sindkhedkar, M. D.; Mali, R. S. *J. Chem. Res. (S)* **1995**, 414.

216. Yamawaki, J.; Kawate, T.; Ando, T.; Hanafusa, T. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1885.

217. Vit, Z.; Nondek, Malek, J. *Collec. Czech. Chem. Commun.* **1982**, *47*, 2235.

218. Muzart, J. *Synthesis*, **1982**, 60.

219. Texier-Boullet, F.; Foucaud, A. *Tetrahedron Lett.* **1982**, *23*, 4927.

220. Villemin, D. *Chem. Ind. (London)* **1983**, 478.

221. Rosini, G.; Ballini, R.; Sorrenti, P. *Synthesis* **1983**, 1014.

222. Rosini, G.; Ballini, R.; Sorrenti, P. *Tetrahedron* **1983**, *39*, 4127.

223. Roudier, J. F.; Foucaud, A. *Synthesis* **1984**, 159.

224. Barot, B. C.; Sullins, D. W.; Eisenbraum, E. J. *Synth.Commun.* **1984**, *14*, 397.

225. Muzart, J. *Synth. Commun.* **1985**, *15*, 285.

226. Varma, R. S.; Kabalka, G. W.; Evans, L. T.; Pagni, R. M. *Synth. Commun.* **1985**, *15*, 279.

227. Rosini, G.; Ballini, R.; Petrini, M.; Sorrenti, P. *Synthesis* **1985**, 515.

228. Villemin, D.; Ricard, M. *Synth. Commun.* **1987**, *17*, 283.

229. Kover, W. B.; Junior, J. J.; deAguiar, A. P.; Von Holleben, M. L. A. *Tetrahedron* **1987**, *43*, 3199.

230. Villemin, D.; Labiad, B. *Synth. Commun.* **1990**, *20*, 3207.

231. Varma, R. S.; Varma, M. *Tetrahedron Lett.* **1992**, *33*, 5938.

232. Beck, A. K.; Seebach, D. *Chem. Ber.* **1991**, *124*, 2897.

233. Ranu, B. C.; Chakraborty, R. *Tetrahedron* **1993**, *49*, 5333.

234. Bell, V. A.; Gold, H. S. *J. Cat.* **1983**, *79*, 286.

235. Bell, V. A.; Carver, R. F.; Dybowski, C.; Gold, H. S. *J. Chem. Soc., Faraday Trans I* **1984**, *80*, 831.

236. Biaglow, A. I.; Gorte, R. J.; White, D. *J. Catal.* **1994**, *150*, 221.

237. Cooke, G.; Schulz, O. *Synth. Commun.* **1996**, *26*, 2549.

238. Villemin, Didier *J. Chem. Soc., Chem. Commun.* **1983**, 1092.

239. Villemin, D.; Ricard, M. *Tetrahedron Lett.* **1984**, *25*, 1059.

240. Villemin, D.; *Chem. Ind. (London)* **1985**, 166.

241. Mélot, J.-M.; Texier-Boullet, F.; Foucaud, A. *Tetrahedron Lett.* **1986**, *27*, 493.

242. Gulyukina, N. S.; Medocks, S. A. Tarasevich, B. N.; Novoselova, M. A.; Kashin, A. N.; Beletskaya, I. P.; Reutor, O. A. *Bull. Acad. Sci. USSR Chem. Ser.* **1986**, *35*, 1869.

243. Ben Alloum, A.; Labiad, B.; Villemin, D. *J. Chem. Soc., Chem. Commun.* **1989**, 386.

244. Villemin, D.; Ben Alloum, A. *Synth. Commun.* **1990**, *20*, 3325.

245. Latouche, R.; Texier-Boullet, F.; Hamelin, J. *Tetrahedron Lett.* **1991**, *32*, 1179.

246. Villemin, D.; Ben Alloum, A. *Synth. Commun.* **1991**, *21*, 63.

247. Villemin, D.; Thibautt-Starzyk, F.; Esprimont, E. *Phosphorus, Sulfur and Silicon* **1992**, *70*, 117.

248. Latouche, R.; Texier-Boullet, F.; Hamelin, J. *Bull. Chem. Soc. Fr.* **1993**, *120*, 535.

249. Villemin, D.; Ben Allouim, A. *Phosphorus, Sulfur and Silicon* **1993**, *79*, 33.

250. Villemin, D.; Martin, B.; Garrigues, B. *Synth. Commun.* **1993**, *23*, 2251.

251. Hellwinkel, D.; Göke, K.; Karle, R. *Synthesis* **1994**, 973.

252. Hellwinkel, D.; Göke, D. *Synthesis* **1995**, 1135.

253. Lu, W.-X.; Yan, C.-G.; Yao, R. *Synth. Commun.* **1996**, *26*, 3719.

254. Texier-Boullet, F.; Foucaud, A. *Synthesis* **1982**, 916.

255. Villemin, D.; Racha, R. *Tetrahedron Lett.* **1986**, *27*, 1789.

256. Texier-Boullet, F.; Lequitte, M. *Tetrahedron Lett.* **1986**, *27*, 3515.

257. Rosini, G.; Marotta, E.; Ballini, R.; Petrini, M. *Synthesis* **1986**, 237

258. Ballini, R.; Petrini, M. *Synthetis,* **1986**, 1024.

259. Rosini, G.; Ballini, R.; Petrini, M.; Marotta, E. *Angew Chem. Int. Ed. Engl.* **1986**, *25*, 941.

260. Ballini, R.; Petrini, M.; Marcontoni, E.; Rosini, G. *Synthesis*, **1988**, 231.

261. Ranu, B. C.; Bhar, S.; Sarkar, D. C. *Tetrahedron Lett.* **1991**, *32*, 2811.

262. Ranu, B. C.; Bhar, S.; *Tetrahedron* **1992**, *48*, 1327.

263. Nakano, Y. Niki, S.; Kinouchi, S.; Miyamae, H.; Igarashi, M. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2934.

264. Clark, J. H. ; Cork, D. G.; Robertson, M. S. *Chem. Lett.* **1983**, 1145.

265. Clark, J. H.; Goodall, D. M.; White, M. S.; *Tetrahedron Lett.* **1983**, *24*, 1097.

266. Clark, J. H.; Cork, D. G.; Gibbs, H. W. *J. Chem. Soc., Perkin I* **1983**, 2253.

267. Laszlo, P.; Pennetreau, P. *Tetrahedron Lett.* **1985**, *26*, 2645.

268. Joucla, M.; LeBrun, J. *Tetrahedron Lett.* **1985**, *26*, 3001.

269. Kaluz, S.; Toma, S. *Collec. Czech. Chem. Commun.* **1986**, *51*, 2199.

270. Mélot, J.-M.; Texier-Boullet, F.; Foucaud, A. *Synthesis* **1987**, 364.

271. Mélot, J.-M.; Texier-Boullet, F.; Foucaud, A. *Tetrahedron 1988*, *44*, 2215.

272. Rao, A. K. S. B.; Rao, G. C.; Singh, B. B. *Synth. Commun.* **1991**, *21*, 443.

273. Caine, P.; Smith, T. L. Jr. *J. Am. Chem. Soc.* **1980**, *102*, 7568.

274. Kan-Fan, G.; Husson, H.-P. *Tetrahedron Lett.* **1980**, *21*, 1463.

275. Varma, R. S.; Kabalka, G. W. *Heterocycles*, **1985**, *23*, 139.

276. Pelletier, S. W.; Venkov, A. P.; Finer-Moore, J.; Mody, N. V. *Tetrahedron Lett.* **1980**, *21*, 809.

277. Hasegawa, M.; Takabatake, T. *Synthesis* **1985**, 938

278. Scott, F.; van Heerden, F. R.; Raubenheimer, H. G. *J. Chem. Res. (S)* **1994**, 144.

279. Thorat, T. S.; Yadav, V. M.; Yadav, G. D. *Appl. Cat. A.* **1992**, *90*, 73.

280. Chihara, T. *J. Chem. Soc.,Chem.Commun.* **1980**, 1215.

281. Ogawa, H.; Chihara, T.; Taya, K. *J. Chem. Soc., Chem. Comm.* **1985**, *107*, 1365.

282. Ogawa, H.; Chihara, T.; Teratani, *S.;* Taya, K. *J. Chem. Soc., Chem Comm.* **1986**, 1337.

283. Ogawa, H; Hiraga, N.; Chihara, T.; Teratani, S.; Taya, K. *Bull. Chem. Soc. Jpn.* **1988**. *61*, 2383.

284. Ogawa, H. *J. Phys. Org. Chem.* **1991**, *4*, 346.

285. Regen, S. L.; Mehrotra, A. K. *Synth. Commun.* **1981**, *11*, 413.

286. Kamata, S.; Higo, M.; Hida, A. *Chem. Lett.* **1993**, 181.

287. Kamata, S.; Hida, A.; Higo, M.; Inadome, H. *J. Phys. Chem.* **1994**, *98*, 1648.

288. Muzart, J.; Genêt, J.-P.; Denis, A. *J. Organomet. Chem.* **1987**, *326*, C23.

289. Posner, G. H.; Okada, S. S.; Babiak, K. A.; Miura, K.; Rose, R. K. *Synthesis* **1981**, 789.

290. Posner, G. H.; Oda, M. *Tetrahedron Lett.* **1981**, *22*, 5003.

291. Bains, S.; Green, J.; Tan, L. C.; Pagni, R. M.; Kabalka, G. W. *Tetrahedron Lett.* **1992**, *33*, 7475.

292. Posner, G. H.; Ellis, J. W.; Ponton, J *J. Fluorine Chem.* **1981**, *19*, 191.

293. Villemin, D.; Hachemi, M.; Laloui, M. *Synth. Commun.* **1996**, *26*, 2461.

294. Ando, T.; Kawata, T.; Yamawaki, J. *Synthesis* **1983**, 637.

295. Nagasawa, K.; Yoshitake, S.; T.; Amiya, T.; Ito, K. *Synth. Commun.* **1990**, *20*, 2033.

296. Nagasawa, K.; Ohhashi, K.; Yamashita, A.; Ito, K. *Chem. Lett.* **1994**, 209.

297. Rao, C. G. *Synth. Commun.* **1982**, 12, 177.

298. Pala Wilgus, C.; Downing, S.; Molitor, E.; Bains, S.; Pagni, R. M.; Kabalka, G. W. *Tetrahedron Lett.* **1995, *36*,** 3469.

299. Kocovsky, P. *Tetrahedron Lett.* **1986**, *27*, 5521.

300. Reitz, A.; Verlander, M.; Goodman, M. *Tetrahedron Lett.* **1982**, *23*, 751.

301. Suzukamo, G.; Fukao, M.; Minobe, M. *Chem. Lett.* **1987**, 585.

302. Buba, T.; Handa, H.; Ono, Y. *Faraday Trans* **1994**, *90*, 187.

303. Radhakrishna, A. S.; Suri, S. K.; Prasad Rao, K.R.K.; Singh, B. B. *Synth. Commun.* **1990**, *20*, 345.

304. McMurray, J.E.; Domain, S. F. *Tetrahedron Lett.* **1977**, *18*, 2869.

305. Tsuboi, S.; Masuda, T.; Makino, H.; Takeda, A. *Tetrahedron Lett.* **1982**, *23*, 209.

306. Tsuboi, S.; Masuda, T.; Takeda, A. *J. Org. Chem.* **1982**, *47*, 4478.

307. Tsuboi, S.; Masuda, T.; Takeda, A. J. *Chem. Lett.* **1983**, 1829.

308. Tsuboi, S.; Masuda, T.; Takeda, A. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3521.

309. Gras, J.-L.; Guérin, A. *Tetrahedron Lett.* **1985**, *26*, 1781.

310. Porter, N. A.; Hogenkamp, D. J.; Khouri, F. F. *J. Am. Chem. Soc.* **1990**, *112*, 2402.

311. Bonin, M.; Romero, J. R.; Grierson, D. S.; Husson, H.-P. *J. Org. Chem.* **1984**, *49*, 2392.

312. Yamamura, S.; Niwa, M.; Itu, M.; Saito, Y. *Chem. Lett.* **1982**, 1681.

313. Tanis, S. P.; Herrinton, P. M. *J. Org. Chem* **1993**, *48*, 4572.

314. Dunstan, T. D. J.; Pincock, R. E. *J. Org. Chem.*, **1985**, *50*, 863.

315. Ozawa, S.; Nakatami, J.; Sato, M.; Ogino, *Y. Bull. Chem. Soc. Jpn.* **1987**, *60*, 4273.

316. Arata, K.; Matsuuran, C. *Chem. Lett.* **1989**, 1797.

317. Tietze, L. F.; Beifuss, O.; Antel, J.; Sheldrick, G. M. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 359.

318. Tietze, L. F. Beifuss, V. *Synthesis*, **1988**, 359.

319. Tietze, L. F.; Ruther, M. *Chem. Ber.* **1990**, *123*, 1387.

320. Yeats, R. B. *Tetrahedron Lett.* **1983**, *24*, 3423.

321. Ganesan, K.; Pillai, C. N. *Tetrahedron*, **1989**, *45*, 877.

322. Lassila, K. R.; Ford, M. E. *Chem. Ind. (London)* **1992**, *47*, 169.

323. See for example, Curtin, T.; McMonagle, J. B. Hodnett, B. K. *Appl. Catal.* **1992**, *93*, 75.

324. Nitta, Y. ; Yamaguchi, T. Tanaka, T. *Heterocycles*, **1986**, *24*, 25.

325. Dressel, J.;Chasey, K. L.; Paquette, L. A. *J. Am. Chem. Soc.* **1988**, *110*, 5479.

326. Grunwell, J. R.; Wempe, M. F.; Mitchell, J.; Grunwell, J. R. *Tetrahedron Lett.* **1993**, *34*, 7163.

327. Nakadaira, Y.; Nomura, T.; Kanouchi, S.; Sato, R.; Kabuta, C.; Sakurai, H. *Chem. Lett.* **1983**, 209.

328. Wadsworth, D. H.; Donatelli, B. A. *Synthesis* **1981**, 285.

329. Lutz, R. P.; Berg, H. A. J.; Wang, P. J. *J. Org. Chem.* **1976**, *41*, 2048.

330. Pogrebnoi, S. I.; Kalyan, Y. B.; Krimer, M. Z.; Smit, V. A. *Tetrahedron Lett.* **1987**, *28*, 4893.

331. Smith, V. A.; Pognebnoi, S. I.; Kalyan, Y. B.; Krimer, M. Z. *Izv. Akad. Nauk SSR, Ser. Khim.*, **1987**, 959.

332. Pogrebnoi, S. K.; Kalyan, Y. B.; Krimer, M. Z.; Smit, V. A. *Izv. Akad. Nauk SSR, Ser. Khim.*, **1991**, 835.

333. Villemin, D.; Ben Alloum, A. *Synth. Commun.* **1992**, *22*, 1351.

334. See also Villemin, D.; Hachemi, M. *Synth. Commun.* **1996**, *26*, 2449.

335. Villemin, D. Hachemi, M. *Synth. Commun.* **1995**, *25*, 2311.

336. Villemin, D. Hachemi, M. *Synth. Commun.* **1995**, *25* , 2305.

337. Alonso, M. E.; Morales, A. *J. Org. Chem.* **1980**, *45*, 4532.

338. Novak, L.; Szantay, C.; Meisel, T.; Aszodi, J. Szabo, E.; Fekete, J. *Tetrahedron* **1985**, *41*, 433.

339. Borodkin, G. I.; Nagi, S. M.; Shakirov, M. M.; Shubin, V. G. *Izv. Akad. Nauk SSR, Ser. Khim.*, **1989**, 133.

340. Victory, P.; Borrell, J. I.; Batllori, X.; Teixidó, J.; Civit, P; Alvarez-Larena, A. *Chem. Lett.* **1993**, 705.

341. Touaux, G.; Klein, B.; Texier-Boullet, F.; Hamelin, J. *J. Chem. Res. (S)* **1994**, 116.

342. Beletskaya, I.P.; Malkhasyan, A. T.; Nazaryan, E. M. Martirosyan, G. T. *Zh, Org. Khim.* **1982**, *18*, 1129.

343. Butler, D. N.; Gupta, I. *Can. J. Chem.* **1982**, *60*, 415.

344. Miki, S.; Marayama, T.; Ohno, T.; Tohma, T.; Toyamae, S. -I.; Yoshida, Z.-I. *Chem. Lett.* **1988**, 861.

345. Parlar, H.; Baumann, R. *Angew. Chem. Int. Ed. Eng.* **1981**, *20*, 1014.

346. Koreeda, M.; Ricca, D.; Luengo, J. I. *J. Org. Chem.* **1988**, *53*, 5586.

347. Hondrogiannis, G.; Pagni, R. M.; Kabalka, G. W.; Anosike, P.; Kurt, R. *Tetrahedron Lett.* **1990**, *31*, 5433.

348. Hondrogiannis, G.; Pagni, R. M.; Kabalka, G. W.; Kurt, R.; Cox, D. *Tetrahedron Lett.* **1991**, *32*, 2303.

349. Kabalka, G. W.; Pagni, R. M.; Bains, S.; Hondrogiannis, G.; Plesco, M.; Kurt, R.; Cox, D.; Green, J. *Tetrahedron: Asymmetry* **1991**, *2*,1283.

350. Bains, S.; Pagni, R. M.; Kabalka, G. W. *Tetrahedron Lett.* **1991**, *32*, 5663.

351. Bains, S. Pagni, R. M. Kabalka, G. W. Pala, C. *Tetrahedron Asymmetry*, **1994**, *5*, 821.

352. Fraile, J. M.; Garćia, J. I.; Mayoral, J. A.; Royo, A. J. *Tetrahedron Asymmetry* **1996**, *7*, 2263.

353. Cativiela C.; Fraile, J. M.; García, J. I.; Mayoral, J. A; Pires, E.; Royo A. J. *Tetrahedron* **1993**, *49*, 4073.

354. Cativiela, C.; García, J. I.; Mayoral, J. A.; Pires, S. E.; Royo, A. J. *Tetrahedron*, **1995**, *131*, 159.

355. Cativiela, C.; García, J. I.; Mayoral, J. A.; Pires, S. E.; Royo, A. J. *Tetrahedron*, **1995**, *51*, 1295.

356. Fraile, J. M.; García, J. I.; Mayoral, J. A.; Pires, E.; Tarnai, T.; Figuera, F. *Appl. Cat. A.* **1996**, *136*, 113.

357. McGinnis, M. B.; Vagle, K.; Green, J. F.; Tan, L. C.; Palmer, R.; Siler.; Pagni, R. M.; Kabalka, G. W. *J. Org. Chem.*, **1995**, *61*, 3496.

358. Itsuno, S.; Kamahori, K.; Watanabe, K.; Koizumi, T.; Ito, K. *Tetrahedron: Asymmetry* **1994**, *5*, 523.

359. Kamitori, Y.; Hojo, M.; Masuda, R.; Yoshida, T. *Tetrahedron Lett.1985*, 26, 4767.

360. Ranu, B.; Majee, A.; Das, A. R. *Synth. Commun.* **1995**, *25*, 363.

361. Ranu, B. C.; Saha, M. *J.Org. Chem.* **1994**, *59*, 8269.

362. Varma, R. S.; Varma, R. S.; Chatterjee, A. K.; *J. Chem. Soc. Perkin Trans 1* **1993**, 999

363. Schmittling, E. Q.; Sawyer, J. S. *Tetrahedron Lett.* **1991**, *32*, 7207.

364. Radhakrishna, A. S.; Rao, K. R. K. P.; Suri, S. K.; Sivaprakash, K.; Singh, B. B. *Synth. Commun.* **1991**, *21*, 379.

365. Ley, S. V.; Mynett, D. M. *Synlett* **1993**, 793.

366. Varma, R. S.; Chatterjee, A. K.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 3207.

367. Varma, R. S.; Chatterjee, A. K.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 4603.

368. Feixas, J.; Capdevila, A.; Camps, F.; Guerrero, A. *J. Chem.Soc., Chem. Commun.* **1992**, 451.

369. Varma, R. S.; Lamture, J. B.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 3029.

370. Feixas, J.; Capdevila, A.; Guerrero A. *Tetrahedron Lett.* **1994**, *50*, 8539.

371. Ceccherilli, P.; Curini, M.; Marcotullio, M. C.; Epifano, F.; Rosati, O. *Synth. Lett.* **1996**, 767.

372. Floor, M.; Kieboom, A. P. G.; van Bekkum, H. *Recl. Trav. Chim. Days-Bas* **1988**, *107*, 362.

373. Breton, G. W.; Fields, J. D.; Kropp, P. J. *Tetrahedron Lett.* **1995**, *36*, 3825.

374. (a)Yadav, V. K.; Kapoor, K. K. *Tetrahedron* **1996**, *52*, 3659; (b) Fraile, J. M.; García, J. Mayoral, J. A.; Figueras, F. *Tetrahedron Lett.* **1996**, *37*, 5995.

375. Sawicki, R. A. *Tetrahedron Lett.* **1982**, *23*, 2249.

376. Foucaud, A.; leRouille, E. *Synthesis* **1990**, 787.

377. Foucaud, A.; Bakouetila, M. *Synthesis* **1987**, 854.

378. Corey, E. J.; Lin, S. *J. Am. Chem. Soc.* **1996**, *118*, 8765.

379. Cheng, Y.-S.; Liu, W.-L.; Chen, S. *Synthesis* **1980**, 223.

380. Savoia, D.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1982**, *47*, 564.

381. Carlsen, P. H. J.; Husbyn, M.; Braeden, J. E.; Eliason, R. *Acta Chem. Scand.* **1989**, *43*, 485.

382. Hirano, M.; Kobayashi, T.; Morimoto, T. *Synth. Commun.* **1994**, *24*, 1823.

383. Vu, M. T. *Bull. Soc. Chim. Belg* **1993**, *102*, 299.

384. Clark, J. H.; Kybett, A. P.; Landon, P.; Macquarrie, D. J.; Martin, K. J. *Chem. Soc., Chem. Commun.* **1989**, 1355.

385. Clark, J. H.; Landon, P.; Barlow, S. J.; Duke, C. V. A.; Martin, K. *Chem. Ind. (London)* **1991**, 800.

386. Lee, D. G.; Chem, T.; Wang, Z. *J. Org. Chem.* **1993**, *58*, 2918.

387. Zhao, D.; Lee, D. G. *Synthesis* **1994**, 915.

388. Villemin, D.; Ricard, M. *Nouv. J. Chim.* **1982**, *6*, 605.

389. Villemin, D.; Ricard, M. *Nouv. J. Chim.* **1984**, *8*, 185.

390. Kim, K. S.; Song, Y. H.; Lee, N. H.; Hah, C. S. *Tetrahedron Lett.* **1986**, *27*, 2875.

391. Delaude, L.; Laszlo, P. *J. Org. Chem.* **1996**, *61*, 6360.

392. Sakamoto, T.; Yonehara, H.; Pac, C. *J. Org. Chem.* **1994**, *59*, 6859.

393. Sterner, O.; Steglich, W. *Liebigs Ann. Chem.* **1988**, 823.

394. Villemin, D.; Ben Alloum, A. *Synth. Commun.* **1992**, *22*, 3169.

395. Hirano, M.; Oose, M.; Morimoto, T. *Chem. Lett.* **1991**, 331.

396. Rienacker, R.; Graefe, J. *Angew. Chem. Int. Ed.Engl.* **1985**, *24*, 320.

397. Savoia, D.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1980** *45*, 3227.

398. Singh, S.; Dev, S. *Tetrahedron* **1993**, *49*, 10959.

399. Fürstner, A.; Seidel, G. *Synthesis* **1995**, 63.

400. Kamitori, Y.; Hojo, M.; Masuda, R.; Yamamoto, M. *Chem. Lett.* **1985**, 253.

401. Ando, T.; Clark, J. H.; Cork, D. G.; Kimura, T. *Chem. Lett.* **1987**, 1315.

402. Hodosan, F.; Servan, N. *Rev. Roumaine Chim.* **1969**, *14*, 121.

403. Santaniello, E.; Farachi, C.; Manzocchi, R. *Synthesis* **1970**, 912.

404. Santaniello, E.; Ponti, F.; Manzocchi, A. *Synthesis* **1978**, 891.

405. Kim, B.; Regen, S. L. *Tetrahedron Lett.* **1983**, *24*, 689.

406. Still, I. W. J.; Ablenas, F. J. *J. Org. Chem.* **1983**, *48*, 1617.

407. Babler, J. H.; Sarussi, S. *J. Org. Chem.* **1983**, *48*, 4419.

408. Alper, H.; Ripley, S.; Prince, T. L. *J. Org. Chem.* **1983**, *48*, 250.

409. Creegan, K. M.; Robbins, J. L.; Robbins, W. K.; Millar, J. M.; Sherwood, R. D.; Tindall, P. J.; Cox, D. M.; Smith, A. B. III; McCauley, J. P. Jr.; Jones, D. R.; Gallagher, R. T. *J. Am. Chem. Soc.* **1992**, *114*, 1103.

410. Verdaguer, X.; Bark, S. C.; Buchwald, S. L. *J. Am. Chem. Soc.* **1995**, *117*, 12641.

411. Hasebe, M.; Lazare, C.; de Mayo, P.; Weedon, A. C. *Tetrahedron Lett.* **1981**, *22*, 5149.

412. Farwaha, R.; de Mayo, P.; Schauble, J. H.; Toong, Y. C. *J. Org. Chem.* **1985**, *50*, 149.

413. Slayton, R. M.; Franklin, N. R.; Tro, N. J. *J. Phys. Chem.* **1996**, *100*, 15551.

414. Homs, N.; Ramirez de la Piscina, P.; Burrull, F. *J. Chem. Soc., Chem. Commun.* **1988**, 1067.

415. Aronovitch, C.; Mazur, Y. *J. Org. Chem.* **1985**, *50*, 149.

416. Barbas, J. T.; Sigman, M. E.; Buchanan, A. C. III; Chevis, E. A. *Photochem. Photobiol* **1993**, *58*, 155.

417. Dabestani, R.; Ellis, K. J.; Sigman, M. E.; Buchanan, A. C. III; Chevis, E. A. *J. Photochem. Photobiol. A.* **1995**, *86*, 231.

418. Pellizzetti, E.; Minero, C.; Carlin, V. *New J. Chem.* **1993**, *17*, 315.

419. Shinoda, K.; Yasuda, K. *Chem. Lett.* **1981**, 1243.

420. Hinkamp, L.; Schäfer, H. J.; Wippich, B.; Luftmann, H. *Ann. Chem.* **1992**, 559.

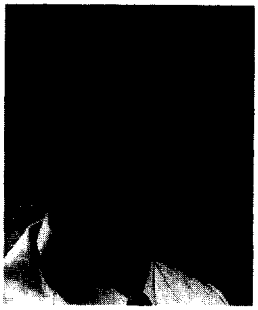
421. Guillemin, J. C.; Denis, J. M. *Synthesis* **1985**, 1131.

422. Ben Alloum, A.; Villemin, D. *Synth. Commun.* **1989**, *19*, 2567.

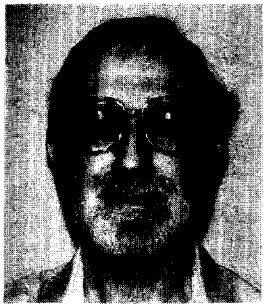
423. Dhavale, D. D.; Patril, P. N.; Mali, R. S. *J. Chem. Res.(S)* **1994**, 152.

(*Received* 19 *January* 1997)

Biographical Sketch



George W. Kabalka



Richard Pagni

George W. Kabalka, a native of Detroit, received a B. S. with Honors in chemistry from the University of Michigan and a Ph.D. from Purdue University under Nobel Laureate H. C. Brown. He joined the Chemistry Department at The University of Tennessee in 1970 and continues to serve as Alumni Distinguished Service Professor in Chemistry. He was appointed Professor and Director of Basic Research at The University of Tennessee Biomedical Imaging Medical Center in 1984 where he also serves as the Robert H. Cole Professor in the Department of Radiology in the Graduate School of Medicine. He is a Consultant to Oak Ridge National Laboratory (Chemistry Division and Medical and Health Sciences Division). He is a member of the Advisory Boards of the International Isotope Society, the International Society for Neutron Capture Therapy, the U. S. A. Boron Research Group and The University of Tennessee Biomedical Imaging Center. He has served on the Advisory Boards of the National Tritium Facility at Lawrence Laboratories, the National Stable Isotope Resource at Los Alamos National Laboratory, and the Society of Nuclear Medicine's Radiopharmaceutical Council. His research interests are focused on the creation of new synthetic pathways which can be utilized for the preparation of physiologically active agents. He enjoys reading, golf and boating.

Richard Pagni, a native of Chicago, received a B.A. degree from Northwestern University and a Ph.D. degree from the University of Wisconsin where he was one of the first chemists to study the di-π-methane rearrangement. After a fifteen month stay at Columbia University as an NIH postdoctoral fellow where he worked on anti-aromaticity, he joined the University of Tennessee where he is Professor of Chemistry. He has also worked part-time at the Oak Ridge National Laboratory. He has worked on a variety of mechanistic and physical organic problems related to reactive intermediates, superacids, molten salts, photochemistry and surface organic chemistry. He enjoys reading, traveling, classical music, and hiking, particularly in the Great Smoky Mountains National Park.