Acyl anion synthons: benzotriazole stabilized compared to classical

Alan R. Katritzky*and Kostyantyn Kirichenko

Center for Heterocyclic Compounds, University of Florida, Department of Chemistry, Gainesville, Florida 32611-7200, USA
E-mail: Katritzky@chem.ufl.edu

Dedicated to Professor Armand Lattes to celebrate his 50 years of great research and teaching activity

Contents

1. Introduction

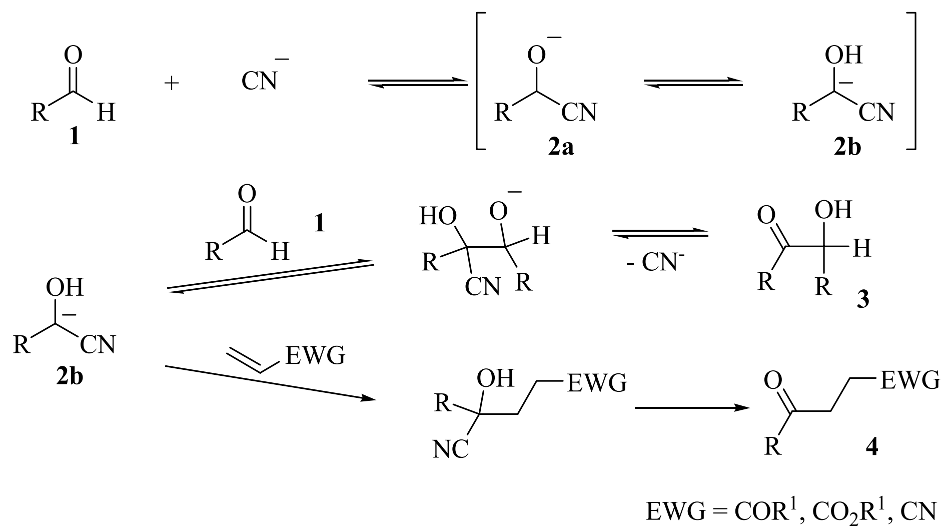
Increasing need for new methods to construct complex molecules, especially natural products with a variety of functionalities, promoted the development of strategies utilizing temporary reversal ("umpolung") of the reactivity of functional groups. This important concept was first introduced in 1962–1965 by Froling and Arens,[1] Truce and Roberts,[2] and Seebach and Corey[3,4] in their applications of thioacetals to the synthesis of carbonyl compounds.[5-7]

The account provides a brief survey on applications of important classical acyl anion synthons to illustrate the advantages and limitations of the major methods available and then attempts to assess the utility of the diverse benzotriazole-stabilized acyl anion synthons, developed by our research group over the last 15 years. The benzotriazole moiety, which can be introduced easily to a molecule, possesses several properties that are relevant to an acyl anion synthon: especially regioselective stabilization of an α-carbanion and ease of removal in the final stage.[8] The methodology has been applied to the synthesis of a large variety of simple and functionalized alkenyl, alkynyl, aryl/heteroaryl, and alkyl ketones plus alkenoyl-, alkynoyl-, aroyl-, and heteroaroylsilanes.

2. Classical acyl anion synthons

2.1. Cyanohydrins

The venerable cyanide ion catalyzed dimerization of aromatic and heterocyclic aldehydes **1** to benzoins **3** by formation of key intermediates **2b**, which are nitrile-stabilized acyl anion synthons (Scheme 1).

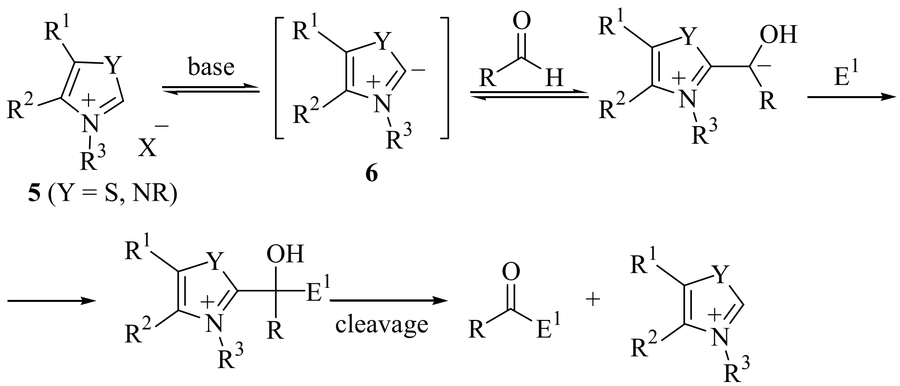


Scheme 1

Carbanions of type **2b** add to double bonds by Michael type addition to give 1,4-diketones, 4-ketonitriles, and 4-ketoesters of general structure **4** (Scheme 1).[9-11]

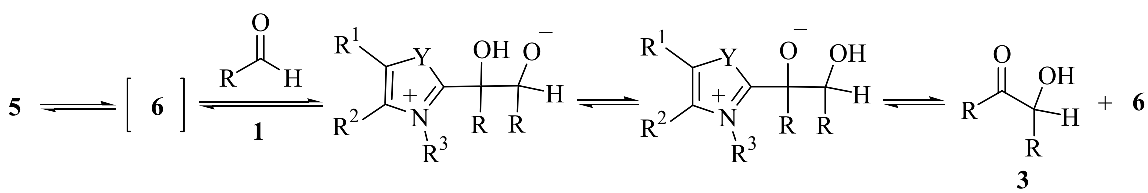
2.2. Azolium stabilized acyl synthons

It is known that vitamin B[1] (thiamine) converts aliphatic aldehydes to acyloins. The catalytic activity is associated with thiazolium part **5** (Y = S) of the vitamin (Scheme 2).[12-16]



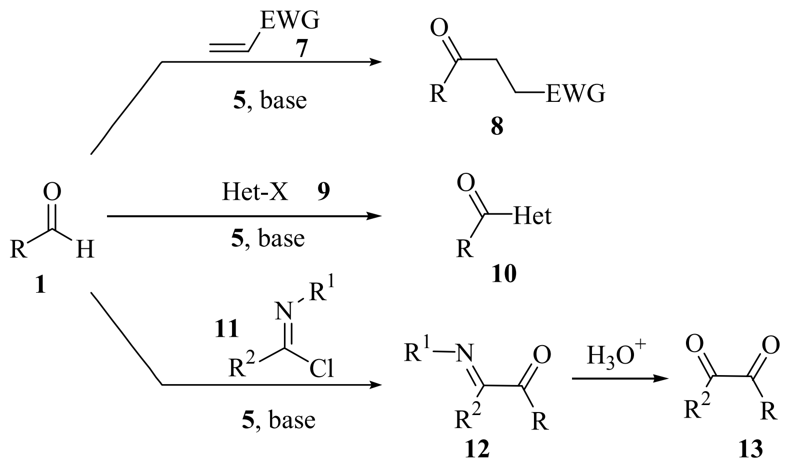
Scheme 2

Thiazolium and other azolium salts of structure **5**, including imidazolium and benzimidazolium, were successfully employed as catalysts in benzoin – acyloin condensations of aliphatic and aromatic aldehydes **1** (Scheme 3).[17]



Scheme 3

Addition of aldehydes **1** to α,β-unsaturated ketones, esters and nitriles of structure **7** (Scheme 4)[9,11] and similar addition of acylsilanes to α,β-unsaturated ketones and esters[18] in the presence of **5** provide access to carbonyl derivatives **8**. Azolium **5** catalyzed syntheses of heteroaromatic ketones **10** and ketimines **12** (and subsequently 1,2-diketones **13**) by the reaction of aldehydes **1** with heteroaryl halides **9**[19] and imidoyl chlorides **11**,[20] respectively, have also been reported.

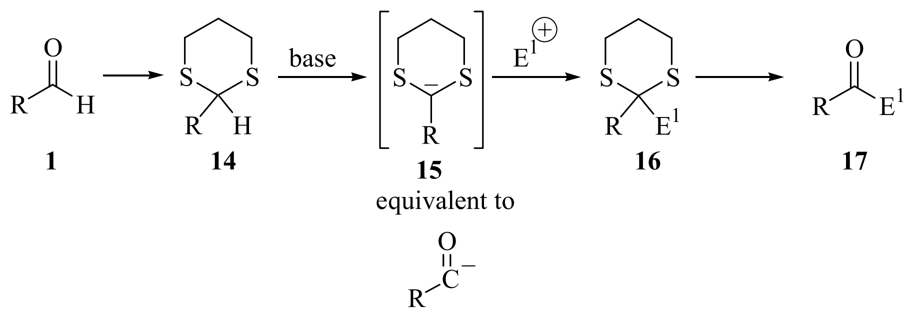


Scheme 4

2.3. Thioacetals[21]

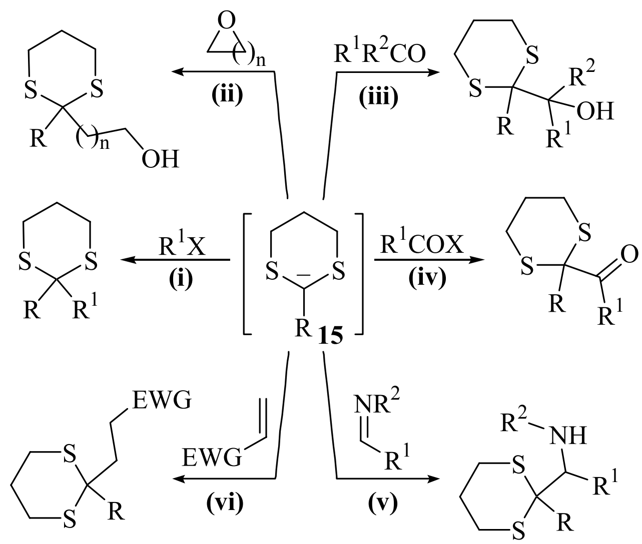
1,3-Dithianes

The nucleophilic acylation by reaction of carbanions **15**, derived from 1,3-dithianes **14**, with electrophiles followed by hydrolysis of the intermediates **16** forming a carbonyl compound **17** is still the most widely used *umpolung* method (Scheme 5).[7,22]



Scheme 5

1,3-Dithianes have been successfully used in reactions with (i) alkyl halides, sulfonates and triflates;[23-28] (ii) oxiranes[23,29-31] and three- to six-membered cyclic ethers;[29] (iii) carbonyl compounds;[23,32,33] (iv) acid halides[34,35] and chloroformates;[29,36,37] (v) imines;[23] and (vi) electron deficient olefins[38-40] (Scheme 6).

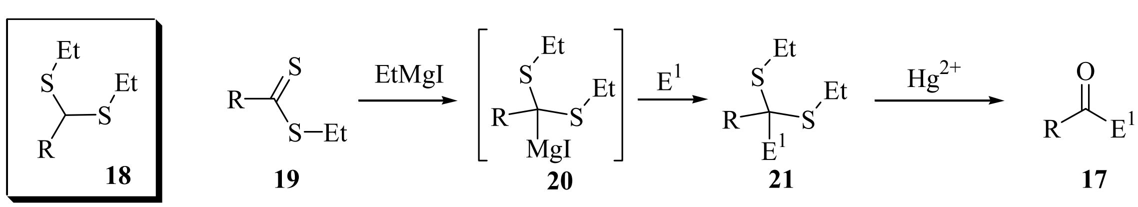


Scheme 6

Unfortunately, the hydrolysis of 1,3-dithianes under mild conditions has proved difficult. High yields of carbonyl compounds were reported in the presence of mercury (II),[25-27,31,38] in few cases with copper (II) ions,[32] or by oxidation (see later).

Bis(alkylthio)acetals

Alkylation of bis(alkylthio)acetals **18** (Scheme 7) using an alkali metal amide followed by reaction with electrophiles occurs in low yields.[1] However, an alternative approach involving initial addition of a Grignard reagent to a dithioester **19** followed by reaction of anion **20** with an electrophile (ketones, aldehydes and chloroformates) is a useful synthetic method. Thus α-hydroxy ketones and α-ketoesters were obtained in good yield but required mercuric ion promoted hydrolysis of thioketals **21**.[41]

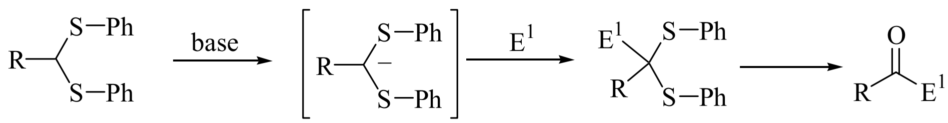


Scheme 7

Bis(arylthio)acetals

The use of bis(phenylthio) acetals **22** rather than bis(alkylthio) acetals **18** results in increased anion **23** stabilization (Scheme 8). Initial studies employed alkali metal amides in liquid ammonia and showed satisfactory results only with alkyl halides.[1] Later, alternative procedures using lithiation of **22** with butyllithium in the presence of TMEDA[42,43] and a copper derivative of

23[44] were introduced. Anions **23** were successfully reacted with alkyl halides,[2,43,45] aldehydes and ketones,[42,43,46,47] acid chlorides,[42] and electron deficient olefins.[44,48,49] However, butyllithium caused carbon – sulfur bond cleavage.[43,50] Similarly with thioketals **16** and **21**, hydrolysis of **24** to ketones **17** requires heavy metal catalysis (Hg^{2+}, Cu^{2+}, Ga^{3+}).[44,45,51] Hydrolysis intermediates **21** with TFA was also reported, but caused in some cases elimination of phenylthio group instead to give a vinyl sulfide.[42]

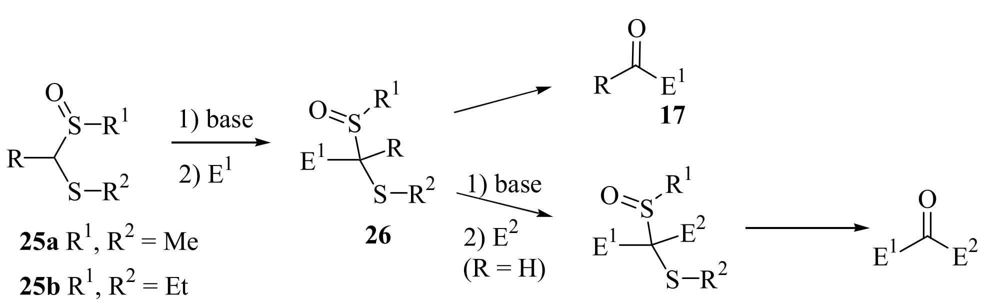


Scheme 8

Oxidized thioacetals

Oxidation of a dithioacetal sulfur atom facilitates generation of a carbanion. Methyl methylthiomethyl sulfoxide **25a**, ethyl ethylthiomethyl sulfoxide **25b** and 1,3-dithiane-1-oxide **25c** have been employed as acyl anion equivalents for the preparation of ketones (Scheme 9). Acyl anion synthon **25a** (R = H) was used for the preparation of symmetrical[52,53] and cyclic[54,55] ketones by reaction with excess base (NaH, KH) and an alkyl halide or a dihaloalkane, respectively. The preparation of α-hydroxyketones has been achieved by the reaction of **25a** (R = alkyl) with LDA and aldehydes.[56] Reagent **25b** (R = H) enabled the preparation of unsymmetrical ketones **28** *via* sequential alkylation with a base (BuLi or LDA) and an alkyl halide.[57] In the reactions with α,β-unsaturated ketones and esters, conjugate addition of lithiated **25b** (R = alkyl) dominated to give 1,4-dicarbonyl systems.[58] 2-Substituted 1,3-dithiane-1-oxides **25c** were readily deprotonated with LDA followed by reaction with a variety of electrophiles, including alkyl halides, aldehydes, and ketones.[59]

Adducts **26** and **27** were converted to ketones **17** and **28** by acidic hydrolysis using hydrochloric acid,[52] or perchloric acid,[57,59] and in the presence of a mercury salt to avoid formation of disulfides.[57,58]

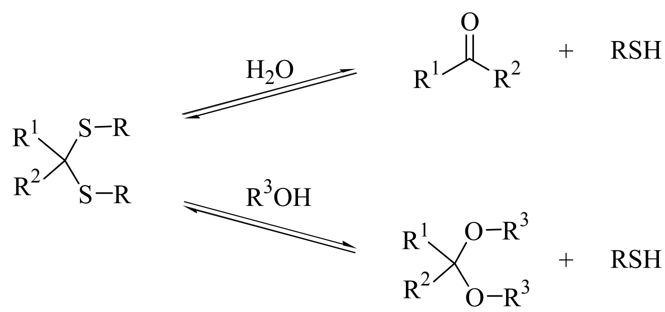


25a R^1, R^2 = Me
25b R^1, R^2 = Et
25c R^1, R^2 = -$(CH_2)_3$-

Scheme 9

Hydrolysis of dithioketals

Hydrolysis of the dithioacetal (ketal) group to a carbonyl group[21,60] is the crucial stage and often extremely difficult to achieve, especially for compounds having complex structure and sensitive groups.[61,62] The problem is that the equilibria of Scheme 10 favor the dithioketal by large factors and only methods which remove the thiol products irreversibly are suitable for the hydrolysis.



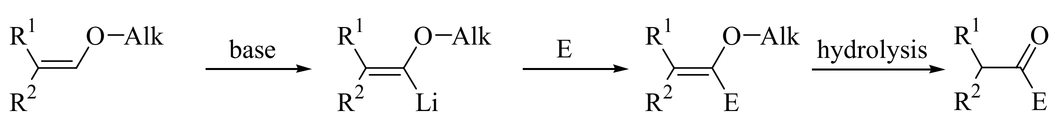
Scheme 10

Frequently utilized procedures for hydrolysis are (i) transition metal ion (Hg, Ag, Cd, Cu, Ga) induced hydrolysis, which involves metal thiolate formation; (ii) oxidation of sulfur to make it less nucleophilic; (iii) alkylation (typically with methyl iodide, trimethyl(or ethyl)oxonium tetrafluoroborate, methyl fluorosulfonate or trityl methyl ether) to a sulfonium salt followed by elimination of sulfide in the presence of base; and (iv) transacetalization to highly reactive carbonyl derivatives using formaldehyde, glyoxylic acid,[62,63] or benzaldehydes.[64]

Trityl methyl ether in the presence of catalytic trityl perchlorate was reported to cleave selectively a diethyl thioketal in the presence of a diphenyl thioketal or 1,3-dithiane.[65] Interestingly, gallium chloride mediated hydrolysis affords transformation of dithioketals into the corresponding ketones whereas dithianes and dithioacetals of aldehydes were unreactive.[51]

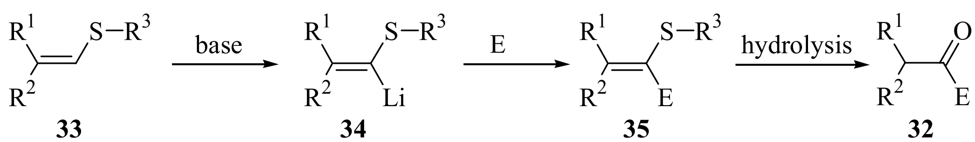
2.4. Alkyl vinyl ethers, vinyl sulfides and vinyl selenides

Alkyl vinyl ethers **29** have been used as acyl anion equivalents (Scheme 11).[66-71] Deprotonation of **29** requires the use of *tert*-butyllithium,[66-73] in some cases in the presence of HMPA[72] or TMEDA.[66,67,71] The system *n*-butyllithium / KOBu^t has also been reported to be suitable for the deprotonation of 1,3-dienyl ethers.[74] Reactions of carbanions **30** with alkyl halides,[67,72,74] aldehydes,[66,67,74] ketones,[67,73] esters,[67] benzonitrile,[67] and alkyl silyl,[68,69,71] alkyl germanium[68,69] and alkyl tin[69] chlorides yield intermediates **31**, which can be hydrolyzed to the corresponding ketones **32** by aqueous acid,[67-71] also in the presence of mercury ion.[66]



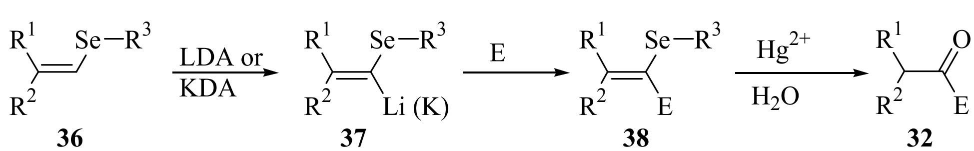
Scheme 11

In a similar manner, vinyl sulfides **33** (R^3 = alkyl, phenyl) have been used as synthons for the preparation of ketones (Scheme 12).[70,75-77] The base / solvent systems used for the generation of vinylanion **34** are: *n*-butyllithium in THF,[70] *sec*-butyllithium[75] in THF – HMPA and *n*-butyllithium / potassium *tert*-butoxide[74,76,77] for alkyl vinyl sulfides (R^3 = alkyl); and *n*-butyllithium – TMEDA,[78] LDA,[79-81] and LTMP[82] for aryl vinyl sulfides (R^3 = Ph). In some cases treatment of phenyl sulfides **33** with organolithium reagents resulted in side reactions involving addition to the double bond[80,82,83] and *ortho*-lithiation[82] of the phenyl ring. Vinyl anion **34** reacts with alkyl halides,[74-77] aldehydes,[74,75,81] acid chlorides,[81] epoxides,[75] trimethylsilyl chloride[76,77] and iminium salts[70] to give masked ketones **35** that may be hydrolyzed to ketones **32** by methods that have been used for the hydrolysis of thioacetals, using mercury salts,[25,75,84] titanium tetrachloride,[70,79,84-86] TFA[79] or methyl iodide[76,77] in aqueous acetonitrile. Hydrolysis of **35** sometimes proved difficult[79] and in some cases the vinyl sulfides could not be hydrolyzed even using mercury salts.[70]



Scheme 12

1-(Phenylseleno)alkenes **36** on treatment with butyllithium at –78 ºC gave products of metalation, cleavage of the C–Se bond and addition (Scheme 13).[87] LDA was found to be an effective reagent for metalation of **36**, but depending on reaction conditions, elimination of phenylselenol with formation of acetylene was observed as well as metalation.[87] Surprisingly, the treatment of 1-(phenylseleno)alkenes **36** with a mixture of potassium diisopropylamide – lithium *tert*-butoxide (KDA) gave selenium stabilized carbanions **37**, which reacted with a variety of electrophiles including alkyl halides, epoxides, aldehydes, and ketones to give products **38** in good yields.[88] Hydrolysis of vinyl selenides **38** to the corresponding ketones **32** was accomplished in the presence of mercury salts,[88-91] strong mineral acids or TFA.[92,93]



Scheme 13

3. Benzotriazole stabilized acyl anion synthons

Over the last 15 years a range of benzotriazole–stabilized acyl anion synthons has been developed (Figure 1). These synthons, obtained by deprotonation of **39–43**, combine the stabilizing influence of a benzotriazolyl group and α-phenoxy-, α-alkoxy-, α-mercapto-, α-carbazolyl-group, or a second α-benzotriazolyl group.

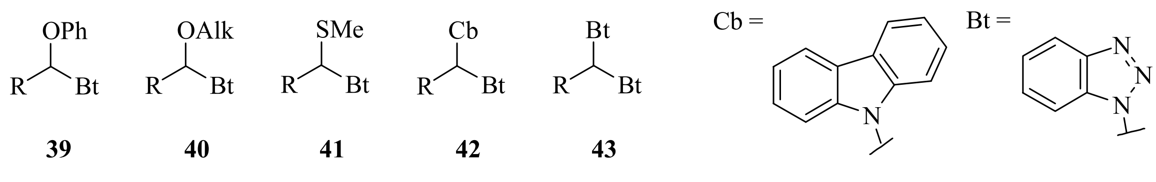
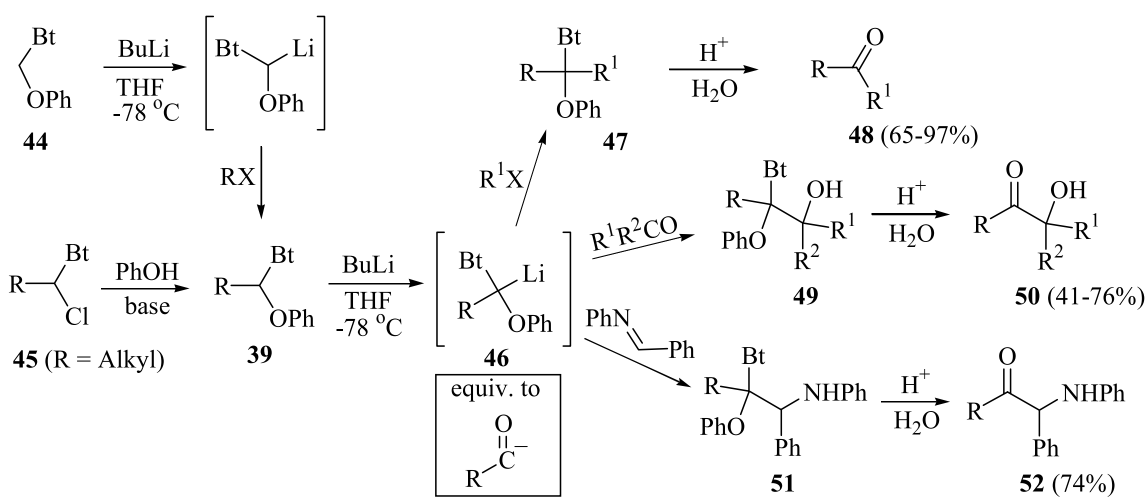


Figure 1. Conjugate acids of benzotriazole stabilized acyl anion synthons.

3.1. Alkyl vinyl ethers, vinyl sulfides and vinyl selenides

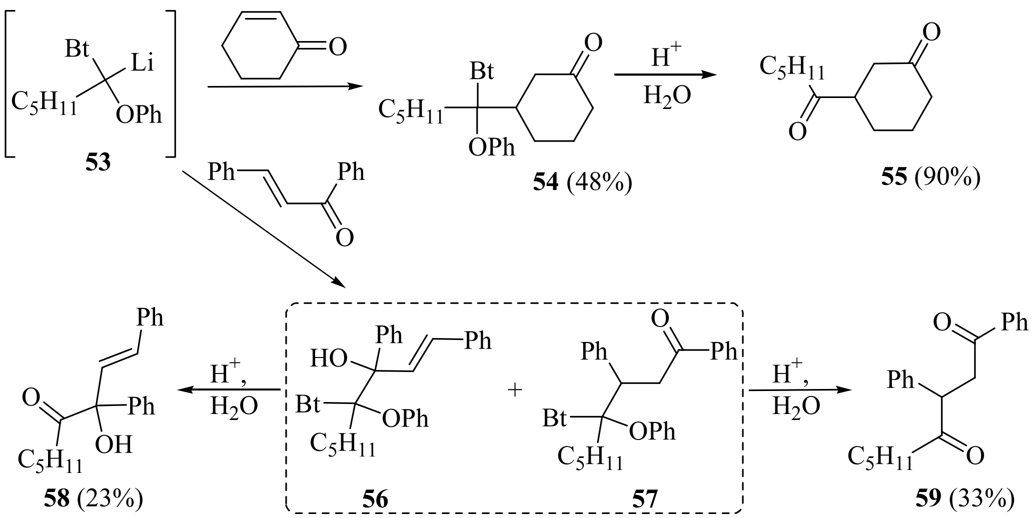
1-(1-Phenoxyalkyl)benzotriazoles **39** usefully combine the activating influence of the phenoxy- and benzotriazolyl- groups (Scheme 14).[94] Compounds **39** are conveniently prepared in good yields (i) from 1-phenoxymethylbenzotriazole **44**[95,96] via lithiation with butyllithium in THF at –78 ºC followed by the reactions with alkyl halides,[94,96,97] or (ii) by the *O*-alkylation of phenol with 1-(1-chloroalkyl)benzotriazoles **45** in the presence of a base.[94,98-100] Compounds **39** can be deprotonated using butyllithium in THF at –78 ºC to give anions **46**, which react with a wide variety of electrophiles to give simple alkyl **47**, α-hydroxyalkyl **49**, and α-aminoalkyl **51** masked ketones.[94] Crude intermediates **47**, **49** and **51** are then hydrolyzed with 5% sulfuric acid in aqueous ethanol under reflux to give good overall yields of ketones **48**, **50** and **52**, respectively.



Scheme 14

1-Phenoxymethylbenzotriazole **44** was also applied to one-pot double-lithiation techniques. Successive treatment of **44** with one equivalent of butyllithium followed by one equivalent of alkyl halide or trialkylsilyl chloride (R = Alk_3Si), then with a second equivalent of butyllithium and finally, with the appropriate second electrophile (alkyl halide, aldehyde, ketone, trialkylsilyl chloride, etc) gave i good yields of ketones **48**, **50** and acyl silanes **48** (R or R^1 = Alk_3Si) after direct hydrolysis of crude products **47** and **49**.

With α,β-unsaturated ketone, 2-cyclohexenone, anion **53** gave exclusively the product of 1,4-addition **54** in 48% yield (Scheme 15). No 1,2-addition product was detected. Intermediate **54** was hydrolyzed to **55** in 90% yield under conditions similar with those used for **48**.



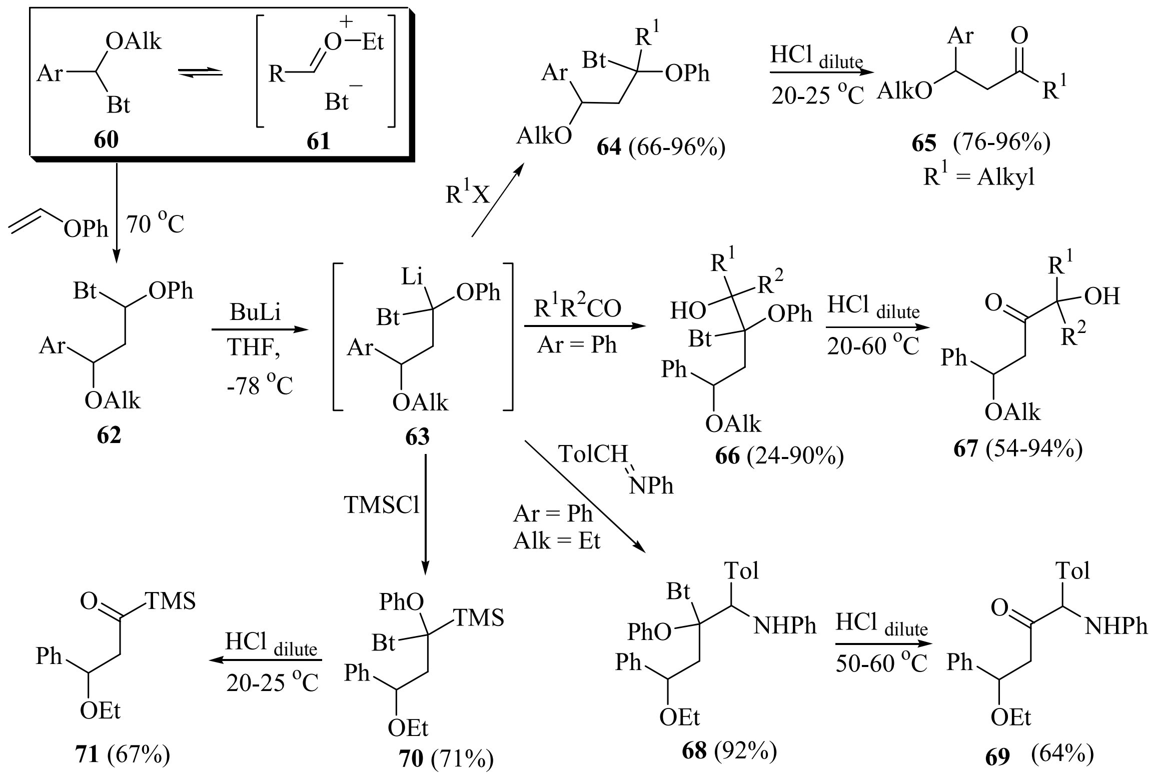
Scheme 15

However, when *trans*-chalcone was used as electrophile to react with anion **53**, both the 1,2-addition **56** and the 1,4- addition products **57** were generated, probably as result of steric hindrance at the γ-position in chalcone (Scheme 15). The crude mixture of **56**/**57** was hydrolyzed with 5% sulfuric acid in aqueous ethanol to give ketones **58** (23%) and **59** (33%).

β-Alkoxy synthons from alkoxymethylbenzotriazoles and phenyl vinyl ether. α'-Functionalized β-alkoxy ketones

An example of the double-addition of Bt-reagents to enol ethers is shown on Scheme 16. Thus, 1-(1-alkoxy-1-arylmethyl)benzotriazoles **60** (available from aromatic aldehydes and benzotriazole with the corresponding alcohol, or trimethyl or triethyl orthoformate)[101-105] add via the ionized form, **61**, to phenyl vinyl ether to give intermediate β-alkoxy acyl anion synthon **62**,[106] of type **39** (Figure 1) and discussed earlier (Scheme 14 and 15).

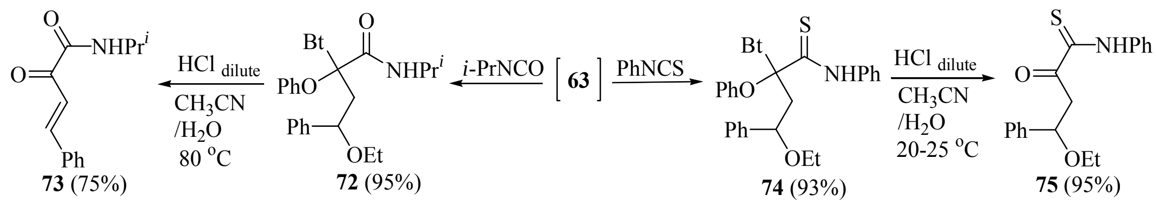
Compounds **62** can be deprotonated with butyllithium in THF at –78 ºC and then reacted with a variety of electrophiles to give intermediates **64**, **66**, **68**, and **70** (Scheme 16). Reaction of anions **63** with alkyl halides gave good yields of masked ketones **64**. In the reactions with carbonyl compounds, aromatic, benzophenone and benzaldehyde, gave excellent (83–90%) yields of intermediates **66**, while reactions with enolizable aliphatic ketones, acetone and cyclohexanone, resulted in low yields of **66** (24–45%, R^1,R^2 = Me, –$(CH_2)_5$–) and recovery of about 50% of **62**. Reactions of anion **63** (Ar = Ph, Alk = Et) with 4-methylbenzylideneaniline or TMS chloride produced masked α-anilino ketone **68** and acyl trimethylsilane **70**, respectively.[106]



Scheme 16

Hydrolysis of compounds **64** with dilute hydrochloric acid in aqueous ethanol (1:1) at room temperature produced β-alkoxy-substituted ketones **65** in 76–96% yields. Compound **70** under the same conditions gave **71**, while hydrolysis at 50–60 °C resulted in partial deethoxylation. Unlike compounds **64** and **70**, hydrolysis of intermediate **68** and some adducts **66** to ketones **69** and **67** required elevated temperature and was achieved with dilute hydrochloric acid in aqueous ethanol at 50–60 °C.[106]

Reactions of anion **63** (Ar = Ph, Alk = Et) with *i*-propyl isocyanate and phenyl isothiocyanate gave excellent yields of corresponding adducts **72** and **74** (Scheme 17). Hydrolysis of compounds **72** and **74** with diluted hydrochloric acid in aqueous acetonitrile gave carbonyl compounds **73** (75%, product of deethoxylation) and **75** (95%).[106]

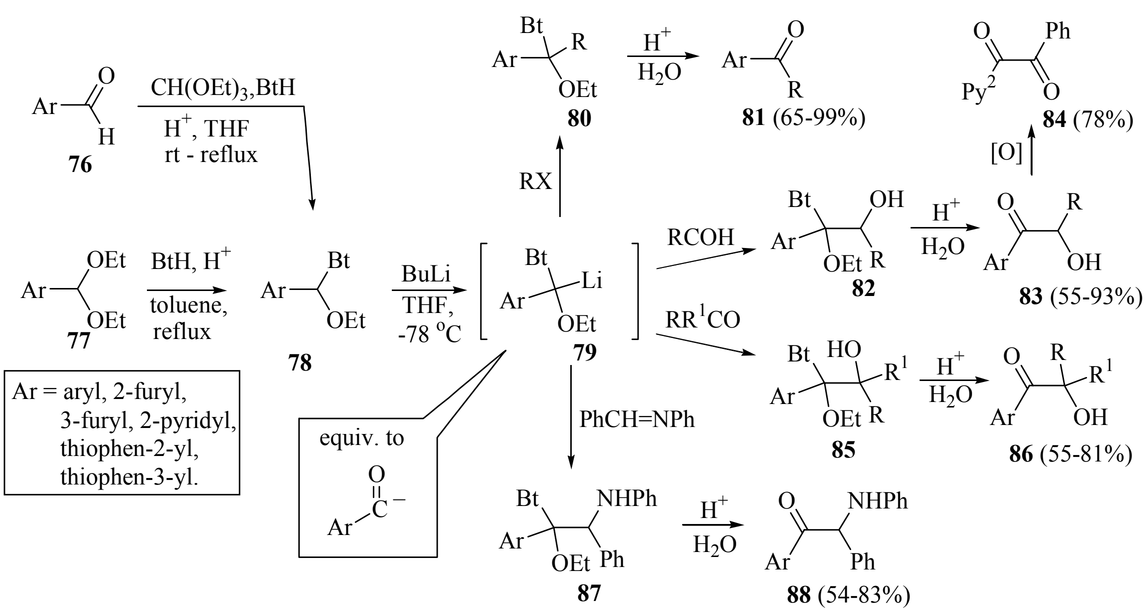


Scheme 17

3.2. *N*-[Ethoxy(aryl)methyl]benzotriazoles - aroyl anion synthons

If an aryl- or heteroaryl- group together with a ethoxy group is already present at the α-position to benzotriazole, then the remaining hydrogen is sufficiently acidic to be deprotonated and replaced by a wide variety of electrophiles as shown in Scheme 18.[101,107]

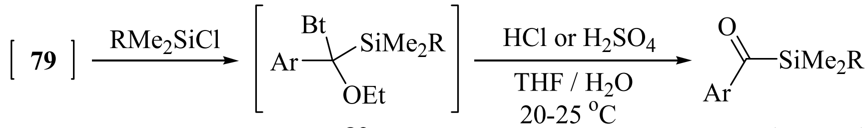
Synthons **78** have been prepared in good yields (51–85%) either from aldehydes **76** or the corresponding acetals **77**.[101,107] Treatment of **78** with butyllithium in THF at –78 ºC for several minutes gave the anions **79**; subsequent reaction with an appropriate electrophile, such as alkyl halides,[101] aldehydes,[101] ketones,[101] and imines[101] at the same temperature for few minutes followed by simultaneous hydrolysis of intermediates **80**, **82**, **85**, and **87** with diluted hydrochloric or sulfuric acid during workup afforded ketones **81**, **83**, **86**, and **88** in good yields. With anion **79** (Ar = 2-pyridyl), reactions with alkyl halides and benzaldehyde were accomplished at room temperature followed by normal hydrolysis of **80** (Ar = 2-pyridyl, R = alkyl) to ketones **81** (Ar = 2-pyridyl, R = alkyl) or hydrolysis / self-oxidation of **82** (Ar = 2-pyridyl, R = Ph) to diketone **84** in 78% yield.



Scheme 18

Deprotonation of the methine group of **78** occurs immediately after the addition of butyllithium. The highly reactive anions **79** are of limited stability in solution, especially in the case of furan and thiophene systems, and therefore immediate quenching with electrophiles is necessary for satisfactory results. Prolonged lithiation times led to partial decomposition of the resulting anion **79** and subsequently to low yields. Two exceptions are the 2-pyridyl ketones **81** (Ar = 2-pyridyl, R = alkyl) and **84** since for these the precursor anion **79** (R = 2-pyridyl) was stable even at 20 °C.

With trialkylsilyl chlorides anions **79** form intermediates **89**; the direct hydrolysis of **89** with dilute hydrochloric or sulfuric acid in aqueous THF give good yields of aroylsilanes **90** (Scheme 19).[107]



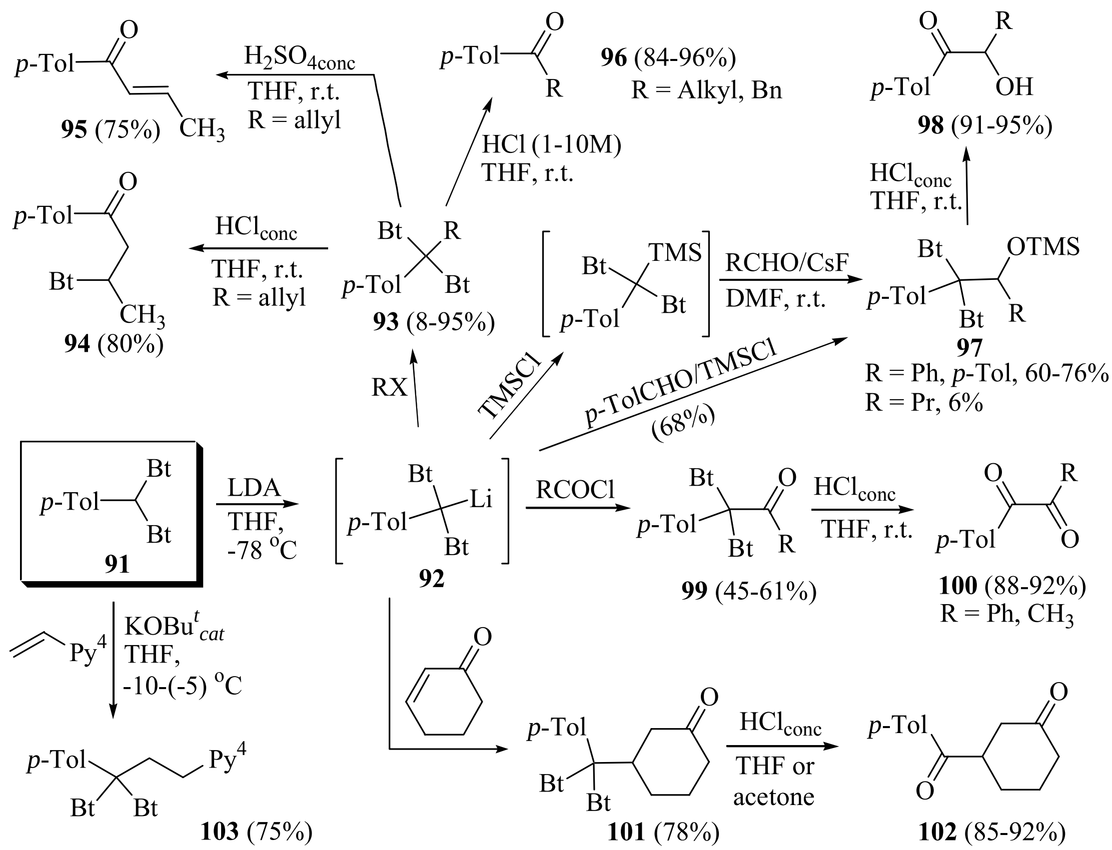
89 **90** (57-97%)

Scheme 19

3.3. Bis(benzotriazolyl)methane derivatives

Bis(benzotriazolyl)arylmethanes **43** (Figure 1, R = Aryl), available from either substituted benzaldehydes with benzotriazole in the presence of thionyl chloride[107] or α,α-dichlorotoluenes with benzotriazole,[108] on treatment with LDA[109] or potassium *tert*-butoxide[110] form carbanion stable at temperatures up to 0 °C.

Reactions of anion **92** (generated from **91**) with alkyl, benzyl, or allyl halides give alkylated intermediates **93** in good yields (52–95%, except for product of the reaction with *sec*-butyl bromide, 8%), as well as reactions with acid halides and cyclohexenone give good yields of masked diketones **99** and exclusive 1,4-addition product **101**, respectively (Scheme 20).[110] However, treatment of anion **92** with 4-vinylpyridine, chalcone, ethyl acrylate, and acrylonitrile gave no reaction. On the other hand, reaction of **91** with 4-vinylpyridine in the presence of catalytic potassium *tert*-butoxide (0.05 equiv) in THF at –10–(–5) °C gave addition product **103** in 75% yield.[111]

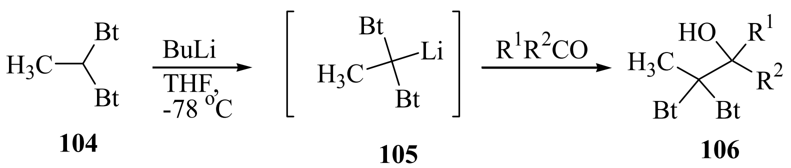


Scheme 20

Unlike previously discussed synthons **39** and **78**, reactions of anion **92** with aldehydes appear to be reversible and result in recovery of starting materials. However, reaction of **92** with *p*-tolualdehyde followed by the addition of trimethylsilyl chloride gave 68% yield of intermediate silyl ether **97** (R = *p*-Tol). Alternatively, compounds **97** were obtained by treatment of anion **92** with trimethylsilyl chloride followed by the reaction with aldehydes in the presence of caesium fluoride in DMF (Scheme 20).[110]

Hydrolysis of intermediates **93**, **97**, **99**, and **101** (except **93**, R = allyl) in THF in the presence of hydrochloric acid at 20–25 °C gives corresponding ketones **96**, **98**, **100**, and **102** in good yields (Scheme 20). Hydrolysis of intermediate **93** (R = allyl) was accompanied by the addition of benzotriazole to allyl group resulted in formation of β-benzotriazolyl ketone **94** (80%). In the presence of concentrated sulfuric acid in THF at 20–25 °C, compound **93** (R = allyl) gave crotonophenone **95** (75%).[110]

Bis(benzotriazolyl)alkanes are also potential alkanoyl anion synthons. The presence of two benzotriazolyl groups in bis(benzotriazolyl)ethane **104** stabilizes carbanion **105** formed on treatment with butyllithium in THF at –78 °C (Scheme 21). At –78 °C, carbanion **105** reacts with ketones including enolizable to give, upon quenching with aqueous ammonium chloride at the same temperature, good yields of masked α-hydroxyketones **106**. However, if the reaction temperature is allowed to rise to 20 °C prior to quenching with aqueous ammonium chloride, the reaction results in recovery of starting material **104**.[112]



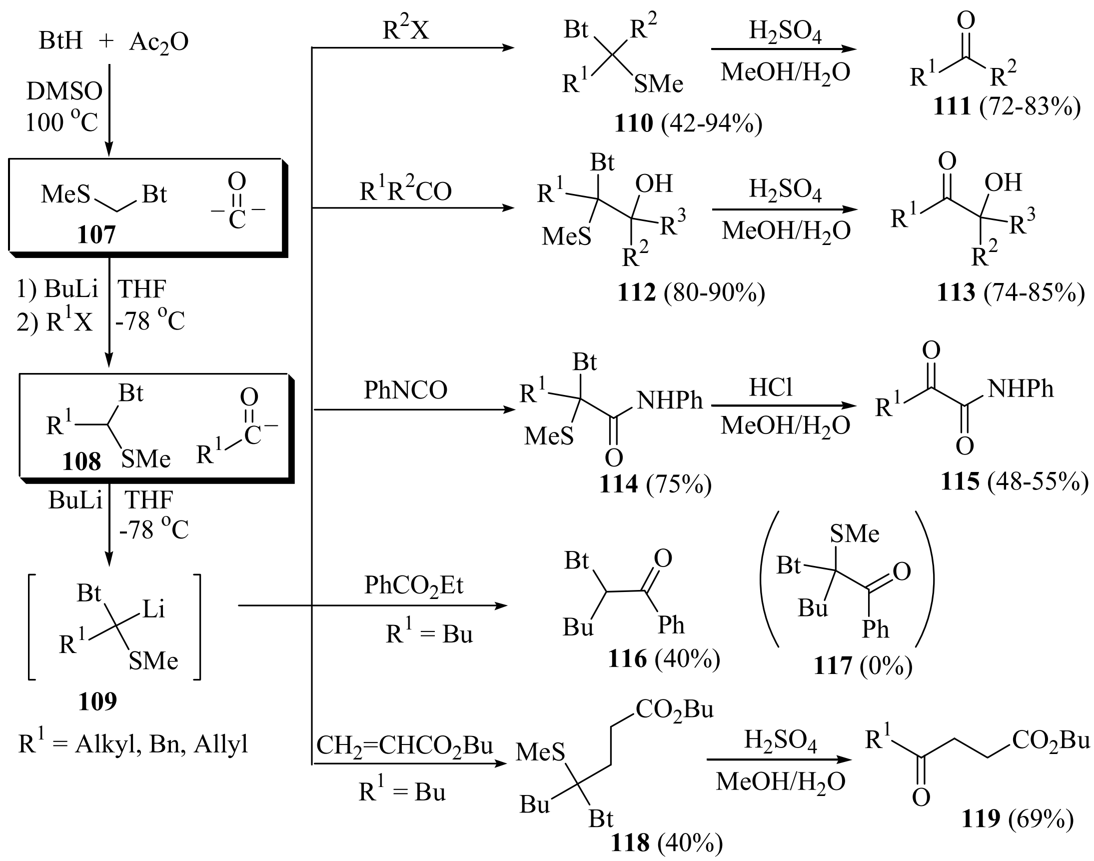
R^1	R^2	%
Me	Ph	90
Ph	Ph	70
$-(CH_2)_4-$		50
$-(CH_2)_5-$		75
Me	*i*-Pr	80

Scheme 21

3.4. 1-(1-Methylsulfanylalkyl)benzotriazoles

(Benzotriazol-1-yl)methyl methyl thioether **107** is conveniently accessible from dimethyl sulfoxide, acetic anhydride, and benzotriazole (98%) (Scheme 22).[113] On treatment with butyllithium in THF at –78 ºC **107** gives the carbanion, which reacts smoothly with alkyl halides, including cyclic, benzyl, and allyl, to form intermediates **108** (55–85%). Compounds **108** can be deprotonated using butyllithium or in some cases LDA to form anions **109**, which react further with various electrophiles, such as alkyl halides, carbonyl compounds (quenching of the reaction mixtures is advantageous at –78 °C due to reverse to starting materials at temperature approaching 20 °C), and phenyl isocyanate to give masked dialkylketones **110** (42–94%), α-hydroxyketones **112** (80–90%), and 2-ketoamides **114** (ca. 75%), respectively. With ethyl benzoate, anion **109** (R^1 = Bu) gave product **116** (40%) instead of expected **117**. With α,β-unsaturated esters, anions **109** either failed to give or gave low yields of the expected Michael addition products, except the adduct **118** formed in 40% yield.[113]

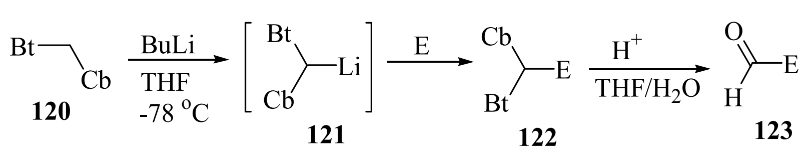
Hydrolysis of intermediates **110**, **112**, **114**, and **118** under mild conditions, 20 °C, with dilute aqueous methanolic solution of sulfuric acid (hydrochloric acid for **114**) provided corresponding ketones **111**, **113**, **115**, and **119** (Scheme 22).[113]



Scheme 22

3.5. 1-(Carbazolylalkyl)benzotriazoles

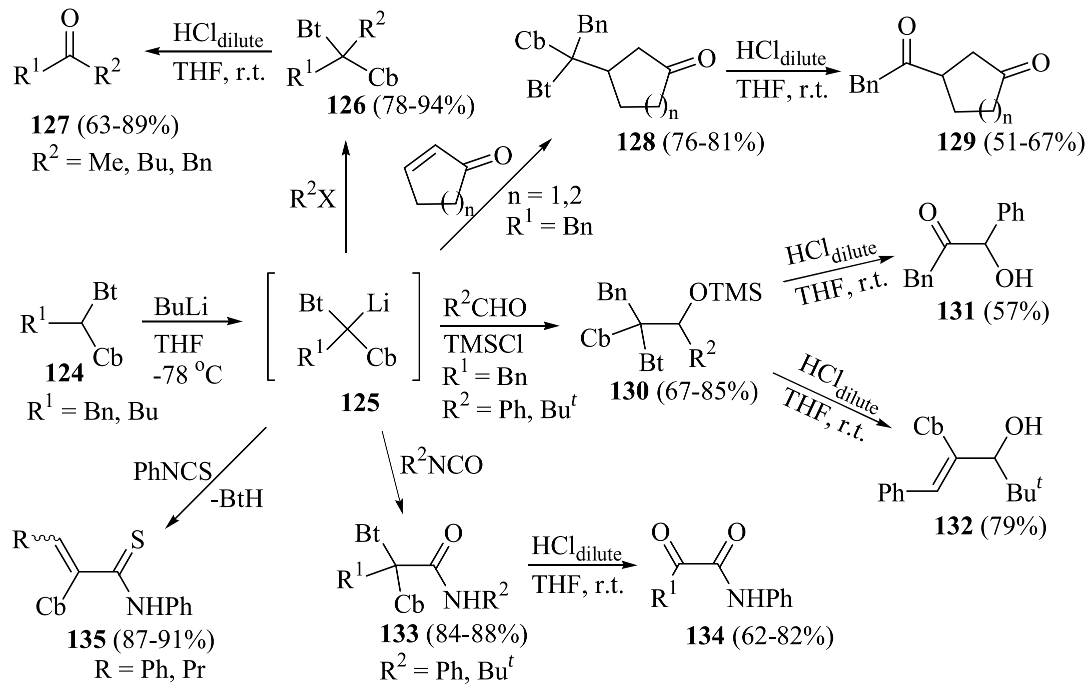
1-(Carbazolylmethyl)benzotriazole **120** on treatment with butyllithium readily formed anion **121**, a versatile formyl anion equivalent,[114] which reacts with variety of electrophiles, including alkyl halides, aldehydes, ketones, isocyanates, isothiocyanates, and esters, to give 71–96% yields of adducts **122** (Scheme 23). Hydrolysis of intermediates **122** with dilute sulfuric acid in aqueous THF at 20–25 °C gave corresponding aldehydes **123**, which were trapped and characterized as 2,4-dinitrophenyl hydrazones.[114]



Scheme 23

Intermediates **122** (E = Alkyl) can be further deprotonated and the resulting anions again react with electrophiles. Thus compounds **124** (Scheme 24) with butyllithium in THF at –78 °C give anions **125**, which further react with electrophiles.[115] With alkyl halides, α,β-unsaturated ketones, and phenyl and *tert*-butyl isocyanates, anions **125** give corresponding alkylated products **126**, exclusively 1,4-addition products **128**, and amides **133**. Reactions of **125** with aldehydes showed to be reversible and addition of trimethylsilyl chloride was necessary to trap products of addition as silyl ethers **130**. Unlike isocyanates, reaction of anions **125** with phenyl isothiocyanate results in the addition followed by the elimination of benzotriazole to give unsaturated thioamides **135**.[115]

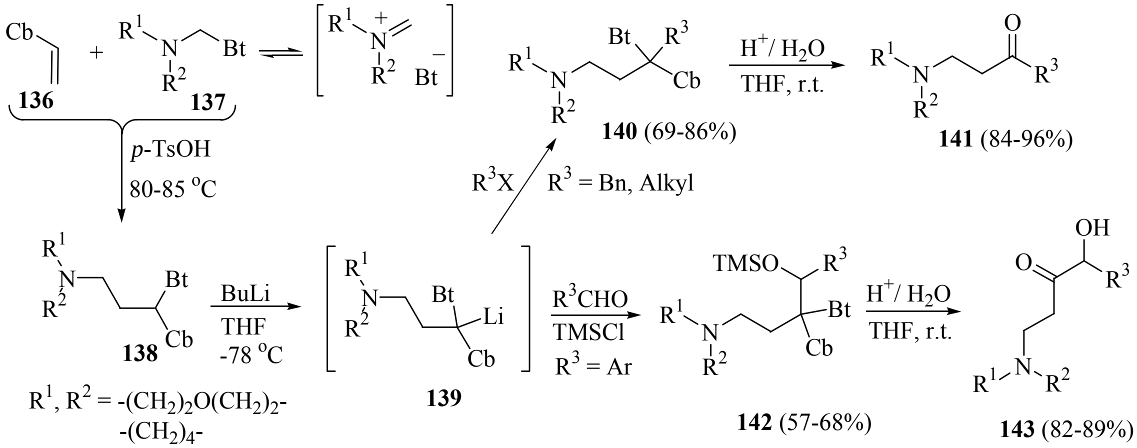
Hydrolysis of compounds **126**, **128**, **130**, and **133** (except adduct **130** of *tert*-butylcarbaldehyde, $R^2 = Bu^t$) to corresponding ketones **127**, **129**, **131**, and **134** was achieved under mild reaction conditions, at 20–25 °C, using dilute hydrochloric acid in THF (Scheme 24). Treatment of compound **130** ($R^2 = Bu^t$) under these conditions resulted in elimination of benzotriazole and formation of product **132**, which is resistant to further hydrolysis to α-hydroxyketone.[115]



Scheme 24

β-Aminoalkanoyl aanion synthons from *N*-vinylcarbazole and *N*-aminomethylbenzotriazoles

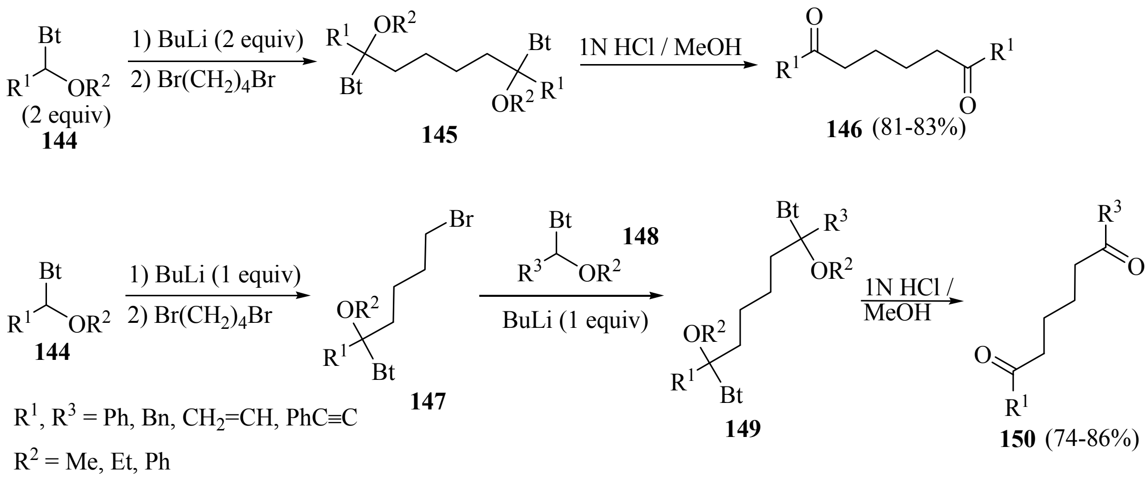
Alkylaminomethylbenzotriazoles **137** exist in equilibrium with the corresponding immonium cation and add to vinyl group of *N*-vinylcarbazole **136** giving adducts **138** (Scheme 25), which are β-amino functionalized acyl anion synthons of type **124** (Scheme 24). Compounds **138** on the treatment with butyllithium form anions **139**, which further react with alkyl halides, or aldehydes in the presence trimethylsilyl chloride to give intermediates **140** (69–86%) and **142** (57–68%), hydrolysis of which with dilute aqueous hydrochloric acid in THF at 20–25 °C provides corresponding β-amino-functionalized dialkyl- **141** (84–96%) and α′-hydroxy- **143** (82–89%) ketones (Scheme 25).[116]



Scheme 25

3.6. Application to the synthesis of 1,6-diketones

An example of the application of benzotriazole mediated acyl anion synthons is shown in the preparation of symmetrical and unsymmetrical alkyl, aryl, alkenyl and alkynyl 1,6-diketones **146** and **150** in Scheme 26.[117] 1,4-Dibromobutane is reacted with two equivalents of the anion derived from the Bt-reagent **144** to give intermediates **145**, which on hydrolysis form the 1,6-diketones **146** in high yields. Alternatively, 1,4-dibromobutane is reacted with a single equivalent of the anion of **144**, to produce intermediates **147**, and then with the anion of the second Bt-reagent **148** to give upon hydrolysis unsymmetrical diketones **150** in good yields. Reaction conditions for hydrolysis of intermediates **145** and **149** depend from nature of groups R^1 and R^3: dilute hydrochloric acid in aqueous methanol at room temperature was used for preparation of alkyl diketones, and mixture of oxalic acid, water and silica gel in dichloromethane at room temperature was applied for mild hydrolysis of sensitive alkenyl or alkynyl derivatives.[117]

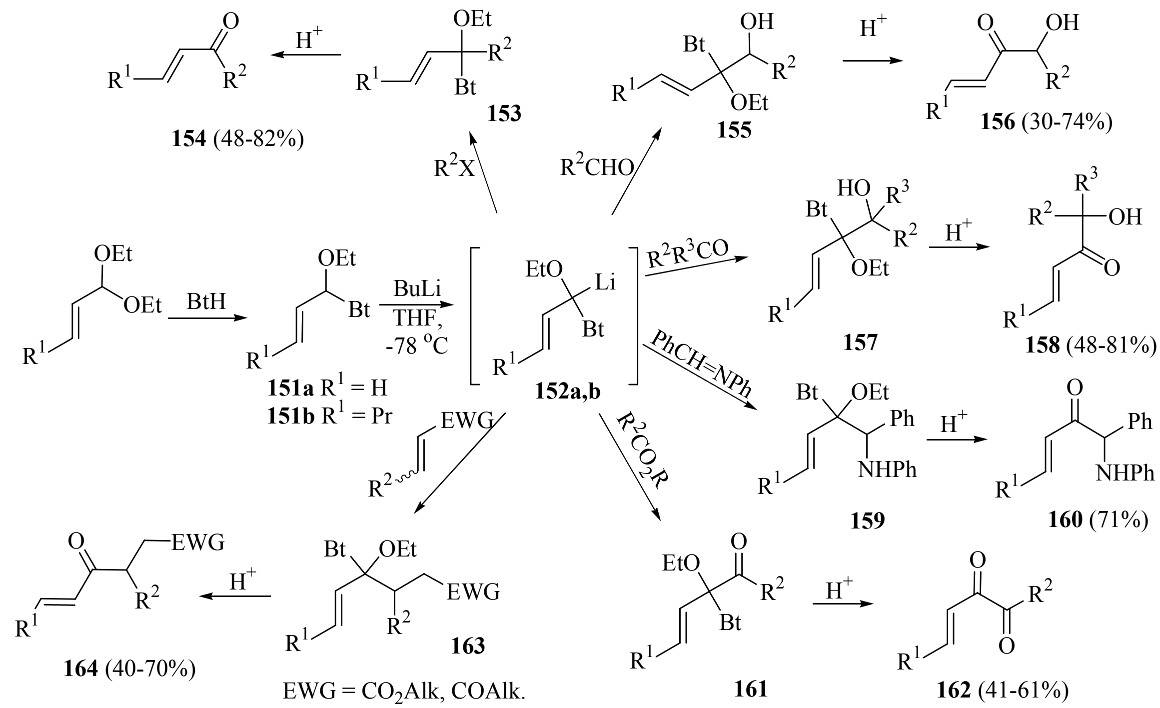


Scheme 26

4. Propenoyl anion synthons

N-(α-Ethoxyallyl)benzotriazoles **151** are excellent propenoyl-anion synthons.[97,107,118–121] The starting materials **151a,b** are easily accessible from the corresponding acetal and benzotriazole.[118–121] The lithiated derivatives **152a,b** (R^1 = H, Pr) react regiospecifically with alkyl halides to form compounds **153**[119] (Scheme 27), which undergo (without further separation) facile hydrolysis under very mild conditions, such as oxalic acid on wet silica (for R^1 = H)[119] or dilute hydrochloric acid (R^1 = Pr),[121] both at 20 ºC to give a variety of vinyl ketones **154** (48–82%).

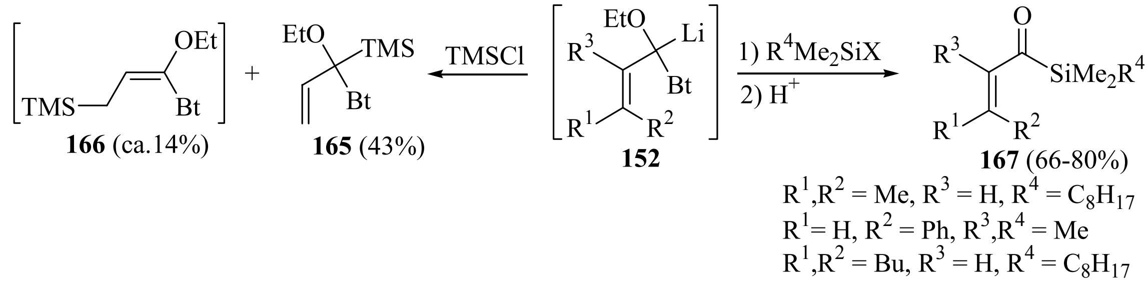
The lithiated derivatives **152a,b** react with α,β-unsaturated ketones and esters in reactions which are doubly regiospecific α to the benzotriazole and β in the α,β-unsaturated ketones (esters) to give intermediates of type **163**.[118,119,121] The minor (ca. 20%) products of 1,2-addition were detected only for addition to β-substituted vinyl ketones (2-cyclohexenone and hex-4-en-3-one).[119] The intermediates **163** can be hydrolyzed under the same mild conditions to give vinyl-ketoesters and 1,4-diketones of common structure **164** in overall 40–70% yields.[118,119,121] Unlike α,β-unsaturated ketones, α,β-unsaturated aldehydes, e. g. cinnamaldehyde, with anion **152b** gave exclusively the product of 1,2-addition **155** (R^2 = PhCH=CH-), the hydroxy group of which can be oxidized with chromic oxide / pyridine to carbonyl followed by hydrolysis to give divinyl 1,2-diketone (not shown) in 39% yield.[97]



Scheme 27

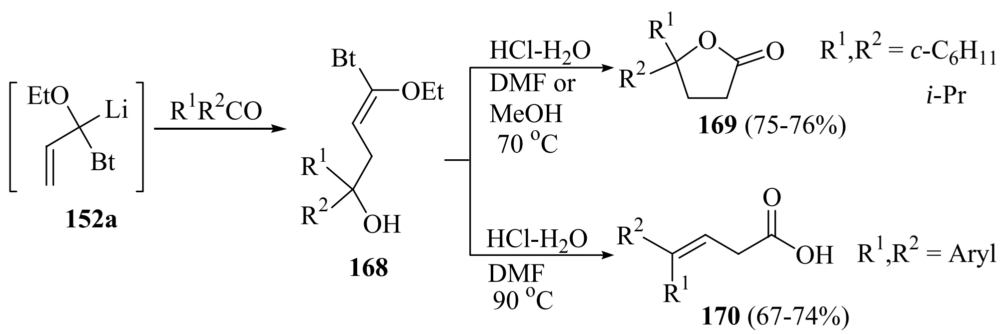
The lithiated derivatives **152a,b** react respectively with aldehydes[119,121] and ketones (except some enolizable or bulky examples, such as heptan-3-one, benzophenone or fluorenone discussed next)[120.121] to form alcohols **155** and **157**, with benzalaniline – to give amine **159**,[121] and with esters of alkyl- or aryl-carboxylic acids – to generate masked diketones **161**.[97] Hydrolysis of these intermediates provides access to α-hydroxy vinyl ketones **156** and **158**,[119–] α-anilinomethyl vinyl ketones **160**,[121] and vinyl 1,2-diketones **162**,[97] respectively.

Reaction of anion **152a** (R^1–R^3 = H), derived from 1-(1-ethoxyallyl)benzotriazole, with trimethylsilyl chloride results in the formation of α- and γ-substituted products **165** and **166** in ratio 3:1 (Scheme 28).[119] Reactions of trialkylsilyl halides with R^1–R^3 substituted anions **152** followed by hydrolysis with dilute hydrochloric acid in aqueous THF give exclusive formation α,β-unsaturated acylsilanes **167**.[107,122]



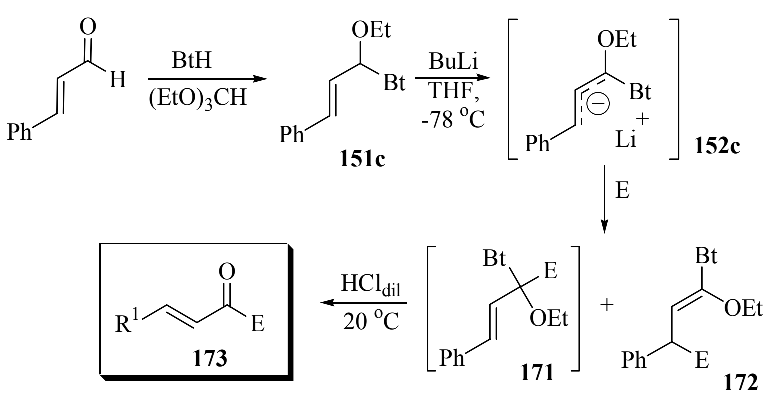
Scheme 28

Reactions of anion **152a** with benzophenone, fluorenone, dicyclohexyl ketone and diisopropyl ketone resulted in exclusive formation of γ-adducts **168** (Scheme 29).[120] Treatment of the crude products **168**, derived from alkyl ketones, with dilute hydrochloric acid in DMF or methanol at 70 °C, and products from aryl ketones in DMF at 90 °C gave hydrolysis / cyclization to lactones **169** and hydrolysis / dehydration to unsaturated acids **170**, respectively, in good yields.



Scheme 29

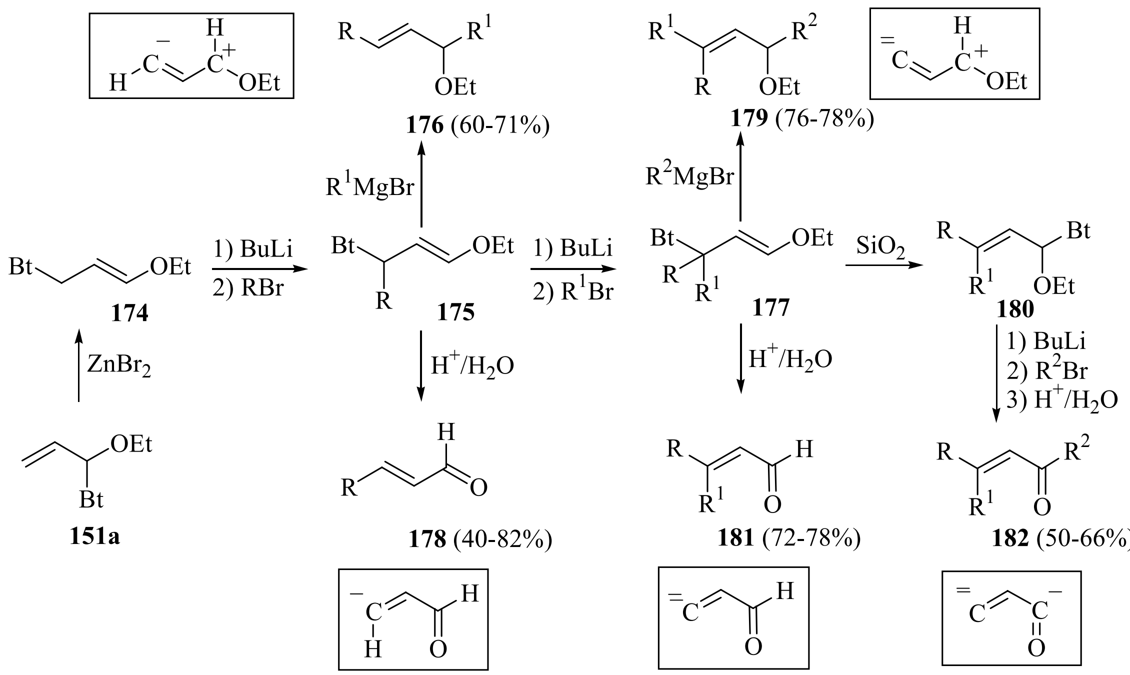
Unlike **152a,b**, reactions of phenylallyl anion **152c** with electrophiles (alkyl halides and carbonyl compounds) produce mixtures of α- and γ- products **171** and **172** (Scheme 30). Treatment of these mixtures with dilute hydrochloric acid at 20 °C gave vinyl ketones **173** while compounds **172** (which are masked acids) appeared to be stable under these conditions.[121] Alkyl halides and aldehydes gave predominantly α-products **173** (55–79%) whereas benzyl bromide gave a major γ-product **172** (E = Bn).[121]



E	**172** (%)	**173** (%)
Et	19	79
C_5H_{11}	23	70
C_8H_{17}	20	68
PhCH(OH)	20	73
4-TolCH(OH)	24	65
C_7H_{15}CH(OH)	27	55
Me_2C(OH)	43	45
$PhCH_2$	86	13

Scheme 30

Further applications of the propenal acetal- derived Bt-reagent **151a** are shown in Scheme 31.[122] Treatment of **151a** with catalytic $ZnBr_2$ causes incipient ionization of the benzotriazole anion, which then adds to the ethoxy-stabilized allyl cation, but because of the steric situation undergoes rearrangement to give **174**. Compound **174** can be lithiated α-to the benzotriazole and then alkylated regiospecifically α-to the benzotriazole to give **175**. Intermediates **175** undergo both hydrolysis to α,β-unsaturated aldehydes **178** or S_N2' reaction with Grignard reagents to give allyl ethers **176**. This process can be repeated with **175** loosing another proton followed by alkylation α-to the benzotriazole to give **177**. Intermediates **177** on hydrolysis or reaction with a Grignard reagent give compounds **181** and **179**, respectively. Finally, if compound **177** is treated with a small amount of a weak Lewis Acid (SiO_2) it will also undergo reversible ionization and an isomerization to form **180**. Compounds **180** contain one further acidic proton that can be removed and replaced by an electrophile (alkyl or trialkylsilyl halide) and finally hydrolyzed to give α,β-unsaturated carbonyl compounds **182**. Thus we have five different synthons as shown in Scheme 31.

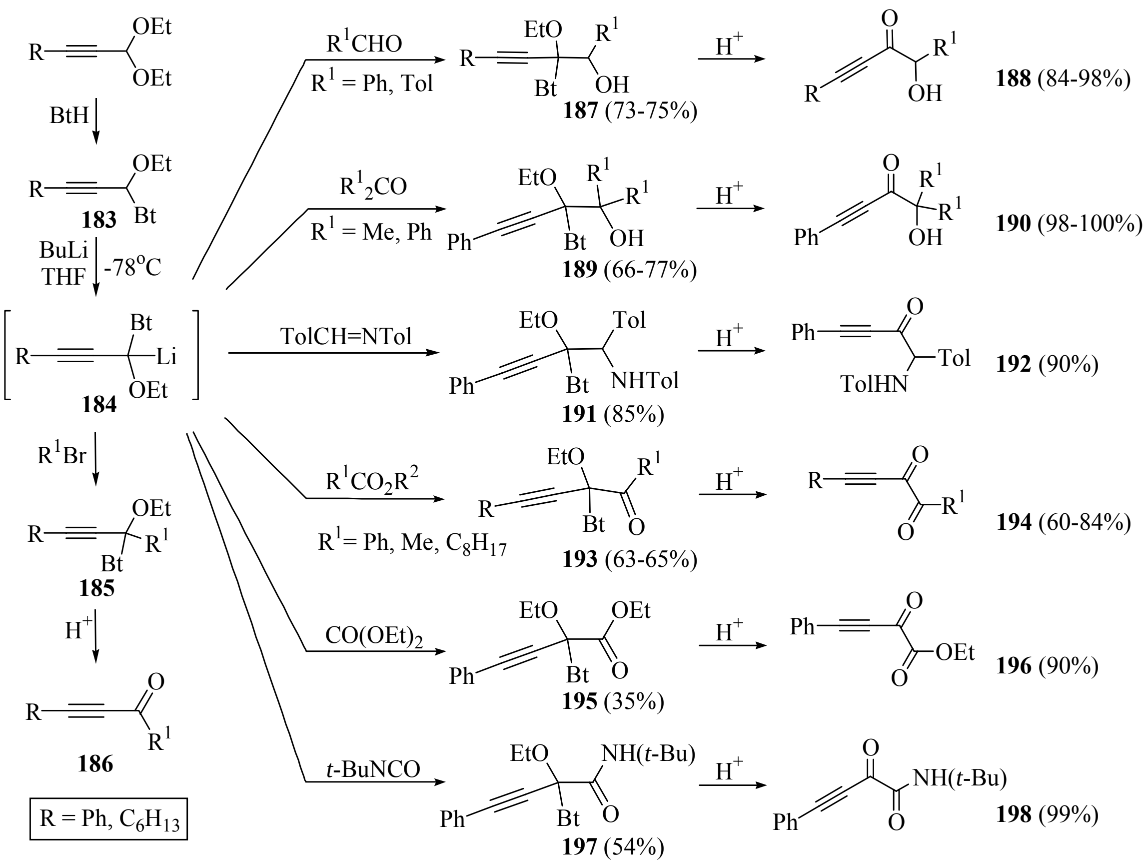


Scheme 31

5. Propargoyl anion synthons

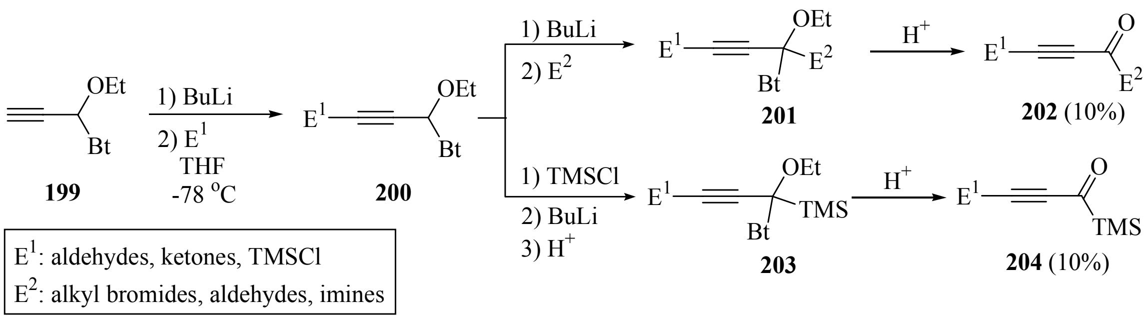
Propargoyl anion synthons **183** are useful for the preparation of various functionalized alkynyl ketones, not easily accessible by other methods (Scheme 32). Readily available propargals are activated by the easy replacement of one of the ethoxy groups to give **183**.[122] In **183** the proton α to benzotriazole can be replaced by lithium using *n*-butyllithium. Anions **184** undergo regioselective alkylation with alkyl halides to give masked ketones **185**.[123,124] Hydrolysis of **185** with dilute hydrochloric acid provides the corresponding acetylenic ketones **186**.[123,124]

Anions **184** can also react with a wide variety of electrophiles.[97,107,123,124] In each case the electrophile reacts regiospecifically α to the benzotriazole group. Thus, the corresponding adducts **187**, **189**, **191**, **193**, **195**, and **197** were obtained with aldehydes, ketones, imines, esters,[97] ethyl carbonate and isocyanates, respectively.[123] All these intermediates can be isolated and characterized in high yields. However, for the preparation of acetylenic carbonyl derivatives it is not necessary to isolate the intermediates, and hydrolysis can be carried out under mild conditions (typically, dilute hydrochloric acid in acetone (methanol or ethanol) for 10–20 min at 5–20 ºC) to give acetylenic hydroxy ketones **188** and **190**, amino-ketones **192**, diketones **194**, keto-esters **196**, and keto-amides **198**, respectively, all in high yields (Scheme 32).[97,123] This kind of compounds were previously little known and requiring rather complex procedures.



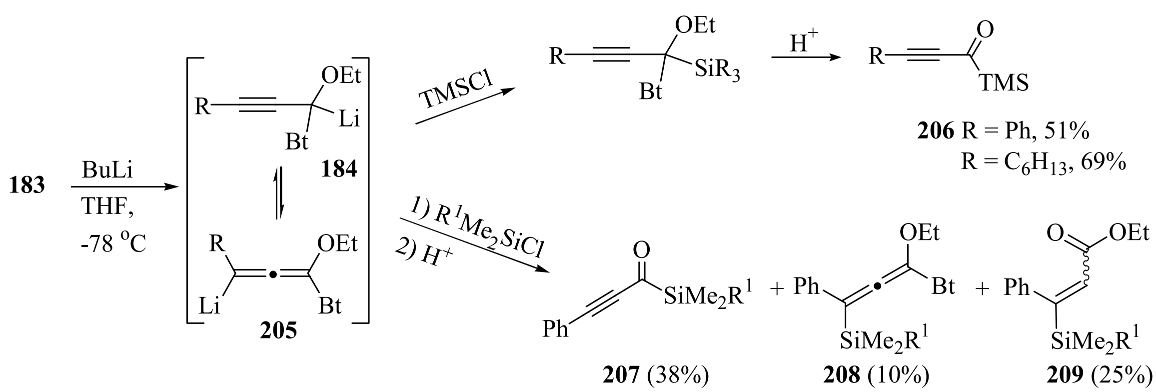
Scheme 32

A general approach to functionalized acetylenic ketones **202** and propargoyl silanes **204** from 1-(1-ethoxy-propargyl)benzotriazole **199** via synthon **200** is shown in Scheme 33. Successive treatment of **199** with butyllithium / electrophile E^1 and again butyllithium / electrophile E^2 (TMSCl / butyllithium for **203**) followed by hydrolysis of intermediates **201** and **203** provides compounds **202** and **204**.[107,123]



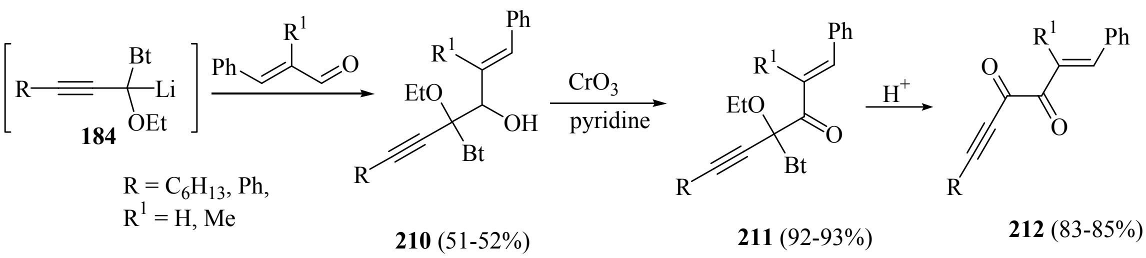
Scheme 33

Reactions of anions derived from compounds **183** with trialkylsilyl chlorides followed by acidic hydrolysis with dilute hydrochloric or sulfuric acid in aqueous THF at 20–25 °C resulted in propargoyl silanes **206** for TMS chloride, or mixture of products **207–209** for octyldimethylsilyl chloride (Scheme 34). Formation of mixture of products **207–209** is presumably caused by steric hindrance of octyldimethylsilyl group and presence of anion **184** in equilibrium with allenic form **205**.[107]



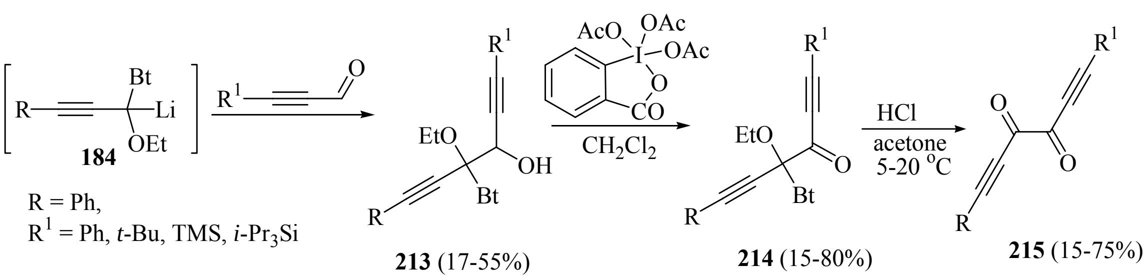
Scheme 34

Attempted preparation of acetylenic 1,2-diketones of type **194** (where R^1 is vinyl) by using α,β-unsaturated esters and α,β-unsaturated acid chlorides as electrophiles in the reactions with anions **184** resulted in complicated mixtures (Scheme 32).[97] On the other hand treatment of anions **184** with *trans*-cinnamaldehydes gave 1,2-addition products **210** (Scheme 35); oxidation of the hydroxy group in **210** with chromium trioxide / pyridine[125] and subsequent hydrolysis of **211** with dilute sulfuric acid at 0–25 °C afforded 1,2-diketones **212** in moderate yields.[97]



Scheme 35

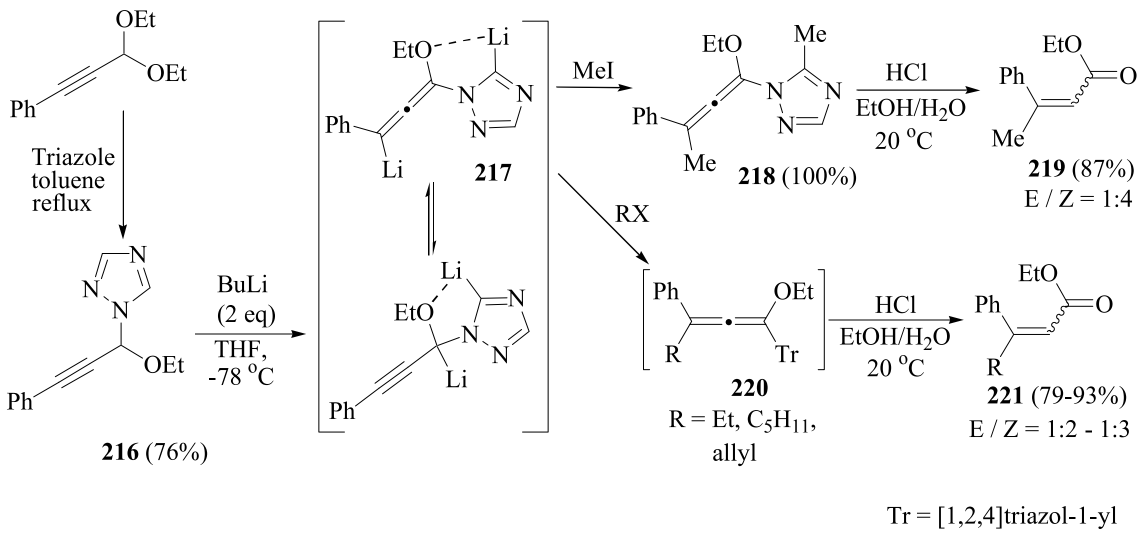
Faust and Weber utilized propargoyl synthon **184** for the synthesis of dialkynyl-1,2-diones **215** (Scheme 36).[126] This approach involves Dess-Martin[127,128] oxidation of intermediate alcohols **213** to **214** and affords diketones **215** in good yields except for the trimethylsilyl-substituted series (R^1 = TMS).



Scheme 36

Inverted regioselectivity of 1,2,4-triazole stabilized allenic anions.

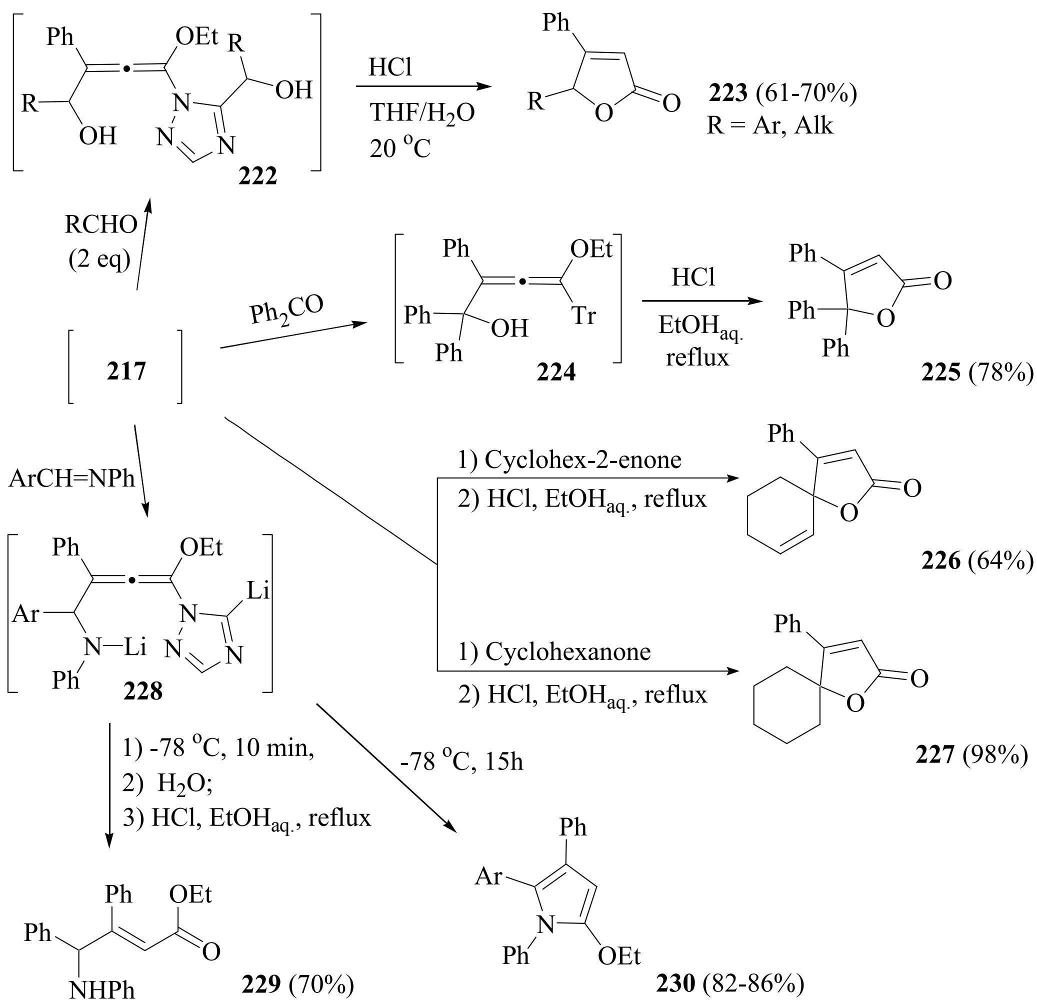
Unlike benzotriazole analog **183**, triazole derivative **216** have two acidic protons and on treatment with butyllithium produces allenic dianion **217** (Scheme 37). This dianion reacts with two equivalents of methyl iodide or only one equivalent of less active alkyl bromides to give adducts **218** and **220**, direct hydrolysis of which with dilute hydrochloric acid in aqueous ethanol (these compounds undergo hydrolysis even on silica gel) provides α,β-unsaturated esters **219** and **221**, respectively, as mixtures of *E* and *Z* isomers.[129]



Scheme 37

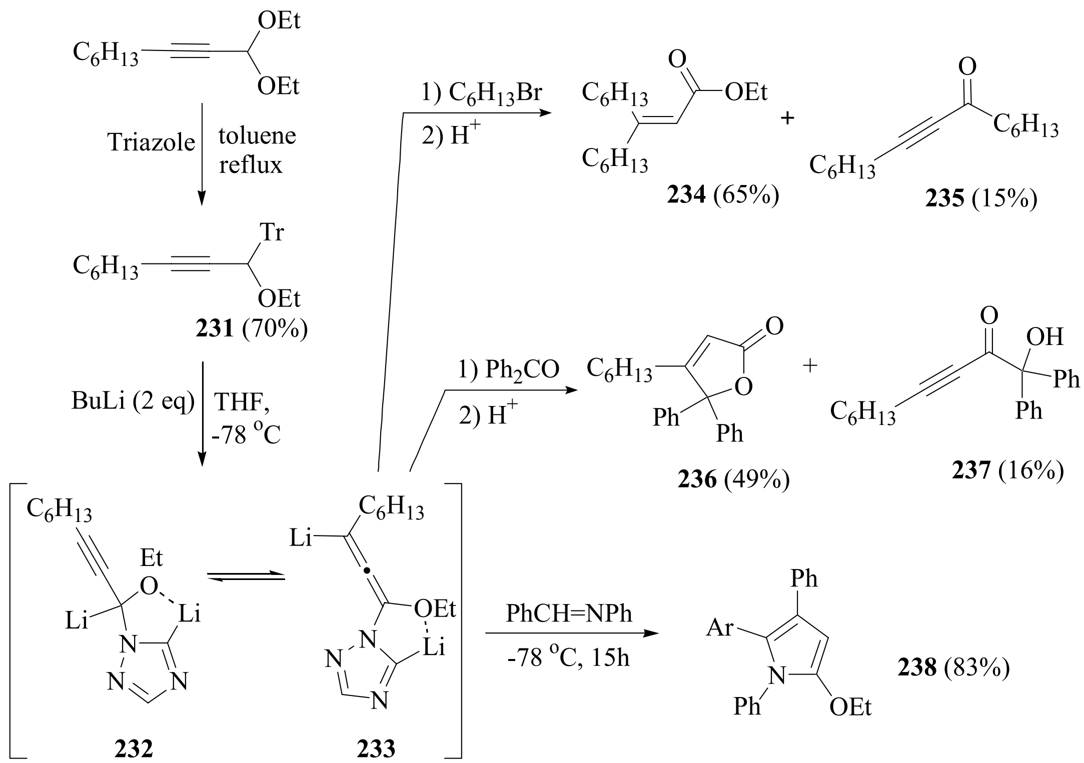
Reactions of dianion **217** with two equivalents of carbonyl compounds gave adducts of type **222** with aldehydes, cyclohexanone, and cyclohex-2-enone (exclusively product of 1,2-addition) and adduct **224** with one equivalent of benzophenone, which under acidic conditions gave lactones **223**, **225–227** (Scheme 38).[129]

Treatment of dianion **217** with imines at –78 °C for several minutes produced adduct **228**, which on quenching with water at the same temperature and subsequent hydrolysis gave product **229** (Scheme 38). In contrast, prolonged keeping of **228** at –78 °C resulted in cyclization by intramolecular substitution of triazole giving pyrrole **230**.[129]



Scheme 38

Reactions of alkyl acetylene derivative **231** with two equivalents of butyllithium followed by treatment with hexyl bromide, or benzophenone, and hydrolysis gave pairs of products **234** / **235** and **236** / **237**, respectively (Scheme 39). Treatment of dianions **232** $\rightleftharpoons$ **233** with benzylideneaniline produced exclusively pyrrole **238**.[129]



Scheme 39

6. References and Notes

1. Froling, A.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1962**, *81*, 1009.
2. Truce, W. E.; Roberts, F. E. *J. Org. Chem.* **1963**, *28*, 961.
3. Corey, E. J.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1075.
4. Corey, E. J.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1077.
5. For a review, see: Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.
6. Ager, D. J. In *Umpoled synthons: a survey of sources and uses in synthesis*; Hase, T. A., Ed.; Wiley: New York, 1987; p. 19.
7. Yus, M.; Nájera, C.; Foubelo, F. *Tetrahedron* **2003**, *59*, 6147.
8. Katritzky, A. R.; Lan, X.; Yang, J. Z.; Denisko, O. V. *Chem. Rev*. **1998**, *98*, 409.
9. Stetter, H.; Kuhlmann, H. *Organic Reactions* **1991**, *40*, 407.
10. Stetter, H.; Schreckenberg, M. Ger. Pat. 2262343, **1974**; *Chem. Abstr*. **1974**, *81*, 505015.
11. Stetter, H. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 639.
12. Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill Book Company: New York, 1969.
13. Breslow, R. *J. Am. Chem. Soc.* **1957**, *79*, 1762.
14. Breslow, R. *J. Am. Chem. Soc.* **1958**, *80*, 3719.
15. Breslow, R.; McNelis, E. *J. Am. Chem. Soc.* **1959**, *81*, 3080.

16. Kuebrich, J. P.; Schowen, R. L.; Wang, M.-s.; Lupes, M. E. *J. Am. Chem. Soc.* **1971**, *93*, 1214.
17. Stetter, H.; Rämsch, R. Y.; Kuhlmann, H. *Synthesis* **1976**, 733.
18. Mattson, A. E.; Bharadwaj, A. R.; Scheidt, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 2314.
19. Miyashita, A.; Matsuda, H.; Iijima, C.; Higashino, T. *Chem. Pharm. Bull.* **1992**, *40*, 43.
20. Miyashita, A.; Matsuda, H.; Higashino, T. *Chem. Pharm. Bull.* **1992**, *40*, 2627.
21. Review: Gröbel, B.-T.; Seebach, D. *Synthesis* **1977**, 357.
22. Smith, A. B., III; Adams, C. M. *Acc. Chem. Res.* **2004**, *37*, 365.
23. Seebach, D.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 231.
24. Seebach, D.; Wilka, E.-M. *Synthesis* **1976**, 476.
25. Seebach, D.; Bürstinghaus, R.; Gröbel, B.-T.; Kolb, M. *Liebigs Ann. Chem.* **1977**, 830.
26. Orsini, F.; Pelizzoni, F. *J. Org. Chem.* **1980**, *45*, 4726.
27. Mori, M.; Chuman, T.; Kohno, M.; Kato, K.; Noguchi, M.; Nomi, H.; Mori, K. *Tetrahedron Lett.* **1982**, *23*, 667.
28. Enders, D.; Schüßeler, T. *Tetrahedron Lett.* **2002**, *43*, 3467.
29. Fang, J.-M.; Chen, M.-Y. *Tetrahedron Lett.* **1988**, *29*, 5939.
30. Smith, A. B., III; Lodise, S. A. *Org. Lett.* **1999**, *1*, 1249.
31. Jiang, B.; Chen, Z. *Tetrahedron: Asymmetry* **2001**, *12*, 2835.
32. Araki, K.; Suenaga, K.; Sengoku, T.; Uemura, D. *Tetrahedron* **2002**, *58*, 1983.
33. Bio, M. M.; Leighton, J. L. *J. Org. Chem.* **2003**, *68*, 1693.
34. Sauers, R. R.; Valenti, P. C.; Crichlow, C. A. *J. Am. Chem. Soc.* **1982**, *104*, 6378.
35. Erni, B.; Khorana, H. G. *J. Am. Chem. Soc.* **1980**, *102*, 3888.
36. Berryhill, S. R.; Price, T.; Rosenblum, M. *J. Org. Chem.* **1983**, *48*, 158.
37. Reimer, L. M.; Conley, D. L.; Pompliano, D. L.; Frost, J. W. *J. Am. Chem. Soc.* **1986**, *108*, 8010.
38. Ziegler, F. E.; Schwartz, J. A. *J. Org. Chem.* **1978**, *43*, 985.
39. Funabashi, M.; Kobayashi, K.; Yoshimura, J. *J. Org. Chem.* **1979**, *44*, 1618.
40. Forns, P.; Diez, A.; Rubiralta, M. *J. Org. Chem.* **1996**, *61*, 7882.
41. Meyers, A. I.; Tait, T. A.; Comins, D. L. *Tetrahedron Lett.* **1978**, *19*, 4657.
42. Blatcher, P.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1074.
43. Ager, D. J. *J. Chem. Soc., Perkin Trans. 1* **1986**, 183.
44. Mukaiyama, T.; Narasaka, K.; Furusato, M. *J. Am. Chem. Soc.* **1972**, *94*, 8641.
45. Alvarez, F. M.; Vander Meer, R. K.; Lofgren, C. S. *Tetrahedron* **1987**, *43*, 2897.
46. Corey, E. J.; Seebach, D. *J. Org. Chem.* **1966**, *31*, 4097.
47. Blatcher, P.; Grayson, J. I.; Warren, S. *J. Chem. Soc., Chem. Commun.* **1978**, 657.
48. Villa, M.-J.; Warren, S. *Tetrahedron Lett.* **1989**, *30*, 5933.
49. Capilla, A. S.; Sánchez, I.; Caignard, D. H.; Renard, P.; Pujol, M. D. *Eur. J. Med. Chem.* **2001**, *36*, 389.
50. Ikehira, H.; Tanimoto, S.; Oida, T. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1223.
51. Saigo, K.; Hashimoto, Y.; Kihara, N.; Umehara, H.; Hasegawa, M. *Chem. Lett.* **1990**, 831.

52. Schill, G.; Jones, P. R. *Synthesis* **1974**, 117.
53. Song, J.; Hollingsworth, R. I. *J. Am. Chem. Soc.* **1999**, *121*, 1851.
54. Ogura, K.; Yamashita, M.; Suzuki, M.; Tsuchihashi, G. *Tetrahedron Lett.* **1974**, *15*, 3653.
55. Ogura, K.; Yamashita, M.; Furukawa, S.; Suzuki, M.; Tsuchihashi, G. *Tetrahedron Lett.* **1975**, *16*, 2767.
56. Fujiwara, K.; Takaoka, D.; Kusumi, K.; Kawai, K.; Murai, A. *Synlett* **2001**, 691.
57. Richman, J. E.; Herrmann, J. L.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, *14*, 3267.
58. Herrmann, J. L.; Richman, J. E.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, *14*, 3271.
59. Fang, J.-M.; Chou, W.-C.; Lee, G.-H.; Peng, S.-M. *J. Org. Chem.* **1990**, *55*, 5515.
60. *Protective Groups in Organic Synthesis*; Greene, T. W. and Wuts, P. G. M.; John Wiley & Sons: New York, 1999.
61. Rieger, D. L. *J. Org. Chem.* **1997**, *62*, 8546.
62. Deprez, P.; Mandine, E.; Vermond, A.; Lesuisse, D. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1287.
63. Muxfeldt, H.; Unterweger, W.-D.; Helmchen, G. *Synthesis* **1976**, 694.
64. Ravindranathan, T.; Chavan, S. P.; Tejwani, R. B.; Varghese, J. P. *J. Chem. Soc., Chem. Commun.* **1991**, 1750.
65. Ohshima, M.; Murakami, M.; Mukaiyama, T. *Chem. Lett.* **1986**, 1593.
66. Schöllkopf, U.; Hänßle, P. *Liebigs Ann. Chem.* **1972**, *763*, 208.
67. Baldwin, J. E.; Höfle, G. A.; Lever, O. W., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 7125.
68. Soderquist, J. A.; Hassner, A. *J. Org. Chem.* **1980**, *45*, 541.
69. Soderquist, J. A.; Hassner, A. *J. Am. Chem. Soc.* **1980**, *102*, 1577.
70. Tietze, L. F.; Brill, G. *Liebigs Ann. Chem.* **1987**, 311.
71. Schinzer, D. *Synthesis* **1989**, 179.
72. Gould, S. J.; Remillard, B. D. *Tetrahedron Lett.* **1978**, *19*, 4353.
73. Paquette, L. A.; DeRussy, D. T.; Rogers, R. D. *Tetrahedron* **1988**, *44*, 3139.
74. Everhardus, R. H.; Gräfing, R.; Brandsma, L. *Recl. Trav. Chim. Pays-Bas* **1978**, *97*, 69.
75. Oshima, K.; Shimoji, K.; Takahashi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1973**, *95*, 2694.
76. Bibang Bi Ekogha, C.; Ruel, O.; Julia, S. A. *Tetrahedron Lett.* **1983**, *24*, 4825.
77. Ruel, O.; Bibang Bi Ekogha, C.; Lorne, R.; Julia, S. A. *Bull. Soc. Chim. Fr.* **1985**, 1250.
78. Yus, M.; Gutiérrez, A.; Foubelo, F. *Tetrahedron* **2001**, *57*, 4411.
79. Cookson, R. C.; Parsons, P. J. *J. Chem. Soc., Chem. Commun.* **1976**, 990.
80. Harirchian, B.; Magnus, P. *J. Chem. Soc., Chem. Commun.* **1977**, 522.
81. Isobe, K.; Fuse, M.; Kosugi, H.; Hagiwara, H.; Uda, H. *Chem. Lett.* **1979**, 785.
82. Cabiddu, M. G.; Cabiddu, S.; Cadoni, E.; Cannas, R.; Fattuoni, C.; Melis, S. *Tetrahedron* **1998**, *54*, 14095.
83. Parham, W. E.; Motter, R. F. *J. Am. Chem. Soc.* **1959**, *81*, 2146.
84. Trost, B. M.; Hiroi, K.; Kurozumi, S. *J. Am. Chem. Soc.* **1975**, *97*, 438.
85. Sato, M.; Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 1609.

86. Takai, K.; Sato, M.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 108.
87. Sevrin, M.; Denis, J. N.; Krief, A. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 526.
88. Raucher, S.; Koolpe, G. A. *J. Org. Chem.* **1978**, *43*, 3794.
89. Corey, E. J.; Shulman, J. I. *J. Org. Chem.* **1970**, *35*, 777.
90. Krief, A. *Tetrahedron* **1980** , *36*, 2531.
91. Petragnani, N.; Rodrigues, R.; Comasseto, J. V. *J. Organomet. Chem.* **1976**, *114*, 281.
92. Piquard, J. L.; Hevesi, L. *Tetrahedron Lett.* **1980**, *21*, 1901.
93. Hevesi, L.; Piquard, J.-L.; Wautier, H. *J. Am. Chem. Soc.* **1981**, *103*, 870.
94. Katritzky, A. R.; Lang, H.; Wang, Z.; Lie, Z. *J. Org. Chem.* **1996**, *61*, 7551.
95. Katritzky, A. R.; Rachwal, S.; Caster, K. C.; Mahni, F.; Law, K. W.; Rubio, O. *J. Chem. Soc., Perkin Trans. 1* **1987**, 781.
96. Katritzky, A. R.; Serdyuk, L.; Xie, L. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1059.
97. Katritzky, A. R.; Wang, Z.; Lang, H.; Feng, D. *J. Org. Chem.* **1997**, *62*, 4125.
98. Katritzky, A. R.; Ji, Y.; Fang, Y.; Prakash, I. *J. Org. Chem.* **2001**, *66*, 5613.
99. Katritzky, A. R.; Kirichenko, K.; Ji, Y.; Steel, P. J.; Karelson, M. *ARKIVOC* **2003**, *vi*, 49.
100. Katritzky, A. R.; Kirichenko, K.; Hür, D.; Zhao, X.; Ji, Y.; Steel, P. J. *ARKIVOC* **2004**, *vi*, 27.
101. Katritzky, A. R.; Lang, H.; Wang, Z.; Zhang, Z.; Song, H. *J. Org. Chem.* **1995**, *60*, 7619.
102. Katritzky, A. R.; Rachwal, S.; Rachwal B. *J. Chem. Soc., Perkin Trans. 1* **1987**, 791.
103. Katritzky, A. R.; Rachwal, S.; Rachwal, B. *J. Org. Chem.* **1989**, *54*, 6022.
104. Katritzky, A. R.; Bayyuk, S. I.; Rachwal, S. *Synthesis* **1991**, 279.
105. Katritzky, A. R.; Xie, L.; Serdyuk, L. *J. Org. Chem.* **1996**, *61*, 7564.
106. Katritzky, A. R.; Feng, D.; Qi, M. *J. Org. Chem.* **1998**, *63*, 1473.
107. Katritzky, A. R.; Wang, Z.; Lang, H. *Organometallics* **1996**, *15*, 486.
108. Katritzky, A. R.; Kuzmierkiewicz, W.; Rachwal B.; Rachwal, S.; Thomson, J. *J. Chem. Soc., Perkin Trans. 1* **1987**, 811.
109. Katritzky, A. R.; Wu, H.; Xie, L. *Tetrahedron Lett.* **1997**, *38*, 903.
110. Katritzky, A. R.; Kuzmierkiewicz, W. *J. Chem. Soc., Perkin Trans. 1* **1987**, 819.
111. Unpublished results by present authors. Treatment of bis(benzotriazolyl)(4-methylphenyl)methane **91** with 4-vinylpyridine (1.1 eq.) in anhydrous THF in the presence of catalytic potassium *tert*-butoxide (0.05 eq.) at –10–(–5) °C for 30 min (deep blue-purple color of the reaction mixture was observed and reaction was complete upon color disappearance) gave 1-[3-(pyridin-4-yl)-1-(4-methylphenyl)-1-(benzotriazol-1-yl)propyl]benzotriazole **103** in 75% yield (purified by column chromatography on silica gel using ethyl acetate / hexanes 1:1), as white prisms from ethyl acetate / hexanes, mp 129–131 °C; ^{1}H NMR δ 8.49 (d, *J* = 6.0 Hz, 2H), 8.04 (d, *J* = 8.1 Hz, 2H), 7.31–7.17 (m, 8H), 7.14 (d, *J* = 6.0 Hz, 2H), 6.91 (d, *J* = 8.3 Hz, 2H), 3.91–3.85 (m, 2H), 2.81–2.76 (m, 2H), 2.43 (s, 3H); ^{13}C NMR δ 149.8, 149.3, 146.5, 139.9, 132.2, 132.0, 129.4, 128.2, 127.8, 124.5, 123.8, 120.3, 111.7, 85.7, 42.8, 30.5, 21.1. Anal. Calcd for $C_{27}H_{23}N_7$: C, 72.79; H, 5.20; N, 22.01. Found: C, 72.43; H, 5.48; N, 21.99.

112. Katritzky, A. R.; Bobrov, S.; Kirichenko, K.; Ji, Y. *J. Org. Chem.* **2004**, *69*, 303.
113. Katritzky, A. R.; Oniciu, D. C.; Ghiviriga, I.; Soti, F. *J. Org. Chem.* **1998**, *63*, 2110.
114. Katritzky, A. R.; Yang, Z.; Lam, J. N. *J. Org. Chem.* **1991**, *56*, 2143.
115. Katritzky, A. R.; Yang, Z.; Lam, J. N. *J. Org. Chem.* **1991**, *56*, 6917.
116. Katritzky, A. R.; Yang, Z.; Lam, J. N. *J. Org. Chem.* **1993**, *58*, 1970.
117. Katritzky, A. R.; Huang, Z.; Fang, Y.; Prakash, I. *J. Org. Chem.* **1999**, *64*, 2124.
118. Katritzky, A. R.; Jiang, J. *J. Org. Chem.* **1995**, *60*, 6.
119. Katritzky, A. R.; Zhang, G.; Jiang, J. *J. Org. Chem.* **1995**, *60*, 7589.
120. Katritzky, A. R.; Jiang, J. *J. Org. Chem.* **1995**, *60*, 7597.
121. Katritzky, A. R.; Feng, D.; Lang, H. *J. Org. Chem.* **1997**, *62*, 706.
122. Katritzky, A. R.; Wu, H.; Xie, L.; Rachwal, S.; Rachwal, B.; Jiang, J.; Zhang, G.; Lang, H. *Synthesis* **1995**, 1315.
123. Katritzky, A. R.; Lang, H. *J. Org. Chem.* **1995**, *60*, 7612.
124. Katritzky, A. R.; Yao, J.; Qi, M. *J. Org. Chem.* **1997**, *62*, 8201.
125. Poos, G. I.; Arth, G. E.; Beyler, R. E.; Sarett, L. H. *J. Am. Chem. Soc.* **1953**, *75*, 422.
126. Faust, R.; Weber, C. *Liebigs Ann.* **1996**, 1235.
127. Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155.
128. Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.
129. Katritzky, A. R.; Feng, D.; Lang, H. *J. Org. Chem.* **1997**, *62*, 715.

7. Authors' biographical data

Kostyantyn Kirichenko was born in Severodonetsk (Ukraine) in 1970. He received his MSc degree (1993) in Chemical Technology of Organic Compounds from Ukrainian State Chemical-Technological University (USCTU, Dnipropetrovsk, Ukraine) and PhD degree (Advisor: Prof. Mati Karelson; 2003) in Organic Chemistry from the University of Tartu (Tartu, Estonia). He worked as a research associate (1993–1996) and later as Assistant Professor (1996–2001) at the Department of Chemical Technology of Organic Compounds at USCTU. In 2001 Dr. Kirichenko joined the research group of Prof. Alan R. Katritzky at the University of Florida with whom he is working on development of new synthetic methodologies for the preparation of heterocyclic compounds, homologation – functionalization of carbonyl compounds, and development of Ionic Liquids based on Energetic Azoles.

Alan Katritzky was born in London, U.K. and educated at Oxford. He was a Founder Fellow of Churchill College, Cambridge, and then Professor/Dean School of Chemical Sciences at the University of East Anglia before crossing the Atlantic to become Kenan Professor and Director of The Center for Heterocyclic Compounds at the University of Florida in 1980. He has researched, published, lectured, and consulted widely especially in heterocyclic chemistry, synthetic methods, and QSPR. In 2000 he created the non-for-profit foundation ARKAT which publishes “Archive for Organic Chemistry” (Arkivoc) completely free on the Internet.