CHEMICAL REVIEWS

REVIEW

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Rongalite: A Useful Green Reagent in Organic Synthesis

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1. INTRODUCTION

Rongalite, also called Rongalit (Rongal-registered trademark of BASF), is sodium hydroxymethanesulfinate dihydrate, which is represented by the chemical formula $Na^+HOCH_2SO_2^-\cdot 2H_2O$. The salt has many names, such as formaldehyde sodium bisulfite adduct, formaldehyde sodium sulfoxylate, formaldehydesulfoxylic acid sodium salt, natrium formaldehydesulfoxylate, natrium hydroxymethanesulfinate, sodium formaldehydesulfoxylate, sodium methanalsulfoxylate, sodium oxymethanesulfinic acid, and sodium sulfoxylate formaldehyde.

Rongalite contains large, transparent, and tubular crystals. It is a strongly hygroscopic substance and should be stored in a dry, cool, dark place, protected from moisture. Rongalite is odorless or possesses a faint leek smell. The loss of purity and hence reactivity is indicated if it smells like fish.

Truter investigated the X-ray crystal structure[1] of rongalite and confirmed the chemical structure shown in Figure 1. There are several methods available in the literature for the preparation[2] of rongalite (**1**), and it is commercially available as lump, powder, and granules to meet the demands of various industrial applications.

The stability of rongalite at various temperatures and under acidic or basic conditions has been a studied thoroughly by Kunin.[3] Rongalite in aqueous solution was found to decompose at 80 °C to decrease the pH of the solution. At 80 °C, in aqueous solution, rongalite was found to decompose to produce sodium sulfite, sodium sulfide, formaldehyde, and water and liberate sulfur dioxide and hydrogen sulfide.[3b] When rongalite was heated at 100 °C, the decomposition was accompanied by an increase in pH owing to the production of sodium hydroxide. Rongalite exhibits maximum stability at pH 6−9. In a 30% solution of rongalite at 100 °C, in a stream of N_2, after 4−10 h, the decomposition products which have been identified include sodium sulfite, sodium thiosulfate, and sodium sulfide.[3a]

In French, "rongeage" means discharge, and rongalite is commonly used as a bleaching agent in the printing and dyeing industry.[4a−k] It is an excellent decolouring agent for some organic compounds and also for sugar juice, caramel, etc.[4k,l] Owing to its reducing property, rongalite constitutes an essential component of various redox-initiator systems for polymerization.[5] Rongalite has been used as an antidote against heavy metal (e.g., Hg, Au, Cu, Ba, Sb, Pb, and Bi) poisoning[6] and also as a photographic developer or an additive to photographic developers.[7] Interestingly, it has shown good bactericidal and fungicidal properties.[8] Rongalite has been widely investigated as a component of veterinary medicines.[9]

Although toxicological properties of rongalite have not been thoroughly explored, it is suspected of causing genetic defects. Rongalite liberates toxic gas on contact with acid. It may be harmful if absorbed through the skin, causes eye irritation, and may be harmful if swallowed or inhaled.[10]

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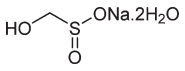

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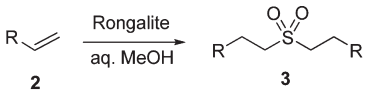
Figure 1. Chemical structure of rongalite.

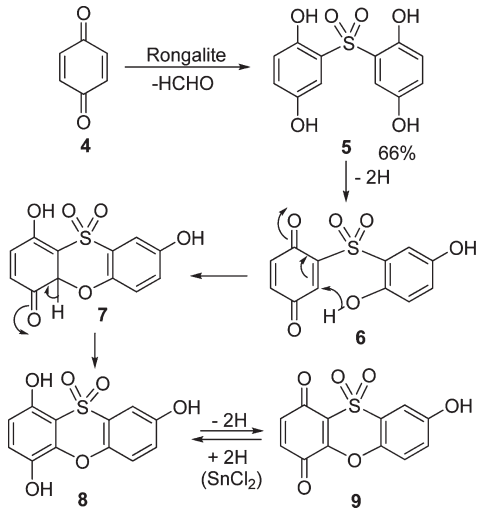
Scheme 1



2 3

R	CO_2Me	CN	CO_2H	$CONH_2$	$COCH_3$	2-pyridyl	4-pyridyl
Yield(%)	90	70	64	77	86	91	86

Scheme 2



4 5 6 7 8 9

2. SYNTHETIC USE OF RONGALITE

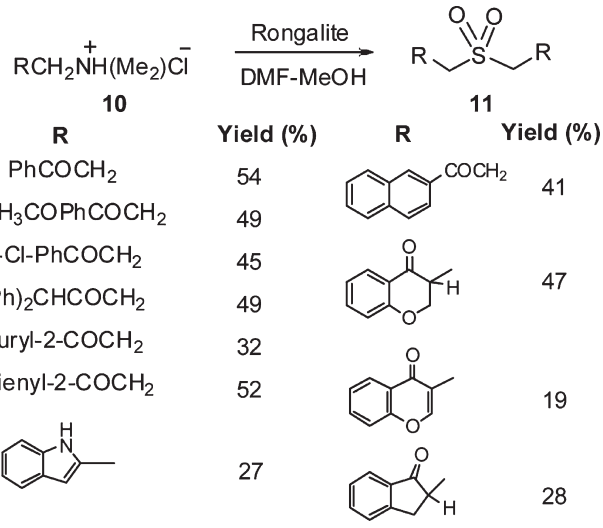
Although a variety of organic transformations are found to be mediated by rongalite, it has remained relatively unexplored in synthetic organic chemistry. Here we present a comprehensive review of literature appearing from 1905 until 2010, demonstrating the applications of rongalite as a versatile reagent in synthetic chemistry. The literature available has been broadly divided into 11 sections which reveal the utility of rongalite in a wide range of chemical reactions.

2.1. Preparation of Sulfones via Rongalite

Sulfone derivatives are preferred starting materials for diversity-oriented synthesis, and the sulfone moiety constitutes a core structural motif for various biologically active molecules.[11] The importance of sulfones and documented difficulties in their preparation[12] have always been of considerable interest to synthetic chemists. In this context, rongalite has been identified as a readily available source of sulfoxylate dianion (SO_2^{2-}) and provides a simple route for the preparation of sulfones.

In 1908, Fromm described[13] the synthesis of dibenzyl sulfone by the treatment of benzyl chloride with rongalite in aqueous alcohol. In 1971, Kerber and Starnick reported[14] the preparation of β,β'-disubstituted diethyl sulfones **3** via rongalite. Activated olefinic substrates such as **2** were reacted with rongalite in aqueous methanol to deliver diverse sulfone derivatives in good to excellent yield (64−91%, Scheme 1).

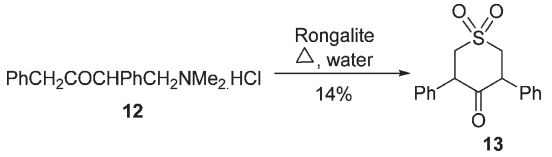
Scheme 3



10 11

R	Yield (%)	R	Yield (%)
$PhCOCH_2$	54	$COCH_2$	41
p-$CH_3COPhCOCH_2$	49		
p-Cl-$PhCOCH_2$	45		47
$(Ph)_2CHCOCH_2$	49		
Furyl-2-$COCH_2$	32		
Thienyl-2-$COCH_2$	52		19
	27		28

Scheme 4



12 13

The reaction of 1,4-benzoquinone (**4**) with rongalite in aqueous medium leads to the formation of symmetrical bis-(dihydroxyaryl) sulfone **5** in 66% yield (Scheme 2).[15] Similar products are observed when rongalite is treated with 1,2-benzoquinone as well as 1,4-naphthoquinone. Oxidation of sulfone **5** leads to intramolecular cyclization by participation of a hydroxyl group to furnish the cyclic sulfone derivative **8**/**9** (Scheme 2).[15]

Messinger and Greve revealed[16] that the hydrochloride salt of Mannich bases **10** can be reacted with rongalite in DMF−methanol to obtain symmetrical sulfones **11** in moderate to good yields (Scheme 3).

When 4-(dimethylamino)-1,3-diphenylbutan-2-one hydrochloride (**12**) was heated with rongalite in aqueous medium, an oil was generated which upon treatment with ethanol furnished cyclic sulfone **13** in 14% yield (Scheme 4).[17]

Dittmer's group has a pioneering contribution toward the expansion of rongalite in organic synthesis. In this regard, the preparation of symmetrical sulfones has been achieved by the treatment of primary halides with rongalite.[18] Various substituted benzyl bromides **14** were heated with rongalite at 80 °C in aqueous DMF in the presence of potassium bicarbonate to furnish dibenzyl sulfones **15** in a moderate to good yield (45−88%). When allyl bromide (**16**) was reacted with rongalite under similar reaction conditions, diallyl sulfone (**17**) was obtained in 20% yield. The cyclic sulfone **19** was obtained (43%) when 1,5-dibromopentane (**18**) was treated with rongalite. When α,α'-dibromo-*o*-xylene (**20**) was treated with rongalite in aqueous DMF at 40 °C, the sultine **21** was obtained in 43%

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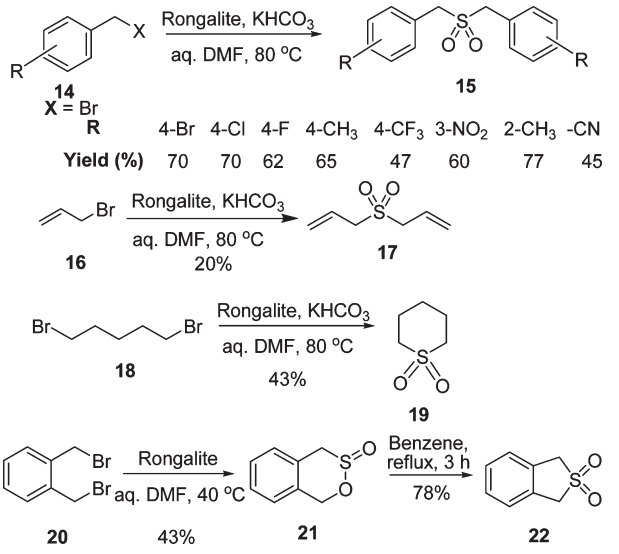
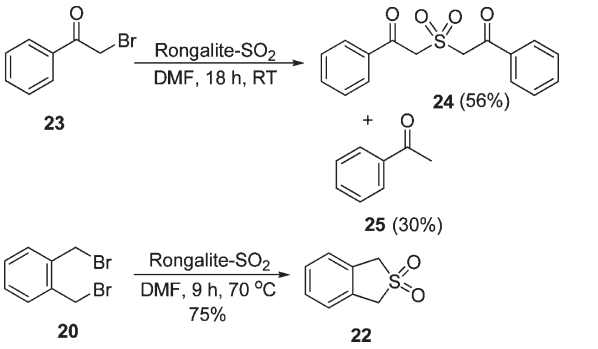
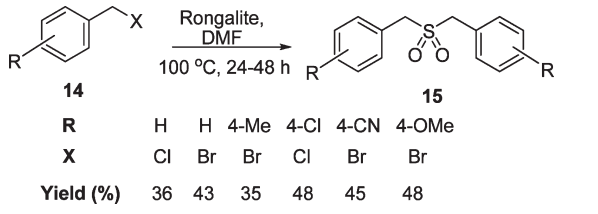
Scheme 5



Scheme 6



Scheme 7

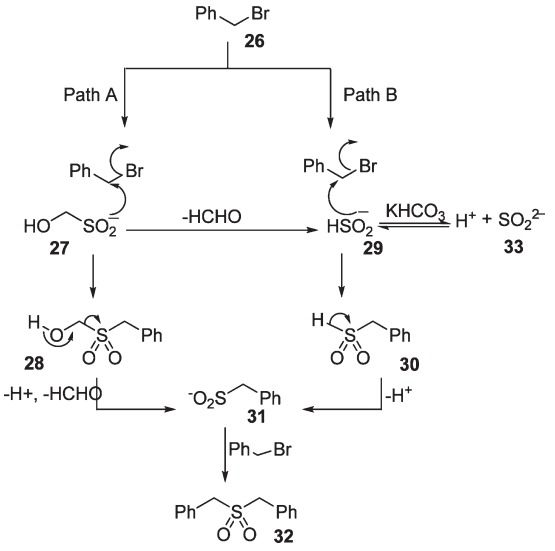


yield, which upon refluxing in benzene for 3 h delivered sulfone **22** in 78% yield (Scheme 5).[18]

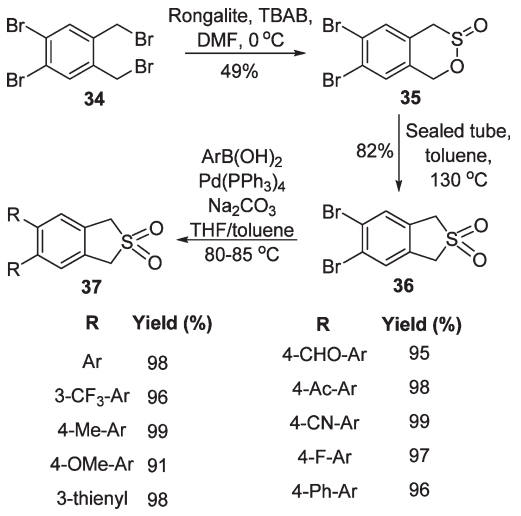
The combination of rongalite and sulfur dioxide has been used toward the synthesis of sulfones. Phenacyl bromide (**23**) reacts with a solution of sulfur dioxide obtained by passing SO_2 into anhydrous DMF and rongalite at room temperature to give diphenacyl sulfone (**24**) in 56% yield and acetophenone (**25**) in 30% yield.[18] Also, α,α'-dibromo-*o*-xylene (**20**) was found to react with rongalite−SO_2 in DMF at 70 °C to furnish sulfone **22** in 75% yield (Scheme 6).[19]

Harris reported[20] the synthesis of several aromatic bissulfones **15** by the treatment of various benzyl halides **14** with rongalite. The reactions were performed in DMF at 100 °C to obtain

Scheme 8



Scheme 9



the variously substituted bissulfones **15** in moderate yields (Scheme 7).

Two possible mechanisms for the formation of sulfone derivatives are shown in Scheme 8.[20] The first path involves the nucleophilic displacement of bromide in benzyl bromide by hydroxymethanesulfinate anion (**27**), followed by the loss of a formaldehyde molecule in the presence of a base, generating a nucleophile, **31**, suitable for the second step. The formation of sulfone can also be explained by the initial nucleophilic displacement by sulfinate anion (**29**) generated from rongalite. Since no intermediates have been isolated, either of these routes appears to be operating simultaneously for the generation of sulfones (Scheme 8). Dittmer and co-workers[18] have recommended that addition of potassium bicarbonate to the reaction mixture leads to the formation of SO_2^{2-} dianion (**33**) via the deprotonation of HSO_2^-, which is a better electron donor than HSO_2^-. Benzyl halides with electrophilic substituents can accept an electron easily from SO_2^{2-} dianion (**33**) and undergo substitution via radical anions.

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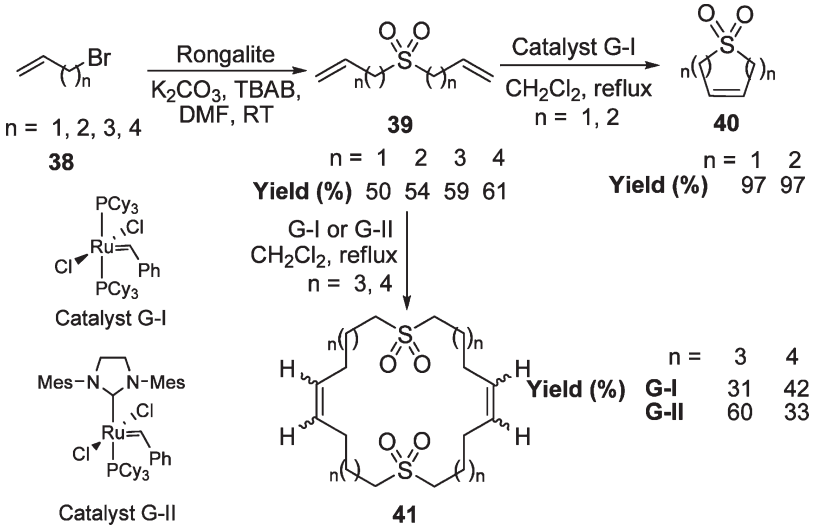
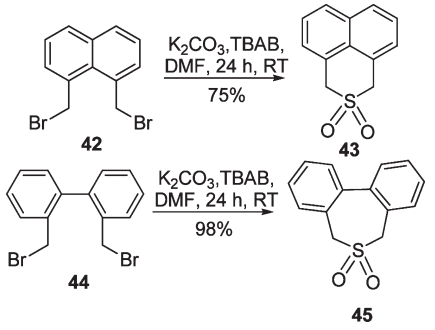
Scheme 10



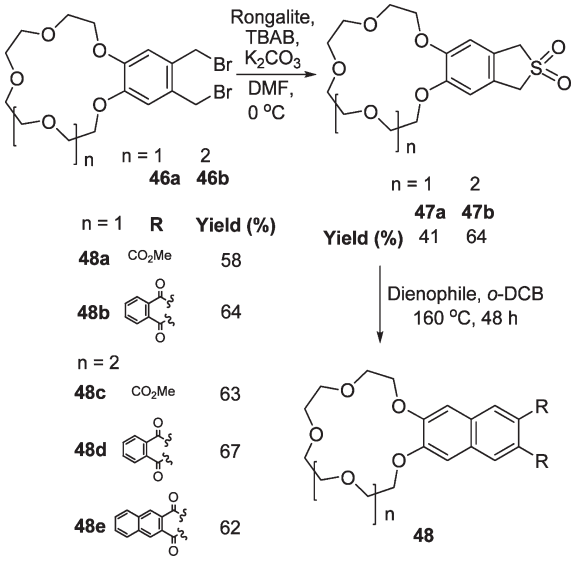
Scheme 11



To expand the utility of rongalite, Kotha and co-workers have demonstrated[21] the synthesis of highly functionalized benzosulfones via rongalite. In view of a report indicating the use of tetrabutylammonium bromide (TBAB) as a phase-transfer catalyst (PTC) in DMF to prepare the sultine,[19] the dibromide **34** was treated with rongalite in the presence of TBAB in DMF to deliver the sultine derivative **35** in 49% yield. The rearrangement of **35** under thermal conditions gave the corresponding sulfone **36**. Later, Suzuki–Miyaura cross-coupling[22] reactions between the dibromosulfone **36** and boronic acids in the presence of Pd(0) catalyst delivered cross-coupling products such as **37** (Scheme 9). Additional functional groups present in the cross-coupling products can serve as a useful handle for further synthetic manipulation. Since a large number of boronic acids are commercially available, this route can be an attractive option for the combinatorial synthesis of sulfone derivatives.

In another example,[23] the open-chain, terminally olefinic sulfones **39** have been obtained by treatment of alkenyl bromides with rongalite. The reaction has been performed at room temperature, and potassium carbonate has been used as a base in the presence of TBAB. Furthermore, symmetrical bisolefinic sulfones **39** have been subjected to a ring-closing metathesis[24] (RCM) protocol to afford the cyclic and macrocyclic sulfones **40** and **41**, respectively (Scheme 10).[23]

Scheme 12



Interestingly, when the substrate, such as 1,8-bis(bromomethyl) naphthalene (**42**), was treated with rongalite and potassium carbonate under PTC conditions, the corresponding six-membered sulfone **43** was produced in 75% yield. Similarly, 2,2′-bis-(bromomethyl)-1,1′-biphenyl (**44**) gave the corresponding seven-membered sulfone **45** in 98% yield (Scheme 11).[23]

Toward the preparation of highly functionalized crown ethers, a straightforward method employing the benzocrown-based sulfone as a key building block has been reported.[25] When the dibromo derivatives **46a** and **46b** were treated with rongalite in the presence of potassium carbonate and TBAB in DMF, the crown-based sulfones **47a** and **47b** were generated, respectively. When sulfones **47a** and **47b** were subjected to a Diels–Alder (DA)[26f,g] reaction with various dienophiles using *o*-dichlorobenzene (*o*-DCB) as a solvent at 160 °C for 48 h, highly functionalized benzocrown ether derivatives **48a**–**e** were obtained in moderate to good

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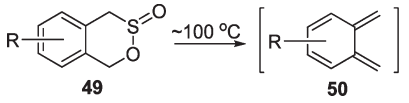
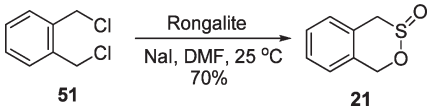
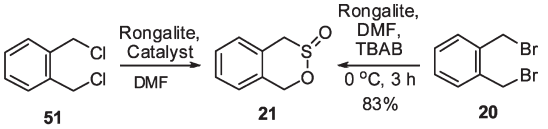
Scheme 13



Scheme 14



Scheme 15



Catalyst	Temp (°C)	Yield(%)	Time (h)
NaI	25	70	26
TBAB	25	73	12
-	60	0	48

yields via a concomitant dehydrogenation of intermediate DA adducts (Scheme 12).[25]

2.2. Preparation of Sultines via Rongalite

The transient intermediates related to *o*-quinodimethane[26] (*o*-QDM) or *o*-xylylene **50** have a remarkable utility in DA chemistry, and they provide easy routes for the synthesis of complex polycyclic compounds. Although several methods are available[26] for the generation of *o*-QDM intermediates, sultine derivatives **49** provide an easy access to *o*-QDM intermediates **50** under mild reaction conditions (Scheme 13).

Dittmer and co-workers have reported[18] a simple procedure for the synthesis of sultines via rongalite. In this regard, α,α'-dibromo-*o*-xylene (**20**) has been treated with rongalite in aqueous DMF to obtain the sultine derivative **21** in 43% yield (Scheme 5). Later, the procedure for the preparation of sultines was improved,[19] and α,α'-dichloro-*o*-xylene (**51**) was treated with rongalite and sodium iodide in DMF at 25 °C to obtain sultine **21** in 70% yield (Scheme 14).

Interestingly, when α,α'-dichloro-*o*-xylene (**51**) was treated with rongalite in the presence of a catalytic amount of TBAB at 25 °C, the sultine **21** was obtained in 73% yield. Dichloro compound **51** was found to be unreactive even at 60 °C when the reaction was performed in the absence of TBAB. The optimum yield (83%) of sultine **21** was obtained in 3 h by performing the reaction of rongalite with α,α'-dibromo-*o*-xylene (**20**) in the presence of TBAB at 0 °C (Scheme 15).[19]

It is interesting to note that constrained dibromoxylenes such as **52** (Figure 2) failed to react with rongalite to furnish desired sultines[27] under Dittmer's conditions.

Fullerenes have been the subject of intense research activity owing to their varied applications in material science, electronics, and nanotechnology.[28] Among the numerous methods available for the generation of *o*-QDM intermediates, sultine derivatives have provided the most convenient route for the preparation of

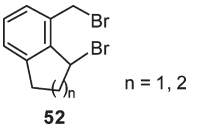
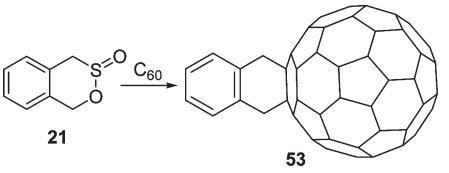


Figure 2. A constrained dibromoxylene derivative fails to furnish sultine.

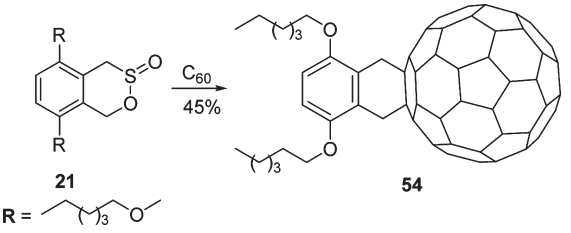
Scheme 16



Ratio 21:C_{60}	Yield (%)[a]		Yield (%)[b]	
5:1	10	12[c]	10	10[c]
2:1	39	44[c]	22	31[c]
2:1	30	44[c]	24	40[c]
1:1.1	23	28[c]	30	47[c]

[a] Yield obtained under microwave irradiation
[b] Yield obtained by conventional heating
[c] Based on recovered C_{60}

Scheme 17



functionalized fullerene derivatives under mild reaction conditions. When the equimolar (1:1.1) mixture of **21** and fullerene C_{60} was refluxed overnight, cycloadduct **53** was obtained in 30% yield (47% based on unreacted fullerene C_{60}) together with a mixture of bisadducts (Scheme 16).[29] The sultine **21** was in turn prepared using rongalite.

Furthermore, *p*-dihexyloxy-substituted sultine **54** prepared via rongalite was subjected to DA reaction with fullerene C_{60} to obtain the functionalized fullerene derivative **55** in 45% yield (Scheme 17).[29]

In 1995, Chung and co-workers synthesized furanosultine **57**, 2,5-dimethylthienosultine **60**, and pyrrolosultine **62** using rongalite.[30] When 3,4-bis(chloromethyl)furan (**56**) was reacted with rongalite and TBAB in DMF at 25 °C, the desired sultine **57** was obtained in 40% yield. The compound **56** was in turn obtained from the diacetate **55** by treatment with aluminum trichloride. The bis(chloromethyl)thiophene **59** has been prepared by the chloromethylation of 2,5-dimethylthiophene (**58**) in 48% yield. Treatment of thiophene derivative **59** with rongalite furnished the thienosultine **60** in 35% yield. Similarly, when 3,4-bis(chloromethyl)-*N*-tosylpyrrole (**61**) was reacted with rongalite, pyrrolosultine **62** was obtained in 62% yield (Scheme 18).

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When furan-based sultine **57** was subjected to DA reaction with 3 equiv of dimethyl acetylenedicarboxylate (DMAD) in benzene at 120−123 °C in a sealed tube for 1 h, 5,6-dimethylidene-7-oxanorbornene **68a** was obtained in 38% yield along with some polymeric byproduct. Similar results were observed when the DA reaction was performed with dienophiles such as diethyl fumarate (DEF), diethyl maleate (DMM), and furanonitrile (FN). Investigations based on DA reaction of 2,5-dimethylthiophenosultine **60** with several dienophiles revealed that the formation of a fused structure of type **67** is preferred rather than the bridged structure **68**. The DA reaction of the sultine **60** with DIMF produced the fused adducts **67** along with thiophene-fused sulfolene **64**. In the absence of dienophile, sultine **60** underwent thermolysis to give sulfolene **64** in 90% yield. A series of experiments revealed that the sulfolene **64** has very low reactivity compared to the corresponding sultine **60** in DA reaction as only starting material could be recovered when it was subjected to DA reaction with DIMF and FN. *N*-Tosylpyrrolosultine **62** reacts with a variety of dienophiles (3 equiv) at 150−170 °C to give three types of products: sulfolene **65**, 1:2 DA adducts such as **69**, and fused adducts of type **67**. When 1 equiv of dimethyl acetylenedicarboxylate was used, only sulfolene **65** and fused adduct **67a** were obtained. When sultine **62** was treated with dimethyl fumarate at 170 °C, a fused adduct, **67a** (63%), and a rearranged sulfolene, **65** (32%), were formed. Interestingly, sulfolene **65** produced **69a** as a sole product upon the treatment with dimethyl acetylenedicarboxylate. The experimental studies have indicated the difference in the reactivities of furano-, thieno-, and *N*-tosylpyrrolo-fused sultines **57**, **60**, and **62** and the corresponding sulfones **63**−**65** (Table 1).[30]

The authors proposed a mechanism which involves the formation of non-Kekule biradicals **66**, followed by DA reaction with a dienophile to form either bridged adducts **68** or fused adducts **67**. Both of these adducts may react with another molecule of dienophile to generate 1:2 adducts **69**. Another possibility involves the first DA reaction on the aromatic side of sultines **57**, **60**, and **62** to give **70**, from which expulsion of SO_2

Scheme 18

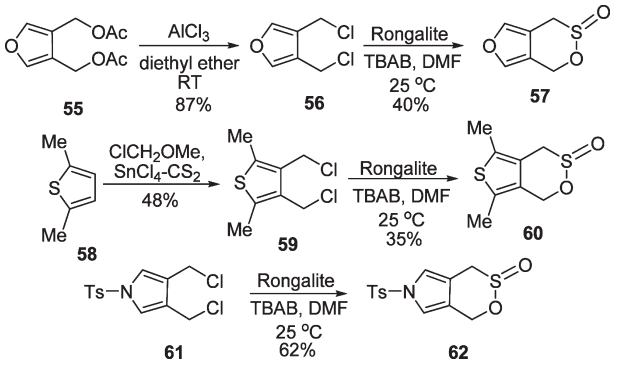

Table 1

	Dienophile	Products (Yield %)
57	DMAD (3 equiv., 120-123 °C)	**68a** (E=CO_2Me) (38)
	DEF	**68b** (E=CO_2Et) (46)
	DMM	**68b** (E=CO_2Me) (38)
	FN	**64b** (E=CN) (53)
60	–	**64** (90)
	DMAD	**64** (44) + Unknown
	DiMF	**64** (49) + **67b** (E=CO_2Me) (40)
62	DMAD (165-170 °C)	**65** (40) + **69a** (E=CO_2Me) (42) + **67a** (E=CO_2Me)(5)
	DMAD (1 equiv., 155 °C)	**65** (40) + **67a** (E=CO_2Me)(9)
	DMAD (110 °C)	**65** (30) + **65a** (E=CO_2Me) (38) + **67a** (E=CO_2Me) (8)
	DiMF	**65** (32) + **67b** (E=CO_2Me) (63)
	FN	**65** (34) + **67b** (E=CN) (50)
64	DiMF (180 °C)	**64** (99)
	FN (180 °C)	**64** (99)
65	DMAD (170 °C)	**69a** (97)
	DMF (170-240 °C)	**65** (73)

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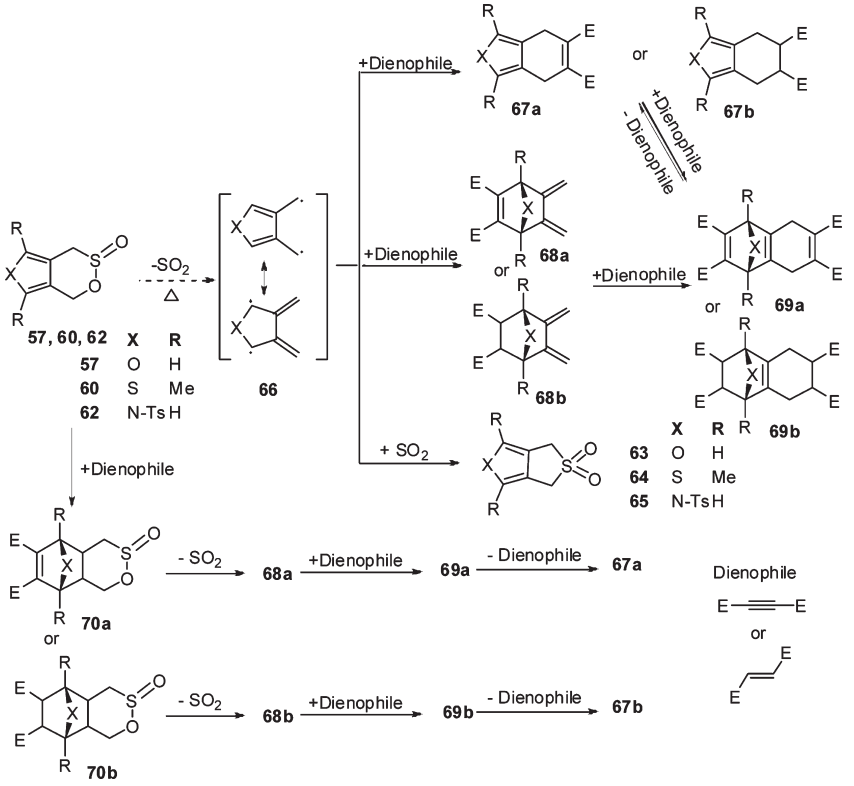
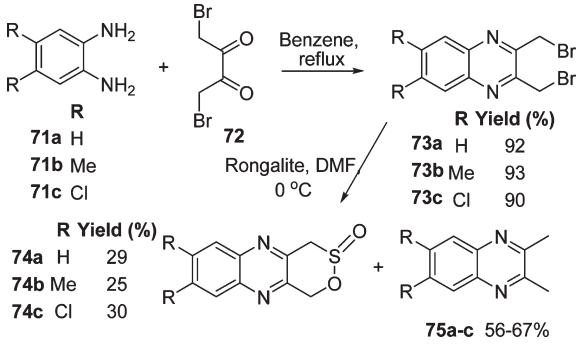
Scheme 19



Scheme 20



occurs to give bridged adducts **68**. Furthermore, the addition of a dienophile to **68** may occur to produce **69**, which can undergo a retro-DA reaction to afford **67** (Scheme 19).[30]

In 1997, Chung and co-workers prepared[31] quinoxalino-fused sultines **74a**−**c** using rongalite. To this end, substituted *o*-diaminobenzene derivatives **71a**−**c** were reacted with 1,4-dibromobutane-2,3-dione (**72**) to obtain the quinoxaline-based dibromides **73a**−**c**. When these dibromides were treated with rongalite, along with the sultines **74a**−**c**, debrominated byproducts **75a**−**c** were formed (Scheme 20).[31] However, these byproducts **75a**−**c** were converted back to dibromo derivatives **73a**−**c** by treatment with *N*-bromosuccinimide.

The DA reactions of sultines **74a**−**c** with various dienophiles (3 equiv) were performed in toluene at 200 °C in a sealed tube (Scheme 20). When DEF or DIMF was used as a dienophile, 1:1 adducts **78a**−**c** and **79a**−**c** were obtained in good yields. When DMAD was used as a dienophile, the DA reaction was found to be accompanied by spontaneous aromatization, resulting in the formation of aromatized products **80a**−**c** in moderate to excellent yields (41−94%) depending upon the nature of the substituents present in the parent system. In the absence of a dienophile, sultine **74a** underwent the thermal extrusion of SO_2 to give cyclobuta[1,2-*b*]quinoxaline **81a** in 96% yield. Thermolysis of **74a** in the presence of methanol or cyclohexa-1,4-diene furnished **77a** in 89−99% yield (Scheme 21).[31]

When **74a**−**c** were treated with an excess amount of *N*-phenylmaleimide at 200 °C, two DA adducts, **83a**−**c** and **84a**−**c**, were obtained. When 1 equiv of NPM was used, 1:1 adducts **82a**−**c** were obtained in 54−72% yields (Scheme 22).[31] 7,8-Disubstituted quinoxalino-fused sultine building blocks **74a**−**c** have a distinct advantage over the corresponding sulfolene derivatives because the former compounds open up at lower temperature and sulfolenes require a high temperature (≥290 °C) to generate *o*-QDM intermediates.

Interestingly, the use of sultines has been extended toward the preparation of highly functionalized fullerene derivatives.[32] In this regard, treatment of dibromides **85a** and **85b** with rongalite in DMF in the presence of a catalytic amount of TBAB furnished the sultine derivatives **86a** and **86b** in 50% and 80% yields, respectively. Similarly, when the dibromide **87** was reacted with rongalite, in the presence of a catalytic amount of TBAB, the desired sultine **88** was obtained in 70% yield. Furthermore, the dibromide **89** reacted with rongalite under the reaction conditions previously described to give the corresponding sultine **90** in 49% yield (Scheme 23).

The sultines **86a**, **86b**, **88**, and **90** were subjected to DA reaction with fullerene C_{60} in refluxing toluene to furnish the

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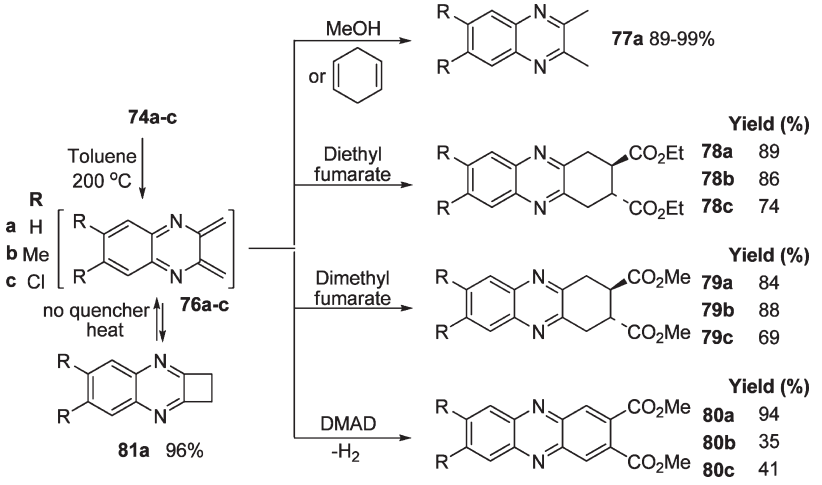
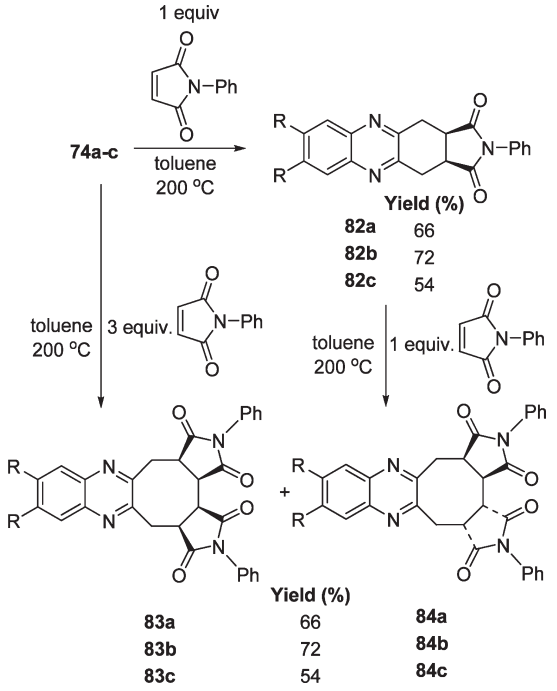
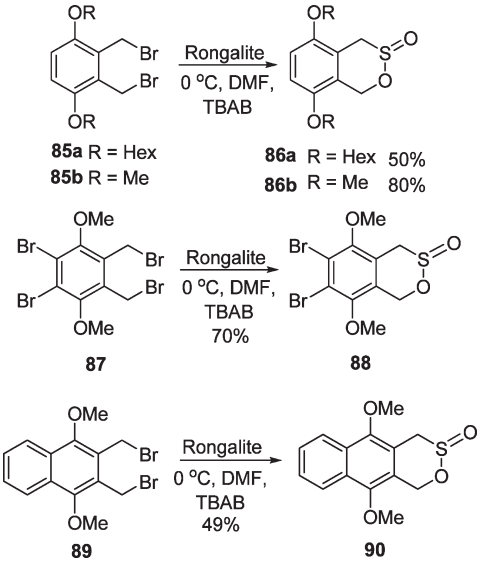
Scheme 21



Scheme 22



Scheme 23



corresponding 1,2-dihydrofullerene derivatives **92a**−**d** in moderate yields (22−45%). The alkyl groups in cycloadducts **92a**−**d** were removed by treatment with the boron tribromide. The dealkylation of **92a** delivered **93a** together with *p*-benzoquinone derivative **94a**. However, **92d** and **92c** were treated with BBr_3 and directly oxidized to deliver **94b** and **94c**, respectively (Scheme 24).[32]

The strategy depicted in Scheme 23 has been extended toward the preparation of sultine **97** in 78% yield.[33] Finally, the DA reaction of sultine **97** with fullerene C_{60} furnished the cycloadduct **98**, which was further converted into the fullerene-based *p*-benzoquinone derivative **99** by treatment with BBr_3 (Scheme 25).[33]

The reaction of 2,3-disubstituted 6,7-dibromomethylquinoxalines **101a**−**c** with rongalite gave quinoxalino-fused sultines **102a**−**c** in 55−76% yields. The dibromides **101a**−**c** were in turn obtained by the *N*-bromosuccinimide (NBS) bromination of the corresponding 6,7-dimethylquinoxaline derivatives **100a**−**c** (Scheme 26).[34]

The DA reactions of sultines **102a**−**c** with 3 equiv of DEF, DIMF, DMM, FN, or *N*-phenylmaleimide were performed in toluene to obtain the corresponding DA adducts. The reaction involves the extrusion of SO_2 from sultine derivatives to generate the quinoxalino-6,7-quinodimethanes **103a**−**c**, which were intercepted by dienophiles to furnish 1:1 adducts **106**−**110**. Minor amounts of sulfones **104a**−**c** were also obtained; however, these did not react with dienophiles even at 210 °C. In the absence of a dienophile, sultines **102a**−**c** underwent thermal extrusion of SO_2 to form cyclobuta[6,7-*g*]quinoxalines **105a**−**c** and the rearranged sulfolenes **104a**−**c** in various ratios depending upon the substituents. The same mixtures were obtained during the pyrolysis of sultines **102a**−**c** in toluene mixed with methanol. Cyclobuta[6,7-*g*]quinoxalines **105a**−**c** did not react with any of the above dienophiles upon heating at 210 °C for 24 h (Scheme 27).[34]

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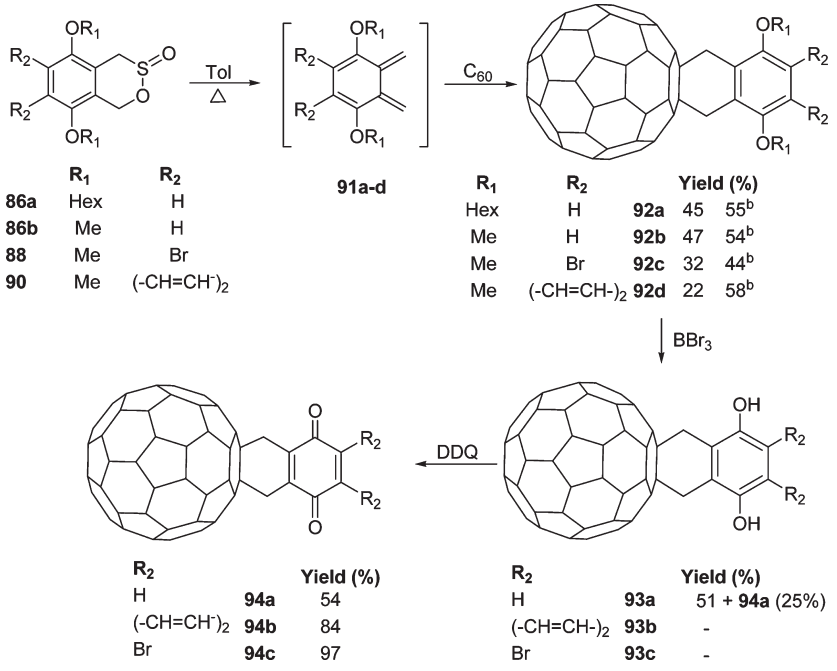
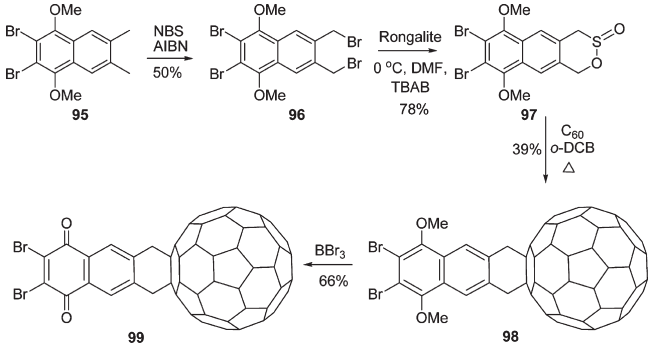
Scheme 24[a]

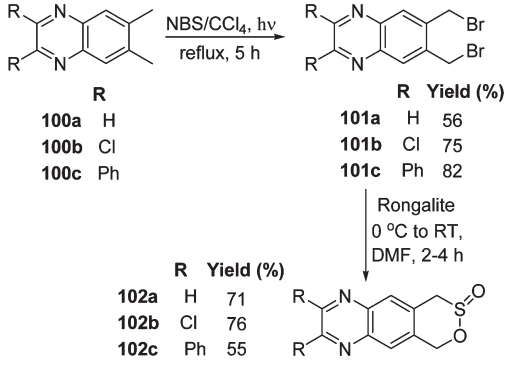


[a] A superscript "b" indicates yields based on consumed C_{60}.

Scheme 25



Scheme 26



The pyrazino-fused sultine **114** has been prepared by the reaction of bisbromide **112** with rongalite in DMF in the presence of a catalytic amount of TBAB. The bisbromide **112** has in turn been obtained by the bromination of commercially available 2,3-dimethylpyrazine (**111**). The sultine **114** was refluxed in toluene in the presence of 1.2 equiv of dienophiles to generate 1:1 DA adducts **117**−**120** in good to excellent yields. In the absence of any quencher, pyrazine-based sulfolene **116** was obtained in 73% yield (Scheme 28).[34]

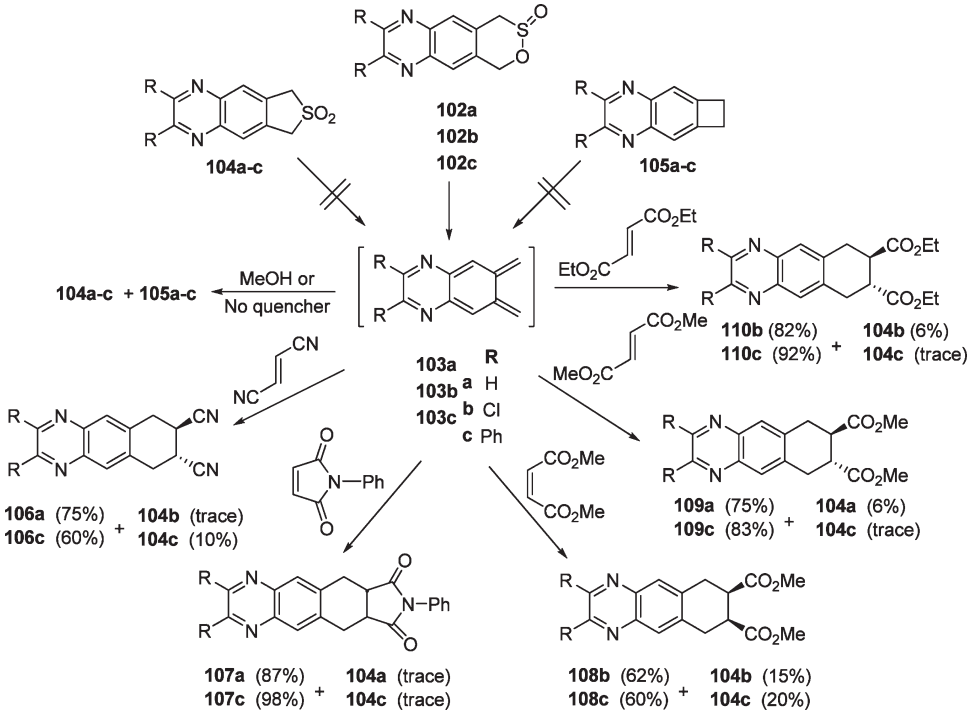
Heterocycle-containing sultines such as quinoxalinosultines **74a**−**c**, **102a**−**c**, and pyrazino-fused sultine **114** were subjected to DA reaction with fullerene C_{60} in *o*-DCB (in toluene for **114**) to obtain the 1:1 cycloadducts in good yields (Scheme 29).[34] Interestingly, the monoaddition product of C_{60} is predominantly formed without detection of an appreciable amount of bisaddition products.

In an interesting piece of work, Chung and co-workers[35] prepared a variety of 3,4-bis(chloromethyl)thiophenes **59** and **125** via the chloromethylation of the corresponding 2,5-disubstituted thiophenes **58** and **124**. The dichloro compounds **59** and **125** react with rongalite in the presence of TBAB to furnish thienosultines **60** and **126**. When thienosultines **60** and **126** were heated in a sealed tube at 180 °C, the corresponding sulfolenes **64** and **127** were obtained in 83−94% yields (Scheme 30).[35]

The various dienophiles were reacted with sultines **60** and **126a,b** to obtain Diels−Alder adducts. For example, sultine **126c** reacts with *N*-phenylmalimide to give DA adduct **128** in 82% yield accompanied by the formation of sulfolene **127c** in 6% yield. Along similar lines, DEF, FN, and DIMF were found to afford the corresponding DA adducts **129**−**131** under the sealed tube reaction conditions with **126c**. All DA reactions were accompanied by the generation of sulfolene **127c** (Scheme 31).[35]

Nucleophilic ring-opening of sultine **126a** with *n*-BuLi generated sulfinyl alcohol **132** in 33% yield. Sultine **60** was found to react with 2-mercaptoethanol in a sealed tube to deliver **133** in 21% yield along with the corresponding sulfolene **64** in 30% yield. When methanol was used as a radical trapping reagent,

Scheme 27



sealed tube reaction of sultine **60** in benzene furnished **134** in 19% yield and rearranged sulfolene **64** in 20% yield (Scheme 32).[35]

In 2004, Chung and co-workers[36] prepared a variety of thienosultines using rongalite and employed DA strategy toward the preparation of highly functionalized fullerene derivatives. Thiophene derivatives **136** and **137** were obtained by lithium exchange of 2,5-dibromothiophene **135**, followed by thiolation. The chloromethylation of thiophene derivatives **136** and **137** gave **138** and **139**, respectively. The reaction of **138** and **139** with rongalite at room temperature in DMF in the presence of a catalytic quantity of TBAB delivered thienosultines **140** and **141**, respectively. Sultine derivatives **140** and **141** underwent DA reaction with fullerene C_{60} in *o*-DCB at the reflux temperature to furnish 1:1 cycloadducts **142** and **143** and 2:1 bisadducts **144** and **145**). Remarkably, when the DA reaction was carried out under the microwave irradiation conditions, the reaction time was decreased considerably compared to that in conventional heating conditions (Scheme 33).[36]

The naphthosultine **149** has been prepared starting with 2,3-naphthalenedicarboxylate **146**. Reduction of the diester **146** with lithium aluminum hydride gave the diol **147** (96%), which upon bromination furnished the dibromo derivative **148** in 70% yield. The naphthosultine **149** was obtained in 63% yield by the reaction of dibromo derivative **148** with rongalite in the presence of TBAB in DMF. The DA reactions of naphthosultine **149** with various electron-deficient dienophiles were performed in a sealed tube at 180 °C to obtain 1:1 cycloadducts **152**−**155** in 67−95% yields. It is interesting to note that formation of DA cycloadducts was accompanied by the formation of sulfone derivative **151**. In the absence of a dienophile, naphthosulfolene **151** was formed in 84% yield (Scheme 34).[37]

Interestingly, benzodisultine **158** has been prepared as a diastereoisomeric mixture in 56% yield by the treatment of 1,2,4,5-tetrakis(bromomethyl)benzene (**157**) with rongalite and TBAB in DMF. The tetrabromide **157** was in turn prepared by the bromination of 1,2,4,5-tetramethylbenzene (**156**) using NBS (Scheme 35).[37]

Townsend and co-workers[38] prepared 6,7-dichloro-1,4-dihydro-2,3-benzoxathiin 3-oxide (**160**), which was used as a precursor for the generation of the corresponding *o*-quinodimethane. In this regard, 1,2-bis(bromomethyl)-4,5-dichlorobenzene (**159**) was reacted with rongalite in the presence of TBAB to obtain the corresponding sultine **160** in quantitative yield. **160** was refluxed in benzene with ethyl (*E*)-3-nitroacrylate to furnish DA adduct ethyl 6,7-dichloro-3-nitro-1,2,3,4-tetrahydro-2-naphthoate (**161**) in 71% yield. When **161** was subjected to NBS bromination with tungsten light, followed by dehydrobromination at −15 °C with triethylamine, compound **162** was obtained in 88% yield (Scheme 36).[38]

Constrained α-amino acid (AAA) derivatives are used extensively in the design and synthesis of a variety of bioactive peptides.[39] In this regard, the sultine **21** has been prepared using rongalite and reacted with methyl 2-acetamidoacrylate (**163**) at toluene reflux temperature to give tetralin-based AAA derivative **164** in 66% isolated yield. In addition, the diiodotetralin derivative **167** has been subjected to Suzuki−Miyaura (SM) cross-coupling reaction to obtain highly functionalized tetralin derivatives **167**. For example, diiodotetralin derivative **167** reacts with *p*-methylphenylboronic acid in the presence of $[Pd(PPh_3)_4]$ catalyst and aqueous sodium carbonate in THF−toluene to afford tetralin-based AAA derivative **168** in 89% yield (Scheme 37).[40a,b] In another example, sultine **166** was directly subjected to SM reaction, and then DA reaction was performed at the sultine part to obtain polycyclic aromatic compounds.[40c]

Toward the preparation of rotaxanes, sultine derivative **173** has been constructed using rongalite.[41] The DA reaction has been performed with sultine **174** to generate various rotaxanes **175**−**177**. In this regard, the protection of the amino group of

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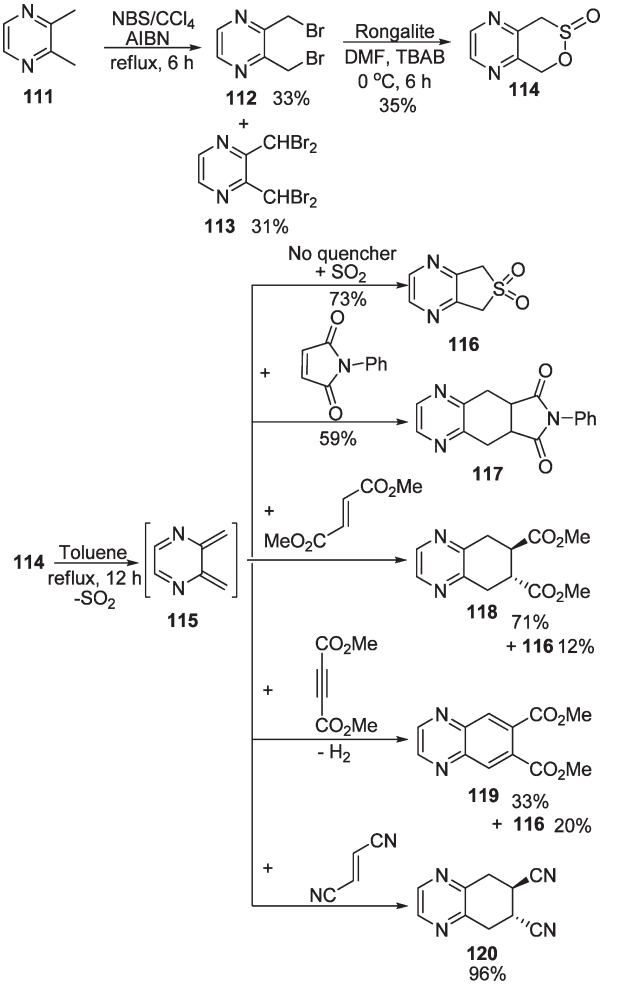
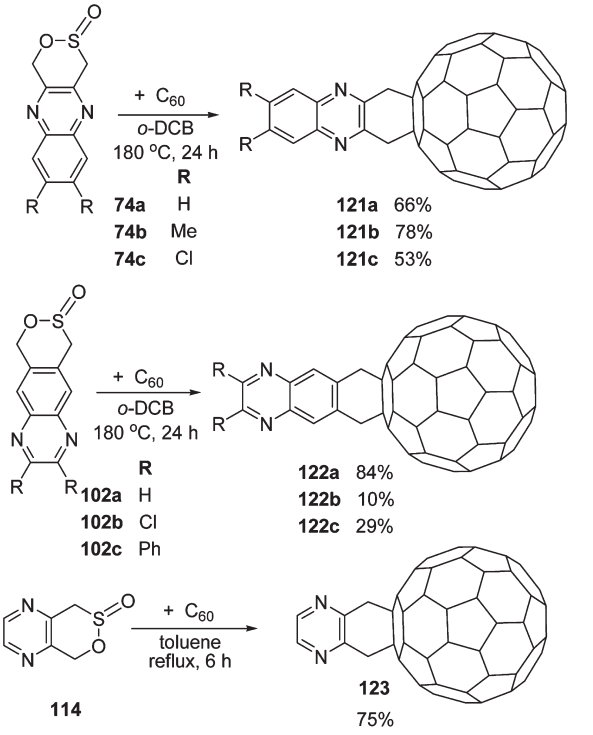
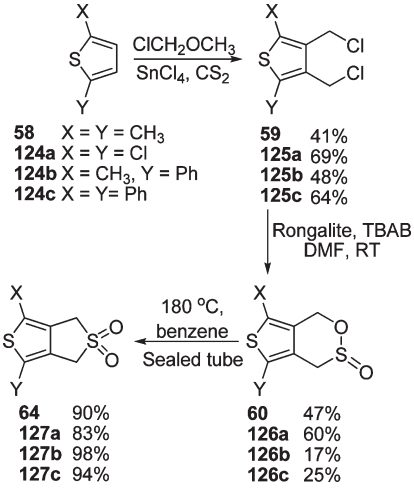
Scheme 28



Scheme 29



Scheme 30



169 as a Boc derivative, **170**, and subsequently acylation of the hydroxy functionality of **170** using acid chloride **171** gave the dibromide **172**. Later, the treatment of **172** with rongalite in the presence of TBAB gave *N*-Boc-sultine **173**. The deprotection of **173** with trifluoroacetic acid (TFA) followed by anion exchange with NH_4PF_6 gave a regioisomeric mixture of sultines **174**. A variety of rotaxanes **175**−**177** were prepared by DA reaction of **174** with different dienophiles in chloroform at 80 °C using dibenzo-24-crown-8 (DB24C8) (Scheme 38).[41]

Synthesis of various highly functionalized benzo-annulated indane-based AAA derivatives were reported via a [4 + 2] cycloaddition strategy using a sultine derivative, **183**, containing an AAA moiety, as a reactive diene component. In this regard the diol **181** has been prepared by [2 + 2 + 2] cyclotrimerization[42] of diyne **180** and 2-butyne-1,4-diol. The diyne **180** was in turn obtained using ethyl isocyanoacetate (**178**) as a glycine equivalent.[43] The diol **181** was transformed into dibromide **182**, which on treatment with rongalite in the presence of TBAB in DMF at 0 °C gave an isomeric mixture of sultine-based AAA derivatives **183** in 72% combined yield (1:1). The sultine **183** was reacted with various dienophiles to deliver the corresponding DA adducts, which on subsequent oxidation gave the aromatized products **184**−**186** (Scheme 39).[44]

In view of various applications of fullerene-based AAA derivatives in bioorganic chemistry,[45] an isomeric mixture of sultine **183** was reacted with buckministerfullerene (C_{60}) and C_{70} in toluene at reflux temperature to obtain the DA products **187** and **189**, respectively. The bisadducts **188** and **190** were obtained as minor products (Scheme 40).[46]

1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid (Tic) is a constrained analogue of phenylalanine (Phe).[47] A unique synergistic combination of [2 + 2 + 2] and [4 + 2] cycloaddition reactions have been employed toward the synthesis of Tic derivatives.[48] The diol building block **193** has been assembled via a [2 + 2 + 2] cyclotrimerization of the alkyne building block **192** and 2-butyne-1,4-diol. The diol **193** was treated with PBr_3 in dry benzene to give the corresponding dibromo derivative **194** in

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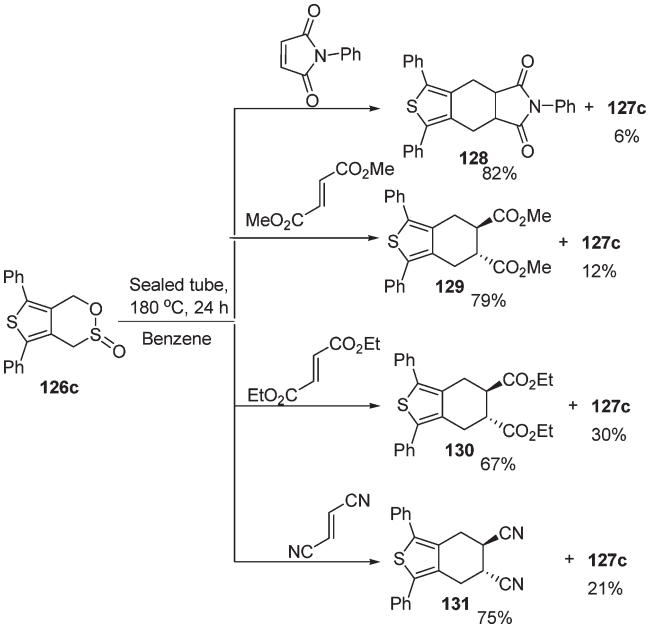
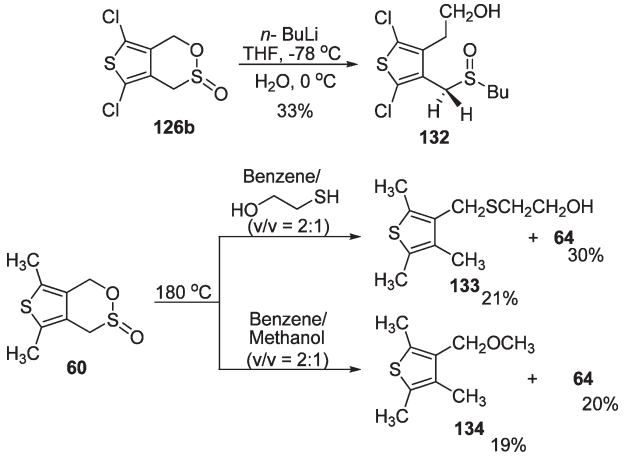
Scheme 31



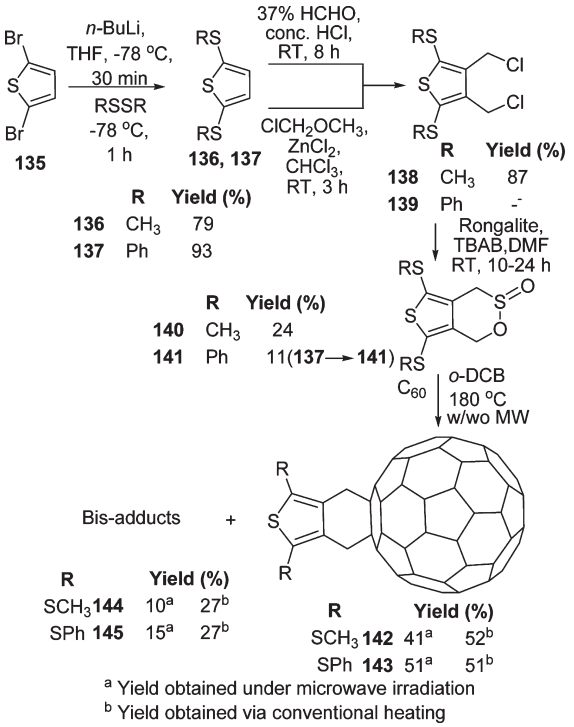
Scheme 32



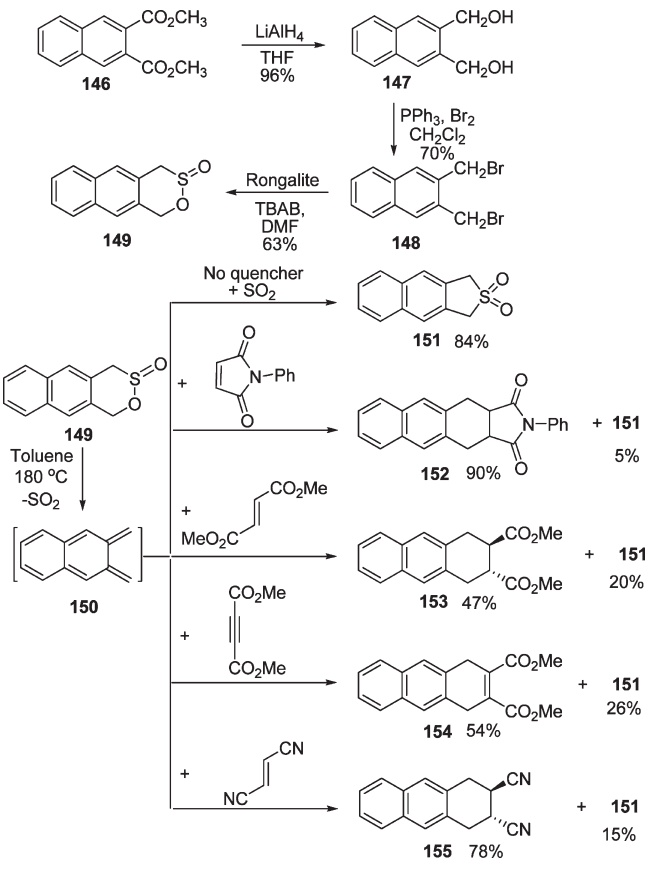
83% yield. Thus, treatment of the dibromo derivative **194** with rongalite in the presence of TBAB in dry DMF furnished the sultine derivative **195** as a mixture of diastereomers. The sultine derivative **195** was then heated at 85−90 °C in the presence of an excess amount of dienophiles to obtain the DA adducts. The DA adducts were slightly contaminated with the aromatized product, and therefore, no attempts were made to isolate the DA adducts. Aromatization of the DA adducts was achieved using activated MnO_2 to furnish the Tic derivatives **196** (Scheme 41).[48]

Kotha and co-workers have conceived an interesting approach for the synthesis of the hybrid benzocyclobutene[26e] (BCB) derivatives **202** and **203** embedding two *o*-QDM precursors of differential reactivity.[49a] The intriguing aspect of these hybrid molecules[50] is the possibility of generating *o*-QDM intermediates on a single molecular frame in a stepwise manner by taking advantage of the fact that benzosultine and benzosulfone can be

Scheme 33



Scheme 34



opened at different temperatures compared to the BCB unit. Rongalite has been used as a key reagent to prepare these hybrid

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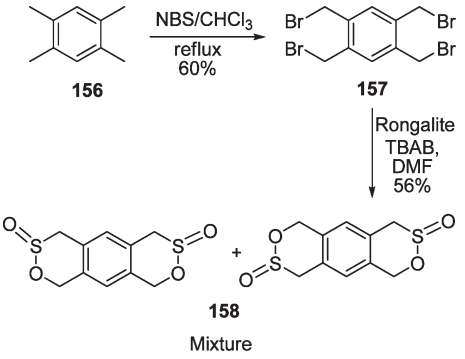
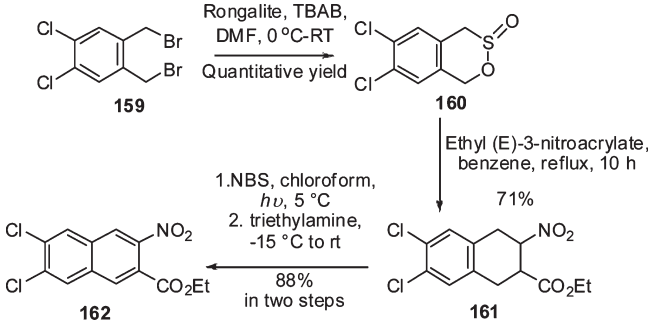
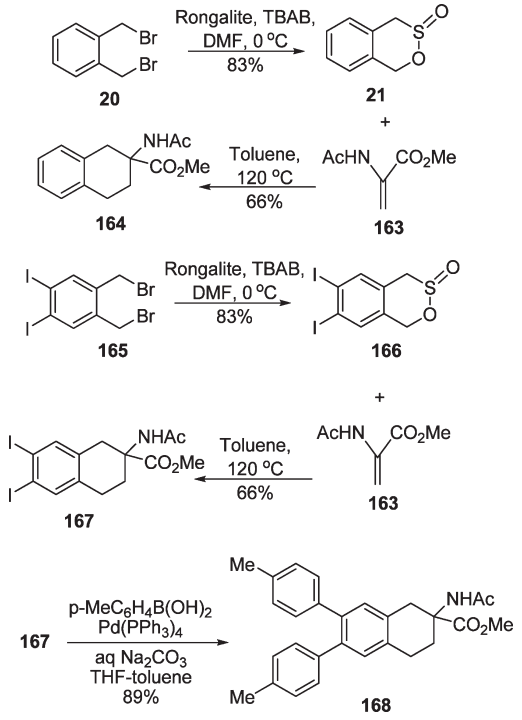
Scheme 35



Scheme 36



Scheme 37



molecular entities. Toward the preparation of hybrid molecular entity **202**, the diyne **197** and DMAD (**198**) were subjected to [2 + 2 + 2] cyclotrimerization reaction to obtain the diester **199** in 35% yield. Later, reduction of **179** generated the diol **200** (67%), which upon treatment with the sodium bromide in the presence of $BF_3 \cdot OEt_2$ gave the corresponding dibromide **201** in 55% yield. When the dibromide **201** was reacted with rongalite, the sultine derivative **202** was obtained in 75% yield. The selective DA reaction at the sultine functionality of **202** was with DMAD (**198**) to obtain the cycloadduct **203** and sulfone **204**. The MnO_2 oxidation of cycloadduct **203** furnished benzo-annulated BCB derivative **205** in almost quantitative (95%) yield (Scheme 42).[49a] The methodology has been extended for the synthesis of other benzocycloalkane-based sultines and sulfones.[49] The DA reaction at the sultine or sulfone terminal followed by aromatization furnished annulated benzocycloalkanes equipped with additional functional groups useful for further synthetic exploitation.

Extending the preparation of hybrid molecular frames containing *o*-QDM precursors of different reactivities, Kotha and co-workers[51] reacted dimethyl 4,5-bis(bromomethyl)phthalate **206** with rongalite in the presence of TBAB in DMF at 0 °C to obtain the sultine derivative **207**, which was converted to the corresponding sulfone derivative **208** by heating in toluene at 100 °C for 7 h. The reduction of diester-containing sulfone **208** was achieved by using KBH_4 and LiCl in refluxing THF to generate the corresponding diol, which upon the treatment with phosphorus tribromide in benzene at 0 °C delivered the dibromosulfone **209** in 73% yield (Scheme 38). The dibromide **209** was converted to the desired benzosultine−sulfone **210** (55%) by treatment with rongalite in the presence of TBAB in DMF at 0 °C. The key building block **210** was subjected to DA reaction with DMAD under refluxing conditions to obtain a DA adduct which was further aromatized with freshly activated MnO_2 in anhydrous dioxane to obtain the sulfone-based diester **211** in 90% yield. Furthermore, benzosultine−sulfone **210** was reacted with methyl 2-acetamidoacrylate (**163**) in refluxing toluene to afford tetralin-based AAA derivative **212** in a moderate yield (57%) along with rearranged benzodisulfone **213** as a side product (Scheme 43).[51]

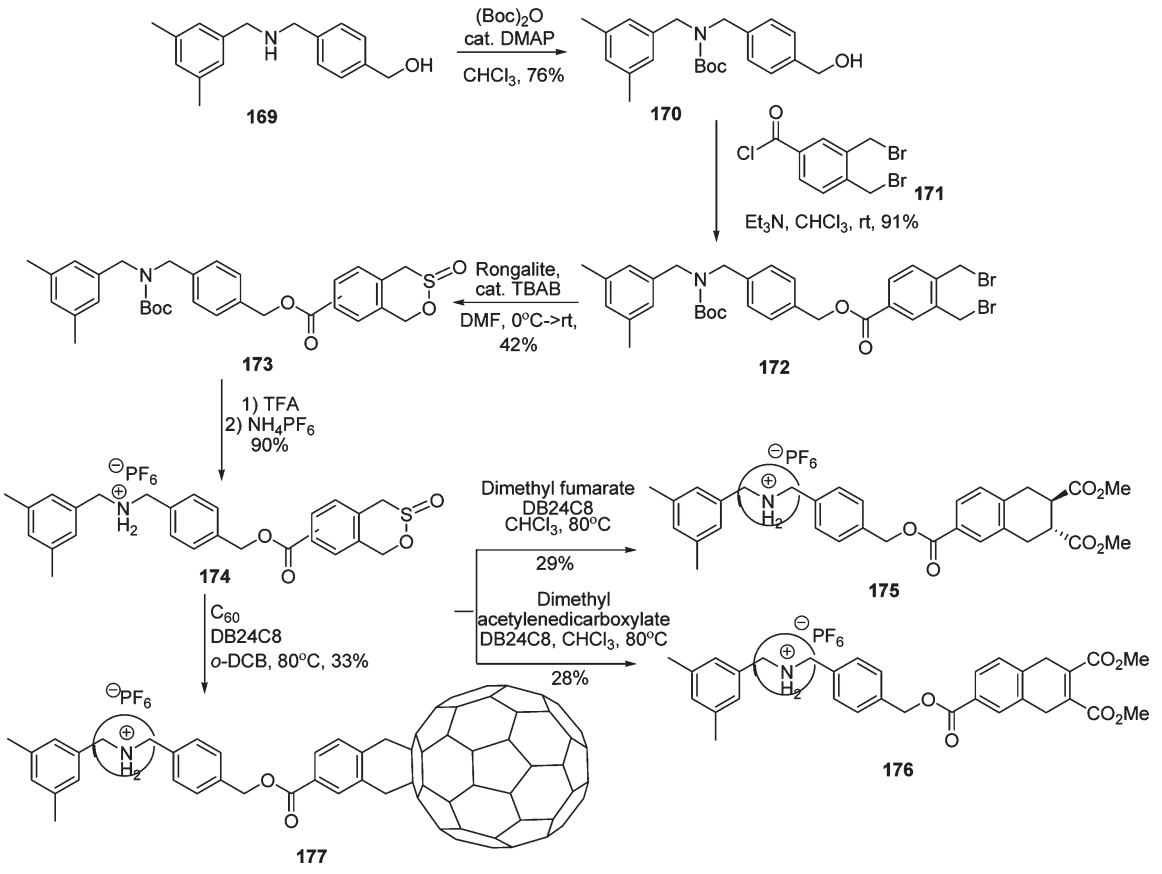
2.3. Tellurium−Rongalite-Mediated Transformations

Tellurium metal is known to be reduced upon the treatment with various reducing agents such as sodium borohydride ($NaBH_4$),[52] triethyllithium borohydride ($LiEt_3BH$),[53] sodium naphthalene,[54] etc. Also, a gentle heating of elemental tellurium with rongalite in dilute aqueous sodium hydroxide is known to generate sodium telluride (Na_2Te_n, generally existing as Na_2Te_2) by reduction of tellurium, producing a wine-red-colored solution.[55] Alkyl halides were found to form dialkyl tellurides upon the reaction with tellurium and rongalite in the presence of sodium hydroxide in aqueous medium.[56] The synthesis of 1,4-thiatellurane (**214**) has been achieved by the reaction of rongalite and tellurium with β,β'-dichlorodiethyl sulfide in aqueous solution in the presence of sodium hydroxide.[57a] When bis-(trimethylsilyl)acetylene was treated with rongalite, tellurium, and sodium hydroxide, tellurophene (**215**) was obtained.[57b] The diazonium salt obtained from 2,2′-diaminobenzophenone reacts with a solution of rongalite, tellurium, and sodium hydroxide to give telluroxanthone (**216**)[57c] (Figure 3).

Various important organic transformations mediated by the tellurium−rongalite recipe will be discussed in this section.

2.3.1. Debromination of Vicinal Dibromoalkanes. Addition of bromine to a double bond and subsequent debromination of a vicinal dibromide to restore the original double bond is one

Scheme 38



of the valuable protecting group strategies for C=C functions in synthetic organic chemistry. Various vicinal dibromoalkanes **217**, **219**, and **221** have been found to undergo debromination easily when treated with sodium telluride obtained by gentle heating of elemental tellurium and rongalite in an aqueous solution of sodium hydroxide. The reaction has been carried out at room temperature, and excellent yields (80−91%) of the corresponding olefins **218**, **220**, and **222** have been obtained (Scheme 44).[58] The most attractive aspect of this transformation is that the other functional groups, such as carbonyl, carboxyl, ester, and nitro groups, present in the molecule remained intact during the debromination. Mechanistically, the elimination of bromine atoms appeared to be stereoselective, and the stereochemical outcome of the reaction supports the concerted *anti*-elimination process involving the initial nucleophilic attack of telluride ion. This strategy serves as a useful alternative to the debromination of vicinal dibromides induced by sodium iodide[59] as it features mild reaction conditions and operational simplicity.

2.3.2. Reduction of Nitroaromatics. The reduction of aromatic nitro compounds **223** to the corresponding amines **224** has been achieved using sodium telluride, obtained by heating tellurium with rongalite in aqueous sodium hydroxide, in good to excellent yields (55−96%, Scheme 45).[60] The reduction was performed with a catalytic amount of tellurium, since the telluride was regenerated readily when an excess amount of rongalite was used. The reduction was found to be accompanied by the separation of free tellurium, and the formation of bimolecular reduction products such as azo, azoxy, and hydrazo compounds could not be detected. In the substrates containing two nitro groups placed in *ortho* or *para* positions relative to each other, the reaction could be stopped at the nitroamine stage by using less rongalite. Thus, the dinitrobenzenes **223i** and **223j** delivered the nitroamines **224i** and **224j** in 89% and 96% yields, respectively (Scheme 45). When these dinitro compounds **223i** and **223j** were subjected to reduction in the presence of an excess amount (twice as much compared to that in other reactions) of rongalite, the corresponding diamines were obtained in 90% and 93% yields, respectively (Scheme 45).[60]

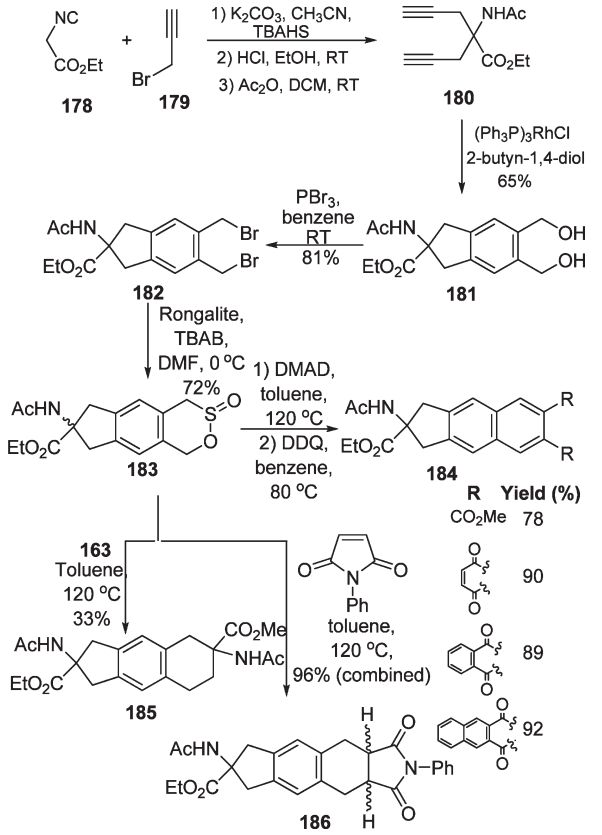
2.3.3. Synthesis of Allylic Alcohols. Dittmer and co-workers have reported[61] the novel use of tellurium−rongalite chemistry toward the synthesis of a variety of allylic alcohols. When 2-substituted 2-chloromethyloxiranes **225** were treated with the telluride ions produced by the reduction of elemental tellurium with rongalite, 2-substituted allyl alcohols **226** were generated in moderate to excellent yields (40−90%, Scheme 46).[61] Several highly functionalized allylic alcohols have been synthesized by the tactical utilization of the tellurium−rongalite protocol.

During the preparation of acetylenic substituted allyl alcohol **226d** via the corresponding epichlorohydrin **225d** and tellurium−rongalite couple, along with the desired allyl alcohol, 2-substituted 4-hydroxymethyltellurophenes **227** were also produced in less than 10% yield (Scheme 47).[62]

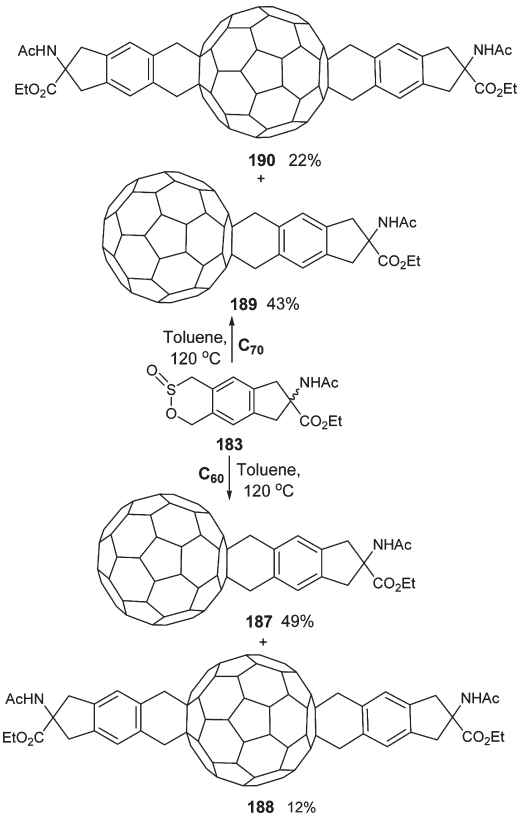
Furthermore, Dittmer and co-workers have extended[63] the utility of tellurium−rongalite chemistry toward the synthesis of diverse optically pure allylic alcohols by combining it with the Sharpless asymmetric epoxidation (SAE). Racemic 1-substituted

dx.doi.org/10.1021/cr100175t |*Chem. Rev.* 2012, 112, 1650–1680

Scheme 39



Scheme 40

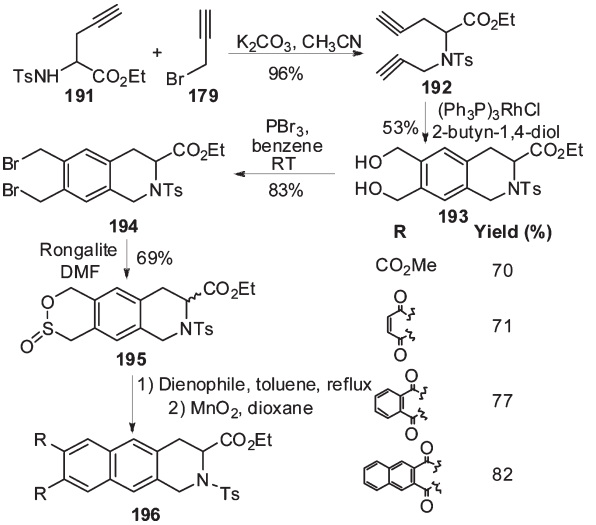


2-propenols have been transformed into one of the enantiomers with high optical purity and chemical yield. The process involves the conversion of one of the enantiomers of racemic allyl alcohol, **228**, into glycidol **229** via epoxidation in Sharpless kinetic resolution, leaving the other enantiomer, **230**, unreacted. The glycidol **229** was transformed into methanesulfonate ester **231** by the reaction with methanesulfonic anhydride and pyridine. The treatment of glycidol methanesulfonate ester **231** with telluride ions generated by the reduction of elemental tellurium with rongalite delivers an enantiomer of allyl alcohol of the same stereochemical configuration as the unreacted enantiomer **230** from the Sharpless–Katsuki resolution (SKR). Thus, a unique combination of SKR and the tellurium–rongalite protocol enables the preparation of a single enantiomer of 1,2-disubstituted allylic alcohols **230** in good yield and high ee, overcoming the limitation of 50% yield by a resolution process (Scheme 48).[63]

Interestingly, vinylcarbinols which are known to react slowly in the electrophilic SKR process can be obtained readily in high optical purity by combining SAE with tellurium–rongalite chemistry. The procedure involves the SAE followed by conversion of epoxy alcohol **232** to its tosylate and treatment with telluride ion (Te^{2-}) generated in situ by the reduction of elemental tellurium by rongalite. The reaction produces a single enantiomer of a 1-monosubstituted allylic alcohol, **234**. The ee's are high, as the epoxidation step is stereospecific. As indicated in Scheme 49,[64] various 1-monosubstituted allylic alcohols **234** have been prepared by tactical utilization of the reducing property of rongalite.

The reaction proceeds either via a stereospecific 1,3-transposition of the double bond and alcohol functionality or via an

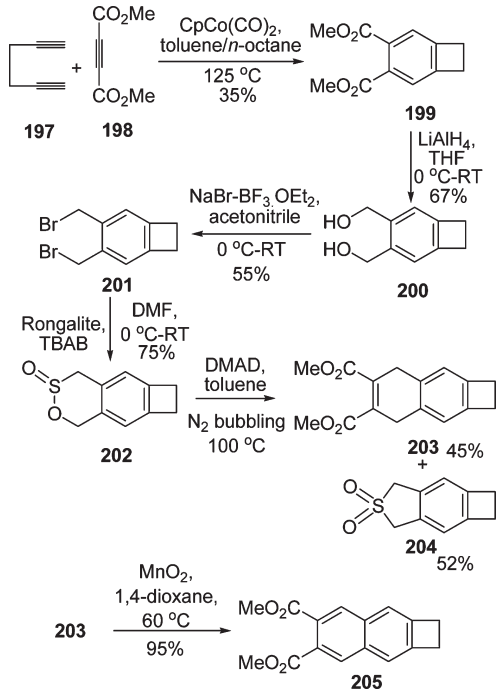
Scheme 41



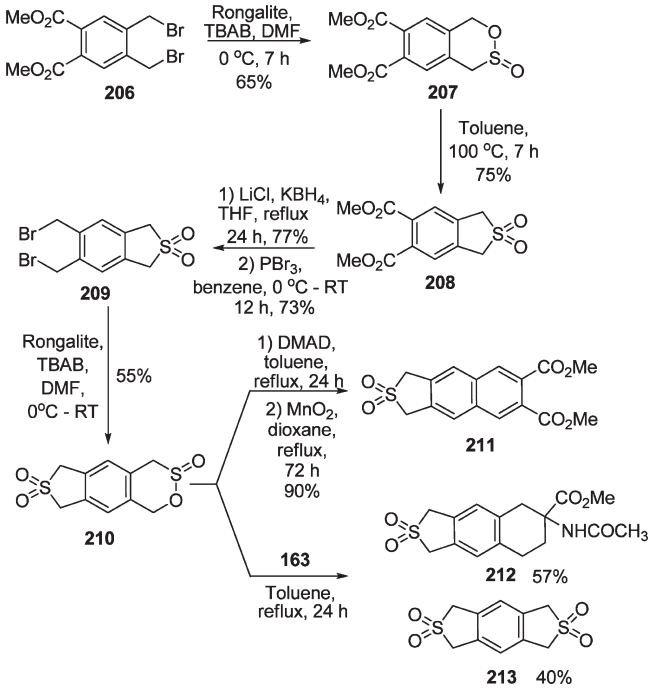
inversion of the alcohol configuration with simultaneous deoxygenation of the epoxide function in epoxy alcohols. The method involves the generation of telluride ion in situ via reduction of the elemental tellurium by rongalite in an aqueous medium. It has been envisaged that the initial attack by telluride ion at the tosylate carbon of **235** is followed by the formation of the epitelluride **237**. Thus, the tellurium atom functions as the nucleophile to effect intramolecular ring-opening of the epoxide **236**. Interestingly,

dx.doi.org/10.1021/cr100175t |*Chem. Rev.* 2012, 112, 1650–1680

Scheme 42



Scheme 43



the tellurium reaction is unique as the proposed epitelluride **237** is unstable and loss of elemental tellurium occurs (Scheme 50).[64]

Tertiary allylic alcohols **240** have been prepared readily by the application of an SAE−Te transposition process to 3,3-disubstituted primary allylic alcohols **239**. As tertiary alcohols are difficult substrates for SKR, SAE combined with tellurium−rongalite transposition provides an excellent route for the preparation of

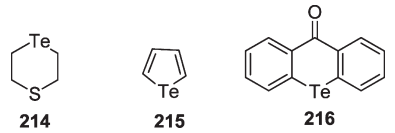
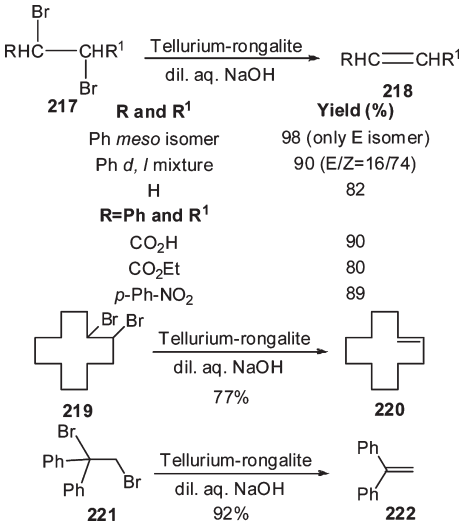
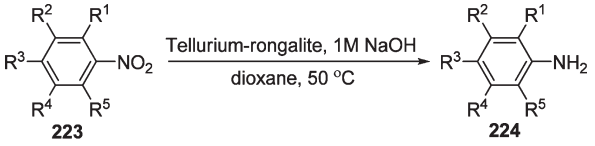


Figure 3. Tellurocycles prepared using rongalite.

Scheme 44



Scheme 45



	R1	R2	R3	R4	R5	Yield (%)	
223a	CH_3	H	CH_3	H	CH_3	95	224a
223b	CH_3	H	CH_3	CH_3	H	87	224b
223c	CH_3	H	$(CH_3)_3C$	H	CH_3	83	224c
223d	H	H	C_6H_5	H	H	66	224d
223e	C_6H_5	H	H	H	H	74	224e
223f	H	H	C_6H_5CO	H	H	90	224f
223g	H	H	C_6H_5CH=CH	H	H	78	224g
			Trans-isomer				
223h	–(CH=CH)2–		H	H	H	55	224h
223i	CH_3	CH_3	NO_2	CH_3	CH_3	89	224i
223j	NO_2	CH_3	CH_3	CH_3	CH_3	96	224j

(+)- and (−)-linalool and (+)-nerolidol in good yield and ee from geraniol and *trans,trans*-farnesol, respectively (Scheme 51).[64]

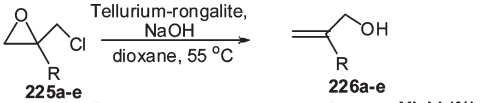
Furthermore, a synthesis of 1,2-disubstituted allylic alcohols **242** has been achieved by application of SAE and tellurium−rongalite transposition of alcohol **241** (Scheme 52).[64]

The SAE of 2,3,3-trisubstituted allylic alcohol **243** with D-(−)-diethyl tartarate [(−)-DET] followed by Te-catalyzed transposition using tellurium−rongalite furnished 1,1,2-trisubstituted allylic alcohol **244** in 41% yield (Scheme 53).[64]

The conversion of glycidyl tosylates or meseylates into the corresponding allylic alcohols is accompanied by oxidation of telluride ion, used in stoichiometric amounts or more, into elemental tellurium. The removal of the precipitated tellurium is

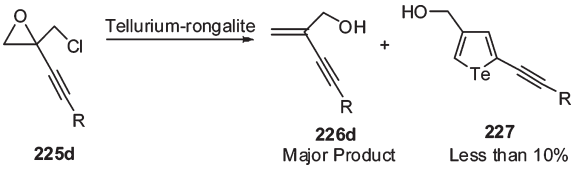
dx.doi.org/10.1021/cr100175t |*Chem. Rev.* 2012, 112, 1650–1680

Scheme 46

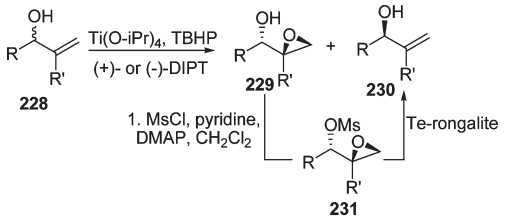


	R		R	Yield (%)
225a	Ph	226a	Ph	90
225b	Et	226b	Et	40
225c	*p*-OCH_3-C_6H_5	226c	*p*-OCH_3-C_6H_5	88
225d	—C≡C—Ph	226d	—C≡C—Ph	90
225e	—CH_2—CH=CH_2	226e	—CH_2—CH=CH_2	43

Scheme 47

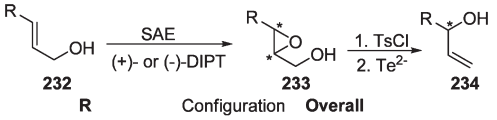


Scheme 48



R' = H	R	%ee	Yield (%)
		92	79
	C_4H_9	94	88
	CH_2CH_2Ph	92	75

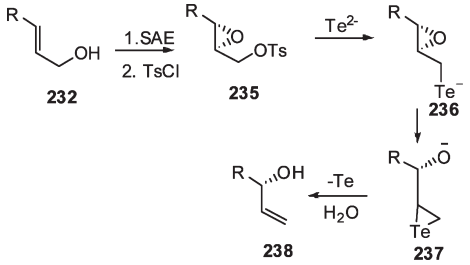
Scheme 49



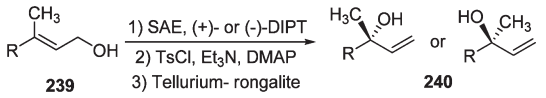
R	Configuration	Overall Yield (%)	%ee
n-C_5H_{11}	(*R*)	88	>95
n-C_6H_{13}	(*R*)	88	>95
Ph	(*R*)	69	90
$PhCH_2OCH_2$	(+)	82	–
$PhCH_2OCH_2$	(*S*)	60	91
$PhCH_2OCH_2$	(*R*)	56	90
tert-Bu	(*R*)	47	>95

difficult on a large scale due to the fine nature of the particles. Dittmer and Kumar[65] improved the synthesis of allylic alcohols and revealed that a catalytic amount of tellurium can be used with an excess amount of rongalite to effect the transposition of allylic hydroxyl groups and carbon−carbon double bonds that proceeds via the epoxy tosylate. The transformations were found to

Scheme 50

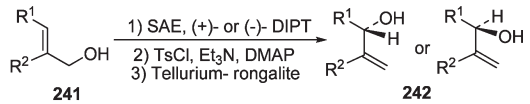


Scheme 51



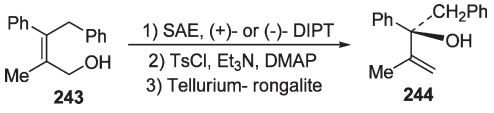
R	Configuration	Overall Yield (%)	%ee
$(Me)_2C=CHCH_2CH_2$	(*S*)	56	95
$(Me)_2C=CHCH_2CH_2$	(*R*)	54	95
$(Me)_2C=CH(CH_2)_2$-$C(CH_3)=CH(CH_2)_2$	(*S*)	86	>95

Scheme 52

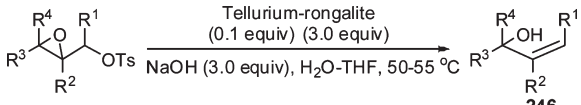


R^1	R^2	Configuration	Overall Yield (%)	%ee
Ph	Me	(*S*)	65	>95
$(Me)_2C=CHCH_2$	Me	(*S*)	38	82
$(Me)_2C=CHCH_2$	Me	(*R*)	49	82
$(CH_2)_4$	$(CH_2)_4$	(*S*)	40	89

Scheme 53



Scheme 54

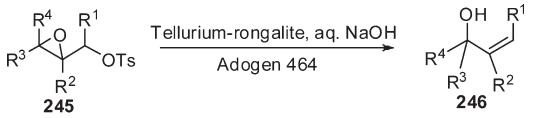


R^1	R^2	R^3	R^4	Yield (%)
H	H	*n*-C_5H_{11}	H	80
H	–$(CH_2)_4$–		H	65
H	H		CH_3	92

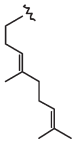
occur with the use of a catalytic quantity of tellurium (0.1 mol equiv of elemental tellurium) in combination with an excess

dx.doi.org/10.1021/cr100175t |*Chem. Rev.* 2012, 112, 1650–1680

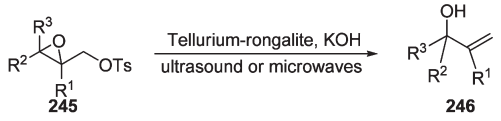
Scheme 55

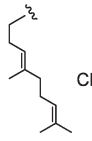


R^1 = H

R^2	R^3	R^4	Yield (%)
H	n-C_5H_{11}	H	93
H	n-C_6H_{11}	H	98
CH_3	Ph	H	99
H	Ph	H	97
H		CH_3	90
H		CH_3	96

Scheme 56

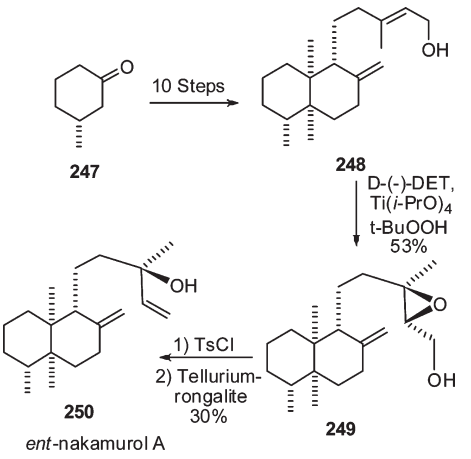


R^1	R^2	R^3	Conditions	Yield (%)
H	n-C_5H_{11}	H	Al_2O_3, Ultrasonication	>95
H	n-C_6H_{11}	H	Al_2O_3, Ultrasonication	90
CH_3	Ph	H	tartaric acid, Ultrasonication	85
CH_3	Ph	H	microwave	50
H		CH_3	Al_2O_3, Ultrasonication	86
H		CH_3	microwave	83
H		CH_3	Al_2O_3, Ultrasonication	89

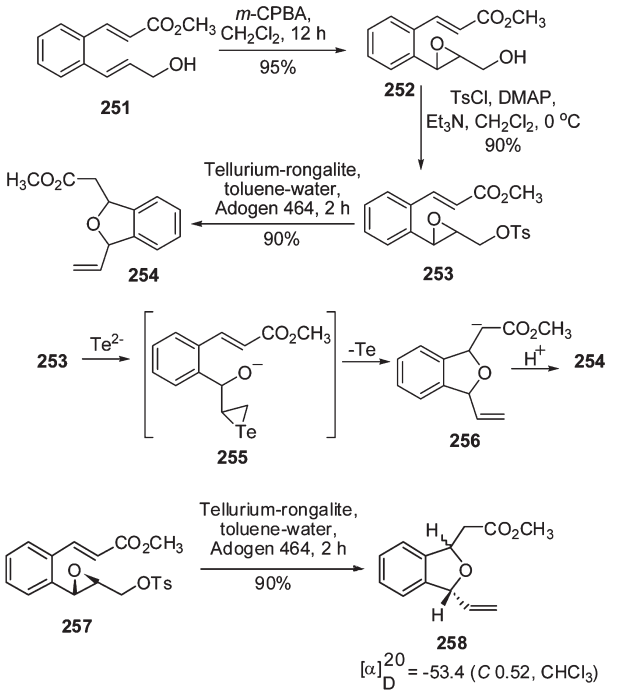
amount (~3 mol equiv) of reducing agent, rongalite. Thus, by adapting this protocol, various allylic alcohols **245** have been synthesized in good to excellent yield (65−92%) from the corresponding epoxides **246** (Scheme 54).[65]

The tellurium−rongalite-mediated route toward the preparation of allylic alcohol can be regarded as a green route as (1) the tellurium is recyclable and can be used in catalytic amounts, (2) during the reaction, the rongalite, which serves as a reducing agent, apparently converts into a water-soluble, nontoxic bisulfite derivative, and (3) only small amounts of organic solvent, typically THF, are used with a large amount of water as a solvent, thereby eliminating the problems associated with the disposal or recovery of the organic solvents. To broaden the scope of the tellurium−rongalite-mediated preparation of allylic alcohols, Dittmer and co-workers reported that epoxy tosylates **245** can be converted into allylic alcohols **246** under the PTC conditions. To a deep red-purple solution of telluride ions produced by the

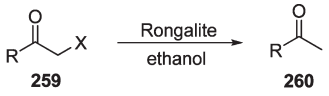
Scheme 57



Scheme 58



Scheme 59



R	Ph	Ph	Ph-NO_2	Ph-Cl	Ph-OMe
X	Cl	Br	Br	Br	Br
Yield (%)	83	79	62	45	77

reduction of elemental tellurium with aqueous rongalite−NaOH are added Adogen 464 and the epoxy tosylate **245** in toluene. The product allylic alcohol was found to be separated in the

dx.doi.org/10.1021/cr100175t |Chem. Rev. 2012, 112, 1650–1680

toluene layer. A catalytic amount of tellurium has been used, and the aqueous layer containing suspended tellurium obtained after reaction can be reused by addition of more rongalite and NaOH. Various allylic alcohols **246** synthesized under PTC conditions are indicated in Scheme 55.[66]

The elemental tellurium can be reduced in the absence of solvent, and this aspect may be considered as an additional green component to the entire transformation. The trituration of Te, rongalite, and KOH in a mortar in an inert atmosphere can produce sodium telluride. In this regard, the neat epoxy tosylates **245** were mixed with the preformed telluride reagent, and the reaction mixture was sonicated or irradiated with microwaves to give the desired allylic alcohols **246** in excellent yields (Scheme 56).[66]

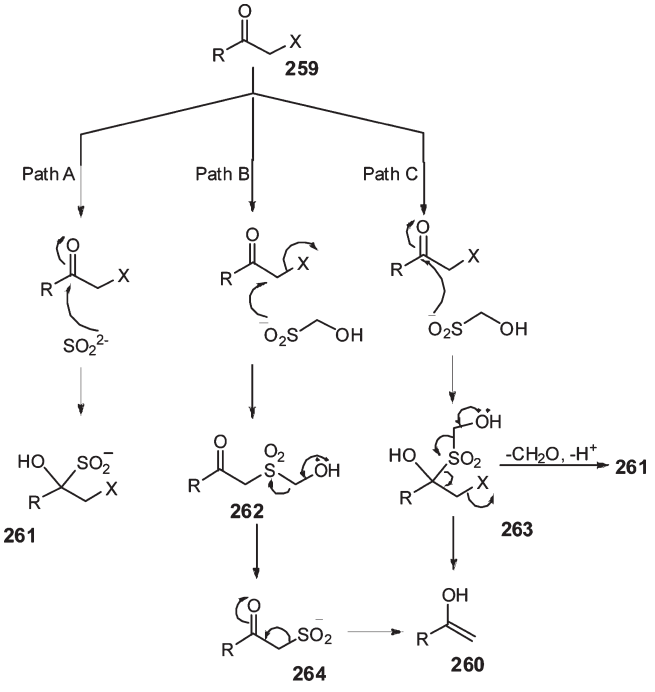
An interesting example[67] of a reductive epoxide ring-opening cascade reaction induced by a Te−rongalite mixture is illustrated by stereocontrolled total synthesis of the marine sponge diterpenoid nakamurol A. The allylic alcohol **248** has been prepared via a synthetic scheme which contains several steps, starting from the commercially available (*R*)-3-methylcyclohexanone (**247**). Stereoselective epoxidation of the allylic alcohol **248** by the SAE method using (−)-DET furnished the desired (13*R*,14*R*)-epoxide **249** in 53% yield. Later, the alcohol was transformed into the corresponding tosylate, which was treated with tellurium in the presence of rongalite in aqueous medium to deliver *ent*-nakamurol A (**250**) in 30% yield (Scheme 57).[67]

A remarkable report[68] by Dittmer and Chao describes the synthesis of dihydroisobenzofuran derivatives via tandem reaction induced by the tellurium−rongalite couple. The carbon−carbon double bond of the allylic alcohol **251** has been epoxidized selectively with *m*-chloroperoxybenzoic acid (*m*-CPBA) to afford an epoxide, **252**, in 95% yield. The epoxy alcohol **252** was converted into the corresponding tosylate **253** by treatment with tosyl chloride in 90% yield. Tosylate **253** underwent tandem intramolecular Michael-type addition of oxyanion **255**, which was generated in close proximity to an α,β-unsaturated ester, in the presence of tellurium−rongalite and PTC (Adogen 464). The resulting 1-substituted 3-vinyl-1,3-dihydroisobenzofuran **254** was isolated in 90% yield. Treatment of optically active epoxy tosylate **257** with telluride ions resulted in the formation of a diastereomeric mixture of two diastereomers of **258** in a 56:44 ratio (Scheme 58).[68]

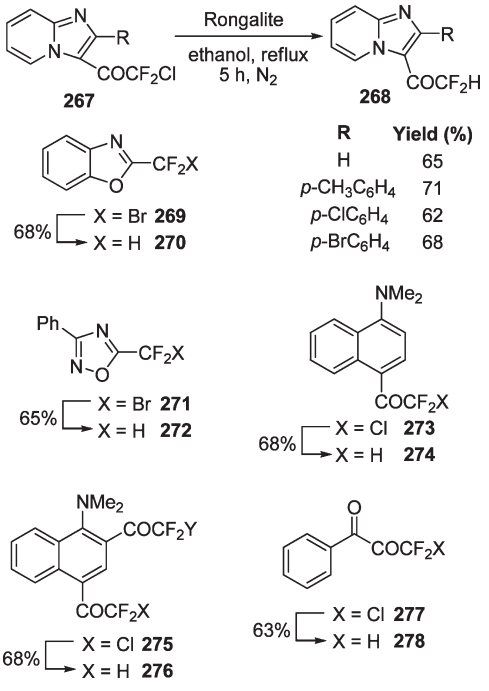
2.4. Rongalite-Promoted Reductive Dehalogenation

Rongalite serves as an efficient reagent for the reductive dehalogenation of phenacyl halides and other α-haloketones.[69−73]

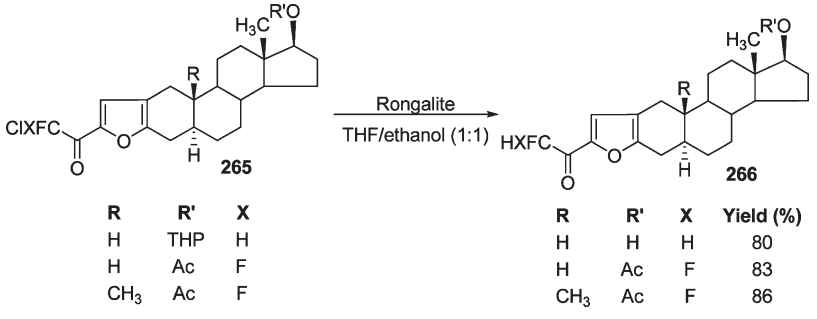
Scheme 60



Scheme 62

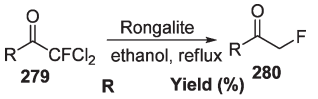


Scheme 61



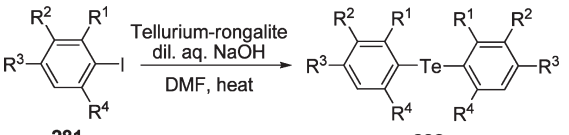
dx.doi.org/10.1021/cr100175t |*Chem. Rev.* 2012, 112, 1650–1680

Scheme 63



R	Yield (%)
Ph	60
p-OCH_3-C_6H_4	65
p-Br-C_6H_4	58

Scheme 64



R^1	R^2	R^3	R^4	Yield (%)
H	H	H	H	71
H	CH_3	H	H	84
H	H	CH_3	H	81
CH_3	H	CH_3	H	94
CH_3	H	CH_3	CH_3	77
H	H	CH_3O	H	74

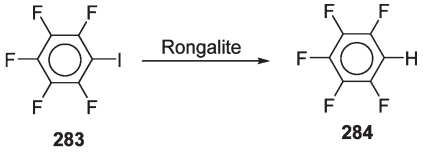
The rongalite−tellurium combination can induce deiodination in nonactivated aryl iodides, leading to the synthesis of diaryl tellurides.[74] Also, perfluoroaryl halides undergo dehalogenation upon treatment with rongalite.[75]

2.4.1. Reductive Dehalogenation of Aldehydes and Ketones. In 1987, Harris demonstrated[69] that rongalite can be used for the reductive dehalogenation of various α-haloketones **259** in mixed aqueous solvent systems. To this end, ethanol was preferred owing to its low cost and comparatively low toxicity. Phenacyl halides **259** are reduced slowly (24 h) in ethanol at room temperature or rapidly (<1 h) at reflux temperature to furnish the corresponding ketones **260** (Scheme 59). During the same time, Dittmer and co-workers reported[18] that the phenacyl chloride reacts with rongalite to produce acetophenone in 93% yield when heated in aqueous DMF at 80 °C for 20 h.

Three possible mechanistic pathways (Scheme 60) have been suggested to rationalize the dehalogenated product from α-haloketone.[69] Path A involves the addition of SO_2^{2-} anion to ketone to give intermediate **261**. Later, a concerted elimination of SO_2 and halide ion delivers the dehalogenated product (path A). Also, a mechanism involving the hydroxy sulfinate attack on the carbonyl group followed by concerted elimination of formaldehyde, SO_2, and halide could not be substantiated by the characterization of intermediate **263** (path C). In view of the pronounced tendency of α-haloketones to undergo halogen displacement by various nucleophiles and as α-hydroxy sulfones **262** are known to be unstable, an alternative mechanism (path B) involving nucleophilic displacement of halide, followed by loss of formaldehyde and SO_2, has been suggested.

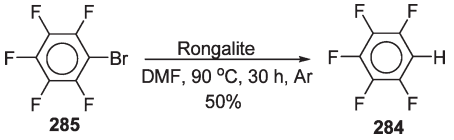
Fluorinated ketones are attractive synthetic targets because they not only serve as useful intermediates for the preparation of other fluorinated compounds but also act as inhibitors of a variety of esterases and proteases.[70] Kumar and co-workers have reported[71] a reductive dehalogenation of chlorofluoroacetyl and chlorodifluoroacetyl steroidal furan derivatives **265** to furnish the corresponding monofluoroacetyl and difluoroacetyl steroidal furans **266** via rongalite. The reaction has been performed in ethanol or a THF/ethanol (1:1) mixture, and fluoromethyl steroidal ketones **266** have been prepared in 80−86% yield (Scheme 61).[71]

Scheme 65

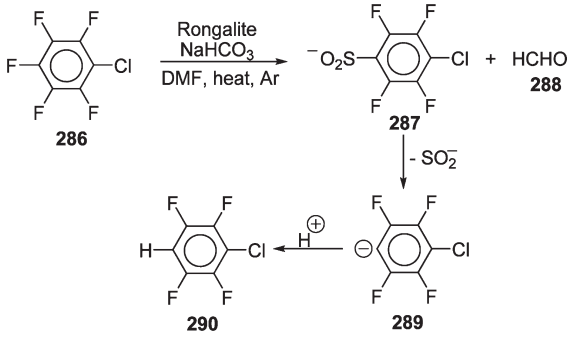


Reaction conditions	Yield (%)
DMF, 19 h, RT	61
DMF, 22 h, 90 °C	36
$NaHCO_3$, aq. MeCN, 12 h, 75 °C	100
CH_3OD-DMF, 20 h, RT (Ph_FD + Ph_FH)	100

Scheme 66



Scheme 67



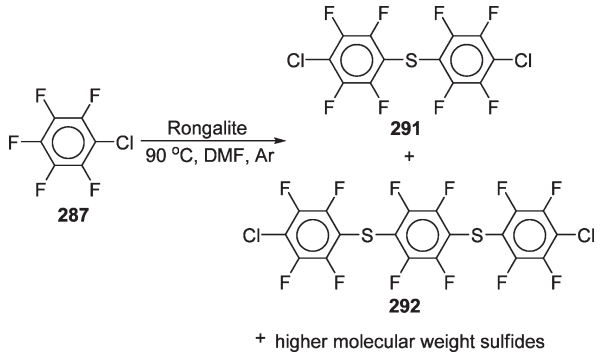
In another instance,[72] rongalite has been used as a single electron transfer reagent for the reductive dehalogenation of a series of halogenodifluoromethylated aromatics and heterocycles such as **267**, **269**, **271**, **273**, **275**, and **277** (Scheme 62). The reaction is believed to involve the electron transfer between the starting material RCF_2X and SO_2^- (or HSO_2^-). Interestingly, perfluoroaryl halides undergo reductive dehalogenation by rongalite to give pentafluorobenzenes. The process is discussed in detail in section 2.4.3.

In 2007, Tsuboi and co-workers demonstrated[73] the reductive dechlorination of dichlorofluoromethyl aryl ketones using rongalite. Various dichlorofluoromethyl aryl ketones **279** have been refluxed in ethanol in the presence of 2 mol equiv of rongalite to deliver the corresponding fluoromethyl phenyl ketones **280** in good yields (58−60%) in less than 1 h (Scheme 63).[73]

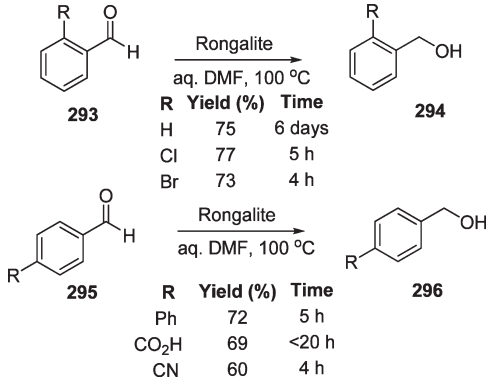
2.4.2. Reductive Dehalogenation Leading to the Synthesis of Dialkyl/Aryl Tellurides. Synthesis of aromatic tellurides is of great value in connection with the development of organometals and new imaging systems.[76] Sodium telluride prepared by reducing tellurium with rongalite in dilute aqueous

dx.doi.org/10.1021/cr100175t |*Chem. Rev.* 2012, 112, 1650–1680

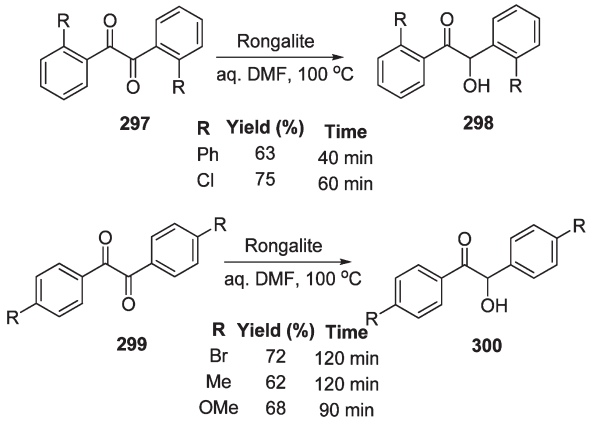
Scheme 68



Scheme 69



Scheme 70



sodium hydroxide reacts smoothly with nonactivated aryl iodides **281** to give symmetrical diaryl tellurides **282** in excellent yields (71−94%).[74] The use of activated aryl iodides to perform the reaction resulted in poor yields of product, probably due to concurrent reductive deiodination. Halides other than iodides were found to be unsuitable for the preparation of tellurides. The use of bromides gave poor yields, and chlorides were found to be unreactive. The sodium telluride prepared from tellurium and rongalite appears to be a highly efficient and handy vehicle for incorporating a tellurium atom into nonactivated aromatic systems (Scheme 64).[74]

2.4.3. Reductive Dehalogenation of Perfluoroaryl Halides. Rongalite has shown an excellent utility in reduction of perfluoroaryl halides. For example, reduction of pentafluoroiodobenzene (**283**) with rongalite was performed in DMF at room temperature to obtain pentafluorobenzene (**284**) in 61% yield. The reaction was essentially performed under an argon atmosphere to avoid the oxidation of reducing species. Performing the reaction at 75 °C in the presence of $NaHCO_3$ delivered a quantitative yield of pentafluorobenzene (**284**) (Scheme 65).[75]

Similarly, bromopentafluorobenzene (**285**) reacts with rongalite in DMF under an argon atmosphere to deliver pentafluorobenzene (**284**) (Scheme 66).[75] The halophilic (S_N2_X) mechanism implicated the formation of pentafluorobenzene via rongalite.

Chloropentafluorobenzene (**286**) reacts with rongalite in the presence of sodium bicarbonate in DMF at elevated temperatures to afford chloro-2,3,5,6-tetrafluorobenzene (**290**) (Scheme 67).[75] Thus, a fluorine *para* to chlorine is found to be reduced, and the reaction may follow an S_NAr mechanism. In iodo and bromo derivatives, the halophilic attack seems to operate predominantly. However, with chloro derivatives the reaction follows the S_NAr mechanism significantly.

In the absence of sodium bicarbonate, a mixture of sulfides was formed, probably by substitution reactions of decomposition products of rongalite. Also, chloropentafluorobenzene (**286**) and rongalite react at 90 °C to give sulfides **291** and **292** and other high molecular weight sulfides (Scheme 68).[75]

2.5. Rongalite-Induced Reduction of Aldehydes and Benzils

In 1983, Heilmann and co-workers observed that benzils can be reduced to the corresponding benzoins in the presence of acid using rongalite.[77] Harris and co-workers extended[78] the utility of rongalite toward the reduction of various aromatic aldehydes and benzils. For example, aromatic aldehydes **293** and **295** have been reduced to the corresponding alcohols **294** and **296** in good yields (60−77%) in aqueous DMF at 100 °C (Scheme 69).[78]

Moreover, benzils **297** and **299**, even those having electron-releasing substituents, underwent a rapid reduction to give the corresponding alcohols **298** and **300** under similar reaction conditions (Scheme 70).[78]

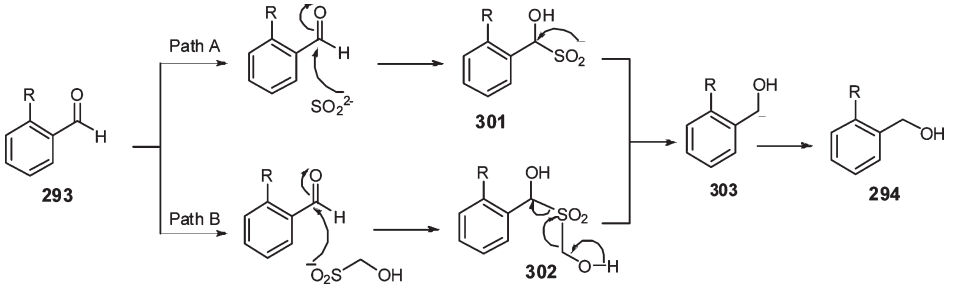
Although no intermediate species (**301** or **302**) could be isolated and characterized mechanistically (Scheme 71),[78] the nucleophilic substitution reaction has been supported by the following observations that (i) the substituents on the aromatic ring have an influence on the reactivity of the substrates and (ii) the reaction occurs in neutral or basic medium. Thus, the initial nucleophilic attack might have occurred through SO_2^{2-} dianion (Scheme 71, path A) or $HOCH_2SO_2^-$ anion (Scheme 71, path B) or both.

2.6. Synthesis of Fluorine-Containing Organic Materials Using Rongalite

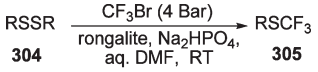
Organofluorine compounds[79] have found a wide range of applications in pharmaceutical and agrochemical materials. This has led to a growth of the literature related to the preparation of fluorine-containing organic materials.

2.6.1. Preparation of α-Halo Thioethers. Wakselman and co-workers have used rongalite in the synthesis of fluorinated sulfides **305**.[80] The reaction involves the treatment of trifluoromethyl bromide with disulfides **304** in the presence of rongalite in aqueous DMF. Disodium hydrogenophosphate was added to the reaction mixture to neutralize the sulfur dioxide formed during the course of the reaction. The stoichiometric amount of rongalite was used, and the transformation was found to be satisfactory when aliphatic as well as aromatic disulfides were used. The condensation

Scheme 71

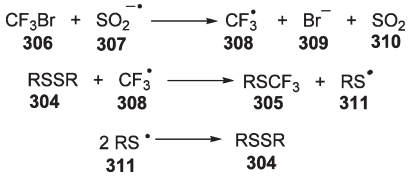


Scheme 72

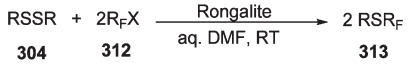


R	Yield (%)
Ph	65
C_4H_9	31
CH_2CO_2Et	55

Scheme 73



Scheme 74



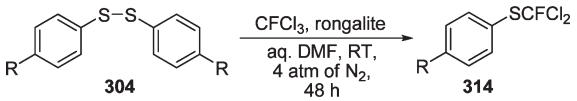
R	R_FX	Yield (%)
$PhCH_2$	C_4F_9I	17
CH_3	$C_8F_{17}I$	20
C_4H_9	$C_6F_{13}I$	22
C_6H_5	$C_6F_{13}I$	40
C_6H_5	CF_2BrCl	72
CH_2CO_2Et	CF_2BrCl	65

was performed generally at room temperature, and alkyl and aryl trifluoromethyl sulfides **305** were obtained in moderate to good yields within a few hours (Scheme 72).[80]

This methodology is based on the formation of perfluoroalkyl radicals **308** under reductive conditions. The weak sulfur−sulfur bond in disulfides **304** is susceptible to the free radical attack, and this aspect seems to be critical for the formation of alkyl or aromatic trifluoromethyl sulfides **305** (Scheme 73).[80]

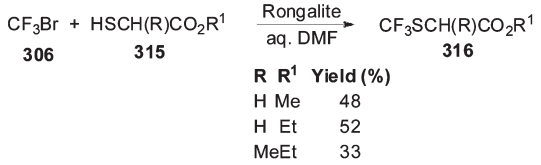
Expanding the utility of the methodology, Wakselman and co-workers have synthesized[81] a variety of perfluoroalkyl sulfides **313** by the treatment of disulfides **304** with a wide range of perhalogenoalkanes **312** in the presence of rongalite. A fairly good solubility of rongalite in DMF allowed the use of a minimum amount of water in the solvent system. Simple

Scheme 75

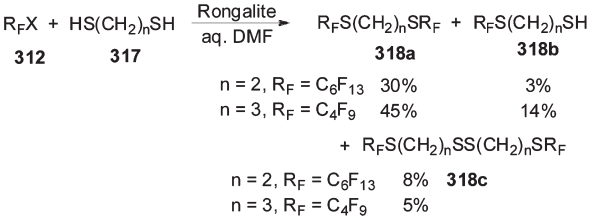


R	Yield (%)
H	52
CH_3	40
Cl	64
NO_2	16

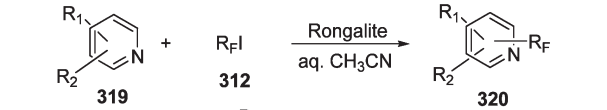
Scheme 76



R	R^1	Yield (%)
H	Me	48
H	Et	52
Me	Et	33



Scheme 77



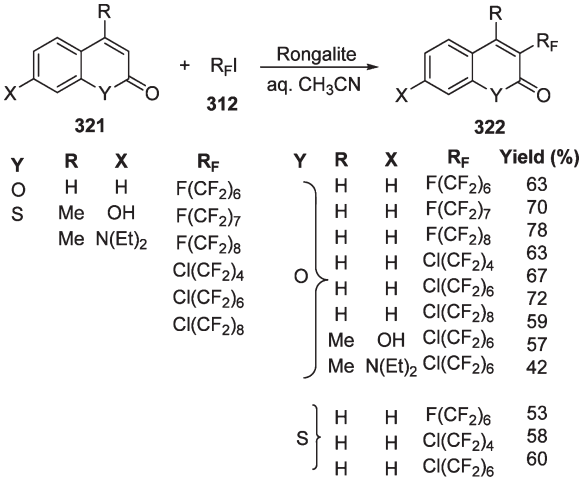
$R_1 = R_2 = H$
$R_1 = 4\text{–}CH_3, R_2 = H$
$R_1 = 3\text{–}CH_3, R_2 = H$
$R_1 = 3\text{–}CH_3, R_2 = 5\text{–}CH_3$
$R_1 = 4\text{–}NH_2, R_2 = H$
Quinoline
Isoquinoline

R_F: C_6F_{13}, C_7F_{15}, C_8F_{17}, ClC_8F_{16}, ClC_4F_8, ClC_6F_{12}

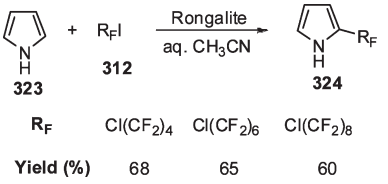
R_1	R_2	R_F	Yield (%)
H	H	C_6F_{13}	57
H	H	C_7F_{15}	62
H	H	C_8F_{17}	68
H	H	ClC_8F_{16}	63
H	H	ClC_4F_8	58
4–CH_3	H	C_6F_{13}	52
4–CH_3	H	ClC_6F_{12}	42
3–CH_3	H	ClC_6F_{12}	46
4–NH_2	H	ClC_6F_{12}	20
Quinoline		ClC_4F_8	44
Isoquinoline		ClC_4F_8	57

dx.doi.org/10.1021/cr100175t |*Chem. Rev.* 2012, 112, 1650–1680

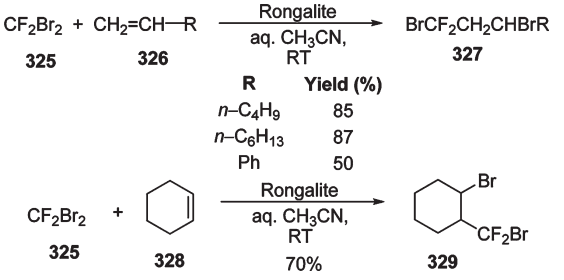
Scheme 78



Scheme 79



Scheme 80



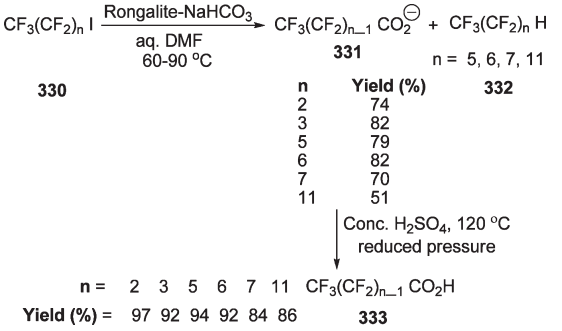
aromatic as well as aliphatic disulfides have been treated with several perfluoroalkanes **312** such as C_4F_9I, $C_8F_{17}I$, $C_6F_{13}I$, CCl_2FCClF_2, and CF_2BrCl to obtain the corresponding fluoroalkyl sulfides **313** (Scheme 74).

The reaction of $CFCl_3$ with diphenyl disulfide **304** in the presence of rongalite gave dichlorofluoromethyl phenyl sulfide **314**. The reaction was carried out in aqueous DMF under a 4 atm pressure of nitrogen. The procedure was generalized for the preparation of various thioethers **314** (Scheme 75).[82]

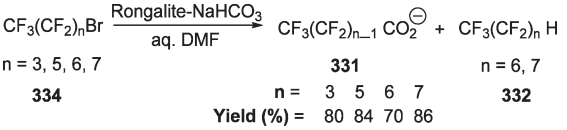
In 2000, Wakselman and co-workers proposed[83] the perfluoroalkylation of mercaptoalkanoic esters **315** via rongalite. The perfluoroalkylation has been realized with trifluoromethyl bromide **306** in the presence of rongalite to afford perfluoroalkyl sulfides **316**. In addition, the perfluoroalkylation has been performed on alkanedithiols **317** to give bisperfluoroalkylated product **318** in 30−45% yield using rongalite (Scheme 76).

2.6.2. Perfluoroalkylation of Heterocycles. The perfluoroalkylation of pyridine and its derivatives **319** with perfluoroalkyl

Scheme 81



Scheme 82



iodides **312** was performed at 70−75 °C in aqueous acetonitrile in the presence of rongalite. To extend this methodology to quinolines and isoquinolines, the reaction mixture was subjected to prolonged heating (Scheme 77).[84]

Extending the utility of perfluoroalkylation using rongalite, C(3)-substituted (perfluoroalkyl)coumarins and -thiocoumarins **322** have also been prepared (Scheme 78).[85] Toward this goal, a variety of coumarins and thiocoumarins **321** have been treated with perfluoroalkyl iodides in aqueous acetonitrile at 70−75 °C to afford 3-(perfluoroalkyl)coumarins **322** in moderate to good yields (Scheme 78).[85] Furthermore, the procedure has been extended for the perfluoroalkylation of 2-quinolones to assemble 3-(perfluoroalkyl)-2-quinolones.

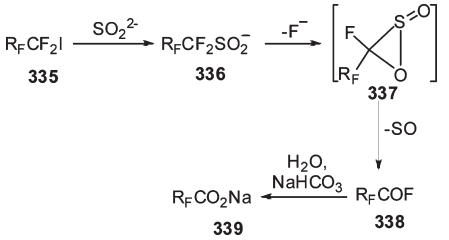
Perfluoroalkylation of pyrroles and other nitrogen-containing heteroaromatic compounds has been achieved in the presence of rongalite. Several perfluoroalkyl iodides **312** were reacted with pyrrole (**323**) in aqueous acetonitrile in the presence of rongalite to furnish 2-perfluoroalkylated pyrrole derivatives **324** in good yields. The reaction proceeds smoothly at 60−70 °C, and sodium bicarbonate was added to keep the reaction medium slightly basic (Scheme 79).[86]

2.6.3. Addition of Dibromodifluoromethane. Synthesis of difluoromethyl-substituted compounds has received considerable attention in view of their utility in pharmaceuticals and agrochemicals.[79] When terminal alkenes **326** and cyclohexene (**328**) were reacted with rongalite and dibromodifluoromethane in aqueous acetonitrile solution at room temperature or at 0 °C, the addition reaction of difluorodibromomethane (**325**) was found to occur across the olefinic double bond. This protocol seems to provide a valuable synthetic route for the incorporation of CF_2Br in organic compounds, and various bromofluoromethylated compounds **327** and **329** have been prepared in good yields (Scheme 80).[87]

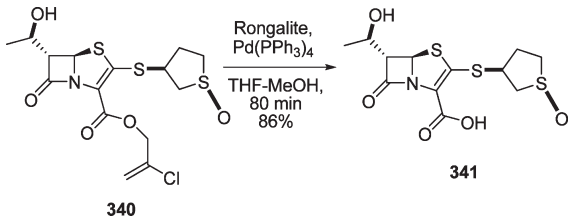
2.6.4. Preparation of Perfluorocarboxylic Acids. The treatment of primary perfluoroalkyl iodides [$CF_3(CF_2)_nI$, n = 2, 3, 5, 6, 7, 11] **330** with rongalite−$NaHCO_3$ in DMF or DMSO gave sodium perfluorocarboxylates [$CF_3(CF_2)_{n-1}CO_2Na$, n = 2, 3, 5, 6, 7, 11] **331** in a moderate to good yield.[88] These perfluorocarboxylates **331** have been converted into the corresponding perfluorocarboxylic

dx.doi.org/10.1021/cr100175t |*Chem. Rev.* 2012, 112, 1650–1680

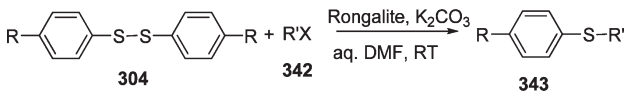
Scheme 83



Scheme 84



Scheme 85

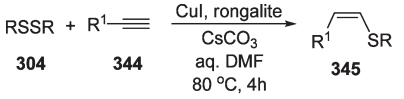


R	R'X	R	R'	Yield (%)
NO_2	MeI	NO_2	Me	97
	EtBr		Et	94
	EtCl		Et	13
	n-PrBr		*n*-Pr	*93*
	n-BuCl		*n*-Bu	12
	$ArCH_2Br$		$ArCH_2$	96
	$ArCOCH_2Br$		$ArCOCH_2$	92
Cl	MeI	Cl	Me	98
	EtBr		Et	95
	EtCl		Et	83
	n-PrBr		*n*-Pr	93
	n-BuCl		*n*-Bu	81
	$ArCH_2Br$		$ArCH_2$	96
	$ArCOCH_2Br$		$ArCOCH_2$	97
H	EtBr	H	EtBr	93
	EtCl		EtCl	82
	n-PrBr		*n*-PrBr	93
	n-BuCl		*n*-BuCl	83

acids $[CF_3(CF_2)_{n-1}CO_2H, n = 2, 3, 5, 6, 7, 11]$ **333** by treatment with sulfuric acid. The process was accompanied by the formation of the corresponding ωH-perfluoroalkanes **332** as byproducts. The optimal reaction temperature range is 60−90 °C, and increasing the reaction temperature above 100 °C was found to increase the formation of **332** (Scheme 81).[88]

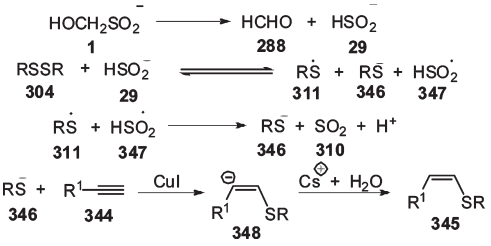
Surprisingly, perfluoroalkyl bromides **334** were found to be relatively inert, and among the various bromides, only nonafluorobutyl bromide, perfluorohexyl bromide, perfluoroheptyl bromide, and perfluorooctyl bromide delivered the corresponding sodium perfluorocarboxylates **331** upon the treatment with rongalite in basic medium (Scheme 82).[88]

Scheme 86



R	R^1	Yield (%)
Ph	p-CH_3-C_6H_4	85
Ph	o-CH_3-C_6H_4	70
Ph	p-OCH_3-C_6H_4	71
Ph	p-NO_2-C_6H_4	74
Ph	C_6H_4NHCO	71
Ph	CO_2Et	63
Ph	n-C_6H_{13}	<5
p-CH_3-C_6H_4	Ph	100
o-NH_2-C_6H_4	Ph	56
p-F-C_6H_4	Ph	87
p-Cl-C_6H_4	Ph	98

Scheme 87



To explain the mechanism for the formation of carboxylates, Grady and Dittmer proposed[89] that the formation of the perfluorcarboxylate **339** occurs via a three-membered cyclic sultine, **337**, that loses sulfur dioxide to furnish an acyl fluoride, **338**, which upon hydrolysis leads to the formation of carboxylate **339** (Scheme 83).

2.7. Deprotection of an Allyl Group by Rongalite

In connection with studies related to the mild deprotection of various allyl derivatives (removal of the allyl group) such as allyl esters, allyl carbonates, allyl carbamates, *O*-allyl ethers, and *N*-allylamines, Nagakura and co-workers have found[90] sulfinic acid or its salt in the presence of a palladium catalyst, $[Pd(PPh_3)_4]$. During these investigations, it has been observed that the 2-chloroallyl ester **340** can be deprotected using rongalite and a catalytic amount of $[Pd(PPh_3)_4]$ in THF−methanol, to give a carboxylic acid, **341**, in 86% yield (Scheme 84).[90] This facile cleavage of the carbon−oxygen bond of allyl ester by rongalite−$[Pd(PPh_3)_4]$ offers a useful allyl deprotection method and may find remarkable applications in the synthesis of complex natural products.

2.8. Synthesis of Sulfides Using Rongalite

One-pot synthesis of aryl alkyl sulfides has been achieved[91] by the reaction of a variety of disulfides **304** with alkyl halides **342** in the presence of rongalite. The reaction has been carried out at room temperature using DMF−water as a solvent system and potassium carbonate as a base. A wide range of alkyl, allylic, and benzyl halides as well as bromoacetophenone have been found to participate in the reaction with disulfide **304**, generating the corresponding sulfides **343** (Scheme 85).[91] The attractive features of this procedure include the operational simplicity, mild reaction conditions, short reaction times, and high yields of products.

A recent protocol developed by Li and co-workers has revealed[92] the utility of rongalite toward the preparation of (*Z*)-1-alkenyl sulfides. The procedure involves the hydrothiolation of

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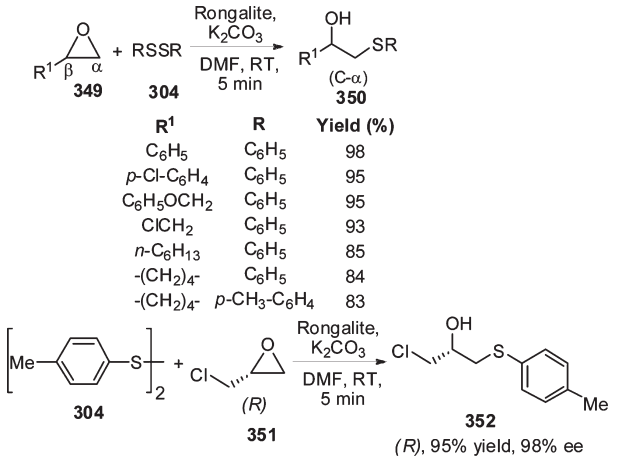
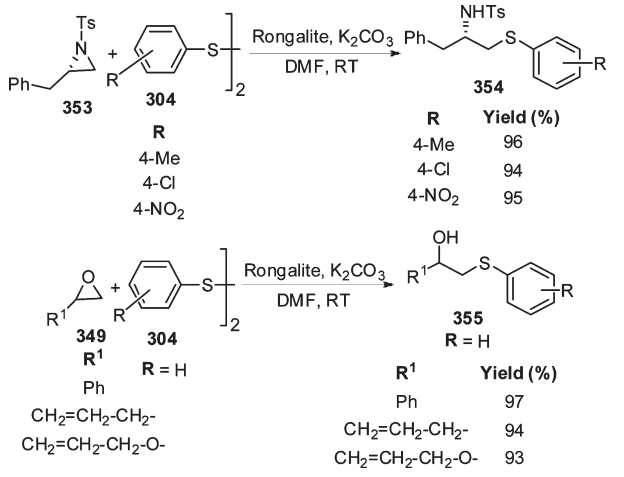
Scheme 88



Scheme 89

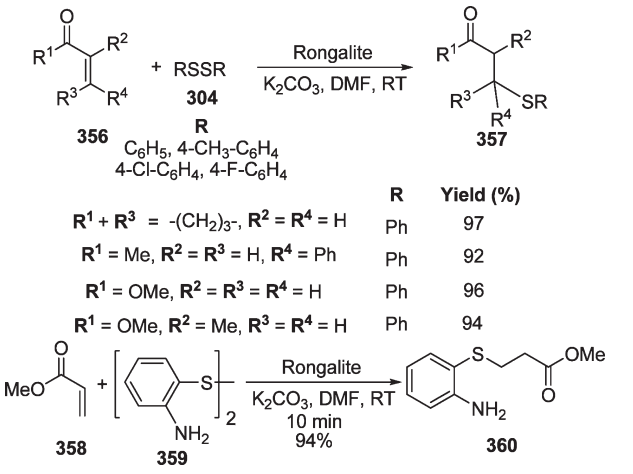


terminal alkynes **344** with diaryl disulfides **304** in the presence of CuI, rongalite, and cesium carbonate. Several disulfides underwent the reaction with a variety of terminal alkynes to yield the corresponding (*Z*)-1-alkenyl sulfides **345** (Scheme 86).[92]

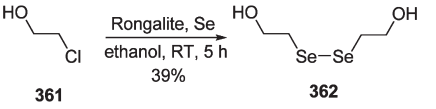
The authors have formulated the mechanism (Scheme 87)[92] involving the formation of HSO_2^- anion (**29**) by the decomposition of rongalite. The anion RS^- (**346**) produced by the reaction of **29** with disulfide **304** undergoes the addition with alkyne **344** to afford the (*Z*)-1-alkenyl sulfide **345**. Addition of CuI seems to improve radical generation, whereas Cs^+ has been considered to support both generation of anion **346** and *cis*-addition with alkyne. The substituents present on alkynes **344** have a profound influence on the stability of anion **348**, and arylalkynes display higher reactivity for hydrothiolations than alkylalkynes due to the electron-withdrawing nature of the aryl moiety.

Wu and co-workers have demonstrated[93] the rongalite-promoted synthesis of β-hydroxy sulfides **350** by thiolysis of epoxides **349** with disulfides **304**. The thiolate anions are produced from disulfides **304** in the presence of rongalite and potassium carbonate and trigger the ring-opening of epoxides to generate β-hydroxy sulfides **350** in 83−98% yield (Scheme 88). The highly regioselective nucleophilic attack of thiolates occurred

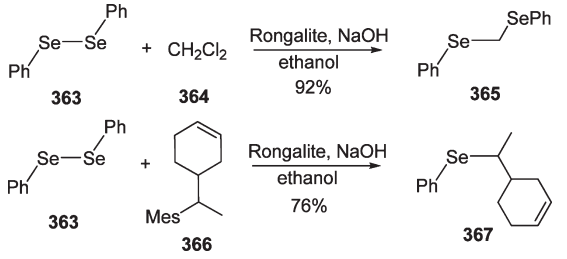
Scheme 90



Scheme 91



Scheme 92

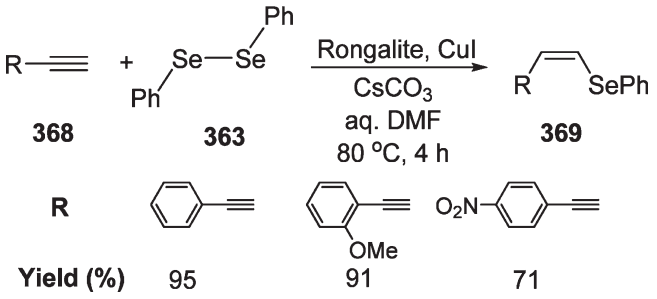


almost exclusively on the less hindered α-carbon of the oxirane ring. Thus, the epoxides derived from styrene, such as 2-phenyloxirane, underwent cleavage with disulfide to afford the corresponding α-addition products selectively. Symmetrical epoxides, such as cyclohexene oxide, upon the reaction with disulfides produce only the *trans*-isomer of the corresponding β-hydroxy sulfides. Furthermore, optically pure (*R*)-2-(chloromethyl)oxirane (**351**) was converted into the corresponding β-hydroxy sulfide **352** without any racemization or inversion using rongalite (Scheme 88).

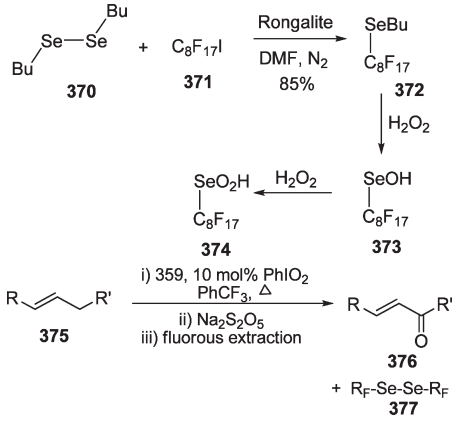
Recently,[94] a report revealed the synthesis of β-amino and β-hydroxy sulfides using rongalite. Phenylalanine-derived aziridine **353** was reacted with various organic disulfides **304** and rongalite in the presence of potassium carbonate in DMF. These experiments revealed that a variety of diaryl disulfides **304** can be cleaved using rongalite in the presence of aziridines to obtain diverse β-amino sulfides **354** in a stereospecific and regioselective manner in excellent yields (Scheme 89).[94] The methodology has been generalized for the synthesis of a variety of β-amino sulfides **354** by varying the aziridine substrates and substitution on the aryl moiety of the disulfides. In addition, β-hydroxy sulfides **355** were prepared by treatment of a range of epoxides **349** with diphenyl disulfide **304**

dx.doi.org/10.1021/cr100175t |*Chem. Rev.* 2012, 112, 1650–1680

Scheme 93



Scheme 94



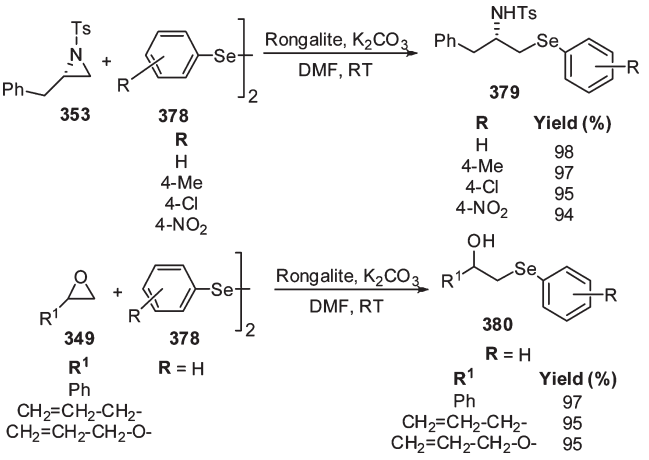
and rongalite in the presence of potassium carbonate. These reactions were found to be extremely facile and took less than 1 h at room temperature for completion.

A recent report[95] describes a simple preparation of β-sulfido carbonyl compounds **357** via thia-Michael addition of thiolate anion to α,β-unsaturated ketones and esters **356**. The thiolate anion in turn has been generated by rongalite and base-promoted cleavage of diaryl disulfides **304**. In this regard, various α,β-unsaturated ketones and esters **356** were treated with diphenyl disulfide **304**, rongalite, and potassium carbonate in DMF to obtain β-sulfido carbonyl compounds **357** in excellent yield (92−97%). The methodology exhibits two avenues to incorporate the diversity in the final product; the first involves the use of differently substituted conjugated carbonyl compounds, and the other one is to employ variously functionalized diphenyl disulfides. The role of rongalite is to cleave the disulfide bond and generate thiolate anion **346** (Scheme 87). Interestingly, the thia-Michael addition of a thiolate generated from diaryl disulfide **359** containing a reactive $-NH_2$ group to methyl acrylate (**358**) generated the corresponding methyl 3-[(2-aminophenyl)thio]propanoate **360** in 94% yield (Scheme 90).[95]

2.9. Synthesis of Selenides Using Rongalite

Similar to tellurium, selenium was found to react with rongalite to deliver the corresponding sodium selenides in the presence of sodium hydroxide.[55] The reaction of long-chain alkyl halides with Na_2Se_2 obtained by refluxing selenium, rongalite, and sodium hydroxide in ethanol affords dialkyl diselenides.[96] However, when rongalite was treated with elemental selenium and 2-chloroethanol (**361**) at room temperature for 5 h, the diselenide **362** was obtained in 39% yield (Scheme 91).[97]

Scheme 95



Reich and co-workers have reported[98] the synthesis of alkyl aryl selenides from the appropriate halide or mesylate using $ArSe^-$ in ethanol, which in turn is produced by the reduction of diselenides using rongalite. In this context, diphenyl diselenide (**363**) in ethanol has been reduced with rongalite in the presence of sodium hydroxide and reacted with dichloromethane (**364**) to give bis(phenylseleno)methane (**365**) in 92% yield. Similarly, the treatment of 1-(3-cyclohexenyl)ethyl mesylate (**366**) with diphenyl diselenide (**363**) and rongalite in the presence of sodium hydroxide furnished 1-(3-cyclohexenyl)ethyl phenyl selenide (**367**) in 76% yield (Scheme 92).[98b]

The hydroselenation of terminal alkynes **368** with diphenyl diselenide (**363**) in the presence of CuI, rongalite, and cesium carbonate has been found to furnish the corresponding (*Z*)-1-alkenyl selenides **369**. Hydroselenation of octyne was unsuccessful; many other alkynes underwent the hydroselenation smoothly to deliver (*Z*)-1-alkenyl selenides **369** in good to excellent yields (71−95%, Scheme 93).[92]

Crich and Zou prepared[99] perfluorooctyl butyl selenide (**372**) in 85% yield by the treatment of dibutyl diselenide (**370**) with perfluorooctyl iodide (**371**) in the presence of rongalite. Treatment of selenide **372** with hydrogen peroxide gave perfluorooctylselenenic acid (**373**), which upon further oxidation furnished fluorous selininic acid **374**. The selininic acid **374** in combination with iodoxybenzene was used to catalyze the allylic oxidation of alkenes to enones in (trifluoromethyl)benzene. Sodium metabisulfite was used during the workup, and catalyst bis(perfluorooctyl) diselenide was recovered by fluorous extraction (Scheme 94).[99]

The treatment of diaryl diselenides **378** with rongalite generates a potentially nucleophilic selenolate anion suitable for the ring-opening of aziridines and epoxides in a regioselective manner. Enantiopure β-amino selenides **379** can be readily obtained by the treatment of *N*-tosylaziridine **353** with variously substituted diphenyl selenides **378** in the presence of rongalite and potassium carbonate. Similarly, oxirane derivatives **349** react with diphenyl diselenides **378**, rongalite, and potassium carbonate in DMF at room temperature to produce the corresponding β-hydroxy selenides **380** in excellent yields (Scheme 95).[94]

The mechanism may involve the generation of anionic species **381** and radical **382** by the transfer of an electron by the sulfinate anion (**29**) to diphenyl diselenide **378**. The selenium radical **382** is also reduced to anion **381** by single-electron transfer (SET). The attack of selenolate anion **381** on aziridine **353** or epoxide

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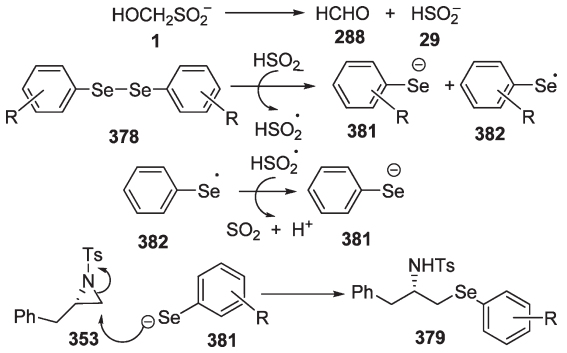
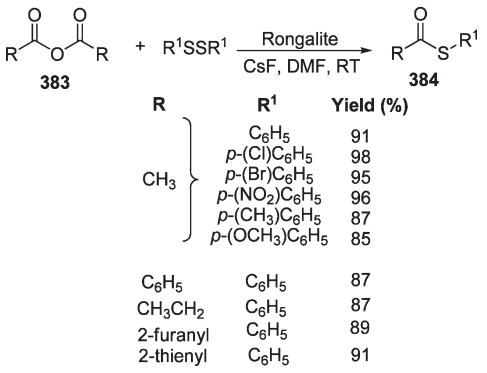
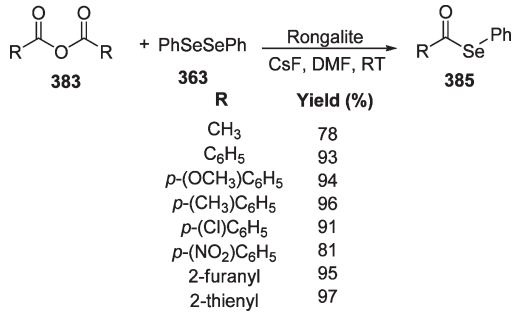
Scheme 96



Scheme 97



Scheme 98



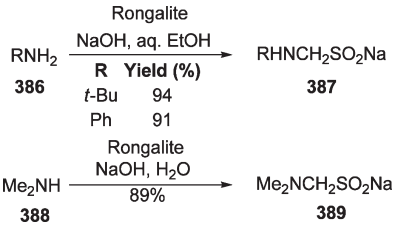
occurs at the less hindered carbon to produce the corresponding β-amino selenides **379** or the β-hydroxy selenide (Scheme 96).[94]

2.10. Synthesis of Thioesters and Selenoesters via Rongalite

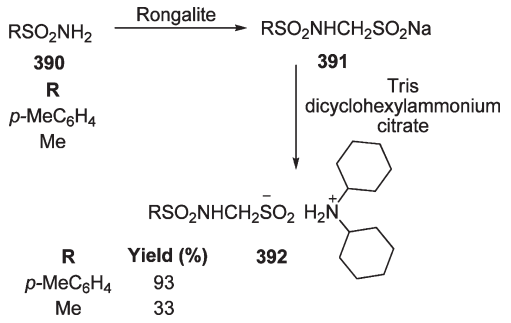
A recent report[100] describes the synthesis of a variety of thioesters and selenoesters via rongalite-promoted cleavage of disulfides followed by acylation reaction. A variety of diaryl disulfides **304** were reacted with anhydrides **383** in the presence of CsF in DMF at room temperature to furnish the thioesters **384** in good to excellent yields (Scheme 97).

Along similar lines, treatment of diphenyl diselenide (**363**) with a variety of anhydrides **383** in the presence of CsF in DMF at room temperature delivered the selenoesters **385** in excellent yields (Scheme 98).[100]

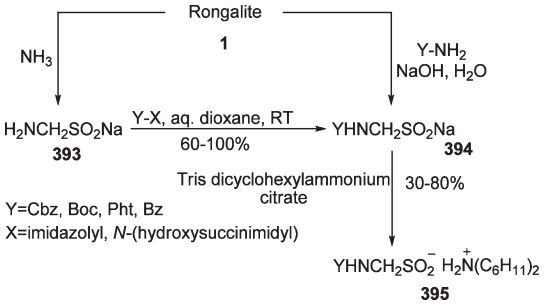
Scheme 99



Scheme 100



Scheme 101



2.11. Synthesis of *N*-Protected α-Aminomethanesulfinate salts with Rongalite

In 1909, Binz and Isaac reported[101] that aniline hydrochloride reacts with rongalite to generate a compound with the molecular formula $C_{27}H_{32}O_3N_4S_2$. The treatment of Me_2NPh with rongalite, formaldehyde, and HCl gave *p*-(dimethylamino)benzyl *p*-(dimethylamino)phenyl sulfone, $Me_2NC_6H_4CH_2SO_2C_6H_4NMe_2$. Furthermore, *o*-toluidine was found to react with rongalite in the presence of HCl to generate $MeC_6H_4NHCH_2SO_2H\cdot NH_2C_6H_4Me$.[102] Later,[103] they prepared a variety of bis(*p*-aminobenzyl) sulfones by the treatment of anilines with rongalite, formaldehyde, and concentrated HCl in aqueous medium.

Leurouin and Mulliez explored[104] the coupling of rongalite with various primary amines **386** and secondary amines **388**. The reaction of primary amines **386** and secondary amines **388** with rongalite in aqueous, basic ethanol generated *N*-substituted α-aminomethanesulfinates **387** and **389**, respectively (Scheme 99).

Investigations revealed[105] that the synthesis of *N*-methanesulfonyl- or *N*-(*p*-toluenesulfonyl)-α-aminosulfinic acid salts **391** can be achieved in a Mannich-type reaction by coupling rongalite with methane- or *p*-toluenesulfonamides **390** in aqueous basic medium. These compounds have been crystallized as dicyclohexylammonium salts **392** (Scheme 100).

Dujols and Mulliez prepared[106] *N*-protected α-aminomethanesulfinate salts **394** by coupling α-aminomethanesulfinate salts **393** with various acylating agents in aqueous basic medium. α-Aminomethanesulfinate salts **393** are prepared by the reaction of rongalite with ammonia. Since sulfinate **393** can be obtained only in aqueous solution, the dioxane is used to solubilize the acylating reagents. The pH of the reaction mixture had been kept above ~5 for the completion of reaction, and the products can be isolated as salts. The sodium salts of **393** are water-soluble and can be separated by extracting organic byproducts and evaporating the aqueous layer to dryness. However, crystallization of compounds **394** as dicyclohexylammonium salts to produce **395** has been recommended in view of the selective solubility of compounds **395** in chloroform (Scheme 101).

3. SUMMARY

The various synthetic methods discussed in this review reveal that rongalite is a powerful reagent for organic synthesis. It is inexpensive and commercially available and can be handled without any special precautions to mediate a wide of variety of synthetic transformations. It serves as a readily available source of SO_2^{2-} anions and facilitates the preparation of sulfone and sultine derivatives which are useful starting materials in diversity-oriented synthesis. Sultines are used immensely toward the preparation of tetracyano-*p*-quinodimethane (TCNQ) and *N*,*N*′-dicyanoquinonediimines (DCNQIs), which are further used to construct materials with high electrical conductivity.[107] The SET reactions promoted by rongalite have been immensely used for the synthesis of sulfide/selenide derivatives and fluorine-containing compounds. In combination with tellurium, it provides excellent reactivity which can be explored in reduction reactions. A tactical utilization of rongalite in synthetic plans may replace tedious organic transformations with simpler routes. We hope that this review may act as a catalyst in boosting the applications of rongalite in organic synthesis.

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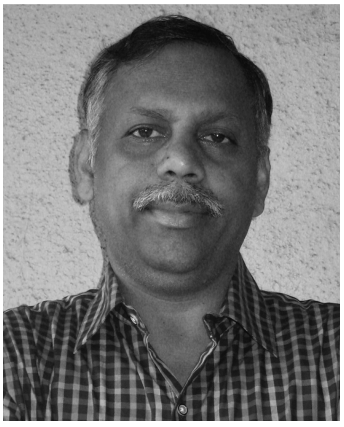
BIOGRAPHIES



Sambasivarao Kotha was born in Amarthalur, Andhra Pradesh, India. He received his Ph.D. degree under the supervision of Professor G. Mehta at the University of Hyderabad in 1985. After spending some time in the United Kindom and United States, he joined the Indian Institute of Technology—Bombay (IIT-B) in 1994 as an Assistant Professor and was promoted to Professor in 2001. He is a recipient of the B. M. Birla Science Prize in Chemistry (1996), N. S. Narasimhan Endowment Award (2000), Chemical Research Society of India bronze medal (2004), Bhagyatara National Award—Punjab University (2005), and Prof. S. C. Bhattacharya Award for Research Excellence in Pure Sciences—IIT-B (2008). Also, he is an elected fellow of the National Academy of Sciences—India and Indian Academy of Sciences. He is a member of various editorial boards (*Indian Journal of Chemistry, Section B*, *Journal of Chemical Sciences*, *Journal of Amino Acids*, and *Catalysis Journal*). Recently, he received a J. C. Bose Fellowship from the Department of Science and Technology and Y. T. Thathachari Award from Bhramara Trust, Mysore. His area of research interest is development of new methods in organic synthesis. At present, he holds Pramod Chaudhari Chair for Green Chemistry and Industrial Biotechnology.

Priti Khedkar was born in Achalpur, Maharashtra, India. She obtained her Ph.D. degree under the supervision of Professor S. Kotha from the Department of Chemistry, Indian Institute of Technology—Bombay in December 2008. She continued as a Research Associate in the same department until July 2010. In August 2010, she joined the Guru Nanak Khalsa College of Arts, Science and Commerce, Matunga, Mumbai, India, as an Assistant Professor. Her research interests are related to development of new methods in organic synthesis.

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LIST OF ACRONYMS

AAA	α-amino acid
Ac	acetyl
aq	aqueous
atm	atmosphere
DA	Diels−Alder
DCE	1,2-dichloroethane
DCM	dichloromethane
o-DCB	*o*-dichlorobenzene

DDQ	2,3-dichloro-5,6-dicyano-*p*-benzoquinone
DEF	diethyl fumarate
DMAD	dimethyl acetylenedicarboxylate
DMF	*N*,*N*-dimethylformamide
DIMF	dimethyl fumarate
DMM	diethyl maleate
ether	diethyl ether
Et	ethyl
equiv	equivalent(s)
FN	furanonitrile
h	hour(s)
Me	methyl
min	minute(s)
MWI	microwave irradiation
NBS	*N*-bromosuccinimide
Ph	phenyl
PTC	phase-transfer catalyst
o-QDM	*o*-quinodimethane
RT	room temperature
Tic	terahydroisoquinoline-3-carboxylic acid
TBAHS	tetrabutylammonium hydrogen sulfate

REFERENCES

(1) (a) Truter, M. R. *J. Chem. Soc.* **1955**, 3064. (b) Truter, M. R. *J. Chem. Soc.* **1962**, 3400.

(2) (a) Sun, F.; Deng, B.; Deng, W. CN 101353354 A, 2009; *Chem. Abstr.* **2009**, *150*, 239781. (b) Yang, Y.; Gu, J.; Xie, X.; Feng, J.; Tang, J. CN 101092422 A, 2007; *Chem. Abstr.* **2007**, *148*, 145642. (c) Boehnke, H.; Frank, J.; Puetter, H.; Schelling, H.; Schneider, R.; Thate, S. DE 10355088 A1, 2005; *Chem. Abstr.* **2005**, *143*, 9536. (d) Huang, H.; Xu, J.; Xue, Y.; Sun, W.; Xu, S.; Xie, X. CN 1121503 A, 1996; *Chem. Abstr.* **1996**, *130*, 170275. (e) Kong, D. CN 1086203 A, 1994; *Chem. Abstr.* **1994**, *123*, 143286. (f) Aleksandrova, A. N.; Budanov, V. V.; Makarov, S. V.; Polenov, Y. V. SU 941356 A1, 1982; *Chem. Abstr.* **1982**, *97*, 181727. (g) Minato, T.; Tetsuhashi, M.; Aoki, M. JP 51001419 A, 1976; *Chem. Abstr.* **1976**, *84*, 150194. (h) Budanov, V. V.; Kibenko, V. D.; Bukin, S. M.; Panov, V. P. SU 303317, 1971; *Chem. Abstr.* **1971**, *75*, 94090. (i) Taguchi, M. JP 32009063 B4, 1957; *Chem. Abstr.* **1957**, *52*, 82706. (j) Postnikov, V. F.; Kunin, T. I. *Zh. Prikl. Khim.* **1940**, *13*, 185. *Chem. Abstr.* **1940**, *35*, 3534. (k) Heyl, F. W.; Greer, F. E. *Am. J. Pharm.* **1922**, *94*, 80. *Chem. Abstr.* **1922**, *16*, 8960. (l) Mitsuoka, S.-I. JP 38776, 1921; *Chem. Abstr.* **1921**, *16*, 12873. Kato, S. JP 34598, 1919; *Chem. Abstr.* **1919**, *14*, 6516. Aoki, N. JP 31544, 1917; *Chem. Abstr.* **1917**, *12*, 2921. (o) Riethof, F. US 1006793, 1911; *Chem. Abstr.* **1911**, *6*, 816. (p) Bazlen, M. *Chem. Ber.* **1905**, *38*, 1057–1068. (q) Reinking, K.; Dehnel, E.; Labhardt, H. *Chem. Ber.* **1905**, *38*, 1069.

(3) (a) Kunin, T. I. *Zh. Prikl. Khim.* **1948**, *21*, 685–691. *Chem. Abstr.* **1948**, *44*, 6458. (b) Kunin, T. I. *Zh. Prikl. Khim.* **1949**, *22*, 199–206. *Chem. Abstr.* **1949**, *44*, 6459.

(4) (a) Robillard, J. J. US 2004259975 A1, 2004; *Chem. Abstr.* **2004**, *142*, 76344. (b) Ouchi, A.; Obata, T.; Oishi, T.; Sakai, H.; Hayashi, T.; Ando, W.; Ito, J. *Green Chem.* **2004**, *6*, 198. (c) Naddeo, R. C. US 2003155085 A1 2003; *Chem. Abstr.* **2003**, *139*, 181826. (d) Osminin, E. N.; Zuikov, A. A.; Kaisina, V. A. SU 1645890 A1, 1991; *Chem. Abstr.* **1991**, *116*, 15080. (e) Arifoglu, M.; Marmer, W. N. US 299174 A0, 1989; *Chem. Abstr.* 1989, *111*, 135969. (f) Grubman, L. P.; Khvorostinskaya, L. V.; Zhukova, T. A.; Arkhipova, E. A.; Fabul'yan, L. V.; Mesnik, O. M.; Ovsyannikov, A. G. SU 1449603 A1, 1989; *Chem. Abstr.* **1989**, *110*, 195206. (g) Stadukhina, V. V.; Vladykina, T. I.; Grubman, L. P.; Arkhipova, E. A.; Mikitevich, I. P.; Zubovich, I. B. SU 1402609 A1, 1988; *Chem. Abstr.* **1988**, *109*, 172605. (h) Slezko, G. F.; Savenko, V. K.; Berezin, Y. E.; Goncharenko, L. K. SU 823477 A1, 1981; *Chem. Abstr.* **1981**, *95*, 44693. (i) Seleznev, M. M.; Gulaya, T. P.; Savenko, V. K.; Shevchenko, V. F.; Slezko, G. F. SU 687155 A1, 1979; *Chem. Abstr.* **1979**, *91*, 194588. (j) Mukherjee, D.; Sarkar, K. T.; Nayudama, Y. IN 103215, 1968; *Chem. Abstr.* **1968**, *81*, 154555. (k) Chappell, N. *J. Soc. Dyers Colour.* **1921**, *37*, 206–210. (l) Kato, S. JP 34598 1919; *Chem. Abstr.* **1919**, *14*, 6516.

(5) (a) Kohut-Svelko, N.; Pirri, R.; Asua, J. M.; Leiza, J. R. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 2917. (b) Ding, F.; Sun, F.; Zhu, X.; Xu, Z. CN 101190956 A, 2008; *Chem. Abstr.* **2008**, *149*, 80773. (c) Cho, K. D.; Kim, Y. S.; Kim, J. G.; Yang, K. H.; Lee, C. H. KR 2007066381 A, 2007; *Chem. Abstr.* **2007**, *148*, 146225. (d) Shirahase, T. JP 2005146194 A, 2005; *Chem. Abstr.* **2005**, *143*, 27405.

(6) (a) Carratala, R. *Hospital* **1942**, *21*, 45. (b) Wolpaw, R.; Alpers, N. *J. Lab. Clin. Med.* **1942**, *27*, 1387. (c) Barnes, J. *Lancet* **1939**, *1*, 89.

(7) (a) Takagi, M.; Iwata, T.; Okujima, K. JP 06118577 A, 1994; *Chem. Abstr.* **1994**, *121*, 191185. (b) Ebato, S.; Ito, N.; Oka, S. JP 49104631 A, 1974; *Chem. Abstr.* **1974**, *82*, 162994. (c) Miller, A. *Br. J. Photogr.* **1925**, *72*, 602. (d) Shimamura, I.; Iijima, Y.; Hayashi, K.; Iwano, H.; Shishido, T. DE 2363585 A1, 1974; *Chem. Abstr.* **1974**, *81*, 84390. (e) Ebato, S.; Ito, N.; Oka, S. JP 49104631 A, 1974; *Chem. Abstr.* **1974**, *82*, 162994.

(8) (a) Rosenthal, S. M. *Public Health Rep.* **1934**, *49*, 908. (b) Miller, J.; Kling, A. US 5270058 A, 1993; *Chem. Abstr.* **1993**, *120*, 99425.

(9) (a) Hacke, W.; Horn, H. US 4386083 A, 1983; *Chem. Abstr.* **1983**, *99*, 76879. (b) Fang, C.; Li, Y.; Liu, Z. CN 101301268 A, 2008; *Chem. Abstr.* **2008**, *150*, 24159. (c) Daoudal, J. EP 271374 A2, 1988; *Chem. Abstr.* **1988**, *110*, 121415.

(10) Data were taken from the safety data sheet available at http://www.sigmaaldrich.com/catalog/DisplayMSDSContent.do for the substance hydroxymethanesulfinic acid monosodium salt dihydrate (accessed Aug 20, 2011).

(11) Simpkins, N. S. In *Sulphones in Organic Synthesis*; Baldwin, J. E., Magnus, P. D., Eds.; Tetrahedron Organic Chemistry Series, Vol. 10; Pergamon: Oxford, U.K., 1993.

(12) Tanaka, K.; Kaji, A. In *The Chemistry of Sulphones and Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C., Eds.; John Wiley & Sons: New York, 1988; p 729.

(13) Fromm, E. *Chem. Ber.* **1908**, *41*, 3397.

(14) Kerber, R.; Starnick, J. *Chem. Ber.* **1971**, *104*, 2035.

(15) Kerber, R.; Gestrich, W. *Chem. Ber.* **1973**, *106*, 798.

(16) Messinger, P.; Greve, H. *Synthesis* **1977**, 259.

(17) Messinger, P.; Greve, H. *Arch. Pharm. (Weinheim, Ger.)* **1977**, *310*, 674.

(18) Jarvis, W. F.; Hoey, M. D.; Finocchio, A. L.; Dittmer, D. C. *J. Org. Chem.* **1988**, *53*, 5750.

(19) Hoey, M. D.; Dittmer, D. C. *J. Org. Chem.* **1991**, *56*, 1948.

(20) Harris, A. R. *Synth. Commun.* **1988**, *18*, 659.

(21) Kotha, S.; Ghosh, A. K. *Indian J. Chem.* **2006**, *45B*, 227.

(22) (a) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633. (b) Kotha, S.; Lahiri, K. *Eur. J. Org. Chem.* **2007**, 1221.

(23) Kotha, S.; Khedkar, P.; Ghosh, A. K. *Eur. J. Org. Chem.* **2005**, 3581.

(24) Selected reviews related to metathesis: (a) Kotha, S.; Sreenivasachary, N. *Indian J. Chem.* **2001**, *40B*, 763. (b) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592. (c) Connon, S. J.; Blechert, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 1900. (d) Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117. (n) McReynolds, M. D.; Dougherty, J. M.; Hanson, P. R. *Chem. Rev.* **2004**, *104*, 2239. (i) Kotha, S.; Lahiri, K. *Synlett* **2007**, 2767. (j) Hoveyda, A. H.; Zhugralin, R. H. *Nature* **2007**, *450*, 243. (k) Kotha, S.; Meshram, M.; Tiwari, A. *Chem. Soc. Rev.* **2009**, *38*, 2065. (l) Burtscher, D.; Grela, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 442. (m) Vougioukalakis, G. C.; Grubbs, R. H. *Chem. Rev.* **2010**, *110*, 1746.

(25) Kotha, S.; Kashinath, D.; Khedkar, P. *Synthesis* **2007**, 3357.

(26) For some reviews related to *o*-QDMs, see: (a) Segura, J. L.; Martin, N. *Chem. Rev.* **1999**, *99*, 3199. (b) Martin, N.; Seoane, C.; Hanack, M. *Org. Prep. Proced. Int.* **1991**, *23*, 237. (c) Charlton, J. L.; Alauddin, M. M. *Tetrahedron* **1987**, *43*, 2873. (d) Funk, R. L.; Vollhardt, K. P. C. *Chem. Soc. Rev.* **1980**, *9*, 41. (e) Mehta, G.; Kotha, S. *Tetrahedron* **2001**, *57*, 625. Books related to DA reactions:(f) Fringulli, F.; Taticchi, A. *Dienes in the Diels–Alder Reaction*; John Wiley & Sons: New York, 1990. (g) Carruthers, W. In *Cycloaddition Reactions in Organic Synthesis*; Baldwin, J. E., Magnus, P. D., Eds.; Tetrahedron Organic Chemistry

Series, Vol. 8; Pergamon: Oxford, U.K., 1990. For preparation of sultines, see: Dittmer, D. C.; Hoey, M. D. A. In *The Chemistry of Sulphinic Acids, Esters, and Their Derivatives*; Patai, S., Ed.; John Wiley & sons: Chichester, England, 1990; Chapter 9, p 239. Large-scale preparation of sultines: Indusegaram, S.; Vonwiller, S. C.; Ridley, D. D.; Silverbrook, K. US 20090043108 A1, 2009; *Chem. Abstr.* 2009, 150, 216089.

(27) Connolly, T. J.; Durst, T. *Tetrahedron Lett.* **1997**, *38*, 1337.

(28) (a) Taylor, R. *The Chemistry of Fullerenes*; World Scientific: Singapore, 1995. (b) Dresselhaus, M. S.; Dresselhaus, G.; Eklund, P. C. *Science of Fullerene and Carbon Nanotubes*; Academic Press: San Diego, CA, 1996. (c) *Fullerenes: From Synthesis to Optoelectronic Properties*; Guldi, D. M., Martín, N., Eds.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 2002. (d) Hirsch, A.; Bettreich, M. *Fullerenes, Chemistry and Reaction*; Wiley-VCH: Weinheim, Germany, 2005. (e) *Fullerenes. Principles and Applications*; Langa, F., Nierengarten, J.-F., Eds.; Royal Society of Chemistry: Cambridge, U.K., 2007. (f) Martín, N. *Chem. Commun.* **2006**, 2093. (g) Delgado, J. L.; Bouit, P.-A.; Filippone, S.; Herranz, M. A.; Martín, N. *Chem. Commun.* **2010**, *46*, 4853.

(29) Illescas, B.; Martin, N.; Seoane, C.; Cruz, P.; Langa, F.; Wudl, F. *Tetrahedron Lett.* **1995**, *36*, 8307.

(30) Chung, W.-S.; Lin, W.-J.; Liu, W.-D.; Chen, L.-G. *J. Chem. Soc., Chem. Commun.* **1995**, 2537.

(31) Chung, W.-S.; Liu, J.-H. *Chem. Commun.* **1997**, 205.

(32) Illescas, B. M.; Martín, N.; Seoane, C.; Ortí, E.; Viruela, P. M.; Viruela, R.; de la Hoz, A. J. *J. Org. Chem.* **1997**, *62*, 7585.

(33) Illescas, B. M.; Martín, N.; Pérez, I.; Seoane, C. *Synth. Met.* **1999**, *103*, 2344.

(34) Liu, J.-H.; Wu, A.-T.; Huang, M.-H.; Wu, C.-W.; Chung, W.-S. *J. Org. Chem.* **2000**, *65*, 3395.

(35) Liu, W.-D.; Chi, C.-C.; Pai, I.-F.; Wu, A.-T.; Chung, W.-S. *J. Org. Chem.* **2002**, *67*, 9267.

(36) Chi, C.-C.; Pai, I.-F.; Chung, W.-S. *Tetrahedron* **2004**, *60*, 10869.

(37) Wu, A.-T.; Liu, W.-D.; Chung, W.-S. *J. Chin. Chem. Soc. (Taipei)* **2002**, *49*, 77.

(38) Zhu, Z.; Drach, J. C.; Townsend, L. B. *J. Org. Chem.* **1998**, *63*, 977.

(39) (a) Trabocchi, A.; Scarpi, D.; Guarna, A. *Amino Acids* **2008**, *34*, 1. (b) Kotha, S.; Lahiri, K. *Curr. Med. Chem.* **2005**, *12*, 849.

(40) (a) Kotha, S.; Ghosh, A. K. *Synthesis* **2004**, *4*, 558. (b) Kotha, S.; Ganesh, T.; Ghosh, A. K. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1755. (c) Kotha, S.; Meshram, M. *Heterocycles* **2011**, *82*, 1663.

(41) Sasabe, H.; Kihara, N.; Furusho, Y.; Mizuno, K.; Ogawa, A.; Takata, T. *Org. Lett.* **2004**, *6*, 3957.

(42) For reviews related to [2 + 2 + 2] cycloaddition reactions, see: (a) Varela, J. A.; Saa, C. *J. Organomet. Chem.* **2009**, *694*, 143. (b) Shibata, T.; Tsuchikama, K. *Org. Biomol. Chem.* **2008**, *6*, 1317. (b) Agenet, N.; Buisine, O.; Slowinski, F.; Gandon, V.; Aubert, C.; Malacria, M. *Org. React.* **2007**, *68*, 1. (k) Chopade, P. R.; Louie, J. *Adv. Synth. Catal.* **2006**, *348*, 2307. (d) Gandon, V.; Aubert, C.; Malacria, M. *Chem. Commun.* **2006**, 2209. (e) Kotha, S.; Brahmachary, E.; Lahiri, K. *Eur. J. Org. Chem.* **2005**, *22*, 4741. (f) Michael, R.; Sromek, A. W.; Gevorgyan, V. *Synlett* **2003**, *15*, 2265. (g) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901. (h) Boese, R.; Sickle, A. P. V.; Vollhardt, K. P. C. *Synthesis* **1994**, 1374. (i) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 525. (j) Vollhardt, K. P. C. *Acc. Chem. Res.* **1977**, *10*, 1.

(43) Kotha, S.; Haldar, S. *Synlett* **2010**, 337.

(44) (a) Kotha, S.; Ghosh, A. K. *Tetrahedron* **2004**, *60*, 10833. (b) Kotha, S.; Ghosh, A. K. *Tetrahedron Lett.* **2004**, *45*, 2931.

(45) Ros, T. D.; Prato, M. *Chem. Commun.* **1999**, 663. (b) Bianco, A.; Ros, T. D.; Prato, M.; Toniolo, C. *J. Pept. Sci.* **2001**, *7*, 208. (c) Ling, R.; Yoshida, M.; Mariano, P. S. *J. Org. Chem.* **1996**, *61*, 4439.

(46) Ghosh, A. K. Ph.D. Thesis, Indian Institute of Technology—Bombay, India, 2004.

(47) Kotha, S.; Sreenivasachary, N. *J. Indian Inst. Sci.* **2001**, *81*, 277.

(48) Kotha, S.; Banerjee, S. *Synthesis* **2007**, *7*, 1015.

(49) (a) Kotha, S.; Khedkar, P. *J. Org. Chem.* **2009**, *74*, 5667. (b) Kotha, S.; Krishna, N. G. *Curr. Sci. India* **2011**in press.

(50) For literature related to hybrid systems, see: (a) Tietze, L. F.; Schneider, G.; Wölfling, J.; Fecher, A.; Nöbel, T.; Petersen, S.; Schuberth, I.; Wulff, C. *Chem.—Eur. J.* **2000**, *6*, 3755. (b) Álvaro, E.; de la Torre, M. C.; Sierra, M. A. *Chem.—Eur. J.* **2006**, *12*, 6403.

(51) Kotha, S.; Chavan, A. *J. Org. Chem.* **2010**, *75*, 4319.

(52) (a) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574. (b) Discordia, R. P.; Murphy, C. K.; Dittmer, D. C. *Tetrahedron Lett.* **1990**, *31*, 5603.

(53) (a) Detty, M. R.; Seidler, M. D. *J. Org. Chem.* **1982**, *47*, 1354. (b) Dittmer, D. C.; Zhang, Y.; Discordia, R. P. *J. Org. Chem.* **1994**, *59*, 1004.

(54) Bhasin, K. K.; Gupta, V.; Sharma, R. P. *Indian J. Chem.* **1991**, *30A*, 632.

(55) Tschugaeff, L.; Chlopin, W. *Chem. Ber.* **1914**, *47*, 1269.

(56) Balfe, M. P.; Chaplin, C. A.; Phillips, H. *J. Chem. Soc.* **1938**, 341.

(57) (a) McCullough, J. D. *Inorg. Chem.* **1965**, *46*, 862. (b) Lohner, W.; Praefcke, K. *Chem. Ber.* **1978**, *11*, 3745. (c) Lohner, W.; Praefcke, K. *Chem.-Ztg.* **1979**, *103*, 265.

(58) Suzuki, H.; Inouye, M. *Chem. Lett.* **1985**, 225.

(59) Young, D. W. In *Protective Groups in Organic Chemistry*; McOmie, J. F. W., Ed.; Plenum Press: London, 1973.

(60) Suzuki, H.; Manabe, H.; Inouye, M. *Chem. Lett.* **1985**, 1671.

(61) Polson, G.; Dittmer, D. C. *Tetrahedron Lett.* **1986**, *27*, 5579.

(62) Discordia, R. P.; Dittmer, D. C. *Tetrahedron Lett.* **1988**, *29*, 4923.

(63) Discordia, R. P.; Dittmer, D. C. *J. Org. Chem.* **1990**, *55*, 1414.

(64) Dittmer, D. C.; Discordia, R. P.; Zhang, Y.; Murphy, C. K.; Kumar, A.; Pepito, A. S.; Wang, Y. *J. Org. Chem.* **1993**, *58*, 718.

(65) Kumar, A.; Dittmer, D. C. *Tetrahedron Lett.* **1994**, *35*, 5583.

(66) Xu, Q.; Chao, B.; Wang, Y.; Dittmer, D. C. *Tetrahedron* **1997**, *53*, 12131.

(67) Díaz, S.; Cuesta, J.; González, A.; Bonjoch, J. *J. Org. Chem.* **2003**, *68*, 7400.

(68) Chao, B.; Dittmer, D. C. *Tetrahedron Lett.* **2000**, *41*, 6001.

(69) Harris, A. R. *Synth. Commun.* **1987**, *17*, 1587.

(70) Rozen, S.; Filler, R. *Tetrahedron* **1985**, *41*, 1111 and references therein.

(71) Kumar, V.; McCloskey, P.; Bell, M. *Tetrahedron Lett.* **1994**, *35*, 833.

(72) Dolbier, W. R., Jr.; Médebielle, M.; Ait-Mohand, S. *Tetrahedron Lett.* **2001**, *42*, 4811.

(73) Barkakaty, B.; Takaguchi, Y.; Tsuboi, S. *Tetrahedron* **2007**, *63*, 970.

(74) Suzuki, H.; Inouye, M. *Chem. Lett.* **1985**, 389.

(75) Wu, F.-H.; Huang, B.-N.; Lu, L.; Huang, W.-Y. *J. Fluorine Chem.* **1996**, *80*, 91.

(76) (a) Petragnani, N.; Stefani, H. A. *Tetrahedron* **2005**, *61*, 1613. (b) Chinchilla, R.; Najera, C.; Yus, M. *Chem. Rev.* **2004**, *104*, 2667. (c) Engman, L. *Phosphorus Sulfur* **1988**, *38*, 105.

(77) Heilmann, S. M.; Rasmussen, J. K.; Smith, H. K., II. *J. Org. Chem.* **1983**, *48*, 987.

(78) Harris, A. R.; Mason, T. J. *Synth. Commun.* **1989**, *19*, 529.

(79) (a) Filler, R. In *Organofluorine Chemicals and Their Industrial Applications*; Banks, R. E., Ed.; Ellis Horwood: Chichester, England, 1979. (b) Welch, J. W.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; John Wiley & Sons: New York, 1991.

(80) Wakselman, C.; Tordeux, M.; Clavel, J.-L.; Langlois, B. *J. Chem. Soc., Chem. Commun.* **1991**, 993.

(81) Clavel, J.-L.; Langlois, B.; Nantermet, R.; Tordeux, M.; Wakselman, C. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3371.

(82) Saikia, A. K.; Tsuboi, S. *J. Org. Chem.* **2001**, *66*, 643.

(83) Anselmi, E.; Blazejewski, J.-C.; Tordeux, M.; Wakselman, C. *J. Fluorine Chem.* **2000**, *105*, 41.

(84) Huang, B.; Liu, J. *Tetrahedron Lett.* **1990**, *31*, 2711.

(85) (a) Huang, B.; Liu, J.; Huang, W. *J. Chem. Soc., Chem. Commun.* **1990**, 1781. (b) Huang, B.-N.; Liu, J.-T.; Huang, W.-Y. *J. Chem. Soc., Perkin Trans. 1* **1994**, 101.

(86) Huang, B.; Liu, J. *J. Fluorine Chem.* **1993**, *64*, 37.

(87) Wu, F.-H.; Huang, B.-N.; Lu, L.; Huang, W.-Y. *J. Fluorine Chem.* **1996**, *80*, 91.
(88) Huang, B.-N.; Hass, A.; Lieb, M. *J. Fluorine Chem.* **1987**, *36*, 49.
(89) Grady, B. J.; Dittmer, D. C. *J. Fluorine Chem.* **1990**, *50*, 151.
(90) Honda, M.; Morita, H.; Nagakura, I. *J. Org. Chem.* **1997**, *62*, 8932.
(91) Tang, R-y.; Zhong, P.; Lin, Q.-l. *Synthesis* **2007**, 85.
(92) Wang, Z.-L.; Tang, R.-Y.; Luo, P.-S.; Deng, C.-L.; Zhong, P.; Li, J.-H. *Tetrahedron* **2008**, *64*, 10670.
(93) Guo, W.; Chen, J.; Wu, D.; Ding, J.; Chen, F.; Wu, H. *Tetrahedron* **2009**, *65*, 5240.
(94) Ganesh, V.; Chandrasekaran, S. *Synthesis* **2009**, 3267.
(95) Guo, W.; Lv, G.; Chen, J.; Gao, W.; Ding, J.; Wu, H. *Tetrahedron* **2010**, *66*, 2297.
(96) Rebane, E. *Ark. Kemi* **1966**, *25*, 363.
(97) Lindgren, B. *Acta. Chem. Scand., Ser. B* **1977**, *31*, 1.
(98) (a) Reich, H. J.; Chow, F.; Shah, S. K. *J. Am. Chem. Soc.* **1979**, *101*, 6638. (b) Reich, H. J.; Shah, S. K.; Chow, F. *J. Am. Chem. Soc.* **1979**, *101*, 6648.
(99) Crich, D.; Zou, Y. *Org. Lett.* **2004**, *6*, 775.
(100) Dan, W.; Deng, H.; Chen, J.; Liu, M.; Ding, J.; Wu, H. *Tetrahedron* **2010**, *66*, 7384.
(101) Binz, A.; Isaac, E. *Chem. Ber.* **1909**, *41*, 3381.
(102) Binz, A.; Marx, T. *Chem. Ber.* **1910**, *43*, 2344.
(103) Binz, A.; Limpach, O.; Janssen, W. *Chem. Ber.* **1915**, *48*, 1069.
(104) Leurouin, F.; Mulliez, M. E. *Phosphorus Sulfur* **1994**, *92*, 201.
(105) Mulliez, M.; Naudy, C. *Tetrahedron* **1994**, *50*, 5401.
(106) Dujols, F. J. M.; Mulliez, M. E. *J. Org. Chem.* **1996**, *61*, 5648.
(107) (a) Martín, N.; Behnisch, R.; Hanack, M. *J. Org. Chem.* **1989**, *54*, 2563. (b) Martín, N.; Segura, J. L.; Seoane, C.; de la Cruz, P.; Langa, F.; Ortí, E.; Viruela, P. M.; Viruela, R. *J. Org. Chem.* **1995**, *60*, 4077. (c) Martín, N.; Navarro, J. A.; Seoane, C.; Albert, A.; Cano, F. H.; Becker, J. Y.; Khodorkovsky, V.; Harlev, E.; Hanack, M. *J. Org. Chem.* **1992**, *57*, 5726. (d) Barranco, E.; Martín, N.; Segura, J. L.; Seoane, C.; de la Cruz, P.; Langa, F.; Gonzá lez, A.; Pingarrón, J. M. *Tetrahedron* **1993**, *49*, 4881. (e) Jannsen, R. A. J.; Christiaans, M. P. T.; Hare, C.; Martín, N.; Sariciftci, N. S.; Heeger, A. J.; Wudl, F. *J. Chem. Phys.* **1995**, *103*, 8840.

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