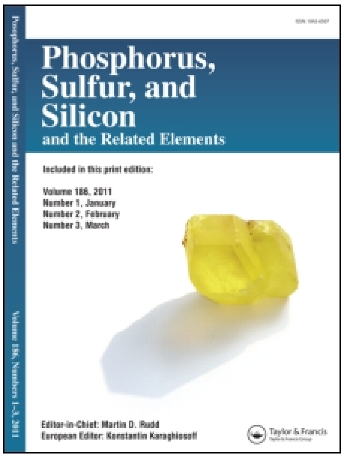

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Chemical Behavior of the Thiophene Ring in 2-Acetylthiophenes

M. A. Metwally[a]; Bakr F. Abdel-Wahab[b]; M. Koketsu[c]
[a] Department of Chemistry, Faculty of Science, University of Mansoura, Mansoura, Egypt [b] Applied Organic Chemistry Department, National Research Center, Dokki, Giza, Egypt [c] Division of Instrumental Analysis, Life Science Research Center, Gifu University, Gifu, Japan

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Review

Chemical Behavior of the Thiophene Ring in 2-Acetylthiophenes

M. A. Metwally,[1] Bakr F. Abdel-Wahab,[2] and M. Koketsu[3]
[1]Department of Chemistry, Faculty of Science, University of Mansoura, Mansoura, Egypt
[2]Applied Organic Chemistry Department, National Research Center, Dokki, Giza, Egypt
[3]Division of Instrumental Analysis, Life Science Research Center, Gifu University, Gifu, Japan

The data on the methods of synthesis and chemical properties of the thiophene ring in 2-acetylthiophenes published over the last several years until mid 2007 are reviewed for the first time. Many of the synthesized compounds exhibit interesting biological activity in various fields and are used in the production of pharmaceuticals, agrochemicals, dyes, and electrophotogeneratoragents.

INTRODUCTION

2-Acetylthiophenes have long been used as precursors for the production of biologically active compounds. Because thiophene moiety shows the wide spectrum of activity, numerous thiophenes substituted with different groups at various positions have been prepared. Despite this importance, 2-acetylthiophene has not been previously reviewed. In recent years, several new methods for the preparation of 2-acetylthiophene have been reported, including Friedel–Crafts acylation of thiophene using various catalysts and oxidation of 2-ethylthiophene. In the present review, the data on the methods of synthesis, chemical properties of thiophene moiety, and some uses of 2-acetylthiophenes published over the last several decades are reviewed for the first time.

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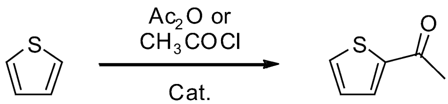
Address correspondence to M. A. Metwally, Department of Chemistry, Faculty of Science, University of Mansoura, P.O. Box 23, Mansoura, Egypt. E-mail: mamegs@mans.edu.eg

SYNTHESES OF 2-ACETYLTHIOPHENES

Friedel–Crafts Acylation

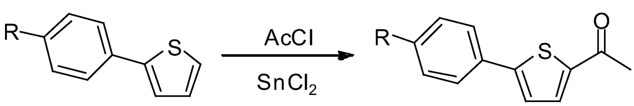
2-Acetylthiophene **1** was prepared by Friedel–Crafts acylation of thiophene in the presence of a catalyst.



1

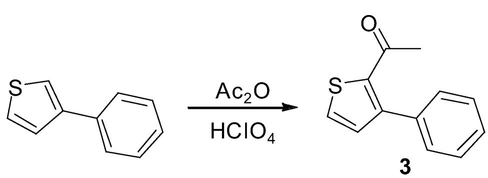
The main catalysts used for the acylation of thiophene are: trifluoromethylsulfonic anhydride [Tf_2O]; phosphotungstic acid; zeolite; molecular sieve; clay-based catalysts; phosphate; micronized beta zeolite; acetic anhydride and iodine as Lewis catalyst; Ytterbium(III) trifluoromethanesulfonate [$Yb(OTf)_3$]; Fe^{3+} exchanged montmorillonite; acetic anhydride and 60% perchloric acid; triacyloxyboranes and tetraacetoxygermane; cationic exchange resins; polyphosphoric acid; boron trifluoride etherate; glauconite; SiO_2-Al_2O_3; zinc chloride; iodine; $SnCl_4$; perchloric acid; magnesium perchlorate ("anhydrone"); tetraacyloxysilanes and acyloxytrichlorosilanes; trifluoroacetic anhydride; aluminum trichloride; silica gel impregnated with an oxide of Ti, Zr, Hf, Th, Fe, Ni, or Co; Nafion-H (fluorocarbon resin sulfonic acid); and 2-(trifluoromethylsulfonyloxy)pyridine.[1–54]

2-Acetyl-5-aryl-thiophenes **2** (R = H, 4-Me, 4-MeO, 4-Cl, and 4-Br) were prepared by acetylation of 2-arylthiophenes with acetyl chloride in benzene containing tin chloride.[55]



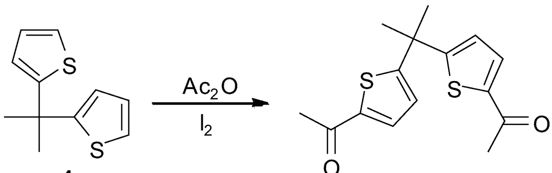
2

2-Acetyl-3-phenyl-thiophene **3** was synthesized by the acetylation of 3-phenylthiophene with acetic anhydride in the presence of 56% perchloric acid.[56]



3

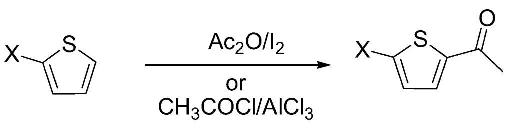
When thiophene was treated with sulfuric acid and acetone, 2,2-di(2-thienyl)propane **4** was obtained. The acylation of **4** with acetic anhydride in the presence of iodine gave 2,2-bis(5-acetylthien-2-yl)propane **5**.[57]



4 **5**

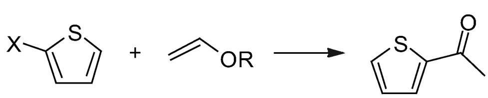
From Halothiophenes

Acetylation of 2-halothiophenes (X = Cl or Br) with acetic anhdride and iodine or with acetyl chloride and aluminum trichloride gave 2-acetyl-5-halothiophene **6**.[58–60]



6

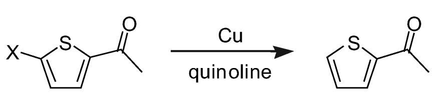
Treatment of halothiophene with vinyl ethers (R = C1–8 alkyl) in the presence of Ni catalyst gave the 2-acetylthiophenes **1**.[61]



1

Dehalogenation of Halothiophenes

Dehalogenation of halothiophenes such as 2-acetyl-5-halothiophene (X = I, Br) **7** with copper and quinoline afforded **1**.[62,63]

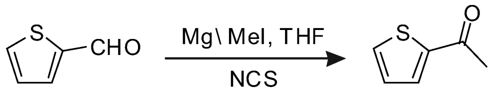


7 **1**

Debromination of 2-bromoacetylthiophene with dibutyl telluride (Bu_2Te) in the presence of triethylamine gave **1**.[64,65]

From Thiophene-2-carbaldehyde

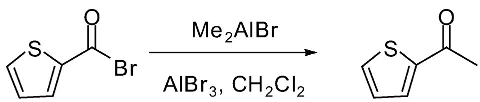
The title compound **1** was prepared from thiophene-2-carbaldehyde **8** by a sonochemical Barbier reaction with magnesium and iodomethane in THF followed by oxidation with *N*-chlorosuccinimide.[66]



8 **1**

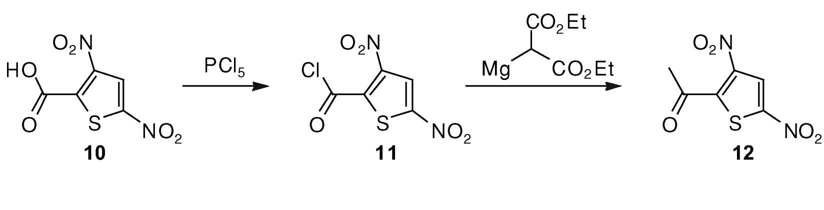
From Acyl Halides

Thiophene-2-carbonyl bromide **9** treated with dimethylaluminum bromide in dichloromethane in the presence of aluminum bromide followed by hydrolysis gave 2-acetylthiophene **1**.[67,68]



9 **1**

3,5-Dinitro-2-thiophenecarboxylic acid **10** was converted into the acid chloride **11** with phosphorus pentachloride. Treatment of **11** with the magnesium derivative of diethyl malonate and subsequent hydrolysis yielded 2-acetyl-3,5-dinitrothiophene **12**.[60]



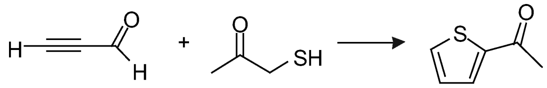
10 **11** **12**

Oxidation of 2-Ethylthiophene

The products of liquid-phase oxidation of 2-ethyl-thiophene, catalyzed by $Co(OAc)_2$ containing sodium bromide or 9,10-dibromoanthracene as promoters, were 2-acetylthiophene and α-methyl-2-thiophenemethyl acetate.[69]

From Propiolaldehyde

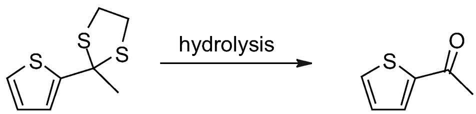
2-Acetylthiophene **1** was prepared by the reaction of propiolaldehyde **13** with 1-mercaptopropan-2-one **14** in sodium methoxide solution.[70]



13 **14** **1**

Hydrolysis of Ethanediyl Dithioacetal

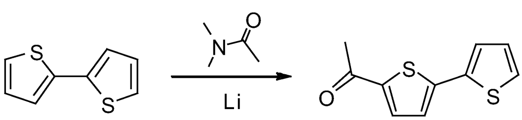
The total hydrolysis of ethanediyl dithioacetal **15** gave 2-acetylthiophene.[71]



15 **1**

Lithiation and Acetylation of Thiophene

5-Acetyl-2,2′-bithiophene **17** can be prepared from 2,2′-bithiophene **16** by lithiation and acetylation with *N,N*-dimethylacetamide.[72]



16 **17**

Carbonylation of 2-Iodothiophene

Carbonylation of 2-iodothiophene by heating it to 120–140°C under a pressure of 20 atm of carbon monoxide with $SnMe_4$, $OP(NMe_2)_3$, and $Ni(CO)_2(PPh_3)$ for 8.5–24 h gave **1**.[73]

Fischer Carbene Synthesis

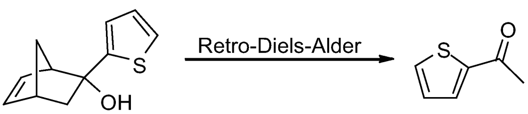
Treatment of pentacarbonyl[(2-thienyl)methoxymethylene]molybdenum with (chloromethyl)lithium gave **1** by a Fischer carbene synthesis.[74]

TABLE I Physical Data of 2-Acetylthiophene[77]

Freezing point°C	10.45
Boiling point at 760 mm,°C	213.9
Change in bp with pressure °C/mm	0.055
Refractive index, n^{20} D	1.5667
n^{20} E	1.5757
n^{20} G	1.6017
Density, g/mL at 20°C	1.1709
Viscosity at 30° centipoises	2.32
Surface tension at 30° dynes/cm	44.5
Solubility	
g 2-acetylthiophene/l00 g water at 30°C	1.4
g water/100 g 2-acetylthiophene at 30°C	2.4

Retro-Diels–Alder Reaction

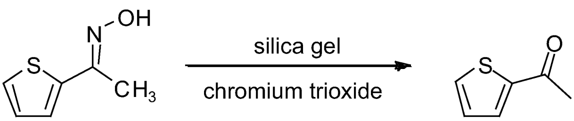
The *retro*-Diels–Alder reaction of the norbornenol **18** gave 2-acetylthiophene **1**.[75]



18 **1**

From the Ketoxime

Efficient oxidative deblocking of the ketoxime **19** to the corresponding ketone was achieved by using silica-gel–supported chromium trioxide.[76]



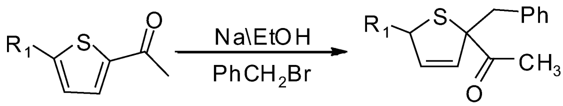
19 **1**

PHYSICAL PROPERTIES OF 2-ACETYLTHIOPHENE (Table I)

REACTIVITY OF THE THIOPHENE RING

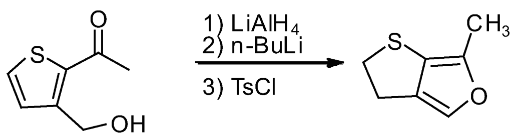
Reduction

2,2-Disubstituted 2,5-dihydrothiophenes [R^1 = H, alkyl, (un)substituted $PhCH_2$] **21** were prepared by reduction of 5-substituted 2-acetylthiophenes **20** with Na/EtOH followed by treatment with benzylbromide.[78–80]



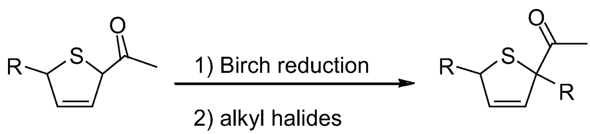
20 **21**

Reduction of 2-acetyl-3-(hydroxymethyl)thiophene with lithium aluminium hydride followed by treatment with n-buthyllithium and subsequently with tosyl chloride led to thienofuran **22**.[81]



22

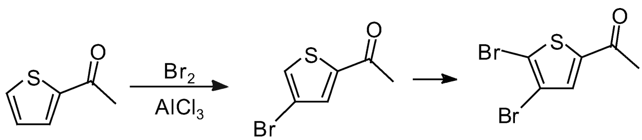
The Birch reduction of 2-acetyl- or 2-acetyl-5-alkylthiophenes **23** (R = H, alkyl) and subsequent alkylation with alkyl halides gave 2-acetyl-2-alkyl- or 2-acetyl-2,5-dialkyl-2,5-dihydrothiophenes **24**.[82]



23 **24**

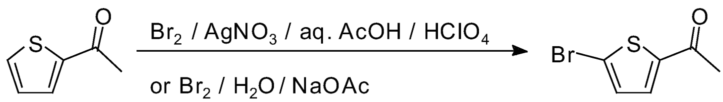
Bromination

Bromination of **1** in the presence of excess aluminum trichloride afforded the 4-bromo derivative **25**, and further on the 4,5-dibromo derivative **26**.[83–85]



1 25 26

The reaction of **1** with bromine, $AgNO_3$, aq. AcOH, and $HClO_4$ at r.t., or with bromine in water containing sodium acetate gave 2-acetyl-5-bromothiophene **27**.[86,87]

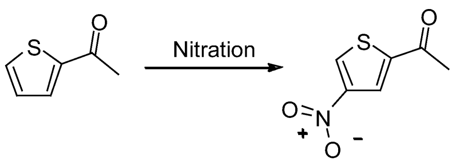


1 27

Bromination of **1** by the use of *N*-bromosuccinimide in acetic anhydride and acetic acid also led to **27**.[88]

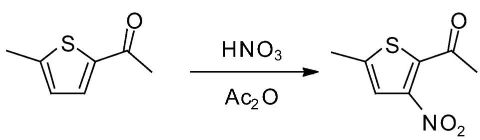
Nitration

Nitration of **1** gave the 4-nitro derivative **28**.[89,90]



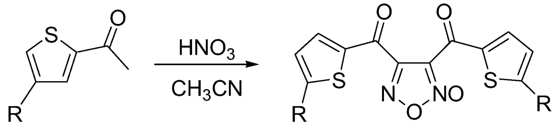
1 28

Nitration of 2-acetyl-5-methylthiophene afforded 2-acetyl-5-methyl-3-nitro-thiophene **29**.[91]



29

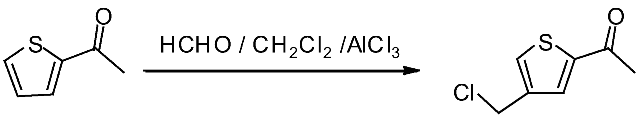
Nitration of the acetylthiophenes **30** (R = H, Et, Br, I) with fuming nitric acid in aceteonitrile afforded the oxadiazoles **31** instead of the expected nitration products.[92]



30 **31**

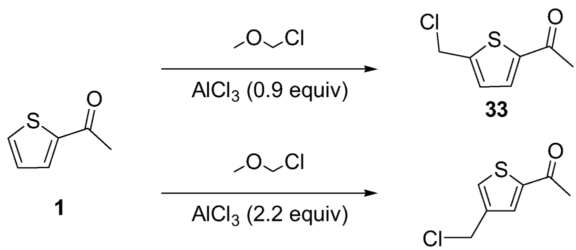
Chloromethylation

(Chloromethyl)thiophene **32** was formed by chloromethylation of **1** by reaction with formaldehyde in dichloromethane in the presence of a catalytic amount of aluminum trichloride.[93]



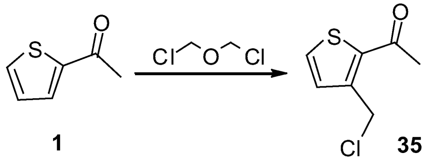
1 32

The chloromethylation of **1** with chloro(methoxy)methane in chloroform or carbon tetrachloride containing 0.9 equiv. of aluminum trichloride gave predominantly the 5-chloromethyl derivative **33.** When 2.2 equivs. of aluminum trichloride were present, the reaction almost exclusively led to the 4-chloromethyl derivative **34**, while the chloromethylation with chloro(chloromethoxy)methane afforded both the 4-chloromethyl and the 5-chloromethyl derivatives.[94,95]



1 **33** **34**

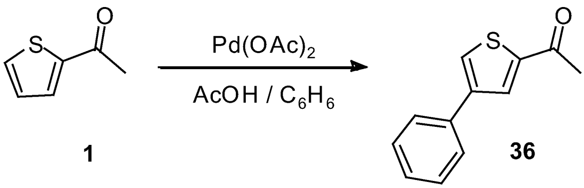
Chloromethylation of **1** in the presence of an excess of aluminum trichloride afforded 2-acetyl-3-chloromethylthiophene **35**.[96–98]



1 **35**

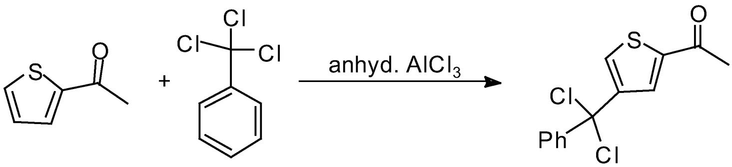
Alkylations

Treatment of **1** with $Pd(OAc)_2$ in AcOH containing benzene at reflux gave 2-acetyl-4-phenylthiophene **36**.[99]



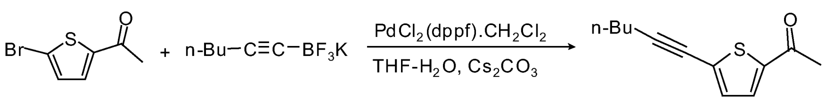
1 36

The reaction of (trichloromethyl)benzene with **1** in the presence of an excess of anhydrous aluminum trichloride was studied. The $PhCCl_2$ group enters into position 4 under the formation of **37**.[100]



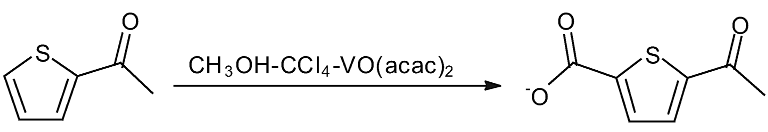
1 37

The palladium-catalyzed cross-coupling reaction of potassium alkynyltrifluoroborates with 5-bromo-2-acetylthiophene **27** afforded the corresponding alkyne **38**.[101]



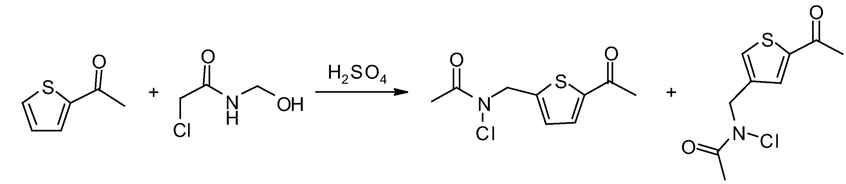
27 38

The reaction of **1** with the $CH_3OH–CCl_4–VO(acac)_2$ system also occurs regioselectively and gives methyl 5-acetylthiophene-2-carboxylate **39**.[102]



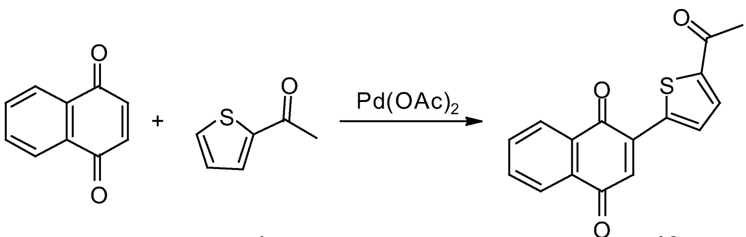
1 39

The reaction of **1** with *N*-(hydroxymethyl)chloroacetamide in concentrated sulfuric acid gave a mixture of the 4- and 5-(*N*-chloroacetylamino)methyl derivatives **40** and **41**.[103,104]



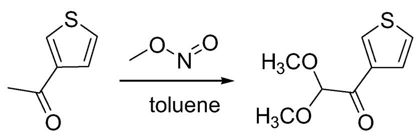
1 40 41

Treatment of 1,4-naphthoquinone with **1** in the presence of palladium diacetate gave the corresponding 2-thienyl-1,4-naphthoquinone **42**.[105]



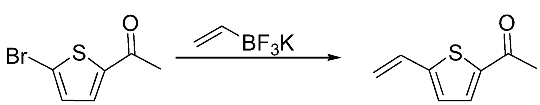
1 42

2,2-Dimethoxy-1-(3-thienyl)-1-ethanone **43** was prepared by reaction of **1** with methyl nitrite in toluene in a multistep reaction.[106]



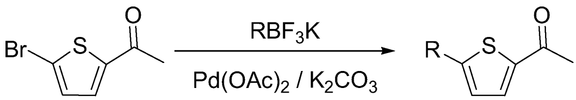
1 43

The Suzuki–Miyaura cross-coupling reaction of potassium vinyltrifluoroborate with 2-acetyl-5-bromothiophene **27** as electrophile gave 2-bromo-5-vinylthiophene **44**.[107]



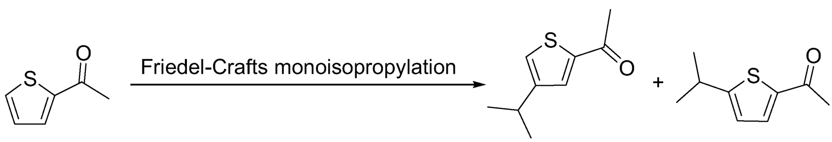
27 44

The ligandless palladium-catalyzed Suzuki cross-coupling reaction of potassium aryl and heteroaryl trifluoroborates (R = aryl or heteroaryl) with 2-acetyl-5-bromothiophene using Pd(OAc)$_2$ as a catalyst in the presence of potassium carbonate afforded 5-substituted 2-acetylthiophenes **45**.[108,109]



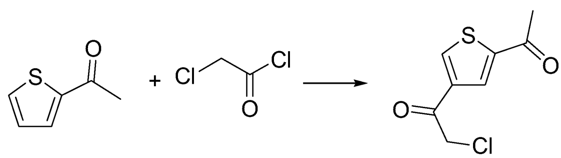
27 45

The Friedel–Crafts monoisopropylation of **1** predominantly led to the 4-isopropyl derivative **46**. Small amounts of the the 5-isopropyl derivative **47** were also formed.[110]



1 46 47

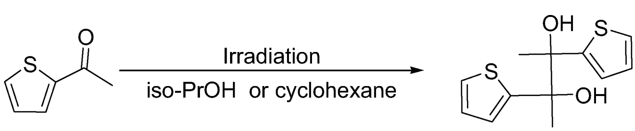
2-Acetylthiophene **1** reacted with chloroacetylchloride in the presence of aluminum trichloride to yield after treatment with aq. HCl 27% of the starting ketone and 56% of crude 2-acetyl-4-chloroacetylthiophene **48**.[111]



1 48

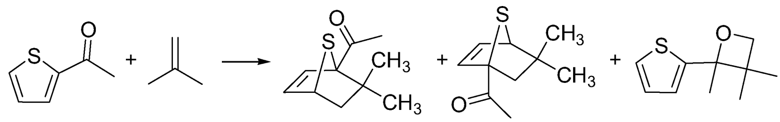
Photochemical Reactions

2,3-Bis(thienyl-2-yl)-2,3-butanediol **49** was prepared by irradiation of 2-propanol or cyclohexane solutions of **1**.[112]



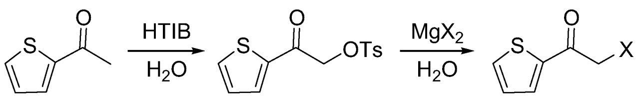
1 49

Irradiation of **1** in the presence of an excess of isobutene gave two major products: 1-acetyl-6,6-dimethyl-7-thiabicyclo[2.2.1]hept-2-ene **50** and 1-acetyl-5,5-dimethyl-7-thiabicyclo[2.2.1]hept-2-ene **51**, as well as 6% of 2,3,3-trimethyl-2-(thien-2-yl)oxetane **52**.[113]



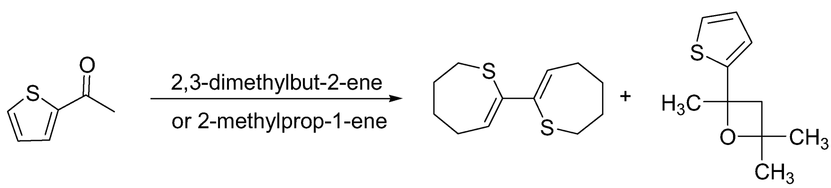
1 50 51 52

Reaction of **1** with HTIB and subsequently with magnesium halide (X = Br, Cl, and I) using microwave irradiation afforded 2-haloacetylthiophene **53**.[114]



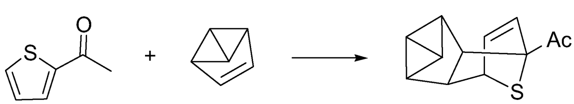
1 53

Irradiation of **1** with 2,3-dimethylbut-2-ene or 2-methylprop-1-ene resulted in [4 + 2] addition of the thiophene to the alkene as the major process to give thiabicycloheptenes, e.g., **54**, as well as a [2 + 2] cycloadduct, e.g., **55**, as the minor products.[115]



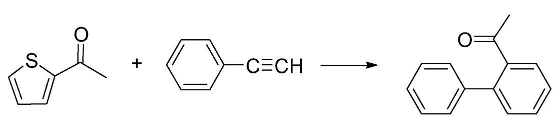
1 54 55

Photocycloaddition of benzvalene with **1** gave bicyclic compounds such as **56**.[116]



1 56

The photochemical reaction between **1** and phenylacetylene gave *ortho*-substituted biphenyls **57**.[117]



1 57

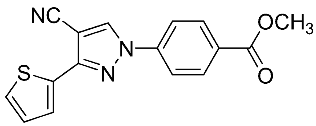
APPLICATIONS

Like many sulfur compounds, acetylthiophenes exhibit antioxidant power toward vitamin C.[118] 2-Acetylthiophene **1** and 2-acetyl-5-methylthiophene have hot spring odor.[119]

Medicinal Applications

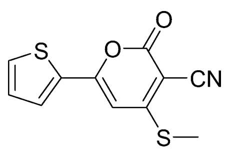
Thiophene compounds or their pharmaceutically acceptable salts are useful as antivirus, anti-inflammatory, and immunostimulant agents.[120,121] 2-Acetyl-5-nitrothiophene, 2-acetyl-4-nitrothiophene, and 5-acetamido-2-acetylthiophene show antibiotic activity.[60]

Methyl 4-[4-cyano-3-(thien-2-yl)-1*H*-pyrazol-1-yl]benzoate **58** is used against buttermilk xanthine oxidase.[122]



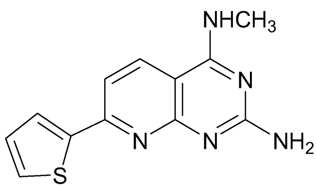
58

3-Cyano-4-methylthio-6-(thien-2-yl)-2*H*-pyran-2-one **59** has hepatoprotective activity.[123]



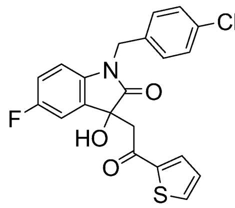
59

The pyrido[2,3-*d*]pyrimidine-2,4-diamine derivative **60** has been useful for the treatment or prevention of PTP-1B mediated diseases, including diabetes, obesity, and diabetes-related diseases.[124]



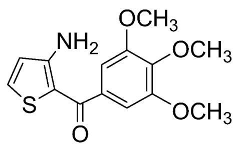
60

The indole derivative **61** is used for the treatment of sodium channel–mediated diseases.[125]



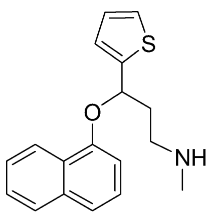
61

Derivatives of 3-amino-2-(3,4,5-trimethoxybenzoyl)thiophene **62** are used as inhibitors of the tubulin polymerization and have antiproliferative activity.[126]



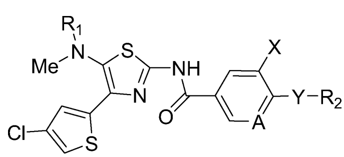
62

2-Acetylthiophene **1** was used in the synthesis of *N*-methyl-γ-(1-naphthalenyloxy)-2-thiophenepropanamine ("duloxetine") **63**, which is applied for the treatment of depression.[127–130]



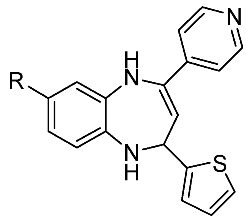
63

Compounds of formula **64** have platelet-increasing effects ($R^1 = n$-Bu, A = N, X = Cl, YR_2 = 4-carboxypiperidino).[131,132]



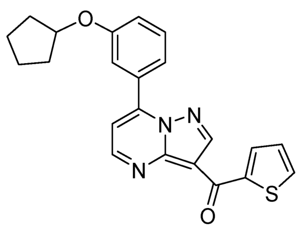
64

8-Substituted 2,5-dihydro-2-(pyridine-4-yl)-4-(thien-2-yl)-1,5-benzothiazepines **65** (R = F, Cl, Br, CH_3, OCH_3 and OC_2H_5) show good antibacterial and antifungal activity.[133]

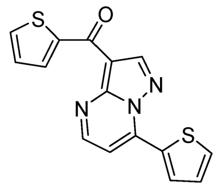


65

The substituted pyrazolo[1,5-*a*]pyrimidines **66** and **67** were used as antiproliferative agents.[134,135]

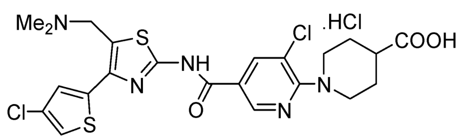


66



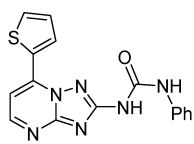
67

2-Acylaminothiazole derivative **68** is used for the treatment of thrombopenia.[136]



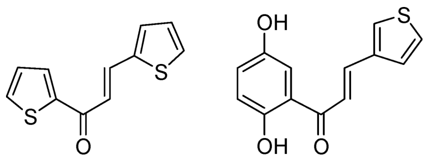
68

1,2,4-Triazolo[1,5-*a*]pyrimidin-2-ylurea derivative **69** is useful for the treatment of autoimmune diseases, allergic diseases, inflammatory diseases, and cancer.[137]



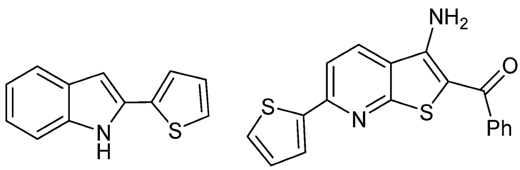
69

Chalcone derivatives **70** and **71** have been used as anti-inflammatories.[138]



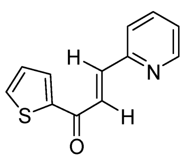
70 **71**

2-(Thien-2-yl)-1*H*-indole **72** is used as an inhibitor of the plasminogen activator inhibitor-1 (PAI-1),[139,140] while thienopyridine derivative **73** is used as a potent anti-tumor agent.[141]



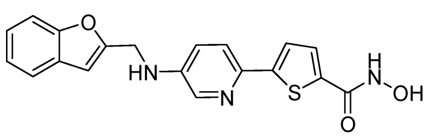
72 **73**

The propenone derivative **74** showed the most significant dual COX/5-LOX inhibitory activity.[142]



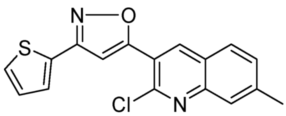
74

The substituted thiophene-2-hydroxamic acid **75** is used as a histone deacetylase inhibitor and is useful against disorders involving increased cell proliferation.[143]

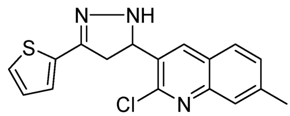


75

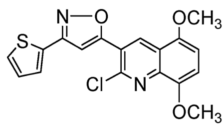
Pyrazoline **76** and isoxazole **77** have antifungal and antibacterial activities.[144]



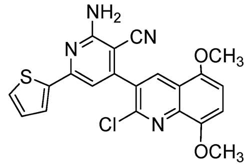
76



77



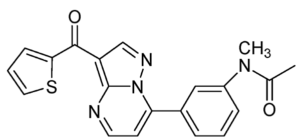
78



79

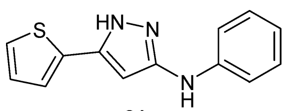
Isoxazole **78** and cyanopyridine **79** exhibit good antimicrobial activity.[145]

N-Methyl-*N*-{3-[3-(2-thenoyl)pyrazolo[1,5-*a*]pyrimidin-7-yl]phenyl} acetamide **80** is used as a sedative-hypnotic, anxiolytic, anticonvulsant, and skeletal muscle relaxant.[146]



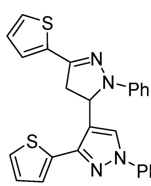
80

Pyrazole derivative **81** is used for inhibiting protein kinase.[147]



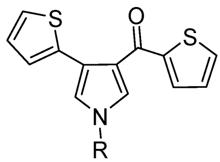
81

Diphenyldithien-2-ylpyrazolylpyrazoline **82** has been is used as a potential component of luminescent composite dyes.[148]



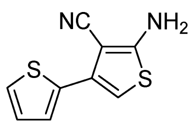
82

The pyrrole derivatives **83** (R = H, Me, Et) are used as a templates for COX-1/COX-2 inhibitors.[149]



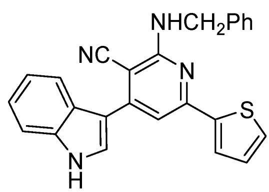
83

5′-Amino-4′-cyano-2,3′-bithiophene **84** shows promising antiradiation activity.[150]



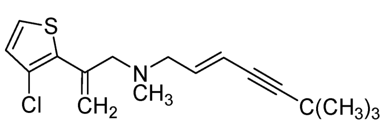
84

3-Indole derivative **85** exhibits antimicrobial activity against several bacterial strains.[151]



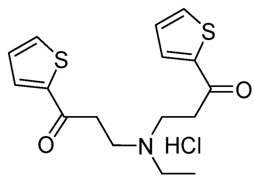
85

Thiophene derivative **86** has been useful for the treatment of athlete's foot and tinea unguium.[152]



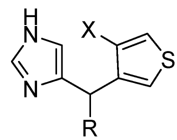
86

The bis-Mannich base *N*-ethyl-*N*,*N*-bis[3-oxo-3-(thien-2-yl)propyl] amine hydrochloride **87** is used as a antimicrobial and cytotoxic agent.[153]



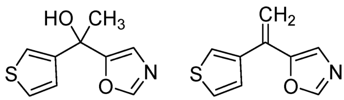
87

The 4-[(thien-3-yl)methyl]imidazoles of formula **88** (R = H, Me; X = 4-chloroalkyl, Br, Cl) show exceptional analgesic activity.[19]



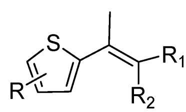
88

The thienyloxazole derivatives **89** and **90** are used as neuroprotective agents.[154]



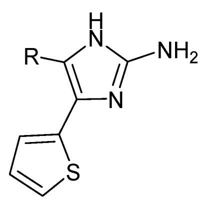
89 **90**

Haloethenylthiophenes **91** are used as pesticides against *Meloidogyne incognita*.[155]



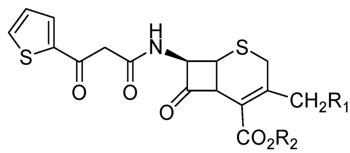
91

The thienylimidazoles **92** (R = H, Br, Cl) exhibit antifungal activity against *Piricularia oryzae* and antibacterial activity against the common pathogenic bacteria *Staphylococcus aureus* and *Escherichia coli*.[156,157]



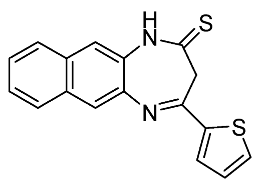
92

Cephalosporins **93** (R = Me, R1 = OAc, R2 = H) were shown to be as active as cephalothin against both Gram-negative and Gram-positive bacteria.[158]



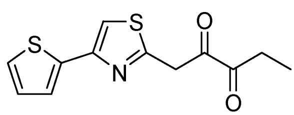
93

1,5-Naphthodiazepine derivative **94** exhibit anti-inflammatory activity.[159]



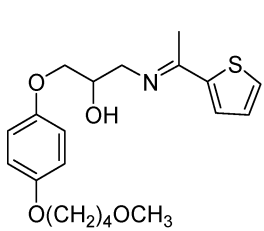
94

The α-diketone **95** is useful for the treatment of asthma.[160]



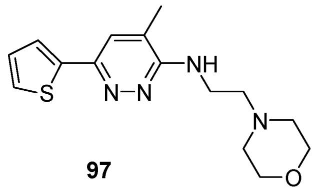
95

1-Aryloxy-3-methyleneaminopropan-2-ol derivative **96** is useful in treating arrhythmia and other heart disorders.[161]



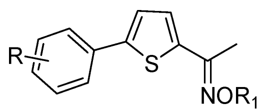
96

N-(2-Morpholinoethyl)-3-pyridazinamine **97** exhibits antidepressant activity.[162]



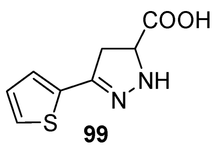
97

Oxime ethers derived from 2-acetyl-5-arylthiophenes **98** have shown mild anti-inflammatory, muscle relaxant, and central nervous system depressant activity.[163]



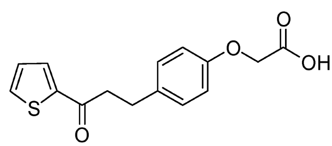
98

4,5-Dihydro-1*H*-pyrazole derivative **99** has been useful as a antihypertensive.[164]



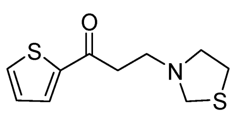
99

The 4-substituted phenoxyacetic acid derivative **100** exhibits antimicrobial activity.[165]



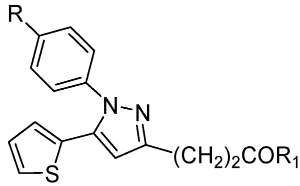
100

3-(Thiazolidin-3-yl)-1-(thien-2-yl)propan-1-ones **101** are used as antihypoxic agents.[166]



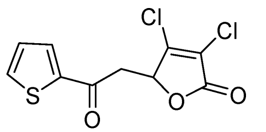
101

Pyrazoles **102** are analogs of tepoxalin, a potent anti-inflammatory agent.[167]



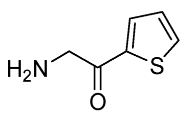
102

Furanone derivatives **103** have been useful as cardiotonics and antiulcer agents.[168]



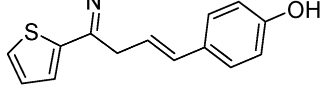
103

2-(2-Aminoacetyl)thiophene **104** exhibits dopamine β-hydroxylase (DBH)-inhibiting and antihypertensive activity.[169]



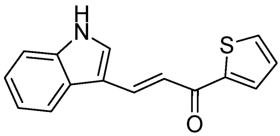
104

Chalcone oxime ether **105** is used as 5-HT2 a receptor antagonist and platelet antiaggregant.[170]



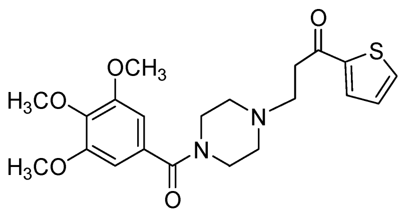
105

Indole **106** demonstrated sedative, positive inotropic, antihypertensive, vasodilatoric, analgesic, diuretic, bronchodilatoric, anti-inflammatory, and capillary permeability decreasing properties.[171]



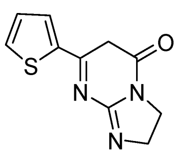
106

Piperazine derivative **107** has been useful in the prophylaxis and treatment of heart diseases, especially ischemia.[172]



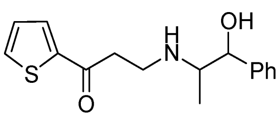
107

Imidazo[1,2-*a*]pyrimidine **108** has been useful as an anti-inflammatory agent.[173]



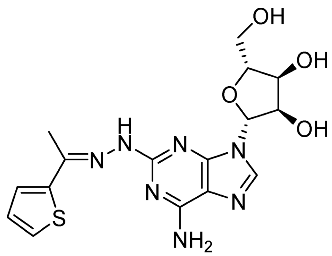
108

2-{3-[*N*-(1-Hydroxy-1-phenyl)prop-2-yl-amino]propionyl}thiophene **109** has shown bronchospasmolytic activity.[174]



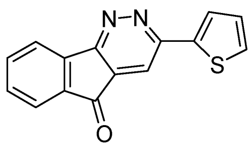
109

2-(N′-2-Thienylidenehydrazino)adenosine **110** is a potent and selective coronary vasodilator.[175]



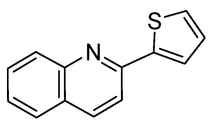
110

5-*H*-Indeno[1,2-*c*]pyridazine derivative **111** has anticonvulsant activity.[176]



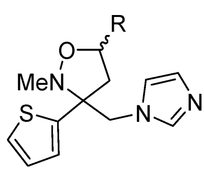
111

2-(Thien-2-yl)quinoline **112** has been useful as an intercalator of DNA, and also inhibits the replication of retroviruses, including HIV.[177]



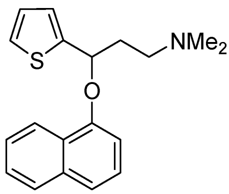
112

5-{[Aryl or aryloxy (or thio)]methyl}-3-(1*H*-imidazol-1-ylmethyl)-3-(2-thienyl)-2-methylisoxazolidine derivatives **113** (R = Ph, 4-ClC_6H_4, 3-$O_2NC_6H_4$, CH_2OAr, CH_2SAr; Ar = Ph, 4-ClC_6H_4, 4-MeC_6H_4) are used as novel antifungal agents.[178,179]



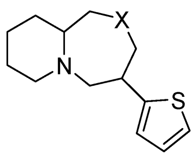
113

Naphthalenyloxypropanamine **114** is used as an antidepressant.[180]



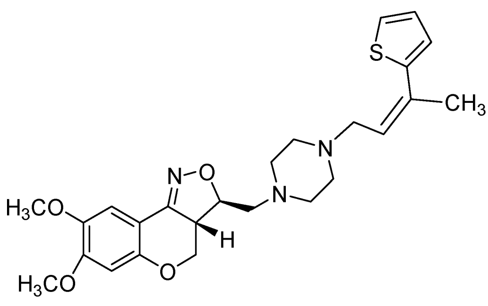
114

Perhydropyrido[1,2-*a*][1,4]diazepine and perhydropyrido[2,1-*c*][1,4]oxazepine **115** (X = O, NMe) has shown anti-inflammatory, central nervous system depressant, and anticonvulsant properties.[181]



115

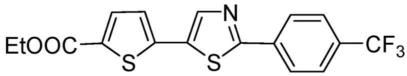
3a,4-Dihydro-3*H*-[1]benzopyrano[4,3-*c*]isoxazole **116** displays combined 5-HT-uptake inhibiting and α_2-adrenoceptor antagonistic activities.[182]



116

Applications as Insecticides

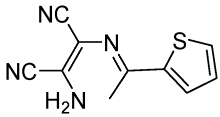
5-(Thien-2-yl)-2-arylthiazole **117** represents a useful photoactive insecticide, acaricide, and nematocide.[183]



117

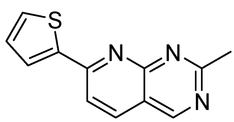
2,2-Disubstituted 2,5-dihydrothiophenes **21**, [R^1 = H, alkyl; R^2 = alkyl, (un)substituted $PhCH_2$], are useful fungicides and insecticides.[184]

2-Amino-3-(methyleneamino)maleonitrile **118** is used as an herbicide.[185]



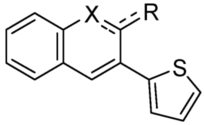
118

7-(Thien-2-yl)-2-methylpyrido[2,3-*d*]pyrimidine **119** has been a useful herbicide antidote.[186]



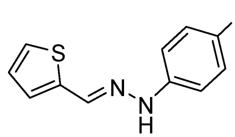
119

Thienylquinoxaline compounds of formula **120** [X = N, R = H, halogen, alkoxy, (substituted) aryloxy, or (substituted) amino; X = NH, R = O] are used as herbicides.[187]



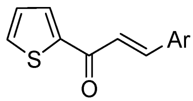
120

The *N*-formylphenylhydrazone **121** is used as a fungicide against *Erysiphe graminis*, *Puccinia recondita*, and *Uromyces fabae*.[188]



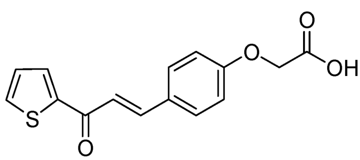
121

Heterocyclic analogs of chalcones **122** used are as potential germicides.[189]



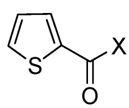
122

Phenoxyacetic acid derivative **123** has been useful as a pesticide.[190]



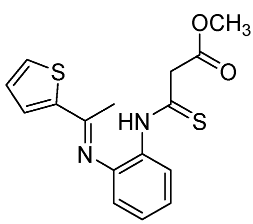
123

2-Haloacetylthiophenes **124** (X = CH_2Cl or CH_2Br) are used as soil fungicides and nematocides.[191]



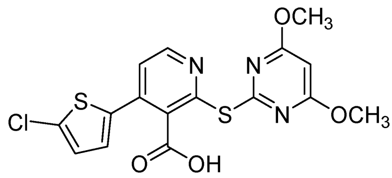
124

Thioallophanate **125** is used as a fungicide.[192]



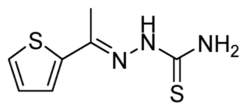
125

4-(5-Chlorothien-2-yl)-2-(4,6-dimethoxypyrimidin-2-ylthio)nicotinic acid **126** has shown herbicidal activity against *Echinochloa crus-galli*.[193]



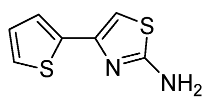
126

Acetylthiophene thiosemicarbazone **127** exhibited bactericidal, fungicidal, and antitubercular activity.[194]



127

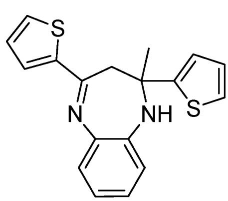
2-Aminothiazole derivative **128** is used as an anesthetic for fish-breeding.[195]



128

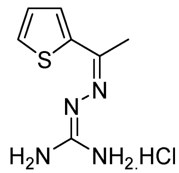
Determination of Metals

2-Methyl-2,4-di(thien-2-yl)-2,3-dihydro-1*H*-1,5-benzodiazepine **129** is used as a highly selective and sensitive plasticized membrane sensor for silver ions.[196]



129

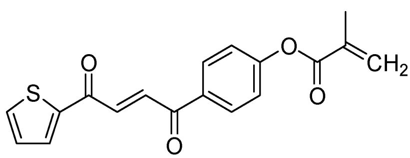
2-Acetylthiophene thiosemicarbazone **127** is also used in the spectrophotometric determination of copper(II) in alloys and edible oils.[197–199] 2-Acetylthiophene guanylhydrazone **130** is used as an analytical reagent for palladium(II) determinations.[200]



130

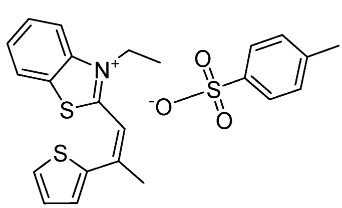
Production of Photosensitizers

The methacrylate **131** represents a useful photosensitizer and photoresistant.[201]



131

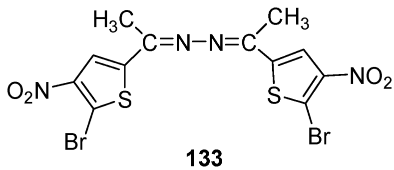
Quaternary salt **132** is used for the production of photographic sensitizers.[202]



132

Production of Azodyes

The azine **133** of 5-acetyl-2-bromo-3-nitro-thiophene is a useful azo dye intermediate.[203]



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