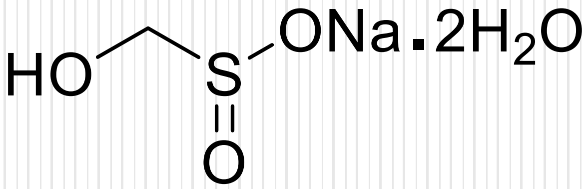
Rongalite: A Useful Reagent in Organic Synthesis

Chris Johnson

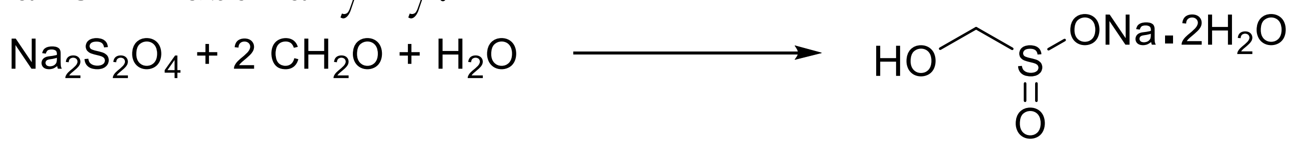
9/5/2013



~50$/kg

Introduction

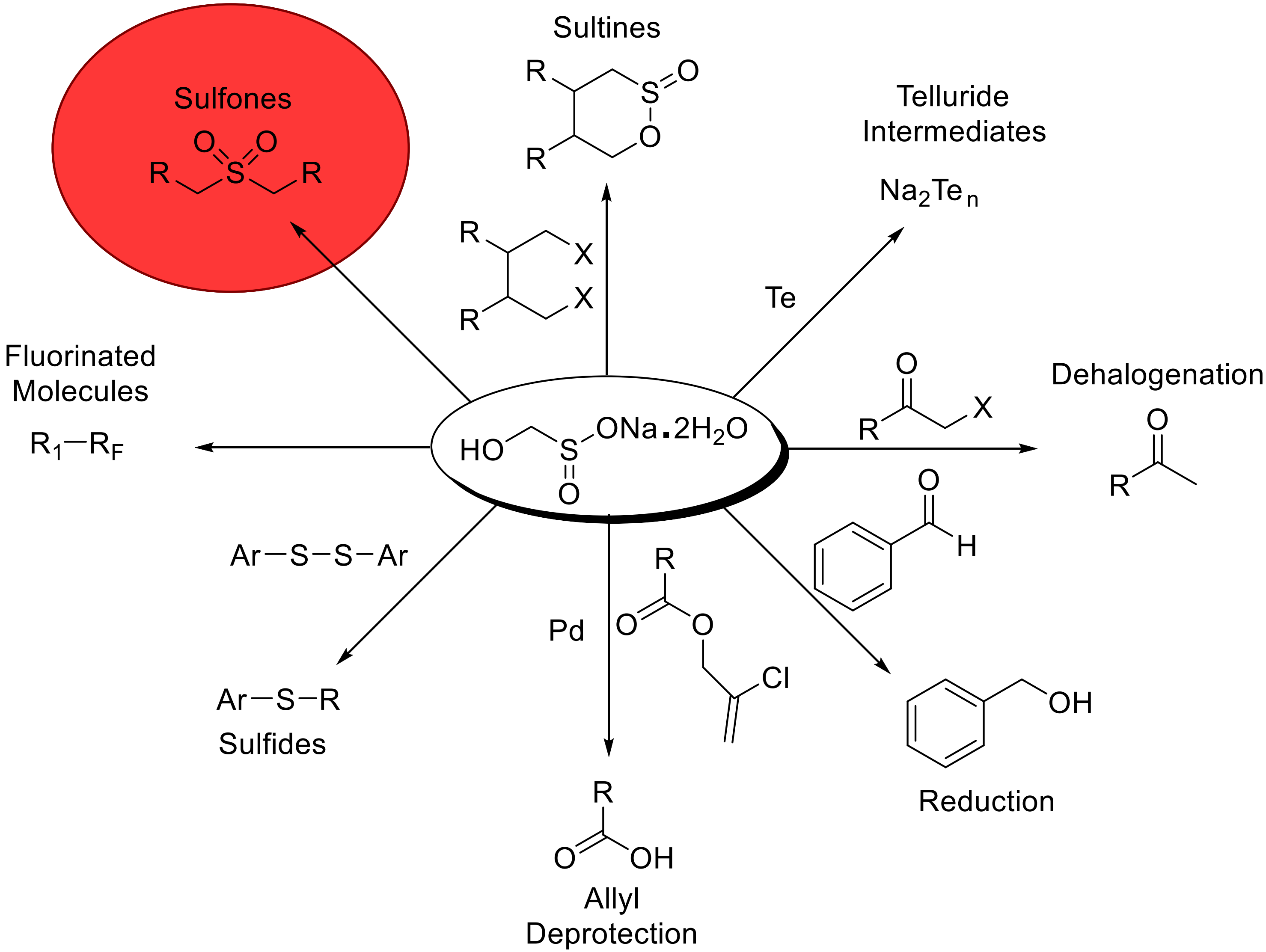
- First literature appearance in Chemische Berichte in 1905
- Made industrially by:



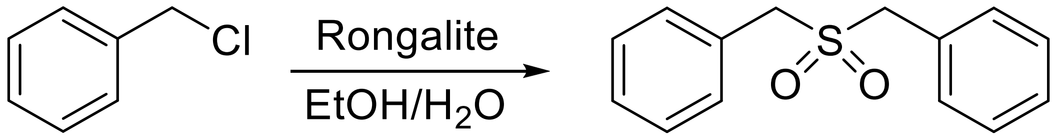
~50$/kg

- The name comes from the french word rongeage, meaning discharge or decolorizing agent.
- When acidified it decomposes into sulfoxylate and formaldehyde
- SO_2^{2-} works as a nucleophile or a reducing agent (1 e^- donor)
- Common uses:
  - Redox initiator source in emulsion polymerization
  - Bleaching agent for printing and dyeing
  - Heavy metal antidote (Hg, Au, Cu, Ba, Sb, Pb, Bi)
  - Photographic developer
  - Reagent in organic synthesis

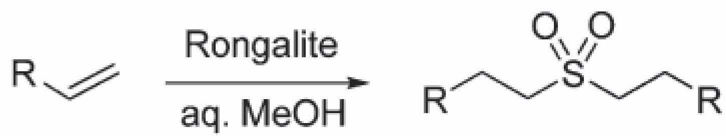
Overview of Reactivity



Sulfones

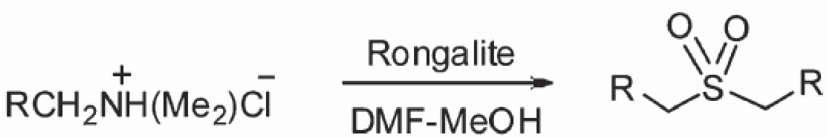


Fromm, E. *Chem. Ber.* 1908, 41, 3397.

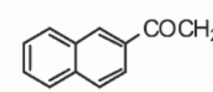
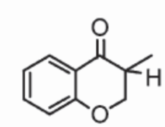
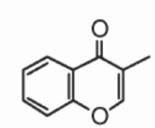
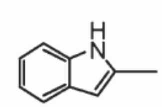
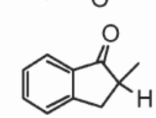


R	CO_2Me	CN	CO_2H	$CONH_2$	$COCH_3$	2-pyridyl	4-pyridyl
Yield(%)	90	70	64	77	86	91	86

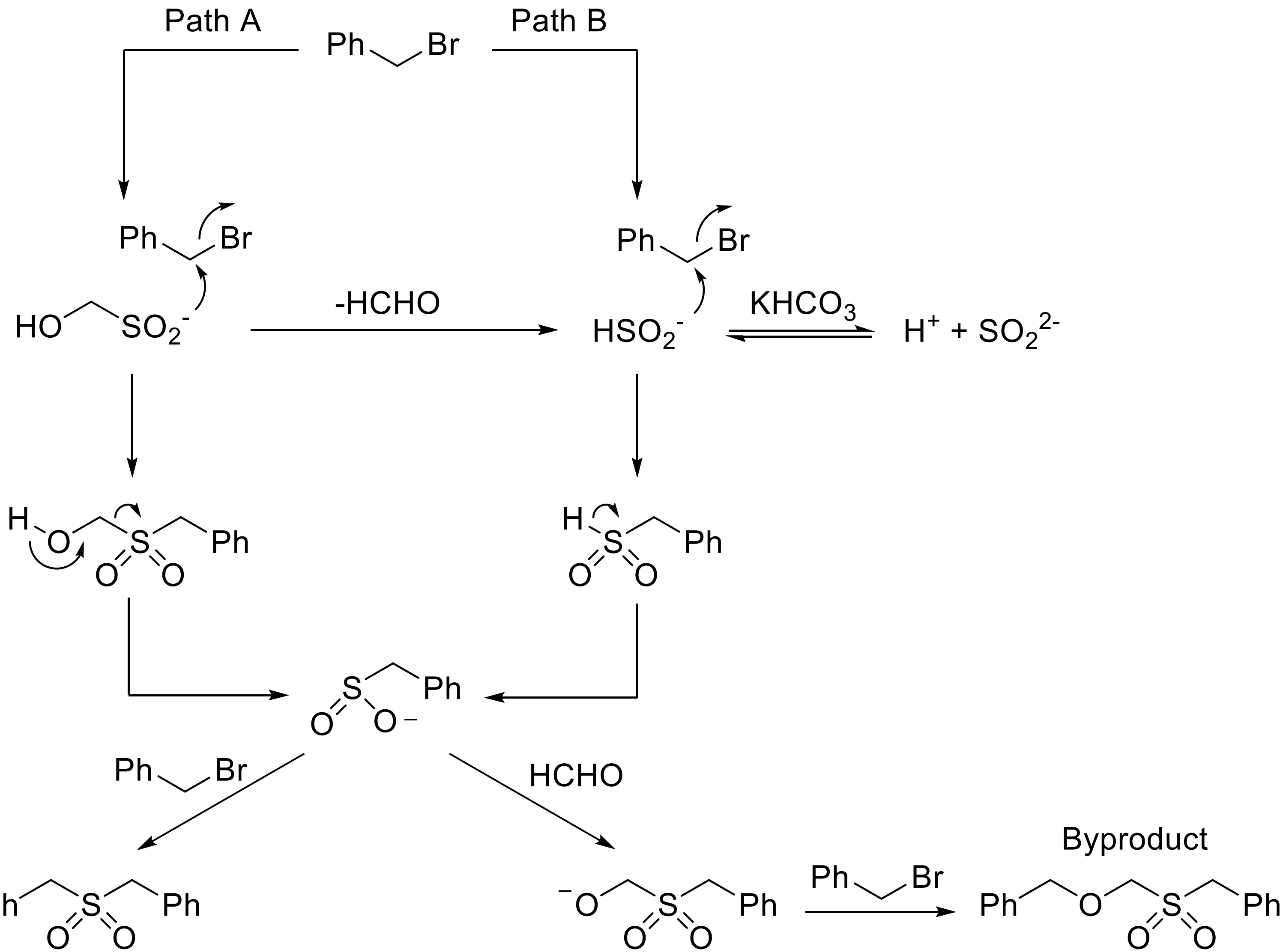
Starnick, J. *Chem. Ber.* 1971, 104, 2035.



Greve, H. *Synthesis* 1977, 259.

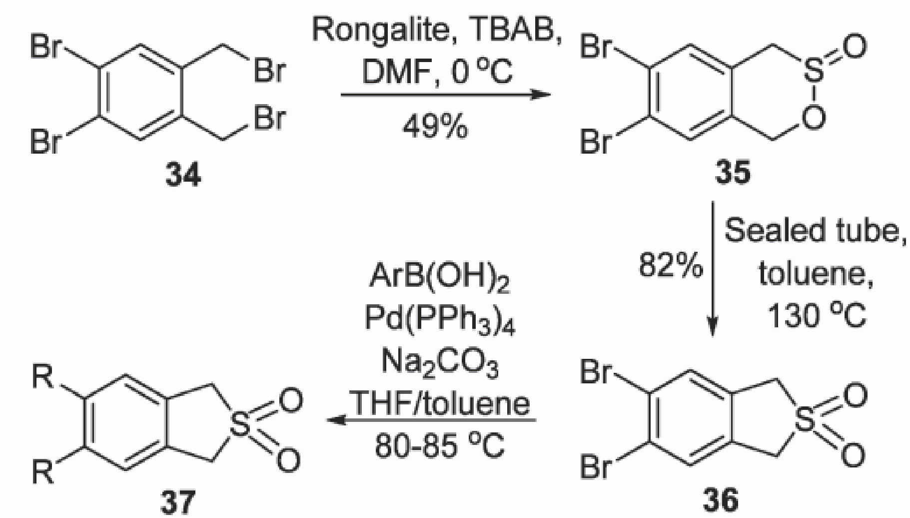
R	**Yield (%)**	**R**	**Yield (%)**
$PhCOCH_2$	54		41
p-$CH_3COPhCOCH_2$	49		
p-Cl-$PhCOCH_2$	45		47
$(Ph)_2CHCOCH_2$	49		
Furyl-2-$COCH_2$	32		
Thienyl-2-$COCH_2$	52		19
	27		28

Sulfone Mechanism



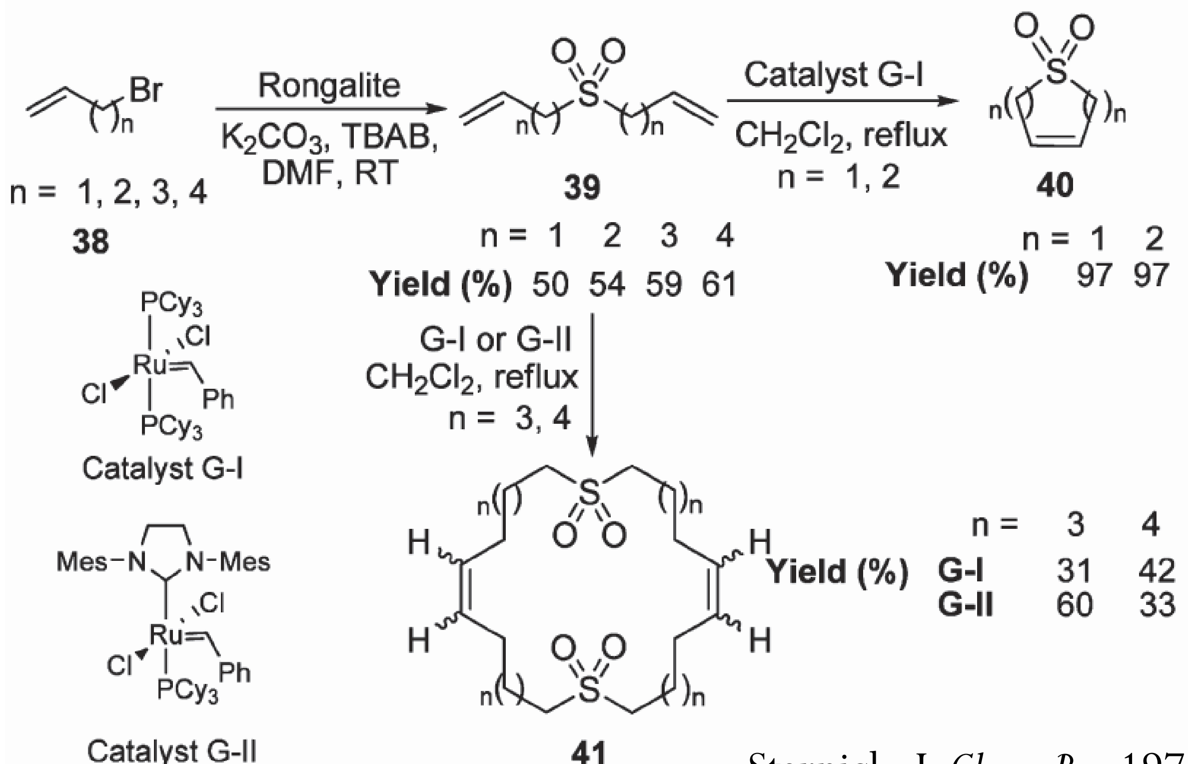
Harris, A. R.; *Synth. Commun.* 1988, 18, 659.

Dittmer, D.C.; *J. Org. Chem.* 1988, 53, 5750.

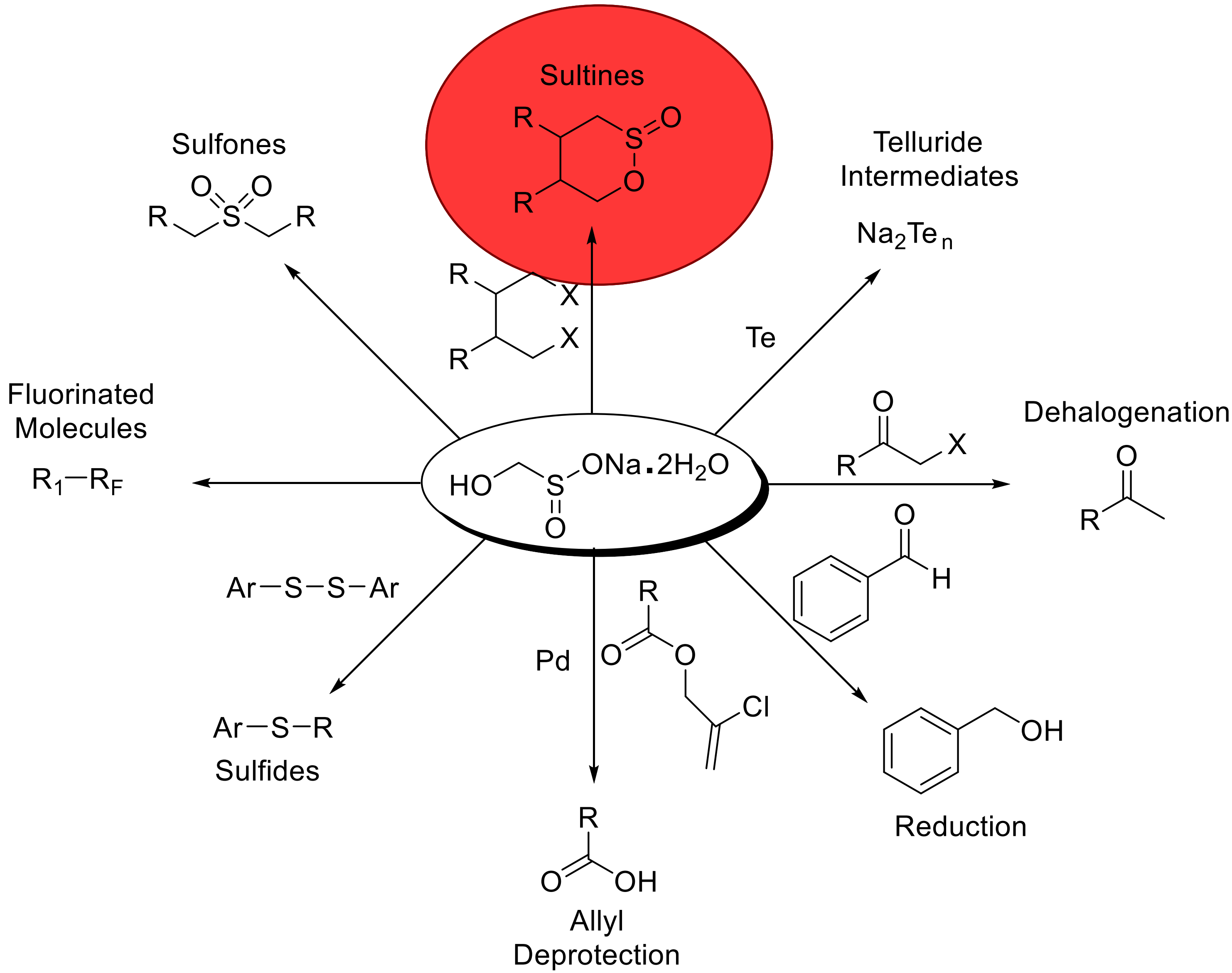


R	Yield (%)	R	Yield (%)
Ar	98	4-CHO-Ar	95
3-CF_3-Ar	96	4-Ac-Ar	98
4-Me-Ar	99	4-CN-Ar	99
4-OMe-Ar	91	4-F-Ar	97
3-thienyl	98	4-Ph-Ar	96

Kahinath, D. *Tetrahedron* 2002, 58, 9633.

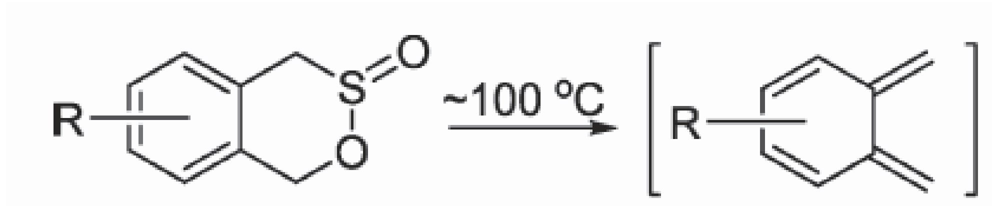


Starnick, J. *Chem. Ber.* 1971, 104, 2035.

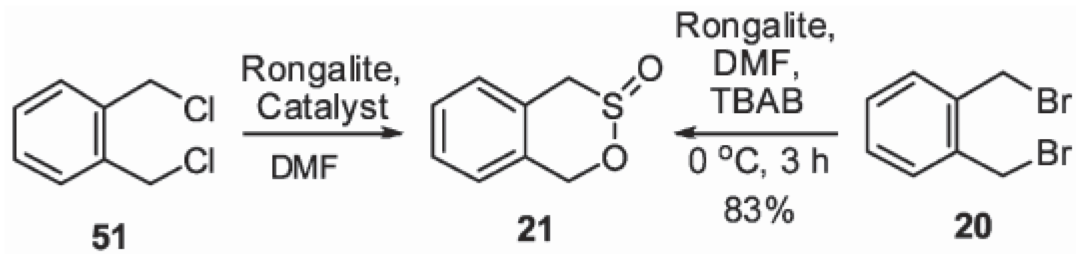


Sultines
Sulfones
Telluride Intermediates
Na_2Te_n
Te
Fluorinated Molecules
R_1-R_F
HO
ONa.2H2O
Dehalogenation
Ar—S—S—Ar
Pd
Ar—S—R
Sulfides
Reduction
Allyl Deprotection

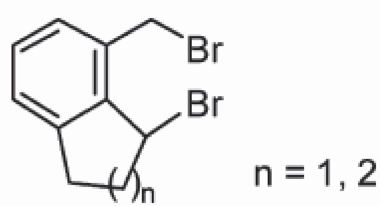
Sultines



Khedkar, P.; *Chem. Rev.* 2012, 112, 1650.



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



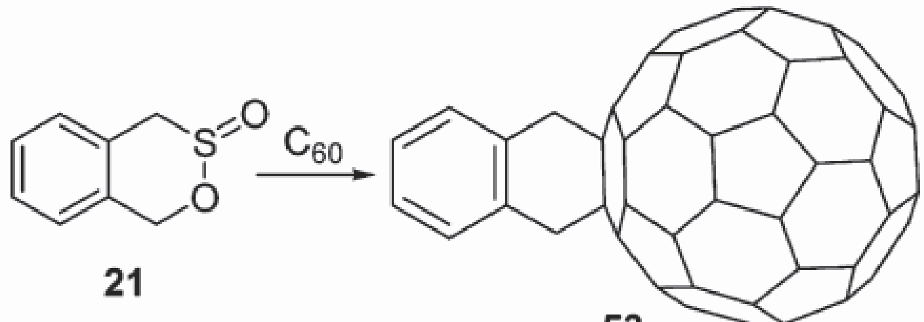
n = 1, 2

52

No Reaction

Dittmer, D.C.; *J. Org. Chem.* 1991, 56, 1948.

Sultines



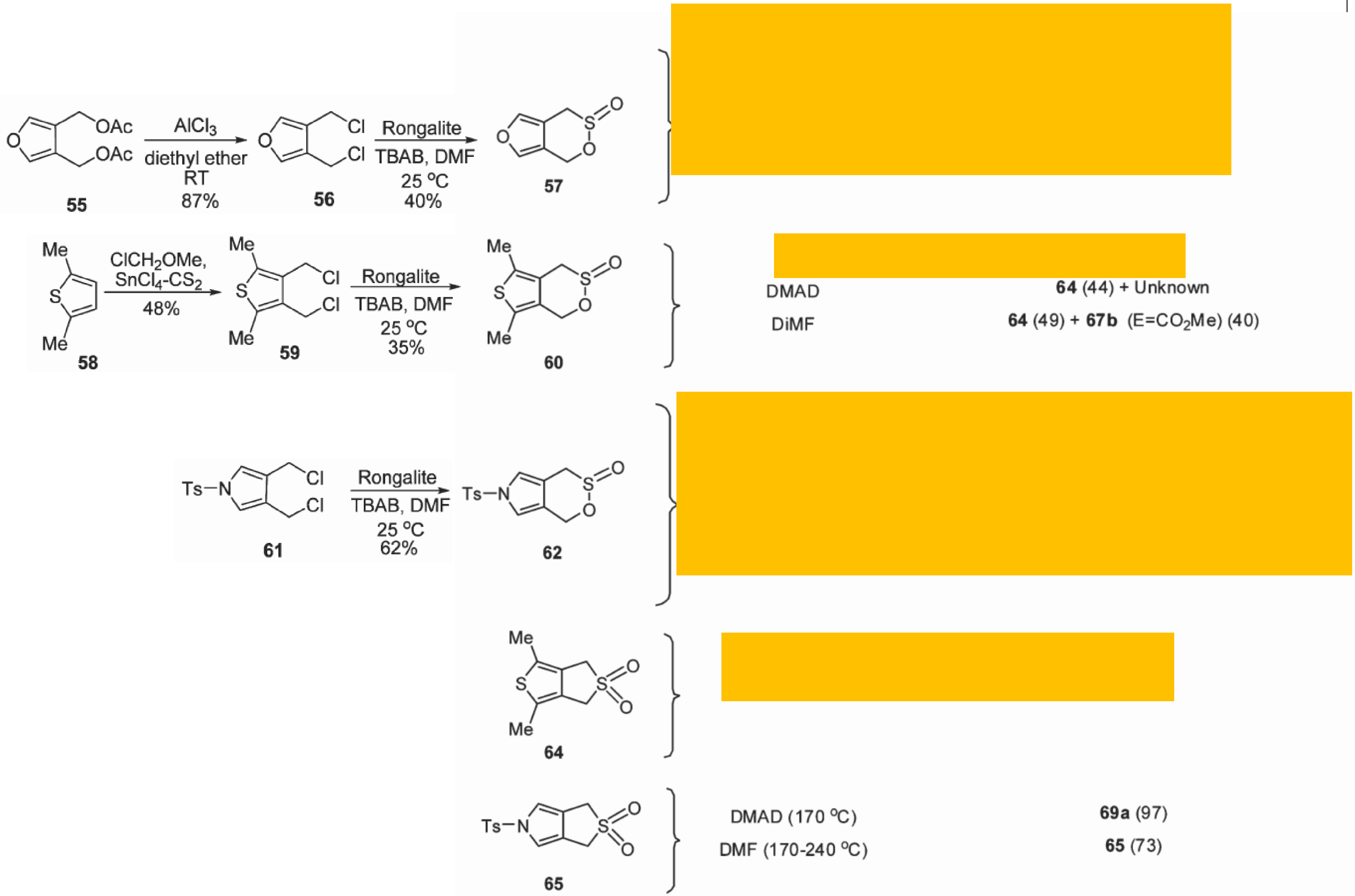
21

53

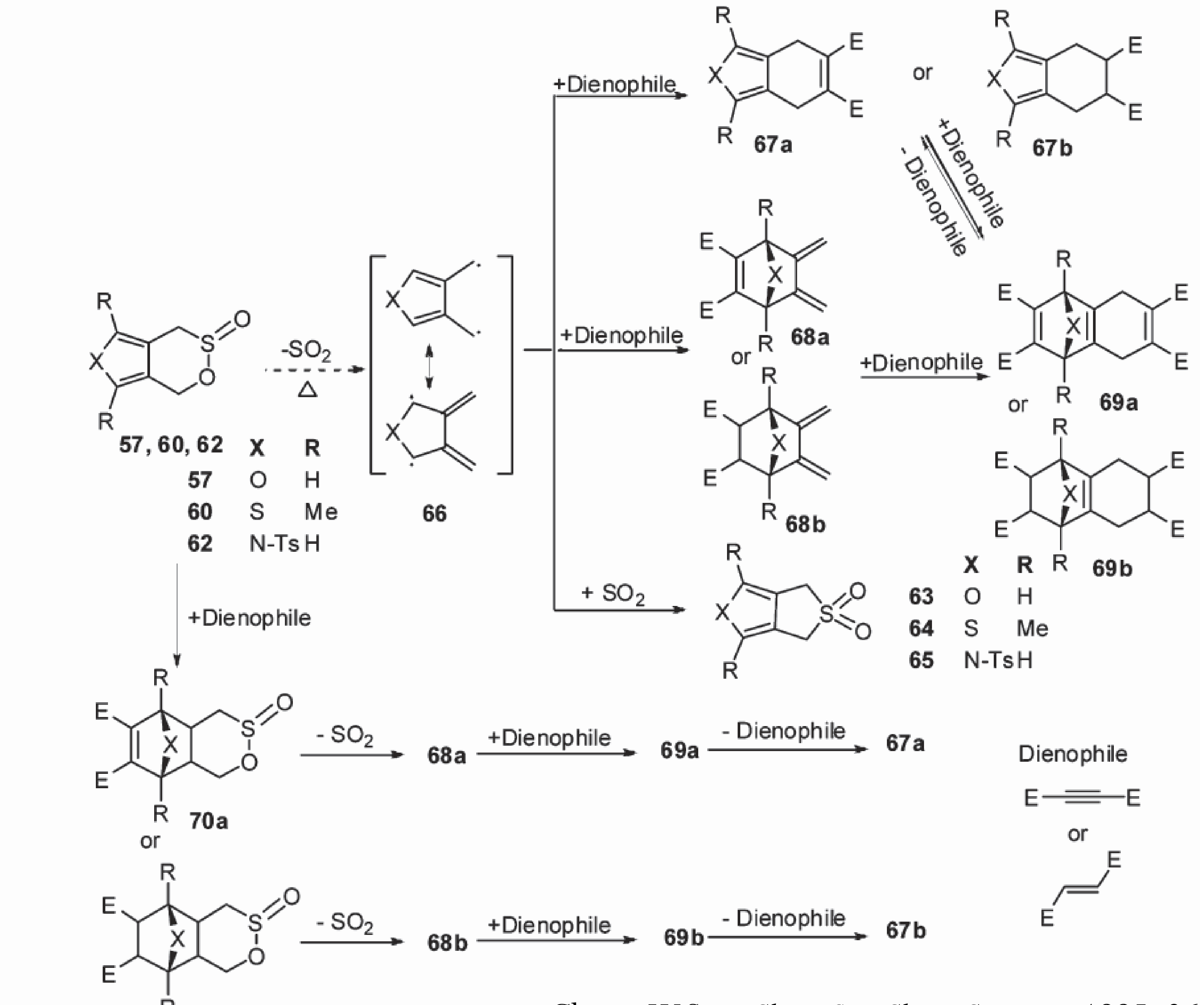
Ratio 21:C_{60}	Yield (%)[a]		Yield (%)[b]	
5:1	10	12[c]	10	10[c]
2:1	39	44[c]	22	31[c]
2:1	30	44[c]	24	40[c]
1:1.1	23	28[c]	30	47[c]

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

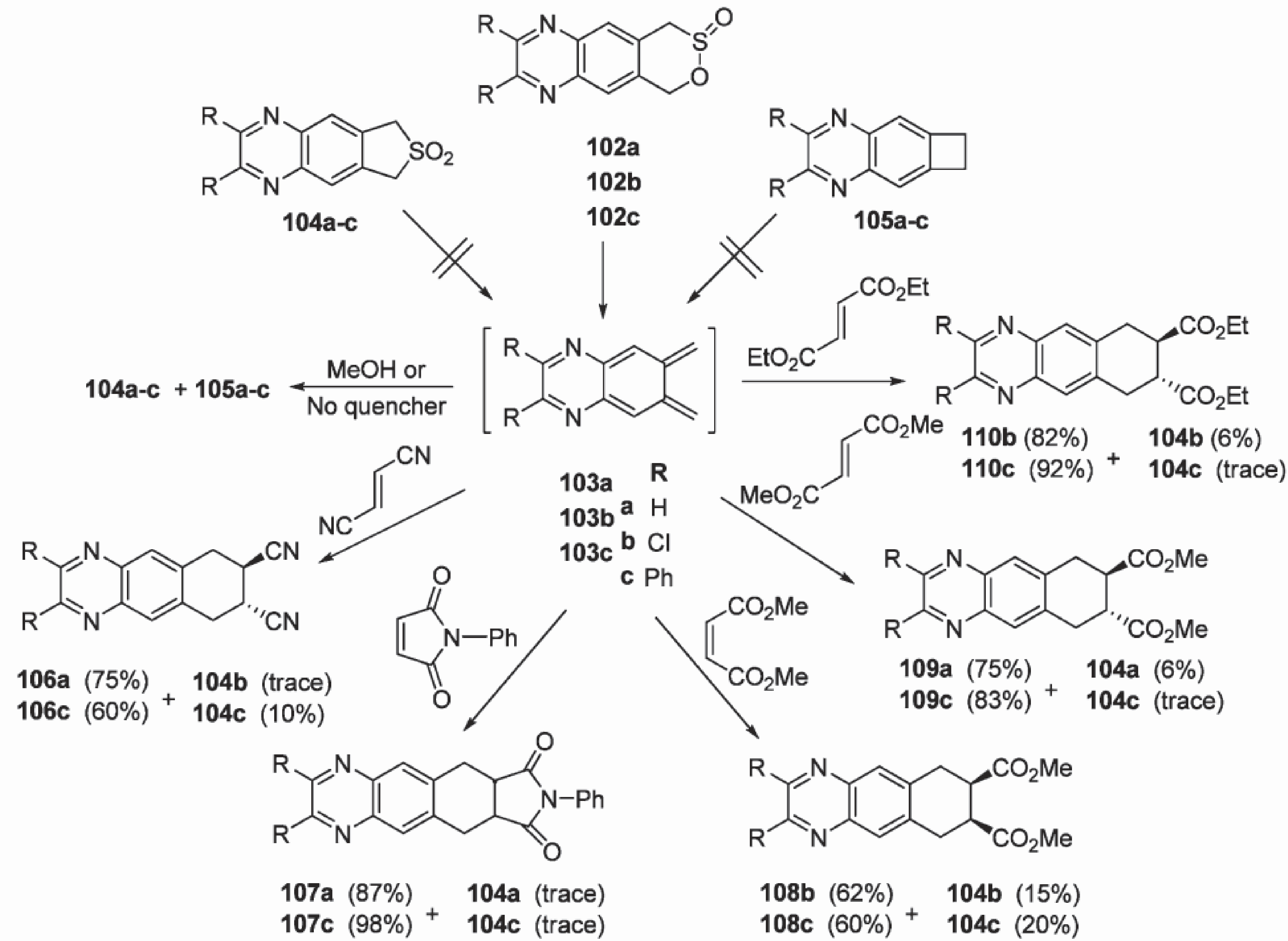
Wudl, F.; *Tet. Lett.* 1995, 36, 8307.



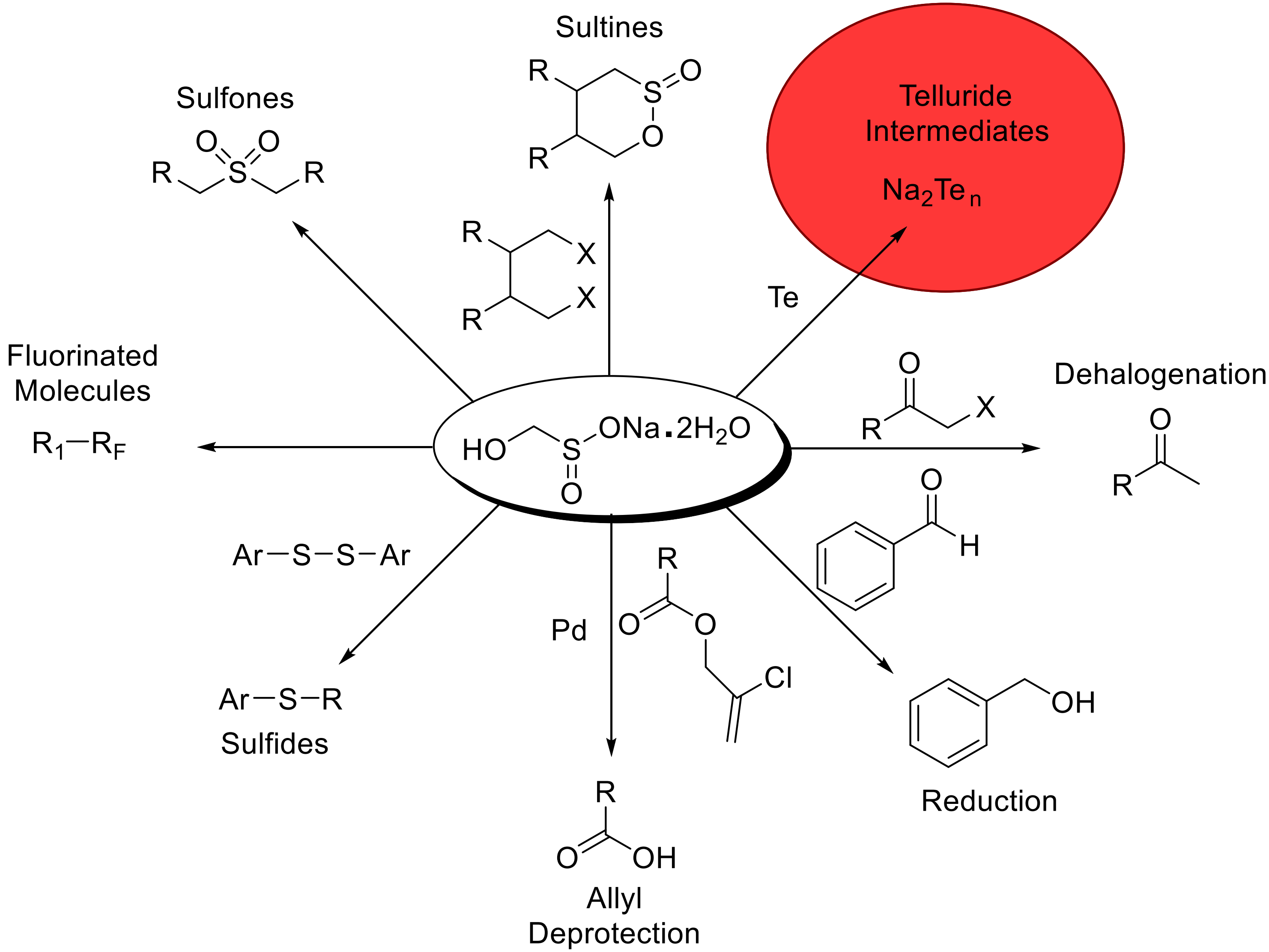
Chung, W.S.; *J. Chem. Soc. Chem. Commun.* 1995, 36, 8307.



Chung, W.S.; *J. Chem. Soc. Chem. Commun.* 1995, 36, 8307.

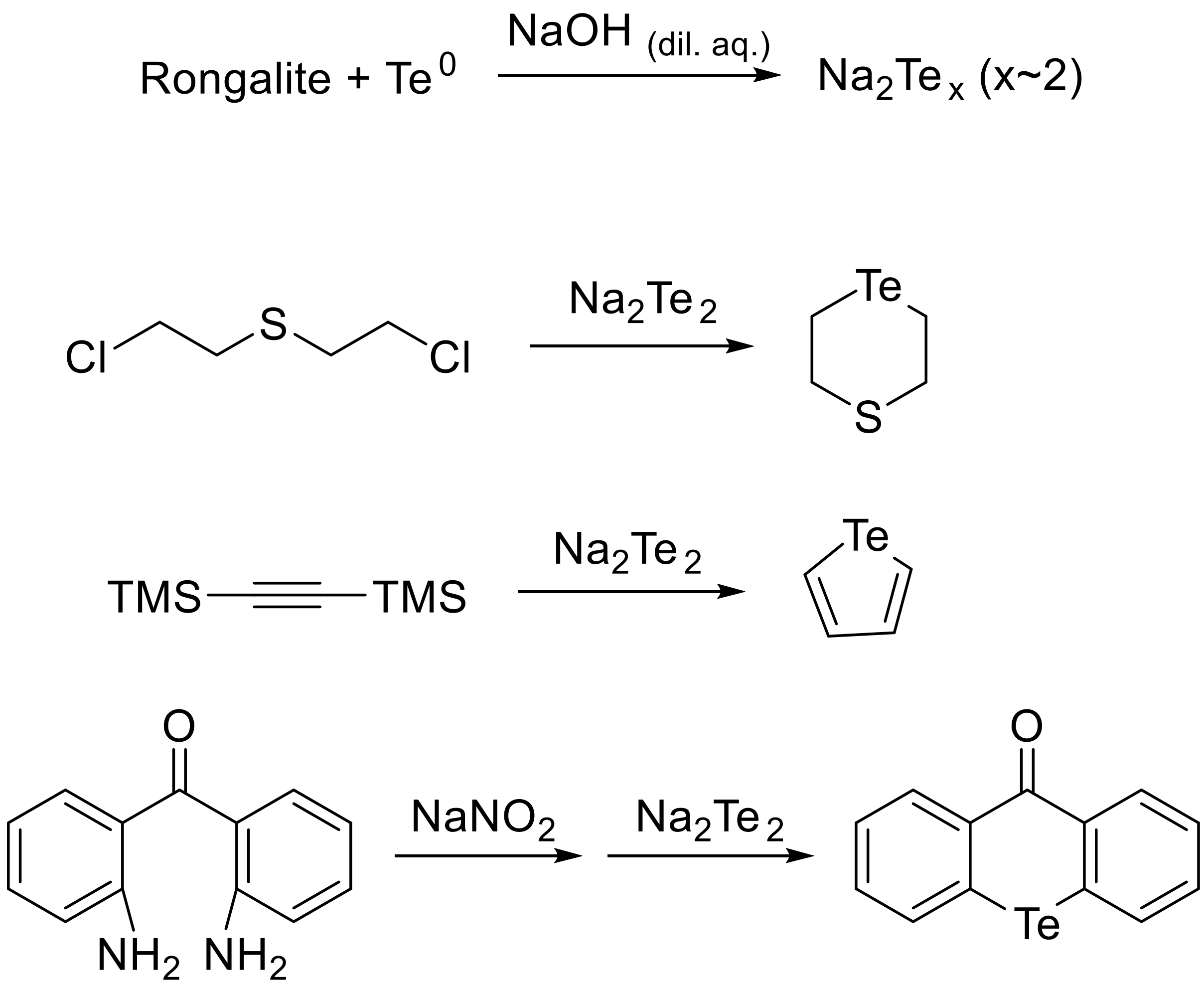


Chung, W.S.; *J. Org. Chem.* 2000, 65, 3395.



Sultines
Sulfones
Telluride Intermediates
Na2Te n
Te
Fluorinated Molecules
R1—RF
HO ONa.2H2O
Dehalogenation
Ar—S—S—Ar
Pd
Ar—S—R
Sulfides
Reduction
Allyl Deprotection

Telluride Chemistry

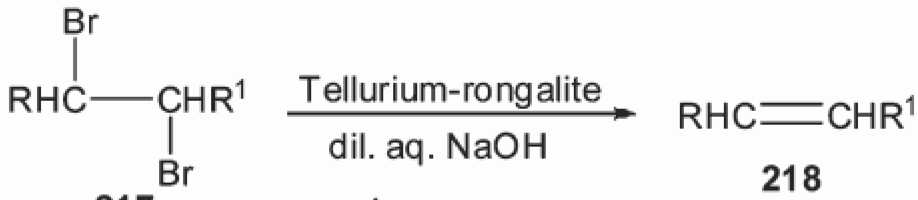


McCullough, J.D.; *Inorg. Chem*. **1965**, 46, 862.

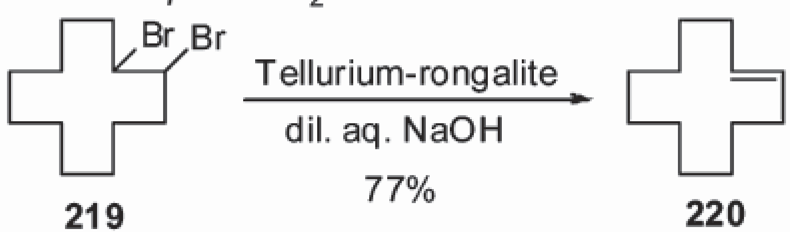
Praefcke, K. *Chem. Ber.* **1978**, 11, 3745.

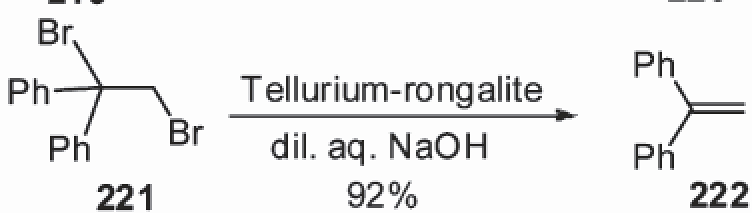
Praefcke, K. *Chem.-Ztg.* **1979**, 103, 265.

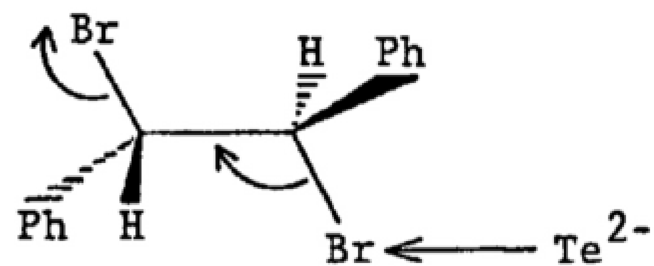
Telluride Debromination



R and R[1]	Yield (%)
Ph *meso* isomer	98 (only E isomer)
Ph *d, l* mixture	90 (E/Z=16/74)
H	82
R=Ph and R[1]	
CO_2H	90
CO_2Et	80
p-Ph-NO_2	89



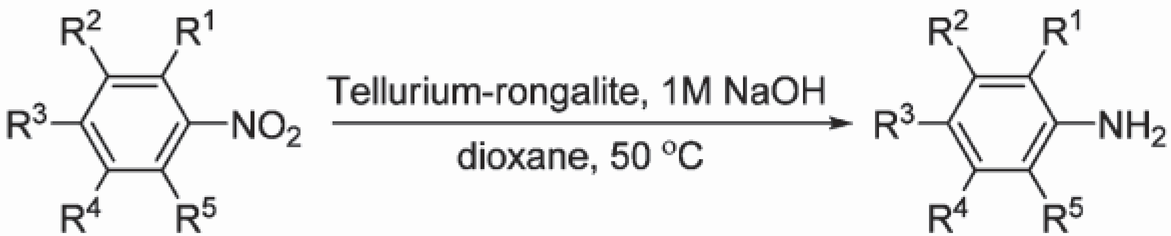




Inouye, M.; *Chem. Lett*. **1985**, 225.

Young, D.W. In *Protective Groups in Organic Chemistry;* Plenum Press: London, 1973.

Reduction of Nitro Aromatics



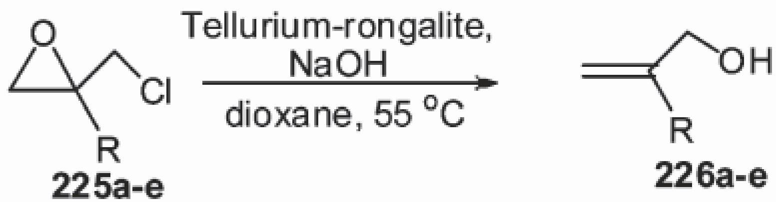
223 → **224**

	R^1	R^2	R^3	R^4	R^5	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	$C_6H_5CH=CH$ *Trans*-isomer	H	H	78	**224g**
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**

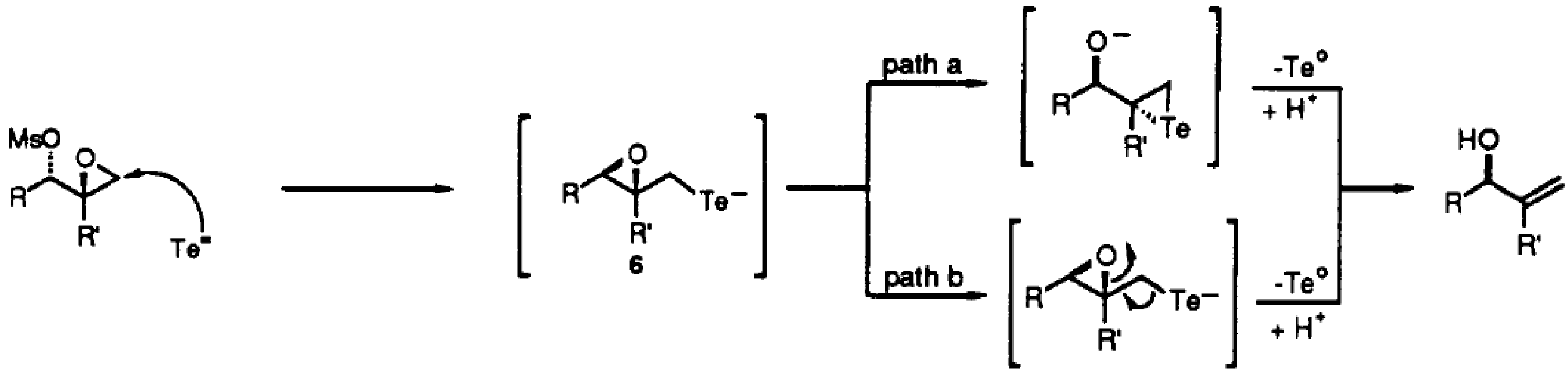
- Catalytic Te
- No bimolecular reduction products
- Mono reduction possible by using less rongalite

Inouye, M. *Chem. Lett.* 1985, 1671.

Synthesis of Allylic Alcohols

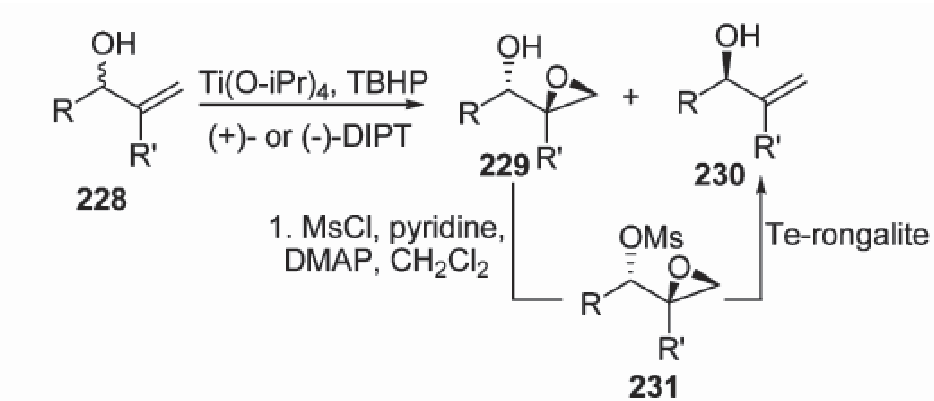


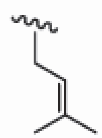
	R		R	Yield (%)
225a	Ph	**226a**	Ph	90
225b	Et	**226b**	Et	40
225c	*p*-OCH_3-C_6H_5	**226c**	*p*-OCH_3-C_6H_5	88
225d	—C≡C—Ph	**226d**	—C≡C—Ph	90
225e	—CH_2—CH=CH_2	**226e**	—CH_2—CH=CH_2	43

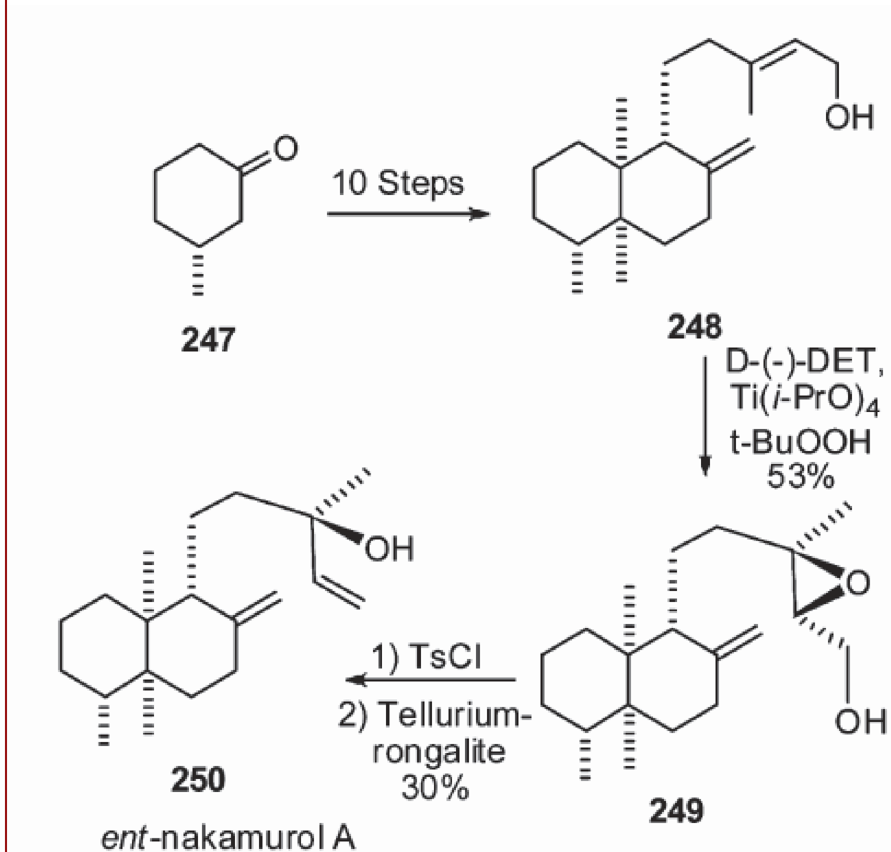


Dittmer, D.C. *Tet. Lett*. 1986, 27, 5579.

Synthesis of Allylic Alcohols

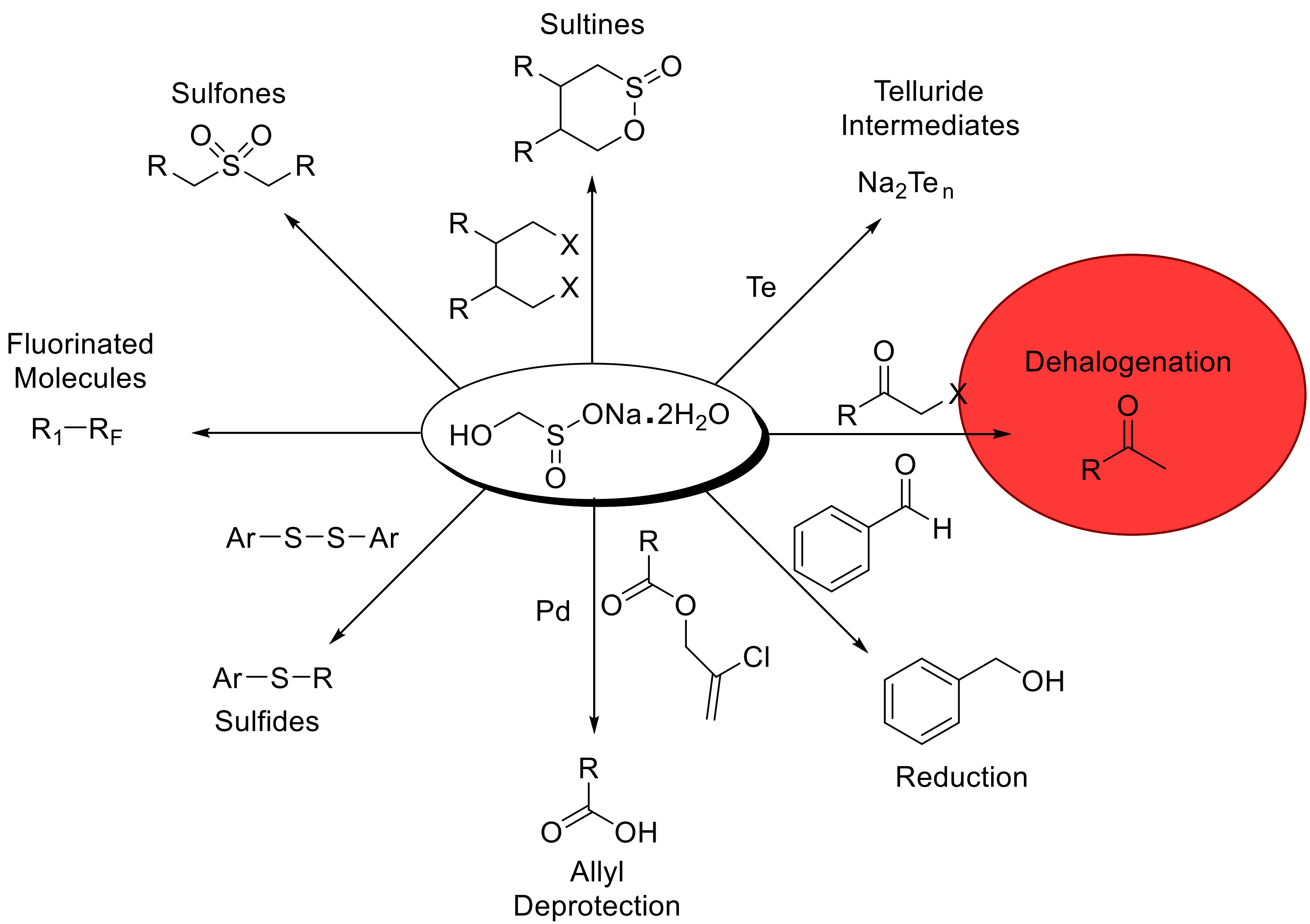


R' = H	R	%ee	Yield (%)
		92	79
	C_4H_9	94	88
	CH_2CH_2Ph	92	75

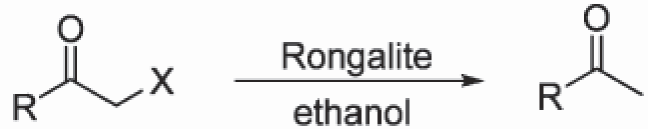


Dittmer, D.C. *J. Org. Chem.* 1990, 55, 1414.

Bonjoch, J. *J. Org. Chem.* 2003, 68, 7400.


Sultines
Sulfones
Telluride Intermediates
Na_2Te_n
Te
Dehalogenation
Fluorinated Molecules
$R_1—R_F$
HO S ONa.2H2O
Ar—S—S—Ar
Ar—S—R
Sulfides
Pd
Allyl Deprotection
Reduction

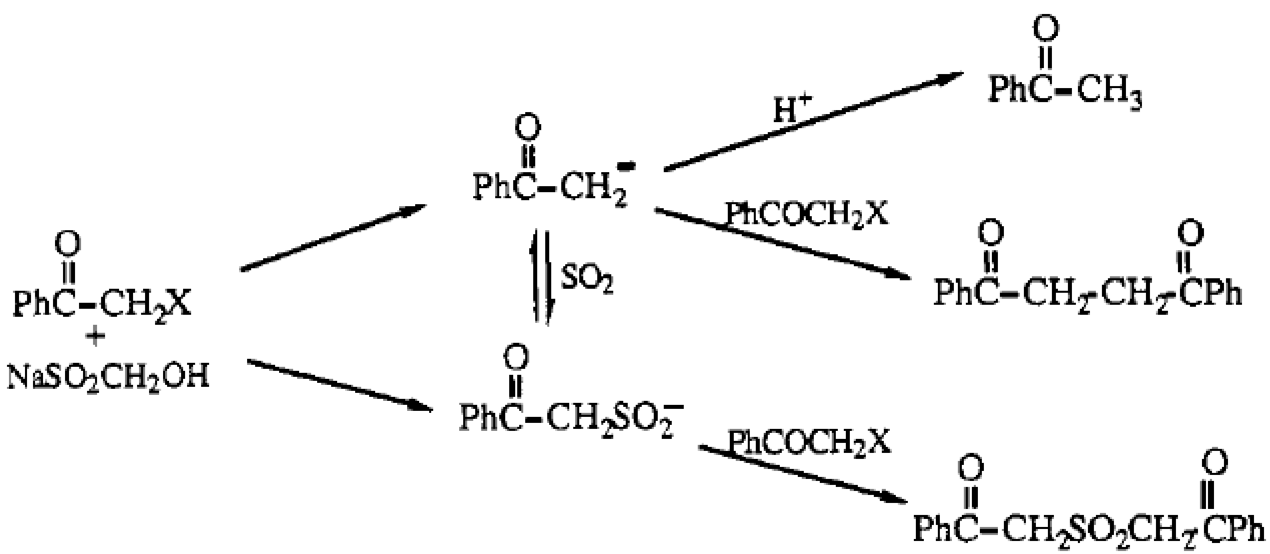
Reductive Dehalogenation



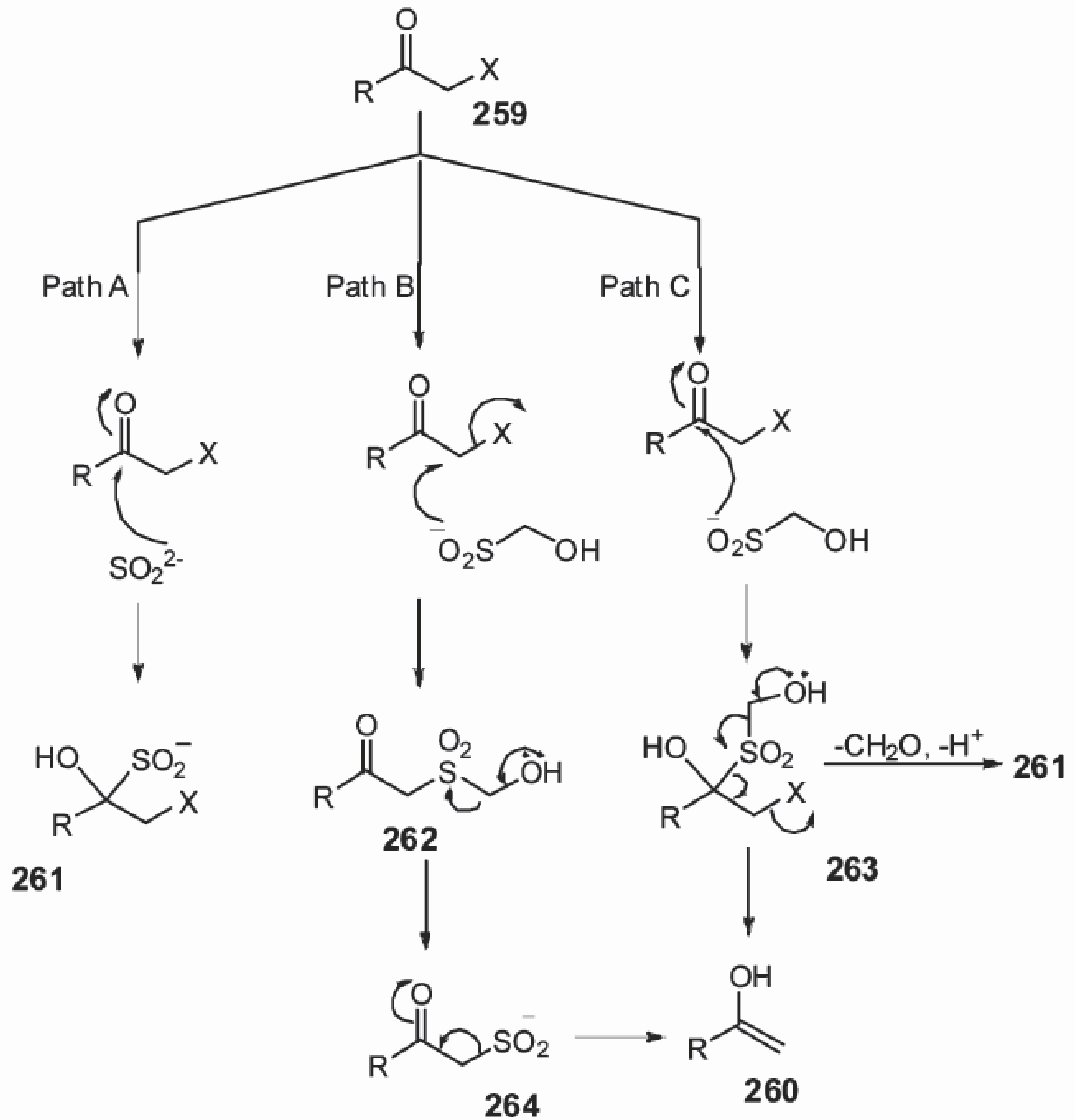
259 → 260

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

Harris, A.R. *Synth. Commun.* 1987, 17, 1587.

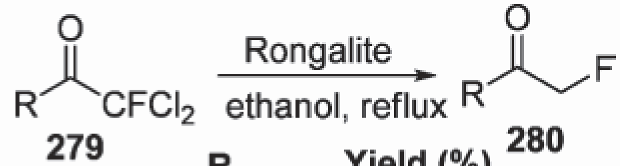


Dittmer, D.C.; *J. Org. Chem.* 1988, 53, 5750.



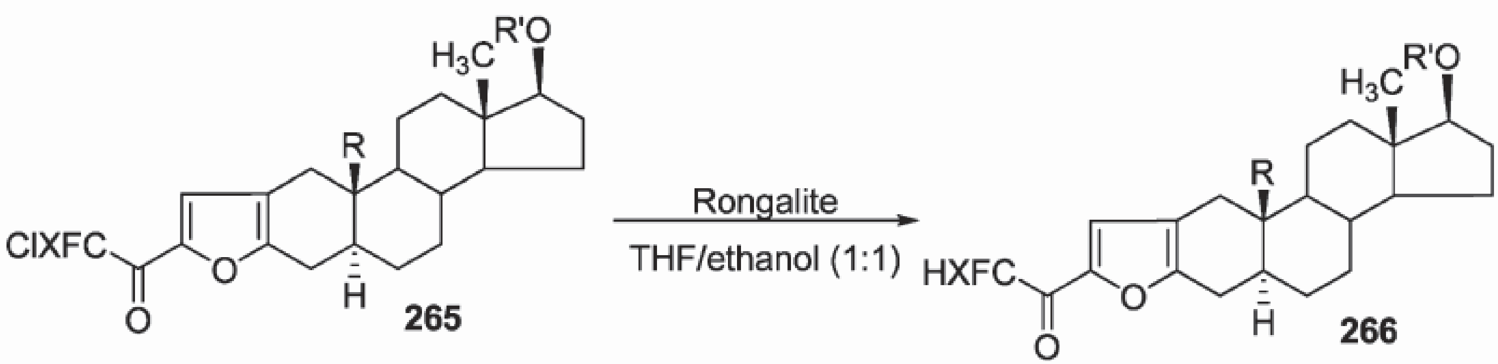
Harris, A.R. *Synth. Commun.* 1987, 17, 1587.

Fluorine Derivatives



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

Tsuboi, S. *Tetrahedron*. 2007, 63, 970.



265

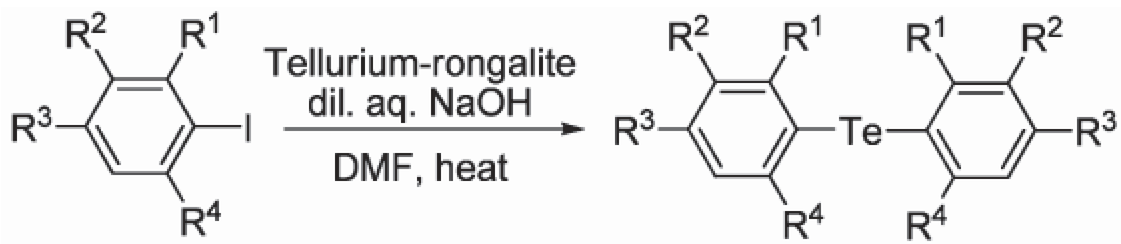
R	R'	X
H	THP	H
H	Ac	F
CH_3	Ac	F

266

R	R'	X	Yield (%)
H	H	H	80
H	Ac	F	83
CH_3	Ac	F	86

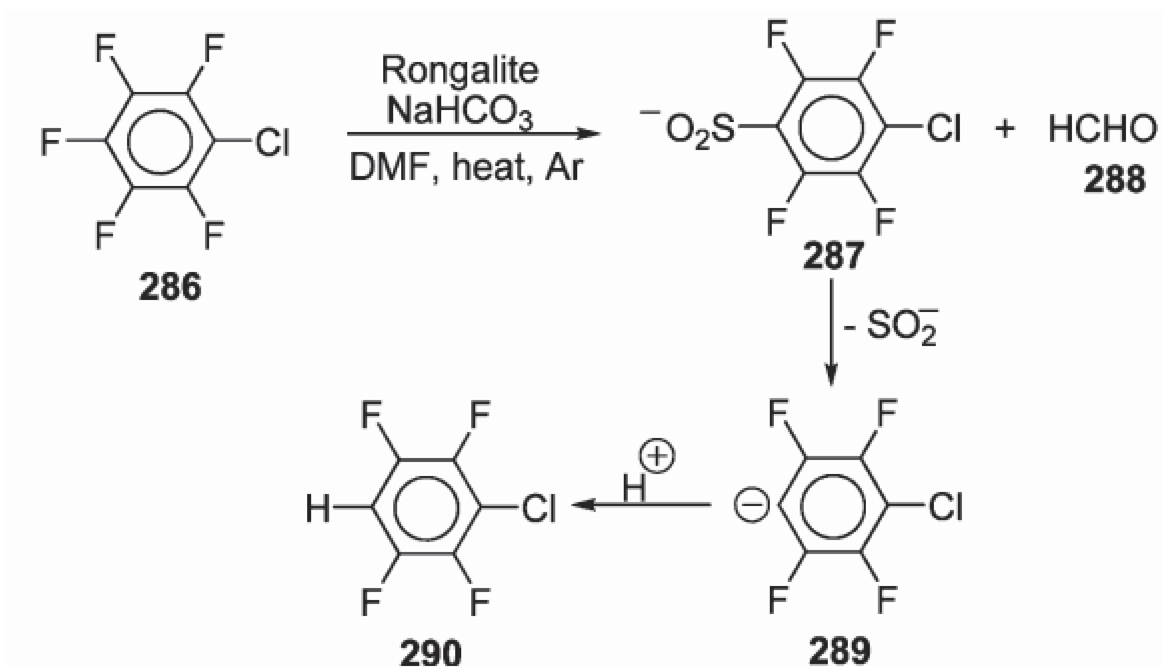
Bell, M.; *Tet. Lett.* 1994, 35, 833.

Aromatic Dehalogenation

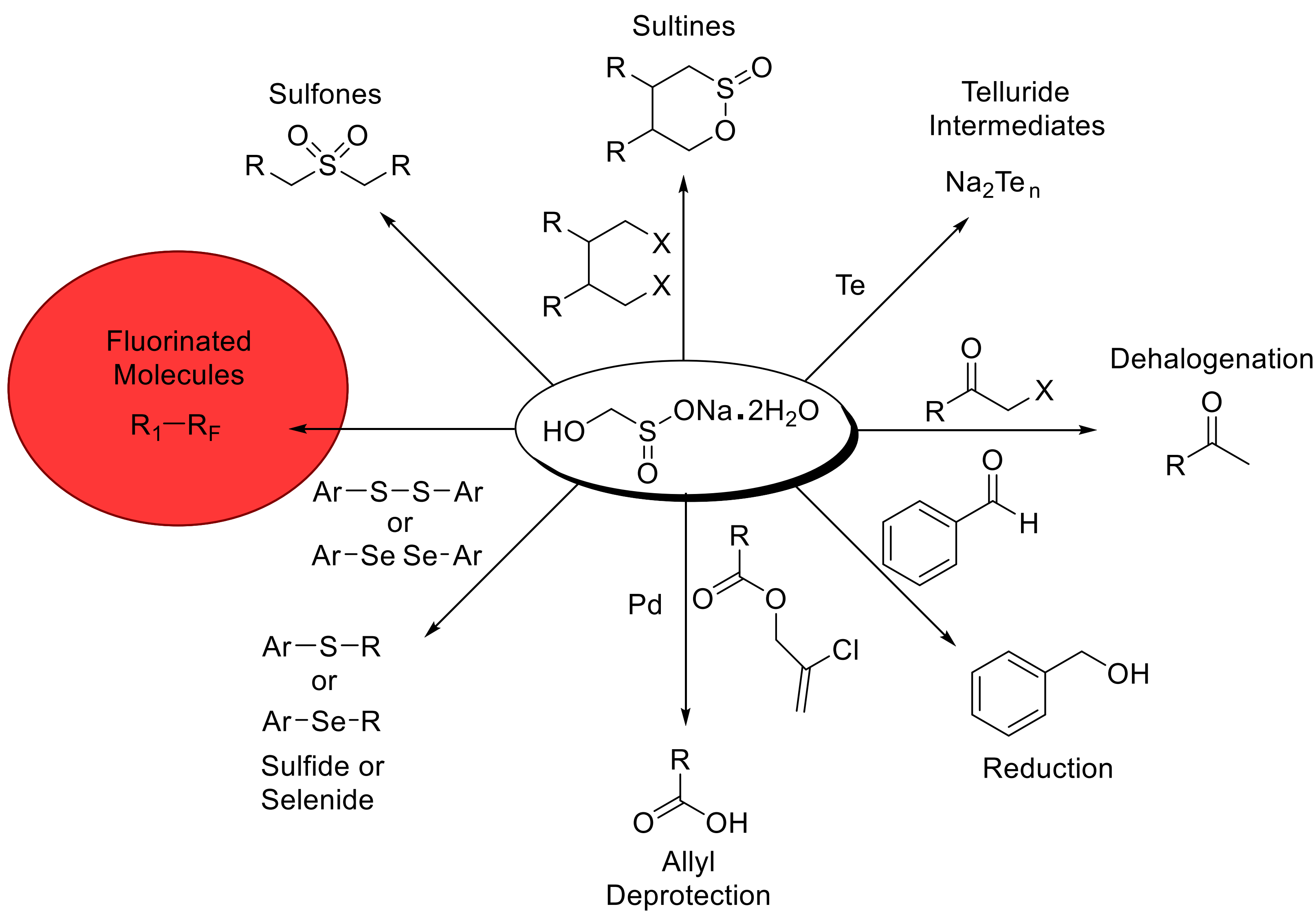


R^1	R^2	R^3	R^4	Yield (%)
H	H	H	H	71
H	CH_3	H	H	84
H	H	CH_3	H	81
CH_3	H	CH_3	H	94
CH_3	H	CH_3	CH_3	77
H	H	CH_3O	H	74

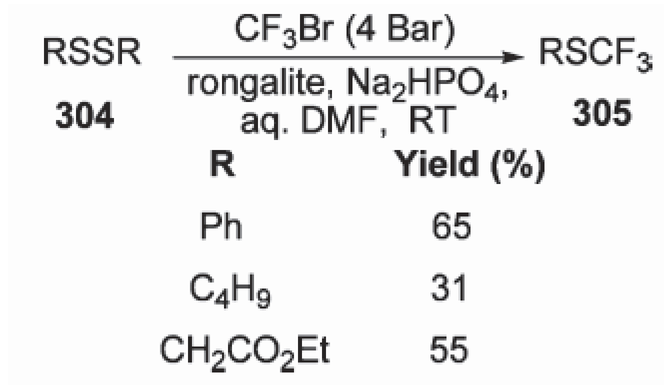
Inouye, M.; *Chem. Lett.* 1985, 389.

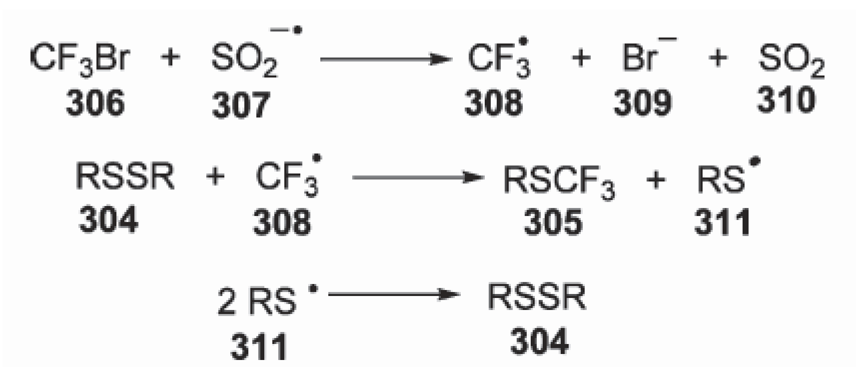


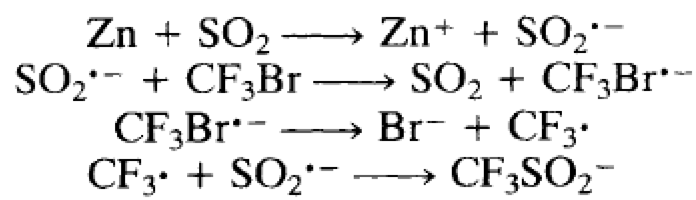
Huang, W.Y.; *Fluorine Chem.* 1996, 80, 91.


Sultines
Sulfones
Telluride Intermediates
Na_2Te_n
Te
Dehalogenation
Fluorinated Molecules
R_1-R_F
HO S ONa.2H2O
Ar-S-S-Ar
or
Ar-Se Se-Ar
Ar-S-R
or
Ar-Se-R
Sulfide or Selenide
Pd
Allyl Deprotection
Reduction

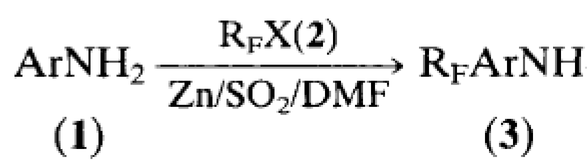
Fluorinated Thioethers





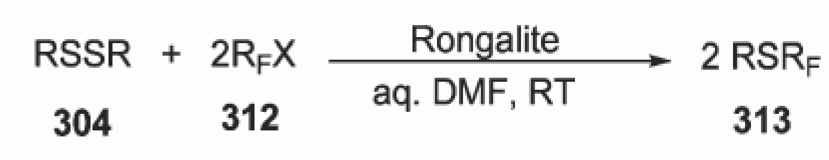


Scheme 1



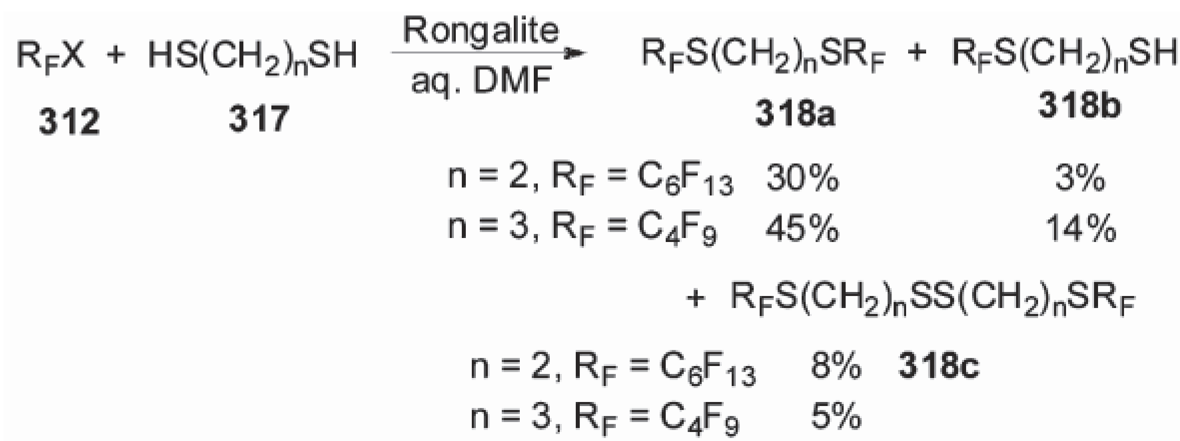
Langlois, B.J.; *J. Chem. Soc., Chem. Commun.* 1991, 993.

Fluorinated Thioethers



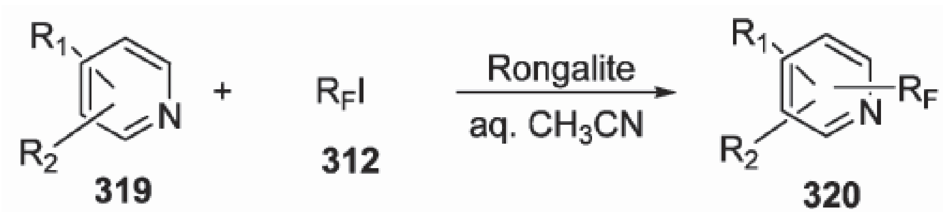
R	R_FX	Yield (%)
$PhCH_2$	C_4F_9I	17
CH_3	$C_8F_{17}I$	20
C_4H_9	$C_6F_{13}I$	22
C_6H_5	$C_6F_{13}I$	40
C_6H_5	CF_2BrCl	72
CH_2CO_2Et	CF_2BrCl	65

Wacselman, C.; *J. Chem. Soc., Perkin Trans. 1* 1992, 3371.



Wacselman, C.; *J. Fluorine Chem.* 2000, 105, 41.

Fluorinated Heterocyles

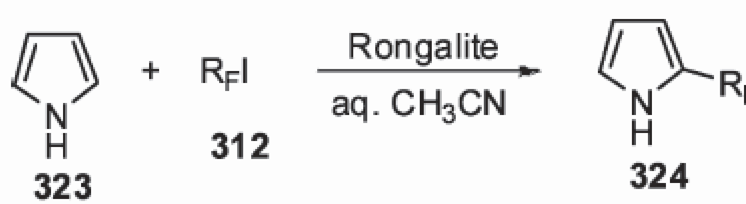


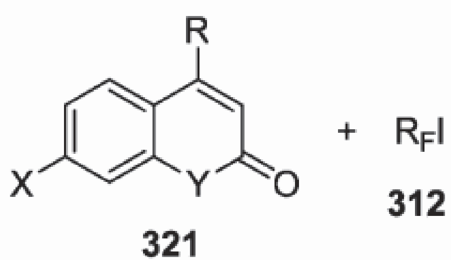
$R_1 = R_2 = H$
$R_1 = 4\text{–}CH_3, R_2 = H$
$R_1 = 3\text{–}CH_3, R_2 = H$
$R_1 = 3\text{–}CH_3, R_2 = 5\text{–}CH_3$
$R_1 = 4\text{–}NH_2, R_2 = H$
Quinoline
Isoquinoline

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

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

Huang, B. *Tet. Lett.* 1990, 31, 2711.





R_F	$Cl(CF_2)_4$	$Cl(CF_2)_6$	$Cl(CF_2)_8$
Yield (%)	68	65	60

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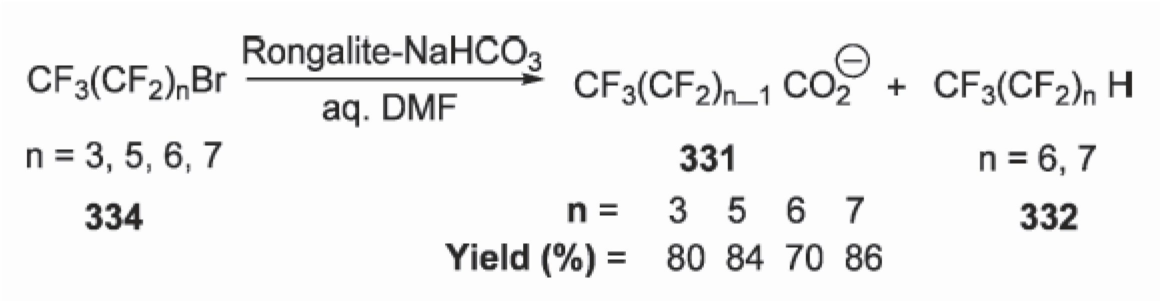
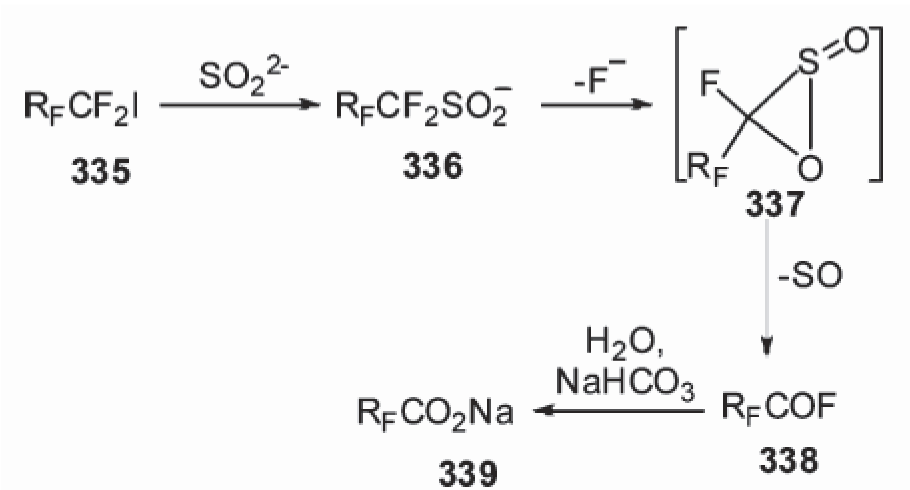
Y	R	X	R_F	Yield (%)
O	H	H	$F(CF_2)_6$	63
O	H	H	$F(CF_2)_7$	70
O	H	H	$F(CF_2)_8$	78
O	H	H	$Cl(CF_2)_4$	63
O	H	H	$Cl(CF_2)_6$	67
O	H	H	$Cl(CF_2)_8$	72
O	Me	OH	$Cl(CF_2)_6$	59
O	Me	$N(Et)_2$	$Cl(CF_2)_6$	57
O	Me	$N(Et)_2$	$Cl(CF_2)_6$	42
S	H	H	$F(CF_2)_6$	53
S	H	H	$Cl(CF_2)_4$	58
S	H	H	$Cl(CF_2)_6$	60

Huang, B. *J. Fluorine Chem.* 1993, 64, 37.; *J. Chem. Soc. Perkin Trans.* 1 1994, 101.

Perfluorocarboxylic Acids

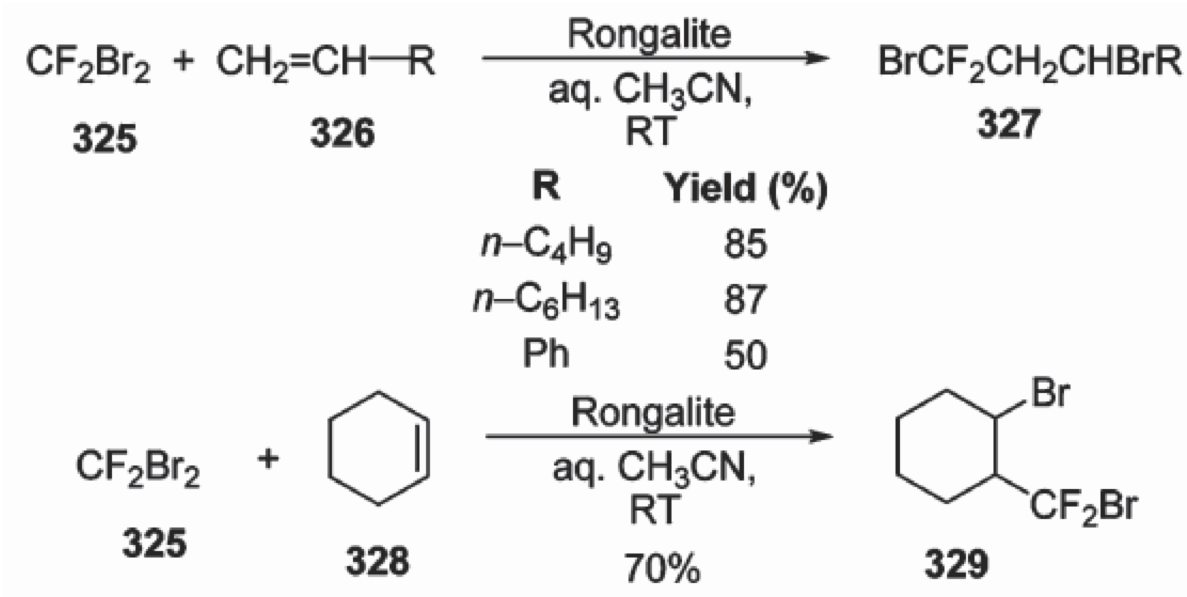


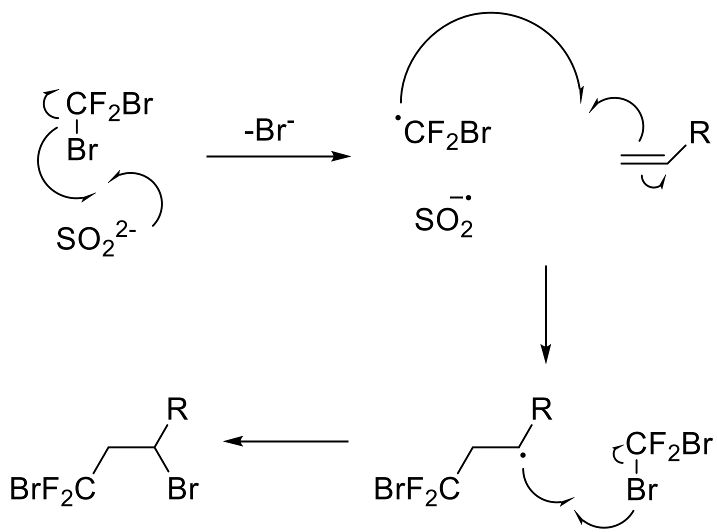
Huang, B.; *J. Fluorine Chem.* 1987, 36, 49.



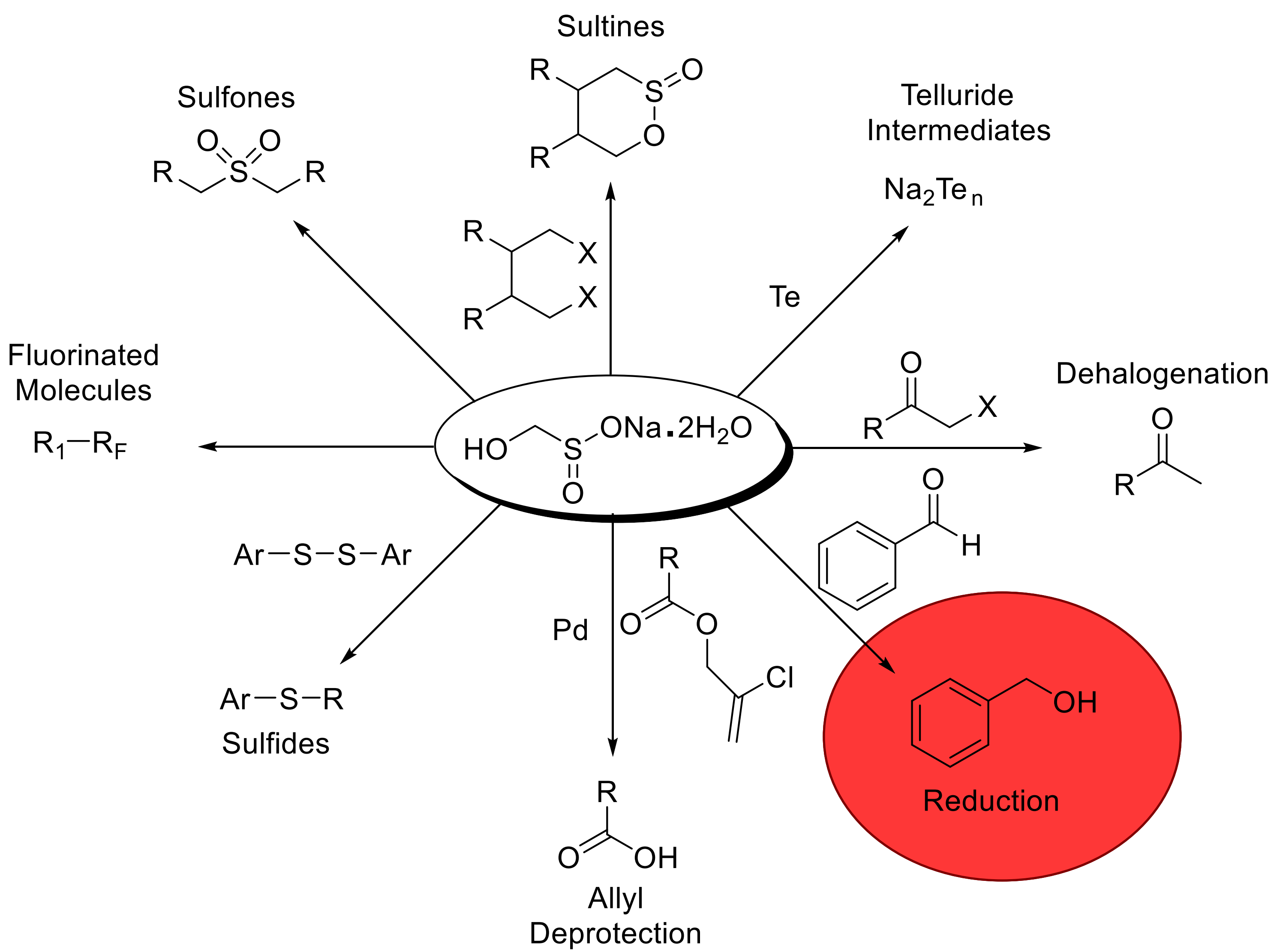
Dittmer, D.C.; *J. Fluorine Chem.* 1990, 50, 151.

Addition of Dibromodifluoromethane



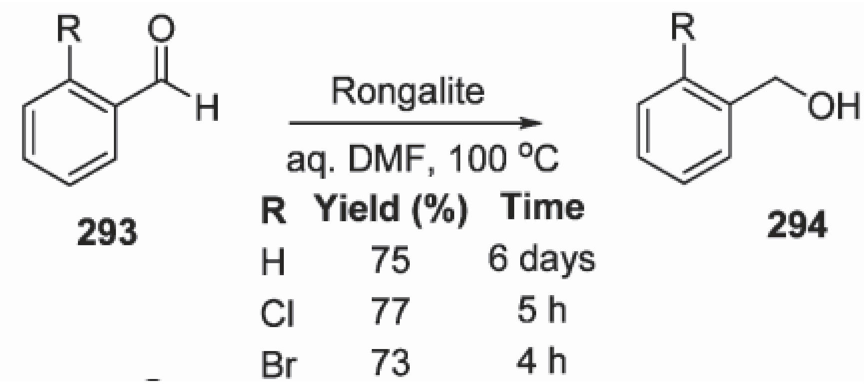


Huang, B.; *J. Fluorine Chem.* 1996, 80, 91.

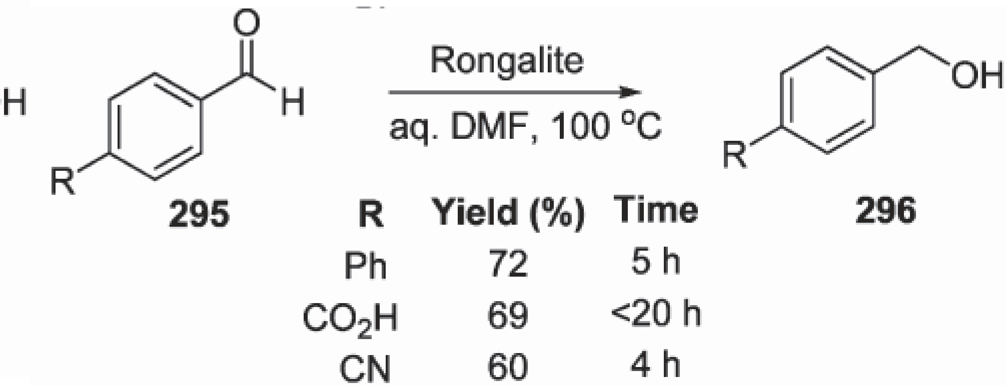


Sultines
Sulfones
Telluride Intermediates
Na_2Te_n
Te
Fluorinated Molecules
$R_1—R_F$
HO
ONa.2H2O
Dehalogenation
Ar—S—S—Ar
Pd
Ar—S—R
Sulfides
Allyl Deprotection
Reduction

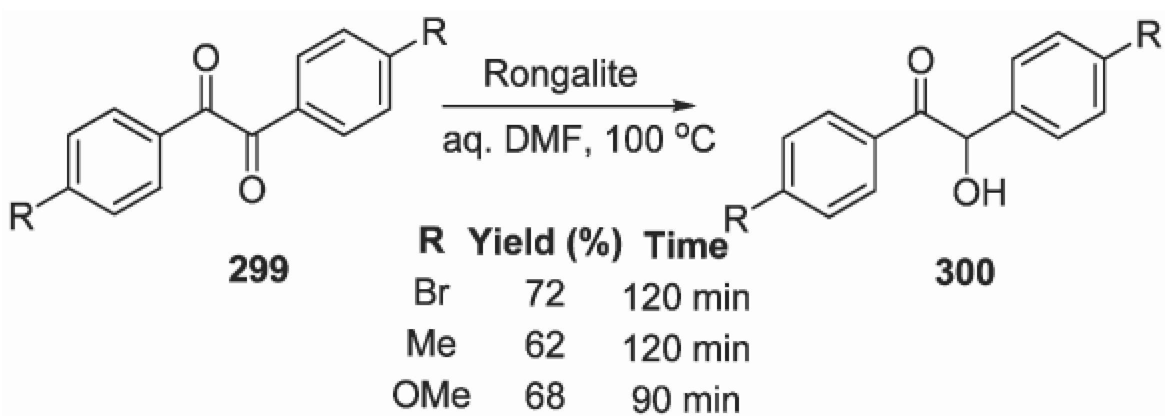
Reduction of Aldehydes and Benzils



R	Yield (%)	Time
H	75	6 days
Cl	77	5 h
Br	73	4 h



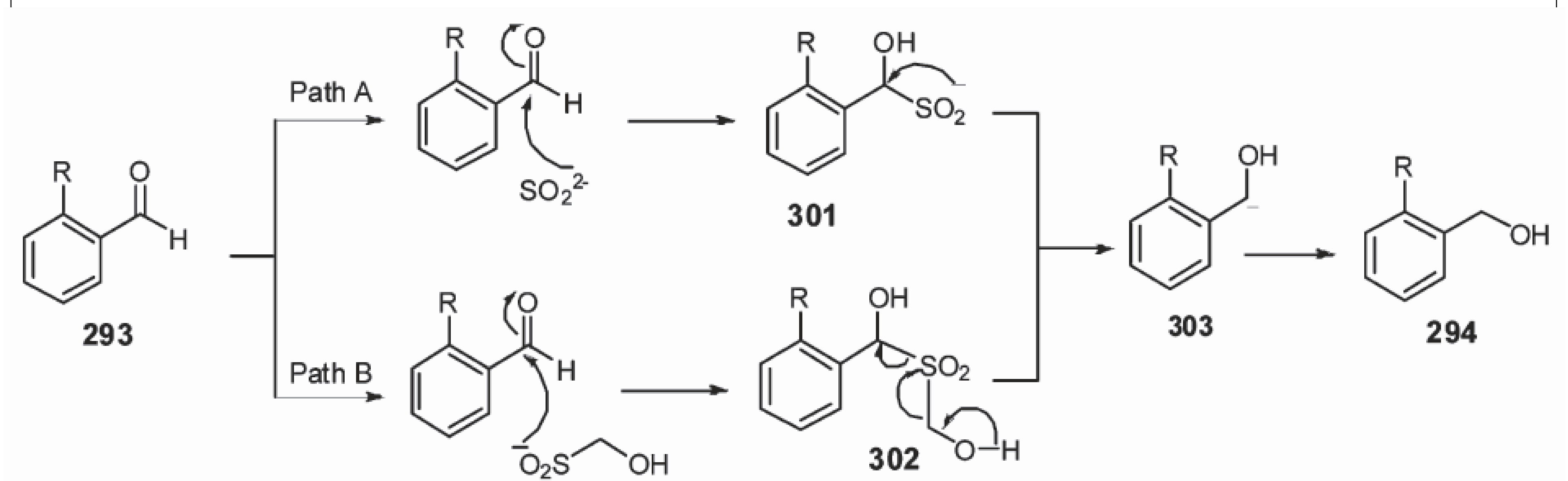
R	Yield (%)	Time
Ph	72	5 h
CO_2H	69	<20 h
CN	60	4 h



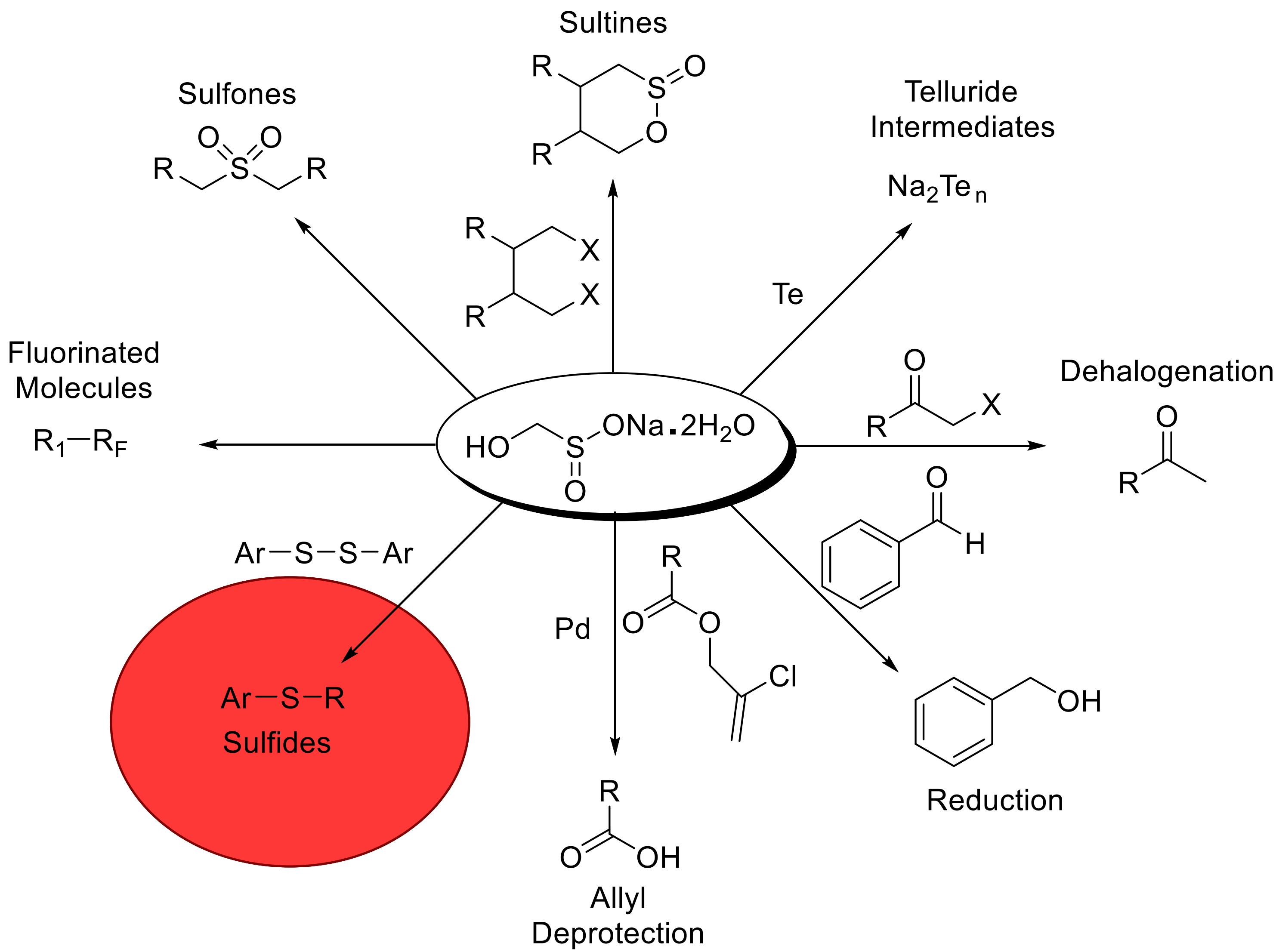
R	Yield (%)	Time
Br	72	120 min
Me	62	120 min
OMe	68	90 min

Mason, T. J.; *Synth. Commun.* 1989, 19, 529.

Reduction of Aldehydes and Benzils



Mason, T.J.; *Synth. Commun.* 1989, 19, 529.



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Sulfones
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Na_2Te_n
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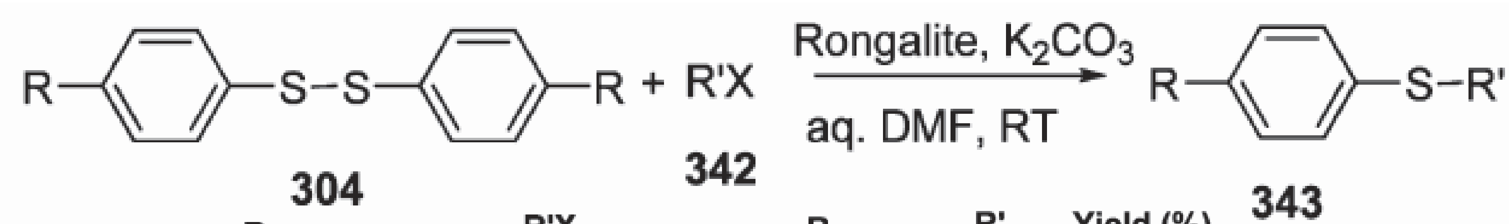
Fluorinated Molecules
R_1—R_F
HO S ONa.2H2O
Dehalogenation
Ar—S—S—Ar
Ar—S—R
Sulfides
Pd
Cl
Reduction
OH
Allyl Deprotection

Sulfide Synthesis



R	R'X	R	R'	Yield (%)
NO_2	MeI	NO_2	Me	97
	EtBr		Et	94
	EtCl		Et	13
	n-PrBr		*n*-Pr	93
Cl	*n*-BuCl	Cl	*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

$$HOCH_2SO_2^- \longrightarrow HCHO + HSO_2^-$$

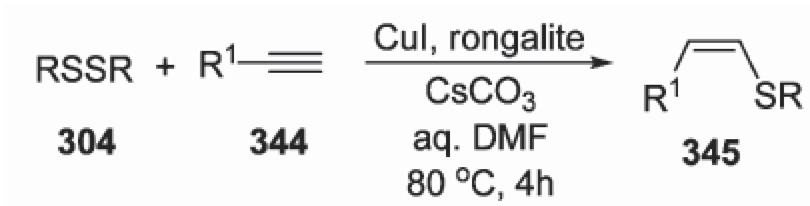
$$ArSSAr + HSO_2^- \rightleftharpoons ArS^\cdot + ArS^- + HSO_2^\cdot$$

$$ArS^\cdot + HSO_2^\cdot \longrightarrow ArS^- + SO_2 + H^+$$

$$ArS^- + RX \longrightarrow ArSR + X^-$$

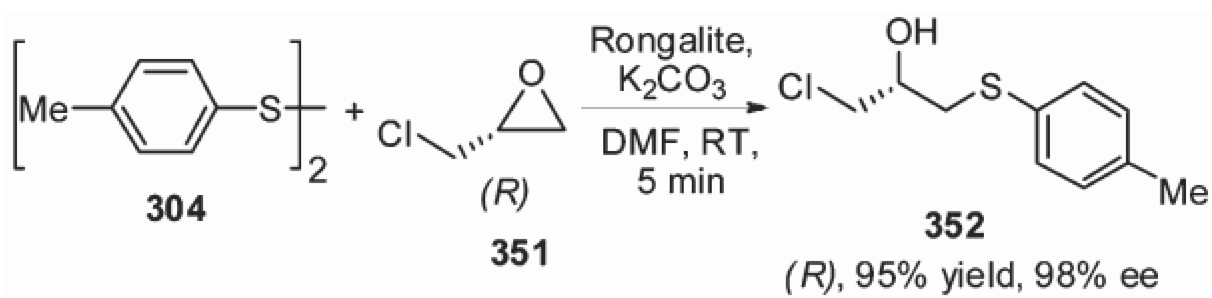
Lin, Q.-L.; *Synthesis* 2007, 85.

Sulfide Synthesis



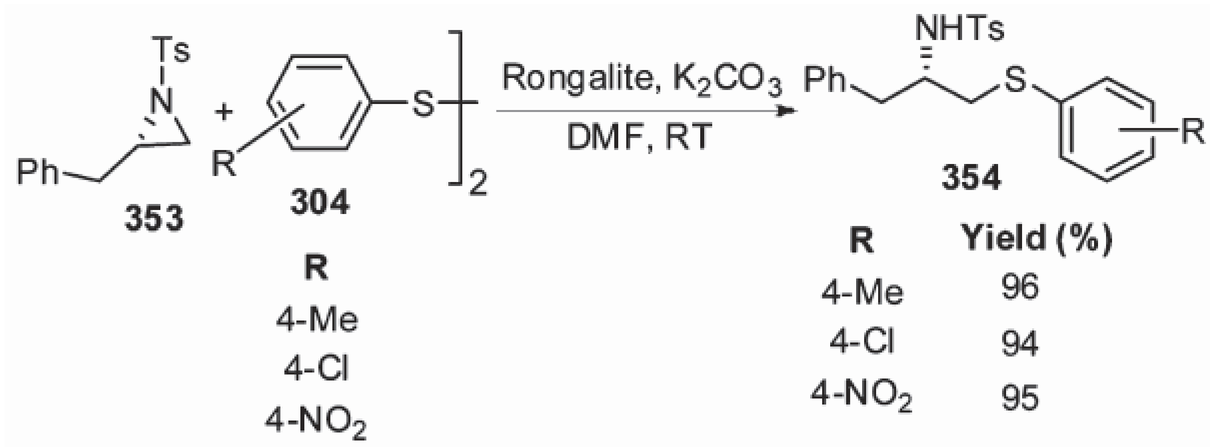
R	R^1	Yield (%)
Ph	*p*-CH_3-C_6H_4	85
Ph	*o*-CH_3-C_6H_4	70
Ph	*p*-OCH_3-C_6H_4	71
Ph	*p*-NO_2-C_6H_4	74
Ph	C_6H_4NHCO	71
Ph	CO_2Et	63
Ph	*n*-C_6H_{13}	<5
p-CH_3-C_6H_4	Ph	100
o-NH_2-C_6H_4	Ph	56
p-F-C_6H_4	Ph	87
p-Cl-C_6H_4	Ph	98

Li, J.-H.; *Tetrahedron* 2008, 64, 10670.

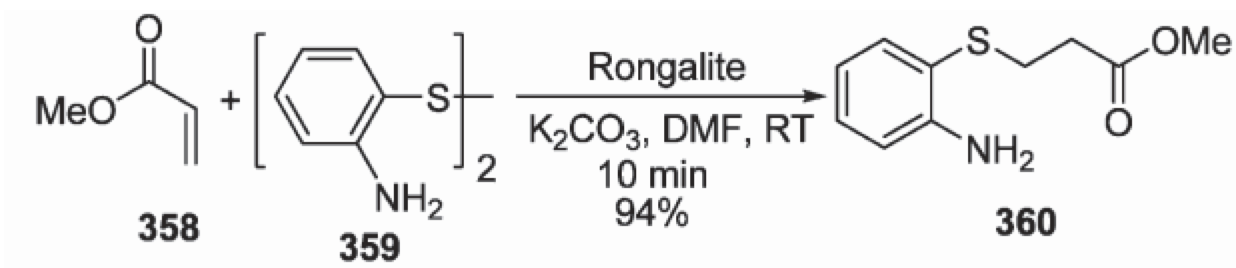


Wu, H.; *Tetrahedron* 2009, 65, 5240.

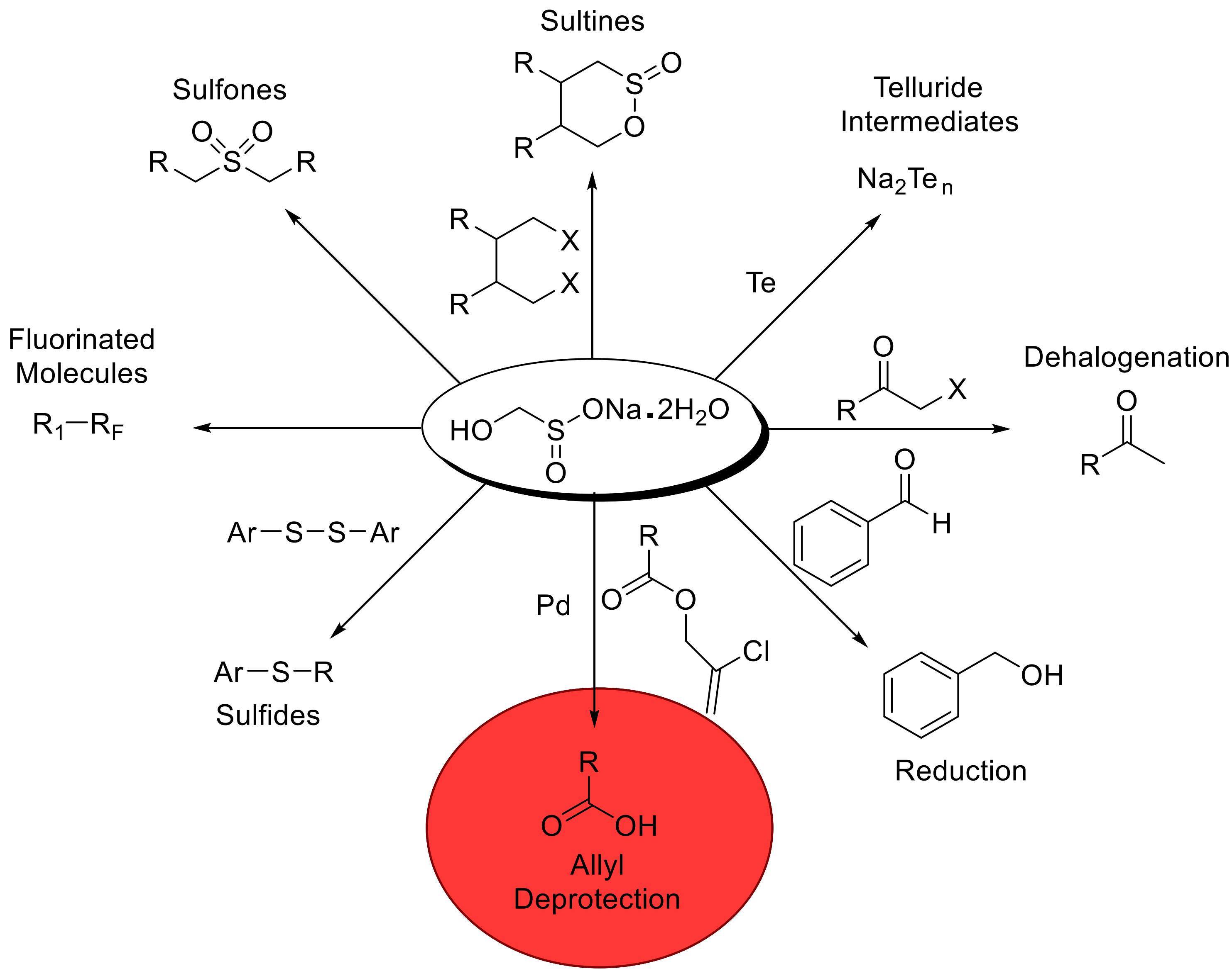
Sulfide Synthesis



Chandrasekaran, S.; *Synthesis* 2009, 3267.



Wu, H.; *Tetrahedron* 2010, 66, 2297.



Sultines
Sulfones
Telluride Intermediates
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R1—RF
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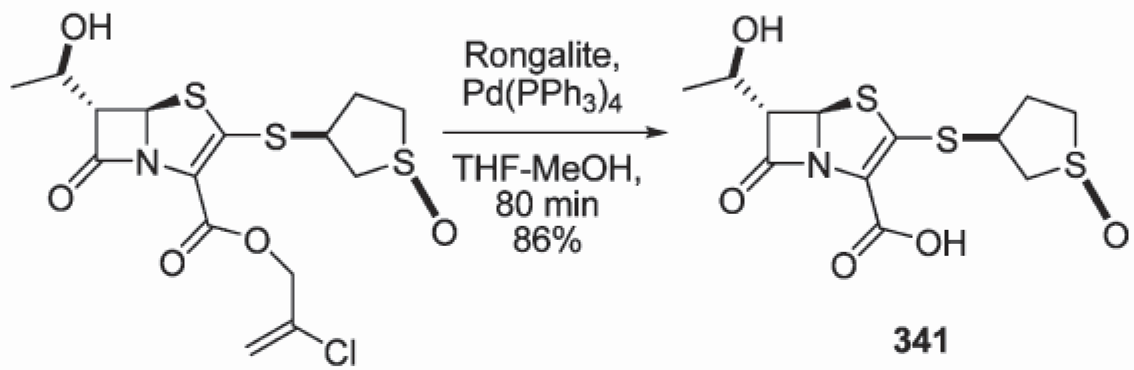
Allyl Deprotection



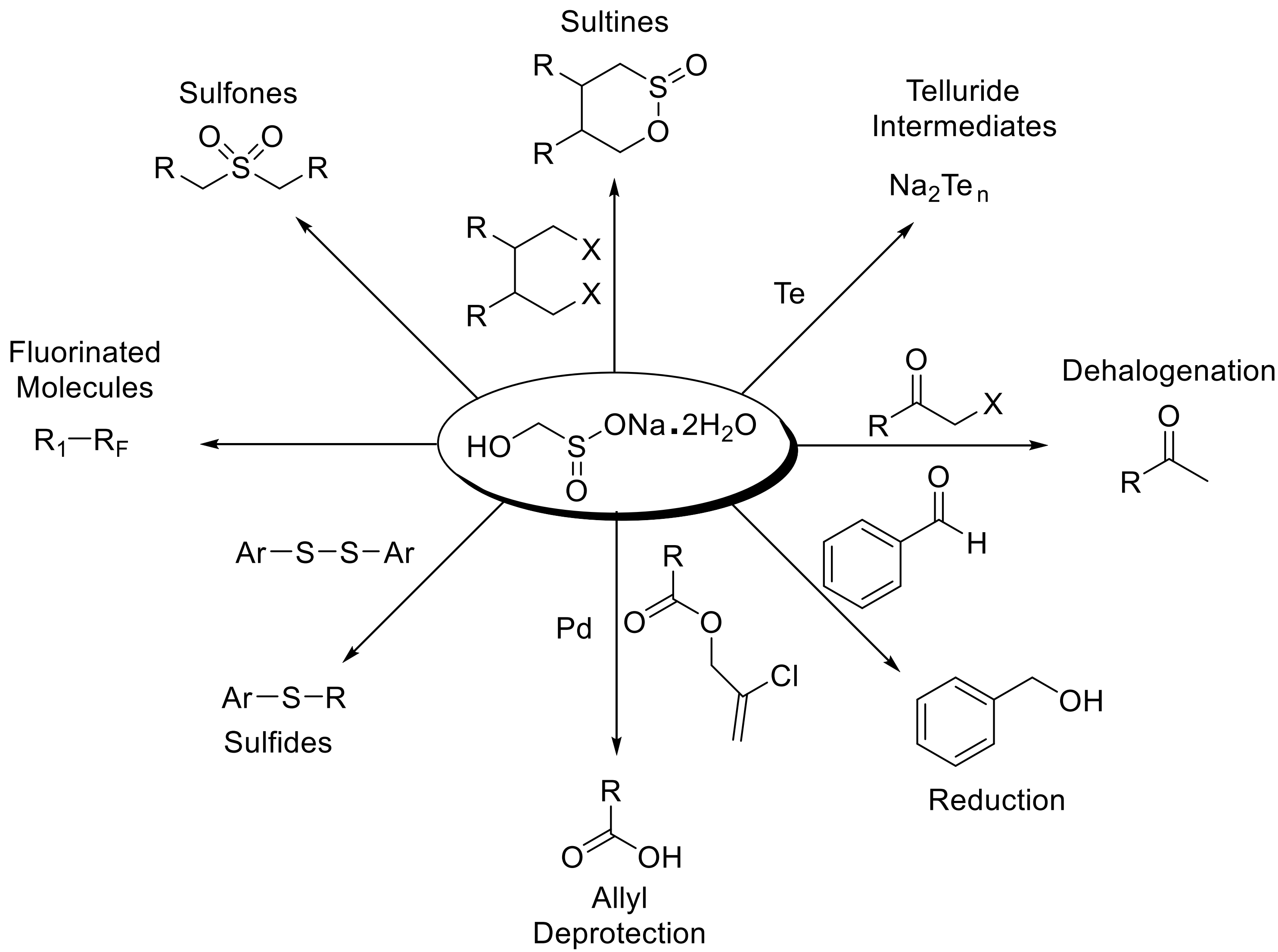
340

341

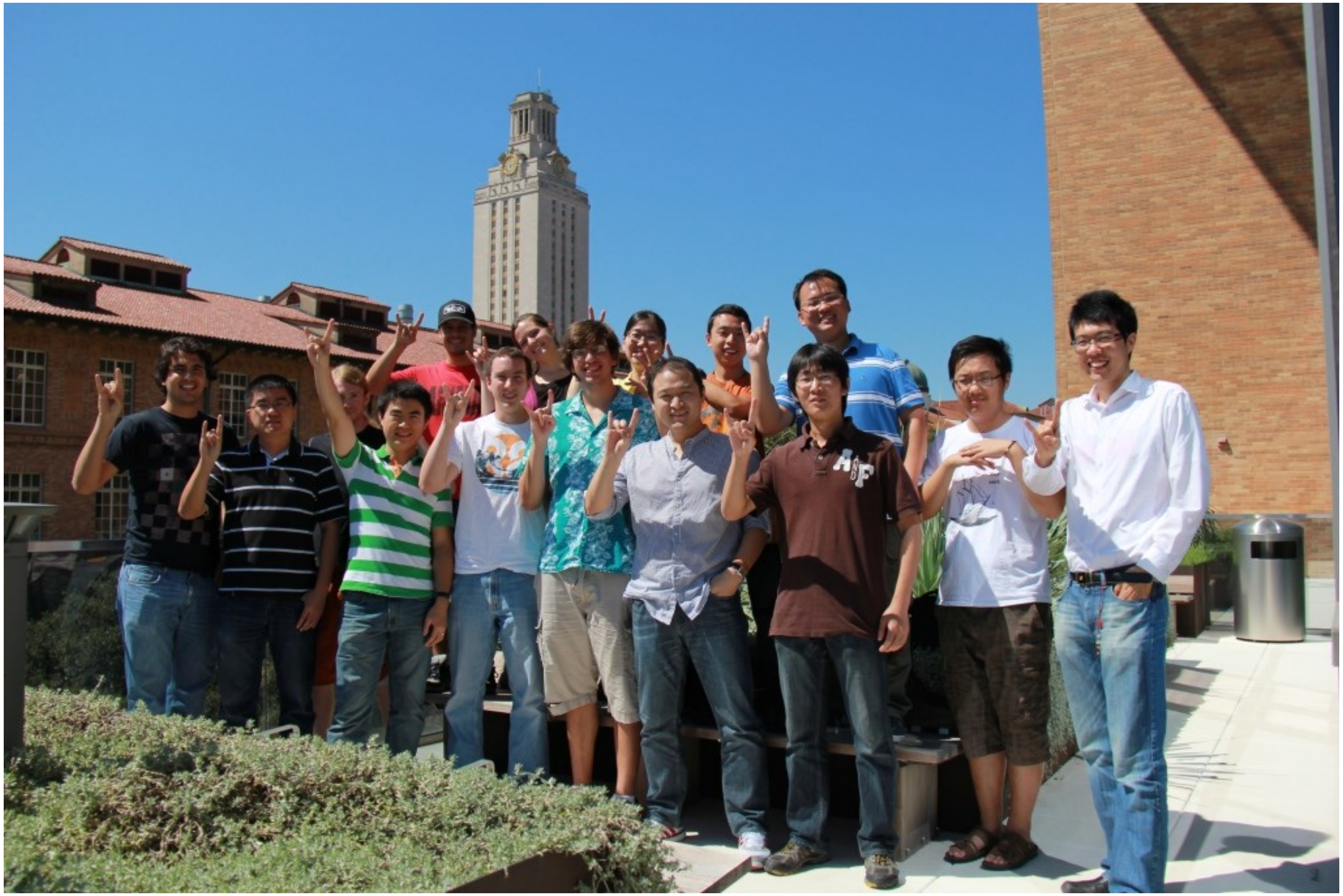
entry	substrate	catalyst: palladium	catalyst: mol %	nucleophile	additive (equiv)	solvent	time (min)	product	yield (%)[b]
2	**1**	Pd(PPh3)$_4$	5.9	TolSO$_2$Na	none	THF/MeOH	105	**6**	97
3	**1**	Pd(PPh$_3$)$_4$	5.4	SEH	PPh$_3$ (0.14)	CH$_2$Cl$_2$	120	**6**	76
4	**2**	Pd(PPh$_3$)$_4$	7.0	TolSO$_2$Na	none	THF/MeOH	130	**6**	94
5	**2**	Pd(PPh$_3$)$_4$	7.7	SEH	PPh$_3$ (0.15)	CH$_2$Cl$_2$	120	**6**	52
6	**1**	Pd(OAc)$_2$	21.2	TolSO$_2$Na	TEP (0.74)	THF/MeOH	80	**6**	80
7	**1**	Pd(OAc)$_2$	20.5	SEH	TEP (0.70)	THF/MeOH	360	**6**	45
8	**1**	Pd(ACN)$_2$Cl$_2$	13.7	TolSO$_2$Na	TEP (0.42)	THF/MeOH	17.5 (h)	**6**	85
9	**1**	Pd(PPh$_3$)$_4$	7.3	STS[c]	none	THF/MeOH	150	**6**	96
10	**1**	Pd(PPh$_3$)$_4$	5.9	SCNBS[d]	none	THF/MeOH	130	**6**	72
11	**1**	Pd(PPh$_3$)$_4$	6.0	*i*-BuSO$_2$Na	none	THF/MeOH	315	**6**	90

Nagakura, I.; *J. Org. Chem.* 1997, 62, 8932.

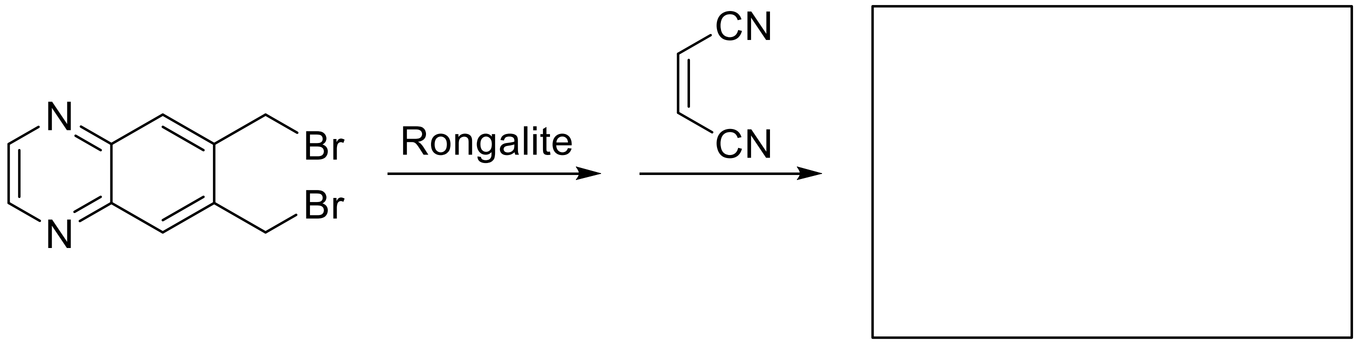
Conclusions

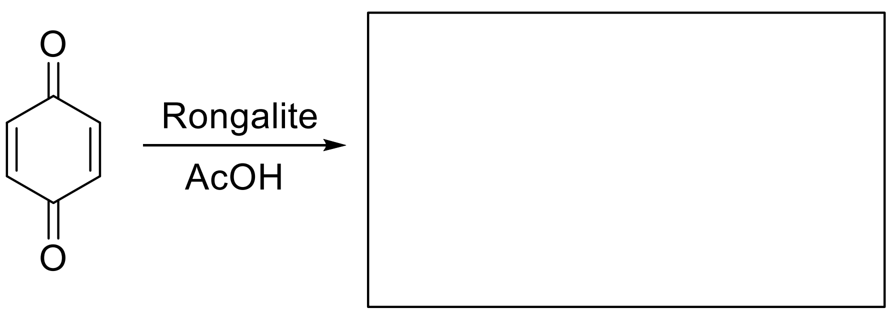


Thanks!!!



Questions!?!?!?





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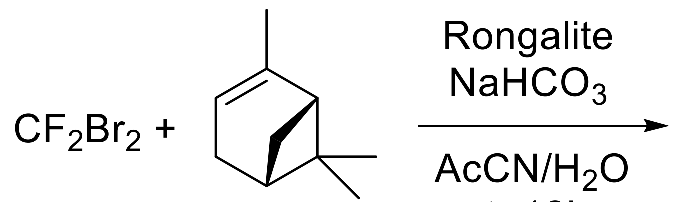
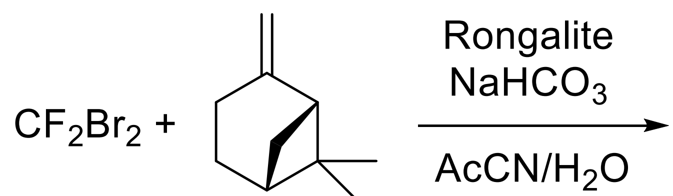
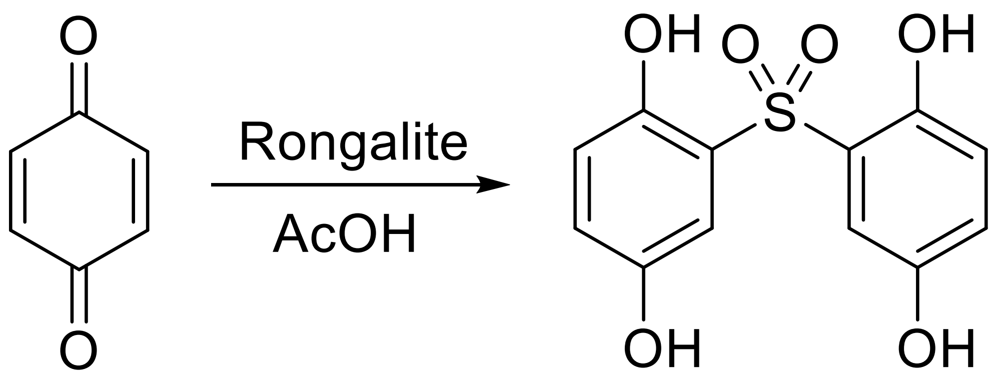


a-pinene



B-pinene



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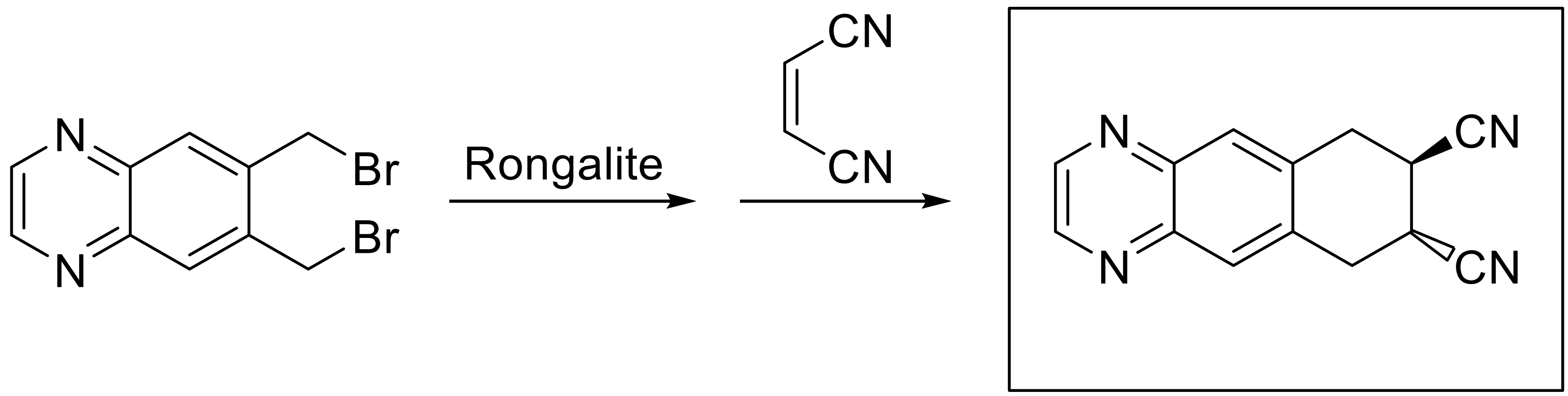
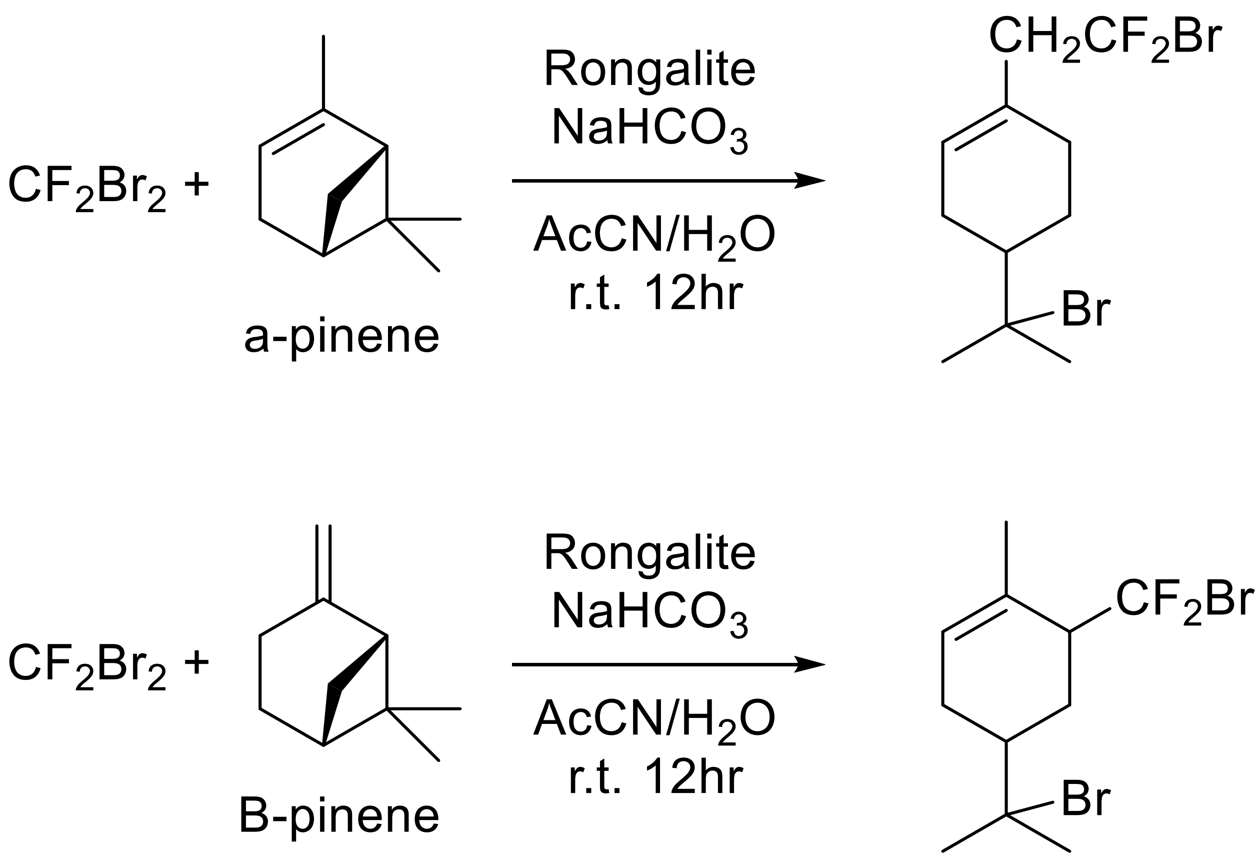


N
N
Br
Br
Rongalite
CN
CN
N
N
CN
CN



CF2Br2 +
Rongalite
NaHCO3
AcCN/H2O
r.t. 12hr
a-pinene
CH2CF2Br
Br
CF2Br2 +
Rongalite
NaHCO3
AcCN/H2O
r.t. 12hr
B-pinene
CF2Br
Br