Azulene Chemistry

What follows is a summary of the synthesis reactions related to Azulene, its generation and its derivatives based on the references I was able to review. I hope that this summary will be of help to those who might be interested in this subject.

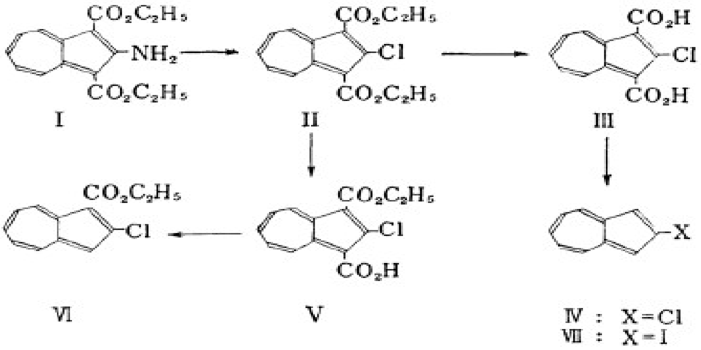
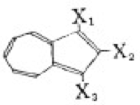


TABLE I. SOME PROPERTIES OF THE REACTION PRODUCTS



Compd. No.	X_1	X_2	X_3	M. p., °C	Color
II	CO_2Et	Cl	CO_2Et	77~ 78	R
III	CO_2H	Cl	CO_2H	260~265(d)	R
IV	H	Cl	H	91~ 92	V
VI	CO_2Et	Cl	H	Oil (pic. 92)	R
VII	H	I	H	125~126	V
IX	CO_2Me	OMe	CO_2Me	61~ 62	O
X	CO_2H	OMe	CO_2Me	145(d)	O
XI	CO_2Et	NHMe	CO_2Et	Oil (TNB 102)	O
XII	CO_2Et	NMe_2	CO_2Et	81~ 82	O
XIII	CO_2Et	NHPh	CO_2Et	141~142	O
XIV	CO_2Et	NHPhBr	CO_2Et	166~168	O
XV	CO_2Et	$NHNH_2$	CO_2Et	Oil (acetate 132)	O
XVI	CO_2Et	NHNHAz	CO_2Et	163~164	O
XVII	CO_2Et	$CH(CO_2Et)_2$	CO_2Et	Oil	R
XVIII	CO_2Et	$CH(CN)CO_2Et$	CO_2Et	116~117	R
XIX	CO_2Et	$CH(Ac)CO_2Et$	CO_2Et	53~ 54	R
XX	CO_2Et	OEt	H	84~ 85	P
XXII	CO_2Et	NHPh	H	Oil (TNB 112)	O
XXIII	H	OMe	H	82~ 83	R.V
XXIV	H	OEt	H	Oil	R.V
XXV	H	NHPh	H	144~145	R.O
XXVI	H	CN	H	77~ 78	B
XXVII	H	$NHNH_2$	H	127~128	R.O
XXVIII	H	HMe_2	H	98~ 99	O
XXX	H	CO_2Me	H	110~111	B
XXXI	H	CO_2H	H	200~203	G
XXXII	CHO	CN	H	180~182	R.V

pic.=picrate, TNB=Trinitrobenzene compound, R=Red, V=Violet, P=Pink, O=Orange, B=Blue, G=Green, Az=1,3-Diethoxycarbonylazulen-2-yl

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Nozoe, T., Seto, S., & Matsumura, S. (1962). Synthesis of 2-substituted azulenes by nucleophilic substitution reactions of 2-haloazulene derivatives. *Bulletin of the Chemical Society of Japan*, *35*(12), 1990-1998.

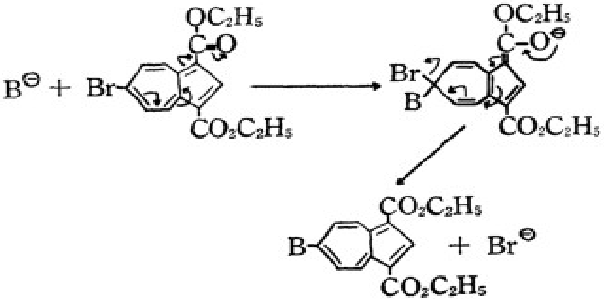
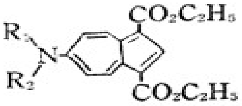
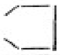
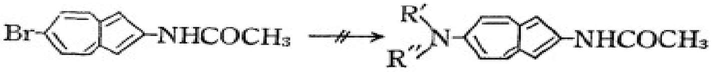


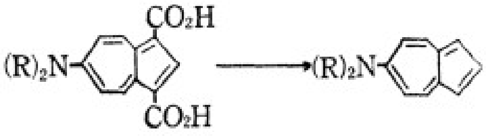
Chart I.



X : $R_1=NH_2$; $R_2=H$
XI : $R_1=R_2=CH_3$
XII : $R_1=R_2=C_2H_5$
XIII : $R_1=CH_2CH_2OH$; $R_2=H$
XIV : $R_1=R_2=CH_2CH_2OH$
XV : $R_1=R_2=CH_2CH=CH_2$
XVI : $R_1+R_2=$ 
XVII : $R_1+R_2=$ 
XVIII : $R_1+R_2=$ 
XIX : $R_1+R_2=$ 
XX : $R_1=CH_2CH_2CH_2$-N O ; $R_2=H$
XXI : $R_1=C_6H_5$; $R_2=H$

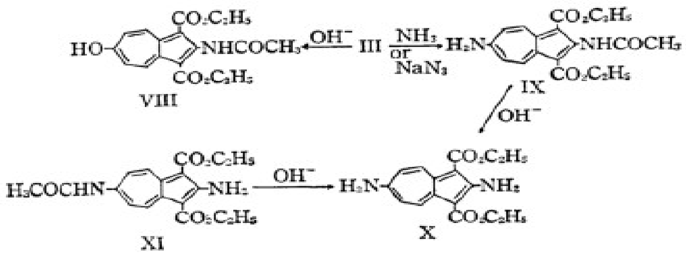


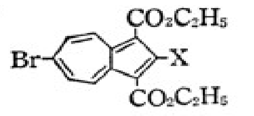
XXII

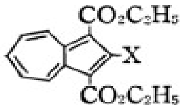


XXIII : $R=CH_3$ XXV : $R=CH_3$
XXIV : $R=C_2H_5$ XXVI : $R=C_2H_5$

Nozoe, T., Takase, K., & Tada, M. (1965). The Anionoid Substitution Reaction of Diethyl 6-Bromoazulene-1, 3-dicarboxylate. *Bulletin of the Chemical Society of Japan*, *38*(2), 247-251.



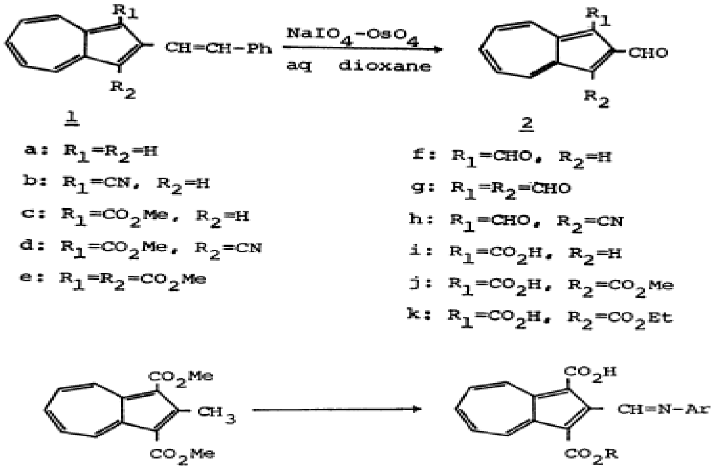




I: $X = H$
II: $X = NH_2$
III: $X = NHCOCH_3$
VII: $X = N(COCH_3)_2$

IV: $X = NH_2$
V: $X = NHCOCH_3$
VI: $X = N(COCH_3)_2$

Tada, M. (1966). The Anionoid Substitution Reaction of Diethyl 2-Acetamido-6-bromoazulene-1, 3-dicarboxylate. *Bulletin of the Chemical Society of Japan*, *39*(9), 1954-1961.

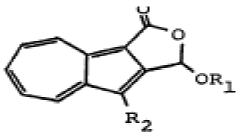


a: $R_1 = R_2 = H$
b: $R_1 = CN$, $R_2 = H$
c: $R_1 = CO_2Me$, $R_2 = H$
d: $R_1 = CO_2Me$, $R_2 = CN$
e: $R_1 = R_2 = CO_2Me$

f: $R_1 = CHO$, $R_2 = H$
g: $R_1 = R_2 = CHO$
h: $R_1 = CHO$, $R_2 = CN$
i: $R_1 = CO_2H$, $R_2 = H$
j: $R_1 = CO_2H$, $R_2 = CO_2Me$
k: $R_1 = CO_2H$, $R_2 = CO_2Et$

8a: $R = Me$, $Ar = p\text{-}(Me)_2NC_6H_5-$
8b: $R = Et$, $Ar = p\text{-}(Me)_2NC_6H_5-$

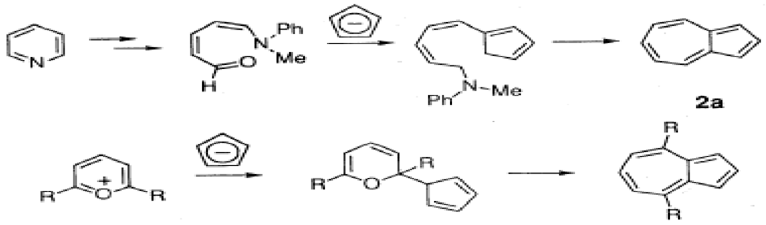
Scheme 2.



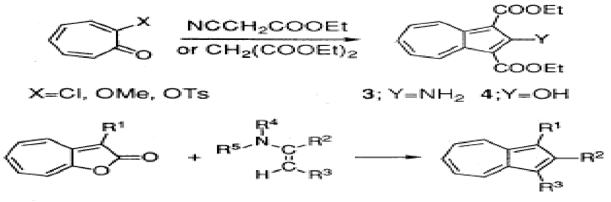
5a: $R_1 = R_2 = H$
5b: $R_1 = H$, $R_2 = CO_2Me$
6a: $R_1 = COMe$, $R_2 = CO_2Me$
6b: $R_1 = COMe$, $R_2 = CO_2Et$

Fig. 1.

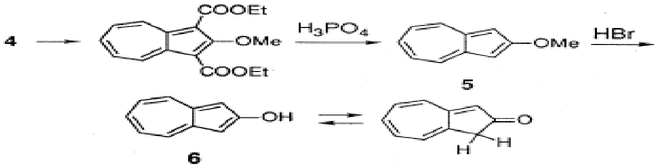
Saito, M., Morita, T., & Takase, K. (1980). Synthesis of 2-Formylazulene and Its Derivatives by Oxidative Cleavage of 2-Styrylazulenes. *Bulletin of the Chemical Society of Japan*, *53*(12), 3696-3700.



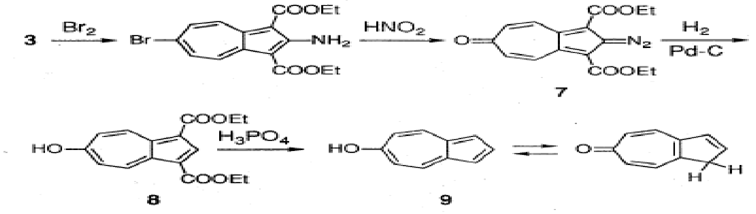
Scheme 2



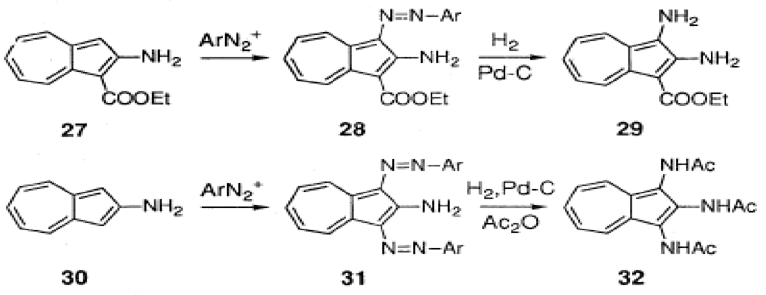
Scheme 3



Scheme 4

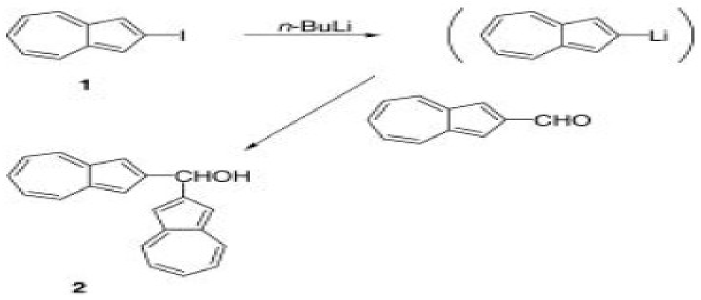


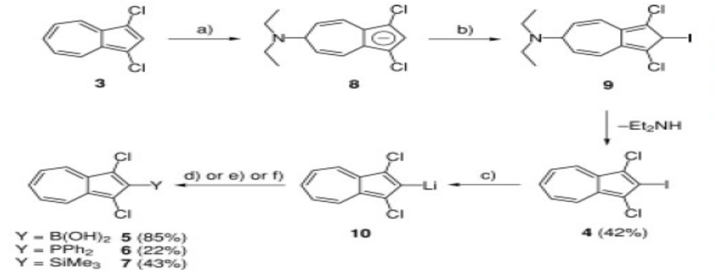
Scheme 5



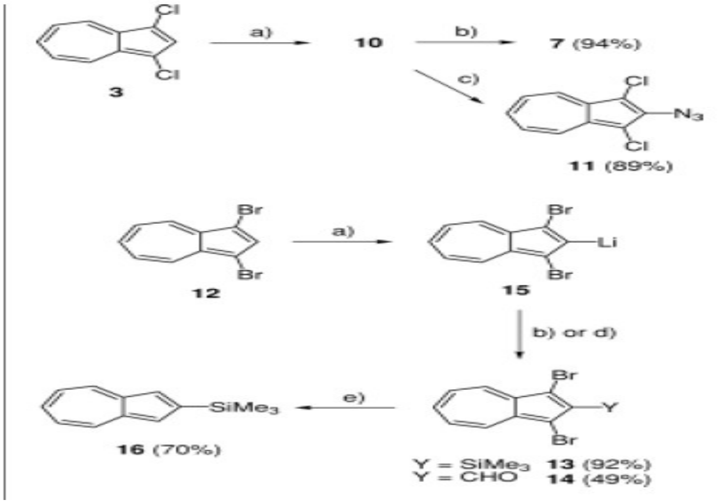
Scheme 11

Asao, T., & Ito, S. (1996). Synthesis and Properties of Novel Azulenic π-Electronic Compounds. *Journal of Synthetic Organic Chemistry, Japan*, *54*(1), 2-14.

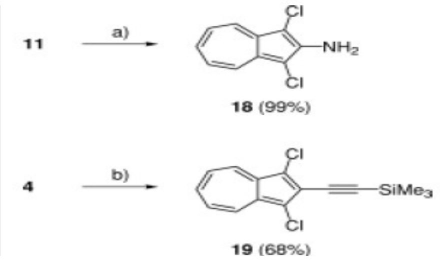




Scheme 2 *Reagents and conditions: a)* Et_2NLi*,* Et_2O*, -70 °C; b);* I_2*, -70 °C; c) PhLi, THF, -70 °C; d)* $B(OMe)_3$*, -70 °C then* H_2O*; e)* Ph_2PCl*, -70 °C; f)* Me_3SiCl*, -70 °C*

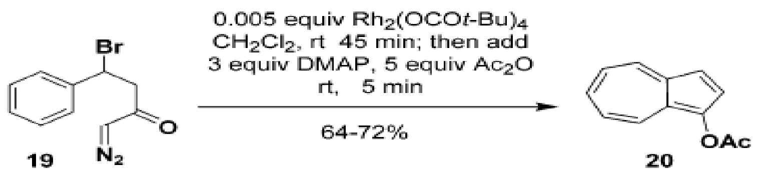


Scheme 3 *Reagents and conditions: a) LTMP, THF, -70 °C; b)* Me_3SiCl*, -70 °C; c)* TsN_3*, -70 °C; d) DMF, -70 °C then* H_2O*; e)* **13***,* $(Ph_3P)_2NiCl_2$*, Zn, NaI, THF-*H_2O*, 50 °C*



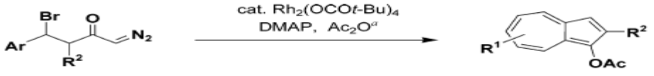
Scheme 5 *Reagents and conditions: a)* $NaBH_4$*, THF, 50 °C; b) trimethylsilylacetylene, CuI,* $(Ph_3P)_2PdCl_2$*,* Et_2NH*, 30 °C*

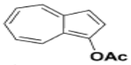
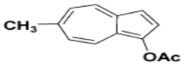
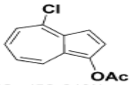
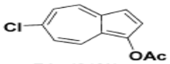
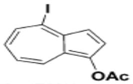
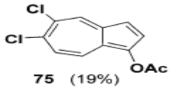
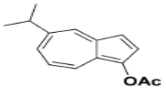
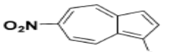
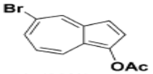
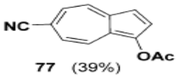
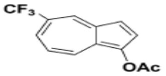
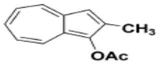
Kurotobi, K., Tabata, H., Miyauchi, M., Mustafizur, R. A., Migita, K., Murafuji, T., ... & Fujimori, K. (2003). The first generation of azulenyl-lithium and-magnesium: A novel, versatile method of introducing a substituent at the 2-position of an azulene skeleton. *Synthesis*, *1*(01), 0030-0034.



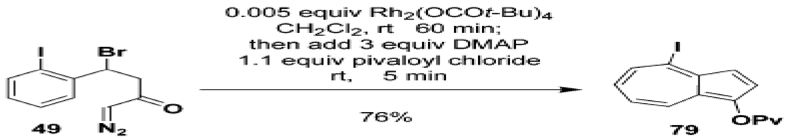
(2)

TABLE 3. Synthesis of Substituted Azulenes



entry	diazo ketone[b] (Ar)	azulene (% yield)[c]	entry	diazo ketone[b] (Ar)	azulene (% yield)[c]
1	**19** (C_6H_5)	 **20**[d] (64-72%)	7	**53** (4-Me-C_6H_4)	 **73** (47%)[e]
2	**48** (2-Cl-C_6H_4)	 **68** (58-61%)	8	**54** (4-Cl-C_6H_4)	 **74** (61%)
3	**49** (2-I-C_6H_4)	 **69** (73%)	9	**55** (3,4-di-Cl-C_6H_3)	 **75** (19%)
4	**50** (3-*i*-Pr-C_6H_4)	 **70** (54%)[f]	10	**65** (4-NO_2-C_6H_4)	 **76** (21%)
5	**51** (3-Br-C_6H_4)	 **71** (39%)	11	**66** (4-CN-C_6H_4)	 **77** (39%)
6	**52** (3-CF_3-C_6H_4)	 **72** (40%)	12	**67** (C_6H_5, $R^2 = CH_3$)	 **78** (58%)

[a] 0.005−0.01 equiv of $Rh_2(OCOt\text{-}Bu)_4$, CH_2Cl_2, rt, 45−90 min; then add 3 equiv of DMAP, 5 equiv of Ac_2O, rt, 5 min. [b] R^2 = H unless otherwise indicated. [c] Isolated yields of products purified by chromatography on silica gel. [d] Asao, T.; Ito, S.; Morita, N. *Tetrahedron Lett.* **1989**, *30*, 6693. [e] Estimated yield; 22% overall yield from 4-methylcinnamic acid (**27**). [f] Et_2O used as solvent.



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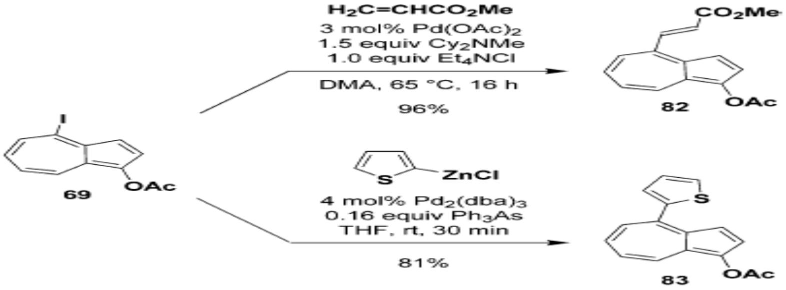
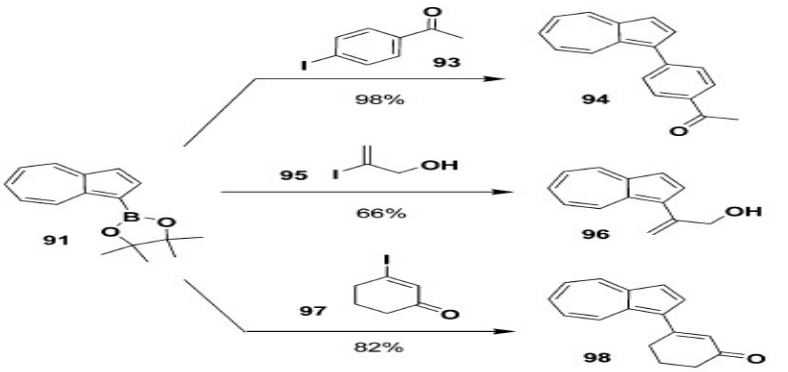
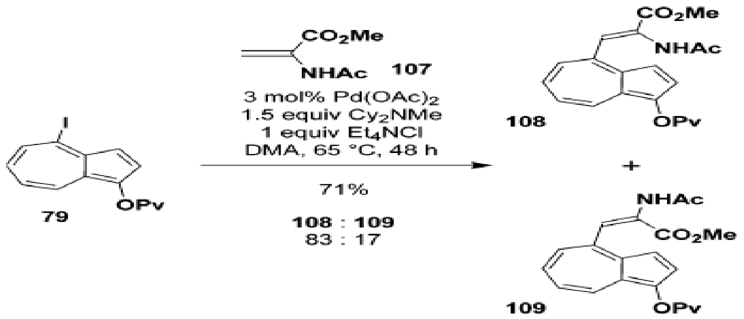


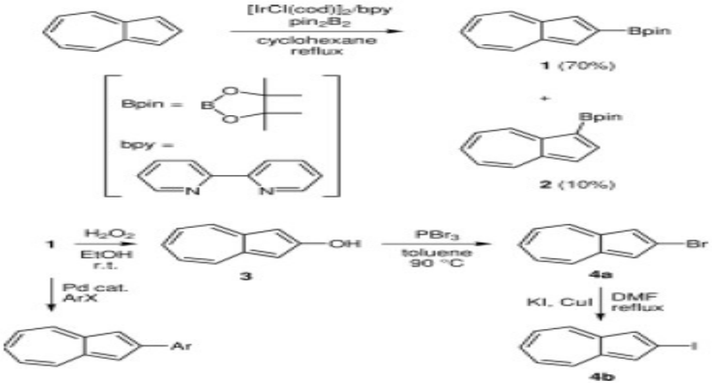


^{a} Reagents and conditions: 1.5 equiv of **91**, 5 mol % of $Pd(OAc)_2$, 20 mol % of (*o*-biphenyl)PCy_2, 3.0 equiv of $Ba(OH)_2$, dioxane–H_2O, 65 °C, 15 min

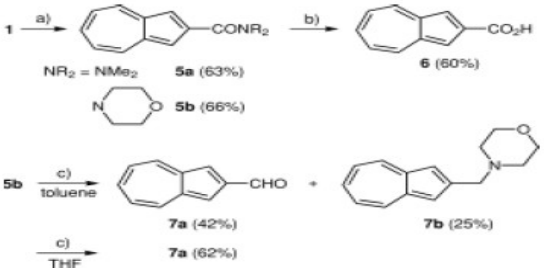


(6)

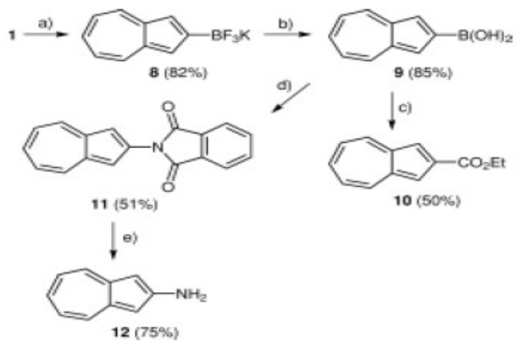
Crombie, A. L., Kane, J. L., Shea, K. M., & Danheiser, R. L. (2004). Ring expansion-annulation strategy for the synthesis of substituted azulenes and oligoazulenes. 2. Synthesis of azulenyl halides, sulfonates, and azulenylmetal compounds and their application in transition-metal-mediated coupling reactions. *The Journal of organic chemistry*, *69*(25), 8652-8667.



Scheme 1

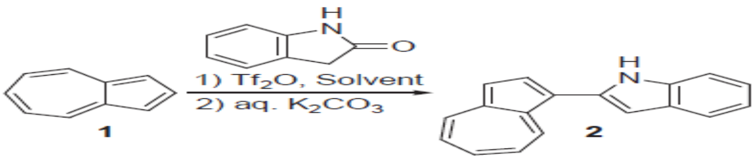


Scheme 2 Reagents and conditions: *a) $PdCl_2(PPh_3)_2$, $ClCONR_2$, CsF, THF, reflux; b) KOH (excess),* **5a**, *EtOH-H_2O, reflux; c) DIBAL-H,* **5b**, *-78 °C.*



Scheme 3 **Reagents and conditions:** *a) KHF_2, MeOH, r.t.; b) Na_2CO_3, MeCN-H_2O, r.t.; c) $Pd(PPh_3)_4$, $K_3PO_4 \cdot nH_2O$, $ClCO_2Et$, toluene, 90 °C; d) $Cu(OAc)_2$, phthalimide, pyridine, H_2O, DMF, r.t.; e) NH_2NH_2, THF, r.t.*

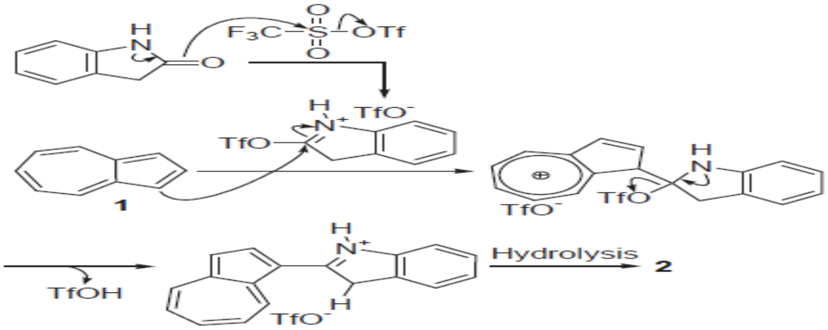
Fujinaga, M., Suetake, K., Gyoji, K., Murafuji, T., Kurotobi, K., & Sugihara, Y. (2008). An Easy Access to 2-Substituted Azulenes from Azulene-2-boronic Acid Pinacol Ester. *Synthesis*, *2008*(23), 3745-3748.



Scheme 1. Reaction of azulene (**1**) with 2-indolinone.

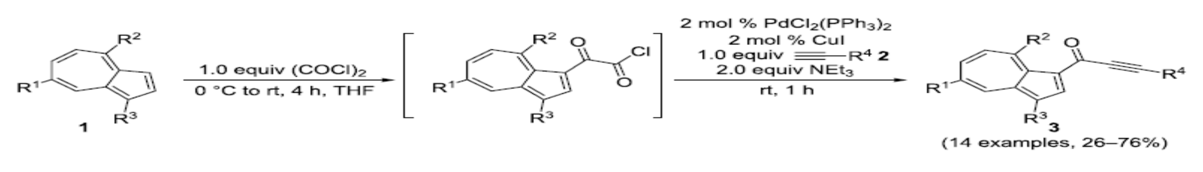
Table 1. Synthesis of 1-(indol-2-yl)azulene (**2**)

Entry	Solvent	Yield of 2 [%]
1	dichloromethane	89
2	1,2-dichroloethane	76
3	toluene	75
4	acetonitrile	59
5	chloroform	33



Scheme 2. Presumed reaction mechanism.

Shoji, T., Inoue, Y., & Ito, S. (2012). First synthesis of 1-(indol-2-yl) azulenes by the Vilsmeier–Haack type arylation with triflic anhydride as an activating reagent. *Tetrahedron Letters*, *53*(12), 1493-1496.



Scheme 4: Three-component synthesis of azulenyl- and guaiazulenylynones 3 by glyoxylation–decarbonylative Sonogashira coupling sequence.

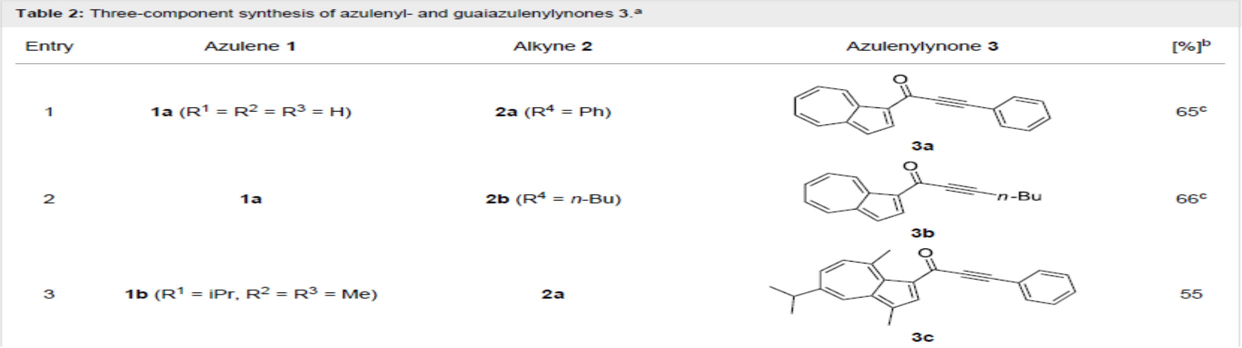
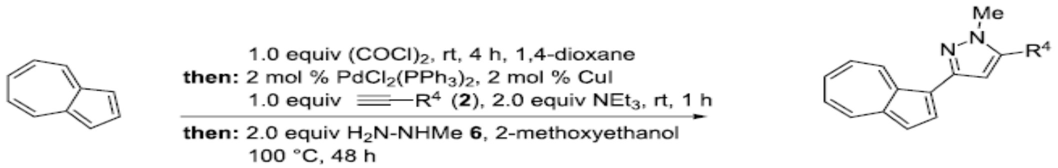


Table 2: Three-component synthesis of azulenyl- and guaiazulenylynones 3.[a]

Entry	Azulene 1	Alkyne 2	Azulenylynone 3	[%][b]
1	**1a** ($R^1 = R^2 = R^3 = H$)	**2a** (R^4 = Ph)	**3a**	65[c]
2	**1a**	**2b** (R^4 = *n*-Bu)	**3b**	66[c]
3	**1b** (R^1 = iPr, $R^2 = R^3$ = Me)	**2a**	**3c**	55

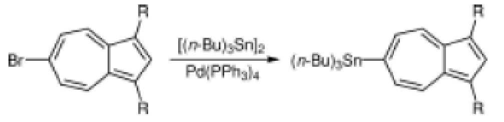


1

7a (R^4 = Ph, 47%)
7b (R^4 = *p*-CNC$_6$H$_4$, 41%)

Scheme 6: Four-component synthesis of pyrazolylazulenes 7 by glyoxylation–decarbonylative Sonogashira coupling–cyclocondensation sequence (yields refer to isolated and purified compounds).

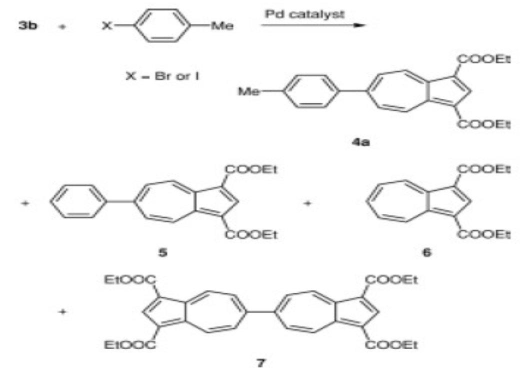
Gers, C. F., Rosellen, J., Merkul, E., & Müller, T. J. (2011). One-pot four-component synthesis of pyrimidyl and pyrazolyl substituted azulenes by glyoxylation–decarbonylative alkynylation–cyclocondensation sequences. *Beilstein journal of organic chemistry*, *7*(1), 1173-1181.



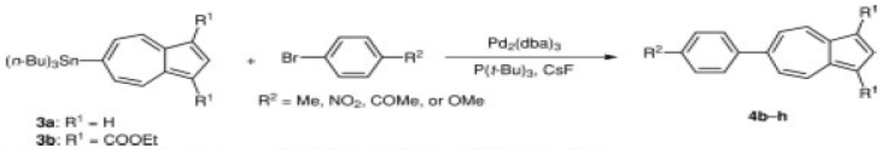
2a: R = H
2b: R = COOEt

3a: R = H 49%
3b: R = COOEt 69%

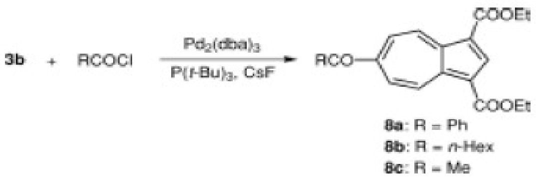
Scheme 1 *Palladium-catalyzed direct stannylation reactions of 6-bromoazulenes with bis(tri-n-butyltin)*



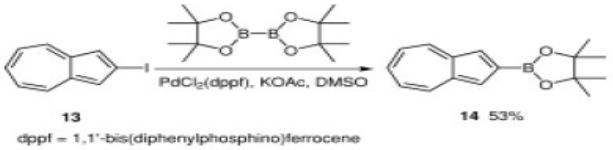
Scheme 2 *Stille cross-coupling reactions of azulenyltin compound* ***3b*** *with 4-bromo- or 4-iodotoluene*



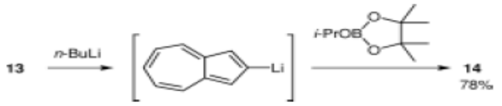
Scheme 3 *Stille cross-coupling reactions of azulenyltin compounds* ***3a*** *and* ***3b*** *with aryl bromides*



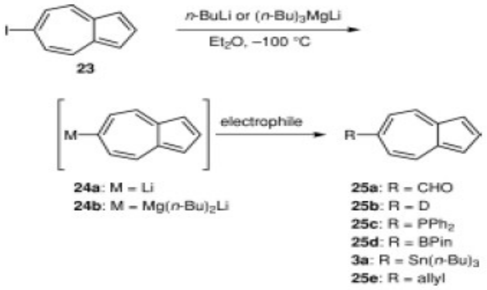
Scheme 4 *Stille cross-coupling reactions of azulenyltin compound* ***3b*** *with acyl chlorides*



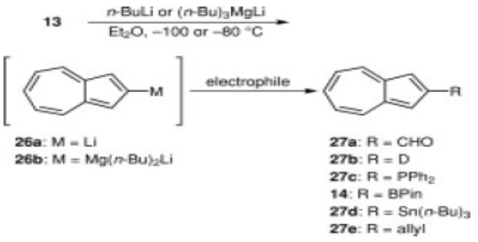
Scheme 5 *Palladium-catalyzed direct azulenylboronate formation*



Scheme 6 *Borylation using azulen-2-yllithium as a reagent*

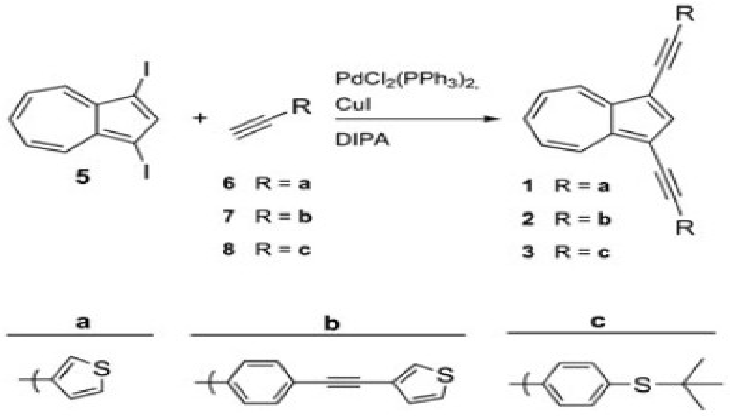


Scheme 9 *Iodine-metal exchange reactions of 6-iodoazulene (**23**) and the reactions of the resulting azulenyl-substituted metallic reagents with electrophiles*

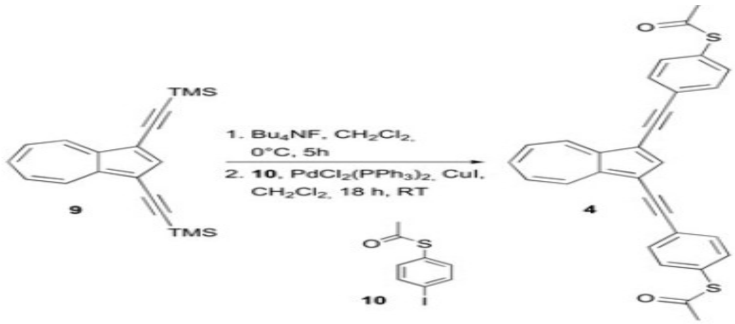


Scheme 10 *Iodine-metal exchange reactions of 2-iodoazulene (**13**) and the reactions of the resulting azulenyl-substituted metallic reagents with electrophiles*

Ito, S., Shoji, T., & Morita, N. (2011). Recent Advances in the Development of Methods for the Preparation of Functionalized Azulenes for Electrochromic Applications. *Synlett*, *2011*(16), 2279-2298.



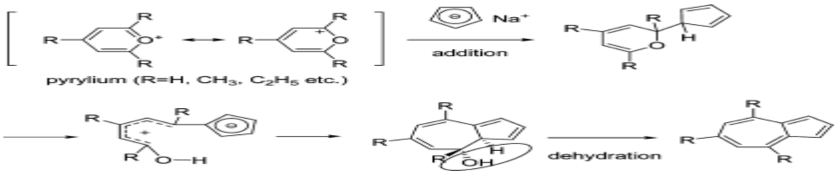
cheme 3. Reaction scheme for the synthesis of **1**, **2**, and **3**



Scheme 4. Reaction scheme for the synthesis of **4**

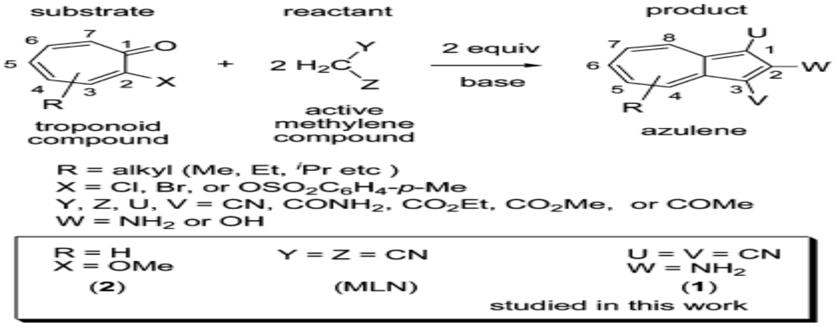
Förster, S., Hahn, T., Loose, C., Röder, C., Liebing, S., Seichter, W., ... & Weber, E. (2012). Synthesis and characterization of new derivatives of azulene, including experimental and theoretical studies of electronic and spectroscopic behavior. *Journal of Physical Organic Chemistry*, *25*(10), 856-863.

Scheme 1. An Example of Hafner's Azulene Synthesis[a]

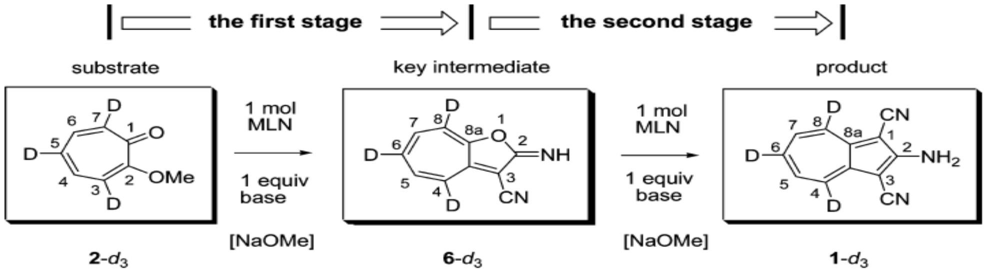


[a]See refs 9−11.

Scheme 2. General and Facile Formation of Polyfunctional Azulenes (Nozoe Azulene Synthesis[12]) from the Reaction between Troponoid Substrates and Active Methylene Compounds[a]

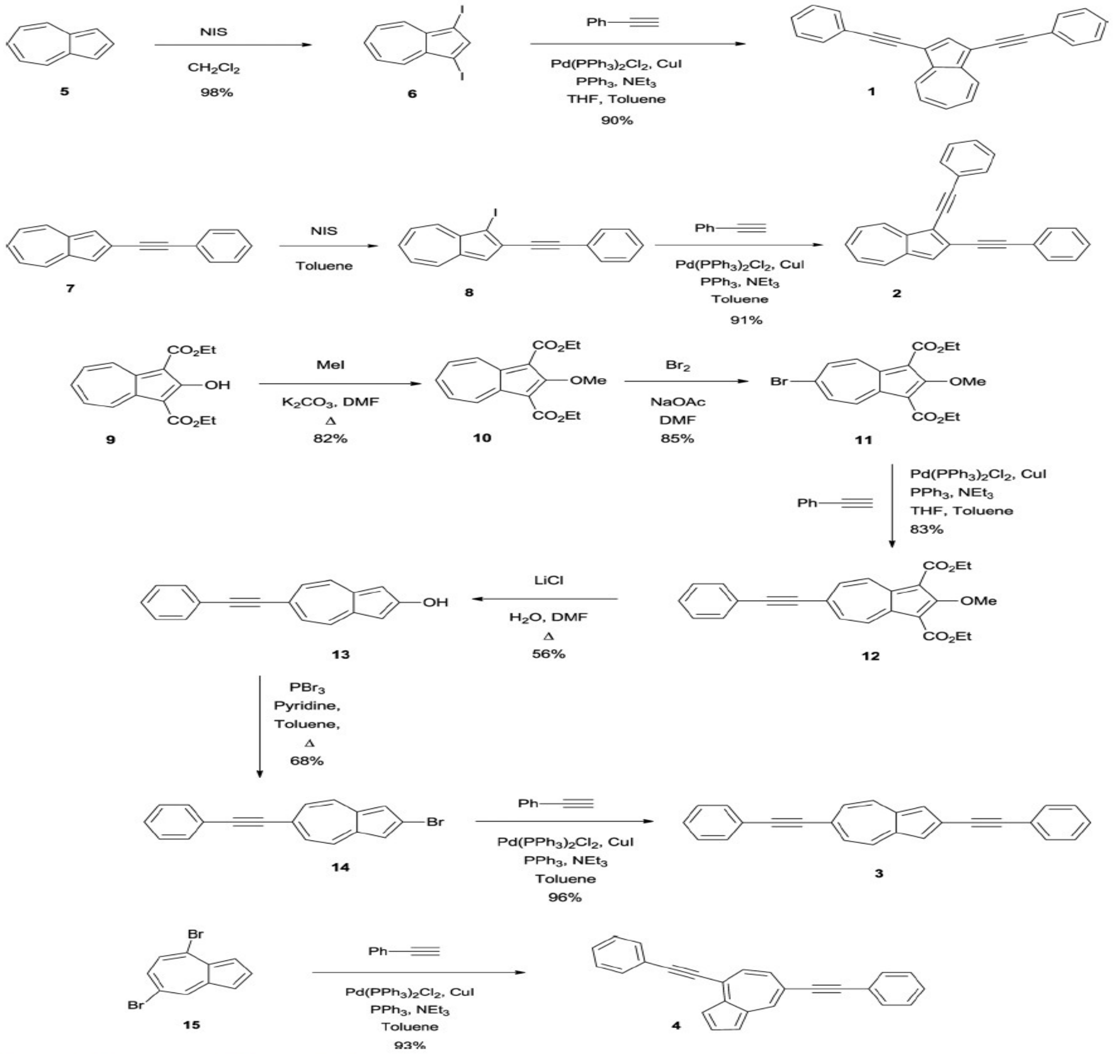


Scheme 3. Key Intermediate and the Position of Three Deuteriums of the Substrate, Key Intermediate and Product in the Nozoe Azulene Synthesis[a]



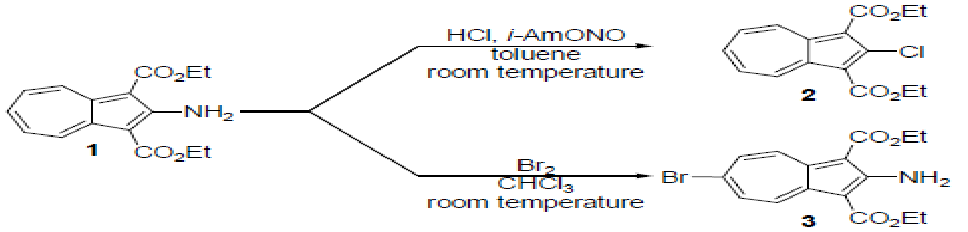
[a]MLN is malononitrile.

Machiguchi, T., Hasegawa, T., Yamabe, S., Minato, T., Yamazaki, S., & Nozoe, T. (2012). Experimental and Theoretical Analyses of Azulene Synthesis from Tropones and Active Methylene Compounds: Reaction of 2-Methoxytropone and Malononitrile. *The Journal of organic chemistry*, *77*(12), 5318-5330.

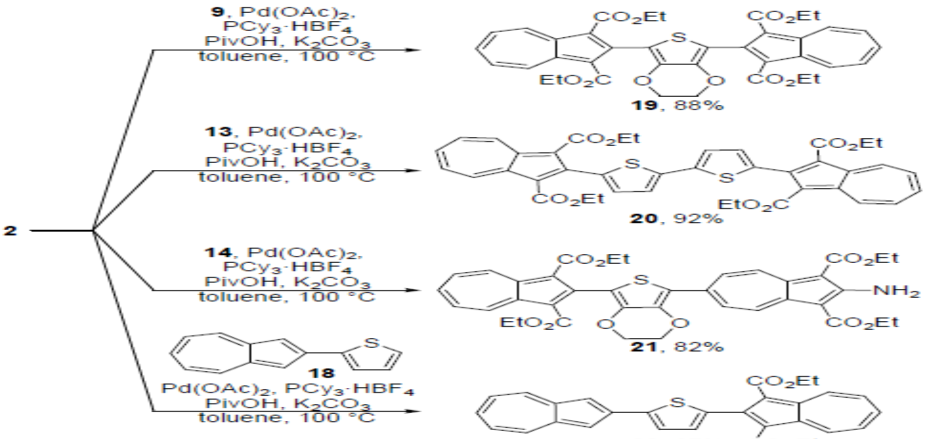


Scheme 1 Synthesis of di(phenylethynyl)azulenes **1**, **2**, **3** and **4**.

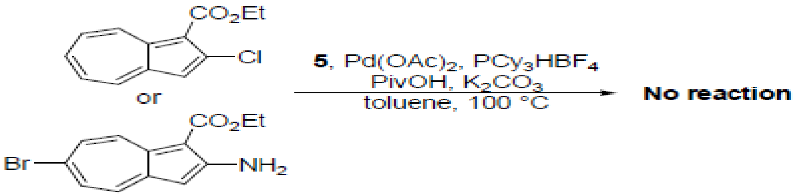
Koch, M., Blacque, O., & Venkatesan, K. (2013). Impact of 2, 6-connectivity in azulene: optical properties and stimuli responsive behavior. *Journal of Materials Chemistry C*, *1*(44), 7400-7408.



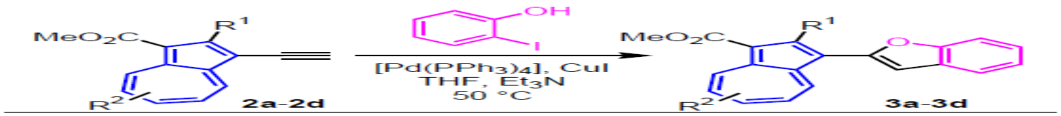
Scheme 1 Synthesis of 2-chloro- and 6-bromoazulene derivatives **2** and **3**.

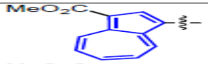
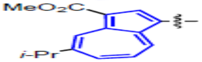
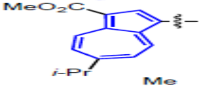
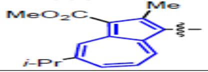


Scheme 4 Preparation of di(azulenyl)thiophene derivatives **19–22**.



Shoji, T., Maruyama, A., Araki, T., Ito, S., & Okujima, T. (2015). Synthesis of 2-and 6-thienylazulenes by palladium-catalyzed direct arylation of 2-and 6-haloazulenes with thiophene derivatives. *Organic & biomolecular chemistry*, *13*(40), 10191-10197.



Entry	Azulene	Product	Yield [%]^a
1		3a	65
2		3b	55[16a]
3		3c	72
4		3d	31

^{a} Isolated yield

Shoji, T., Tanaka, M., Takagaki, S., Miura, K., Ohta, A., Sekiguchi, R., ... & Okujima, T. (2018). Synthesis of azulene-substituted benzofurans and isocoumarins via intramolecular cyclization of 1-ethynylazulenes, and their structural and optical properties. *Organic & biomolecular chemistry*, *16*(3), 480-489.

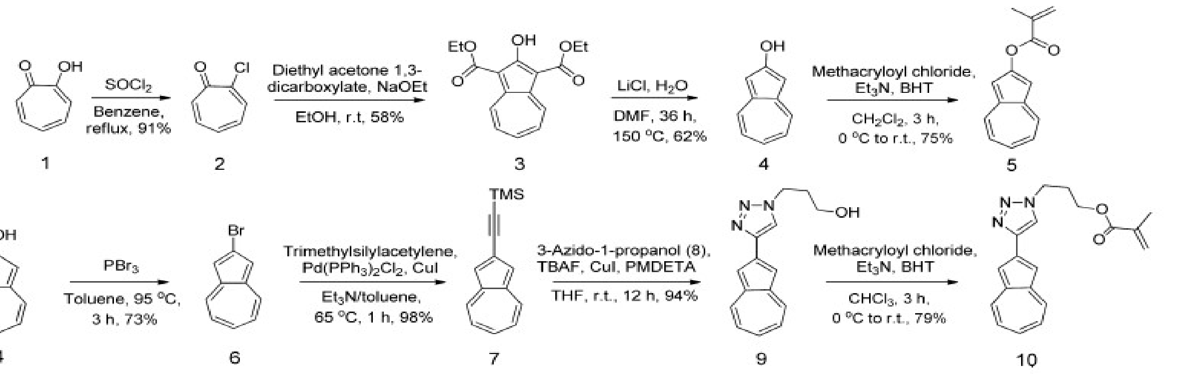


Figure 1. Preparation of azulene methacrylates **5** and **10**.

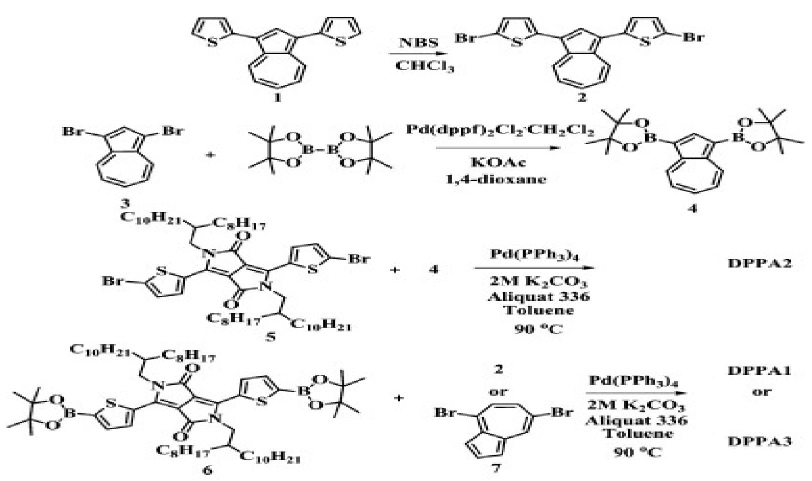
Puodziukynaite, E., Wang, H. W., Lawrence, J., Wise, A. J., Russell, T. P., Barnes, M. D., & Emrick, T. (2014). Azulene methacrylate polymers: synthesis, electronic properties, and solar cell fabrication. *Journal of the American Chemical Society*, *136*(31), 11043-11049.

The following thesis has an excellent synthesis review section.

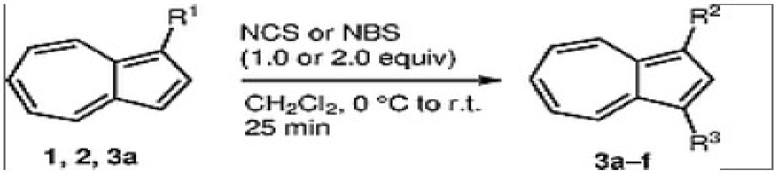
Johansson, N. G. (2014). Framställning av flersubstituerade azulenderivat med fokus på positionerna 1, 2 och 6.

https://helda.helsinki.fi/bitstream/handle/10138/136544/Pro%20gradu,%20Niklas%20G.%20Johansson.pdf?sequence=5

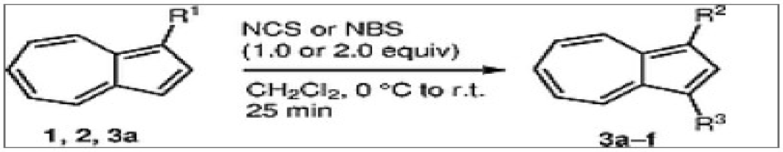
Scheme 2. Synthetic Routes of DPPA1, DPPA2, and DPPA3



Yao, J., Cai, Z., Liu, Z., Yu, C., Luo, H., Yang, Y., ... & Zhang, D. (2015). Tuning the semiconducting behaviors of new alternating dithienyldiketopyrrolopyrrole–azulene conjugated polymers by varying the linking positions of azulene. *Macromolecules*, *48*(7), 2039-2047.



Product	R^1	R^2	R^3	Yield (%)
3a	H	Cl	H	92



Product	R^1	R^2	R^3	Yield (%)
3b	H	Cl	Cl	91
3c	H	Br	H	53
3d	H	Br	Br	98
3e	Cl	Cl	Br	99
3f	CO_2Et	CO_2Et	Br	97

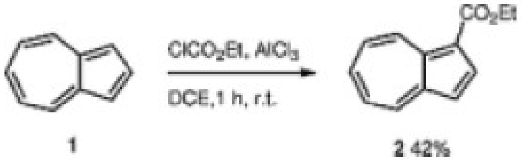
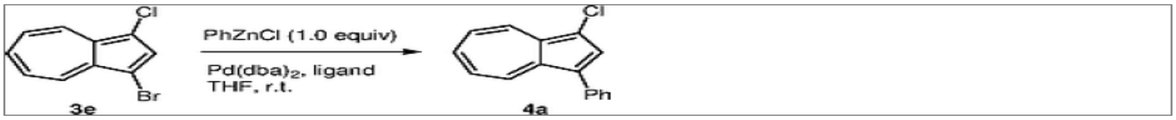
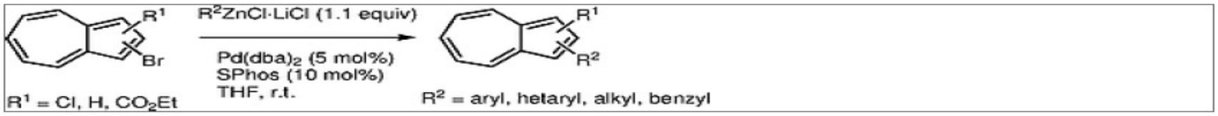


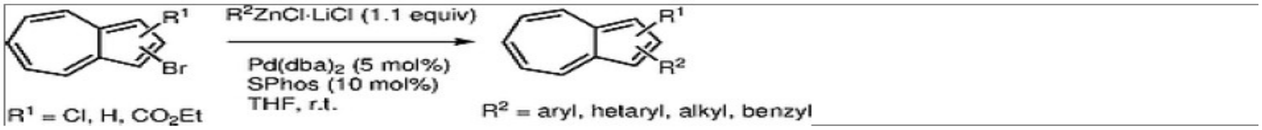
Table 2 Optimization of Catalytic System



Entry	Catalytic system	Conditions	Yield (%)
1	Pd(dba)$_2$ (5 mol%), PPh$_3$ (20 mol%)	24 h, 50 °C	75
2	Pd(dba)$_2$ (5 mol%), SPhos (10 mol%)	45 min, r.t.	70
3	Pd(dba)$_2$ (5 mol%), SPhos (10 mol%), *i*-PrI	30 min, r.t.	76

Table 3 Negishi Cross-Coupling of Monobromoazulenes with Organozinc Reagents





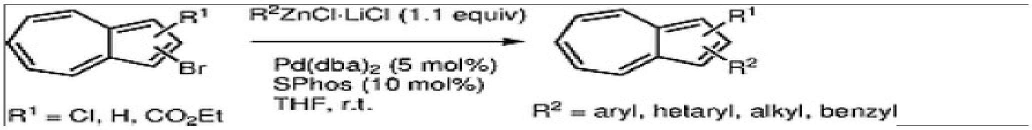
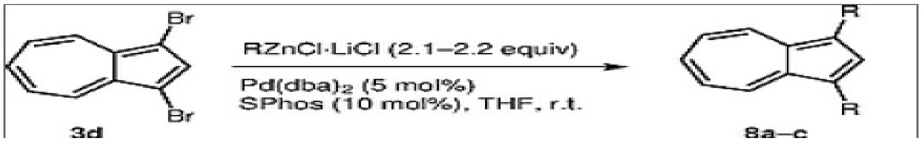
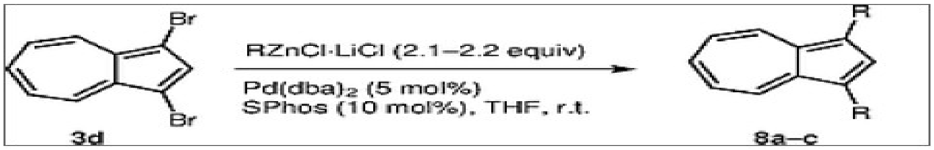
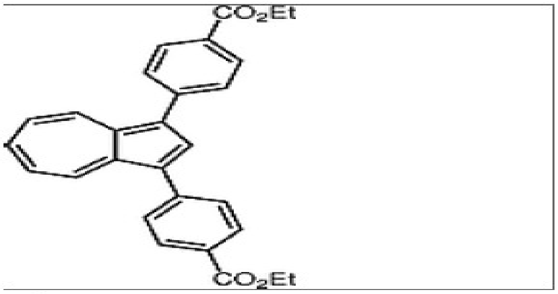
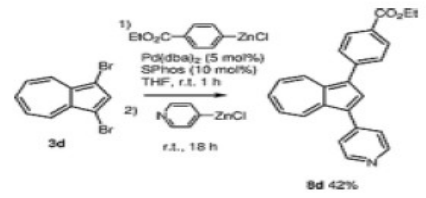


Table 4 Negishi Cross-Coupling of 1,3-Dibromoazulene (**3d**) with Organozinc Reagents





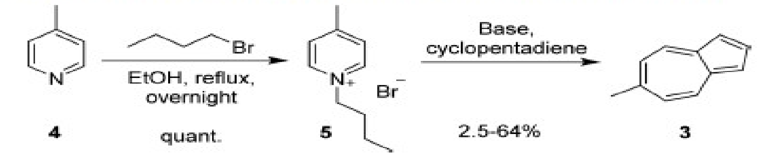
Entry	**Time**	**Product**
2	0.5 h	 **8b** 97%



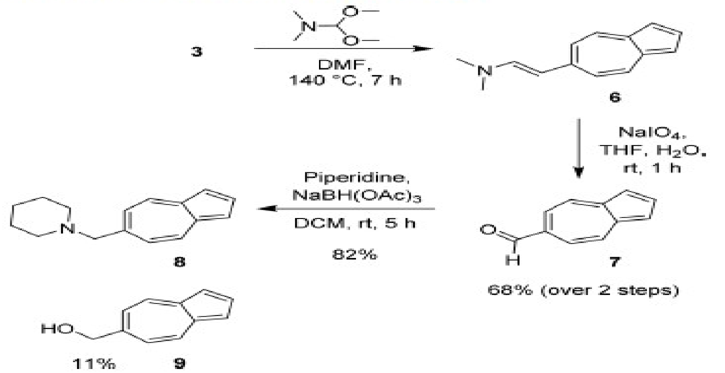
Scheme 2 *One-pot introduction of two different substituents*

Dubovik, J., & Bredihhin, A. (2015). A Convenient Synthesis of Functionalized Azulenes via Negishi Cross-Coupling. *Synthesis*, *47*(04), 538-548.

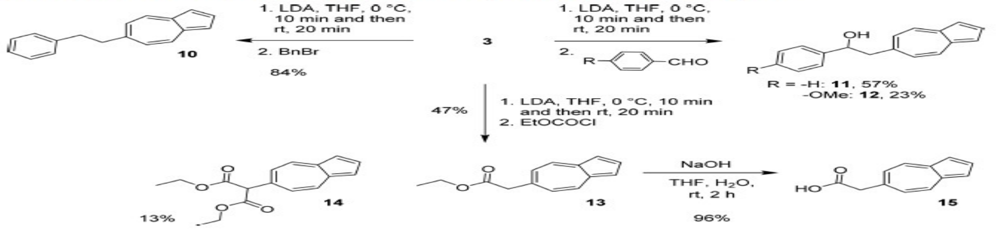
Scheme 1. Two-Step Synthesis of 6-Methylazulene (3)



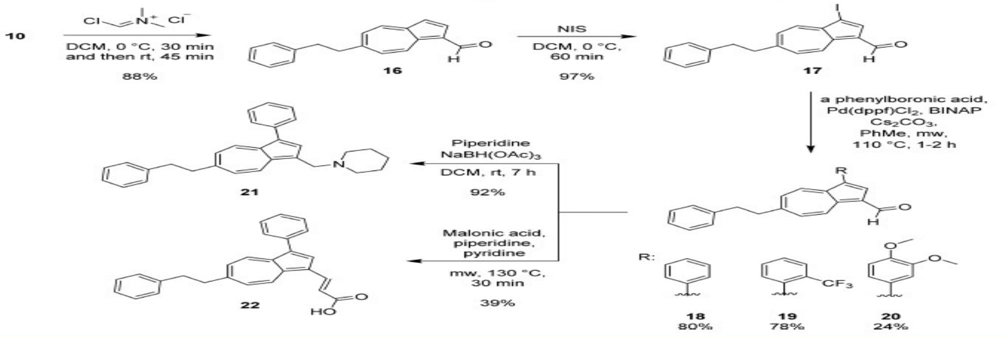
Scheme 2. Functionalization of the Methyl Group of 6-Methylazulene (3) Via a Formyl Group



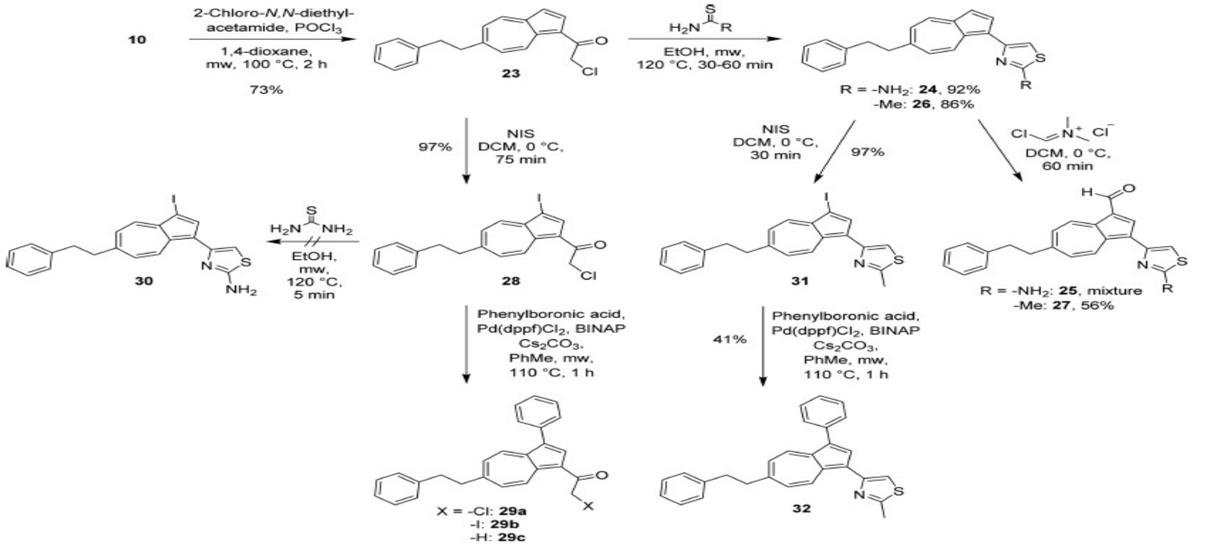
Scheme 3. Deprotonation of 6-Methylazulene (3) Followed by Reactions with Electrophiles



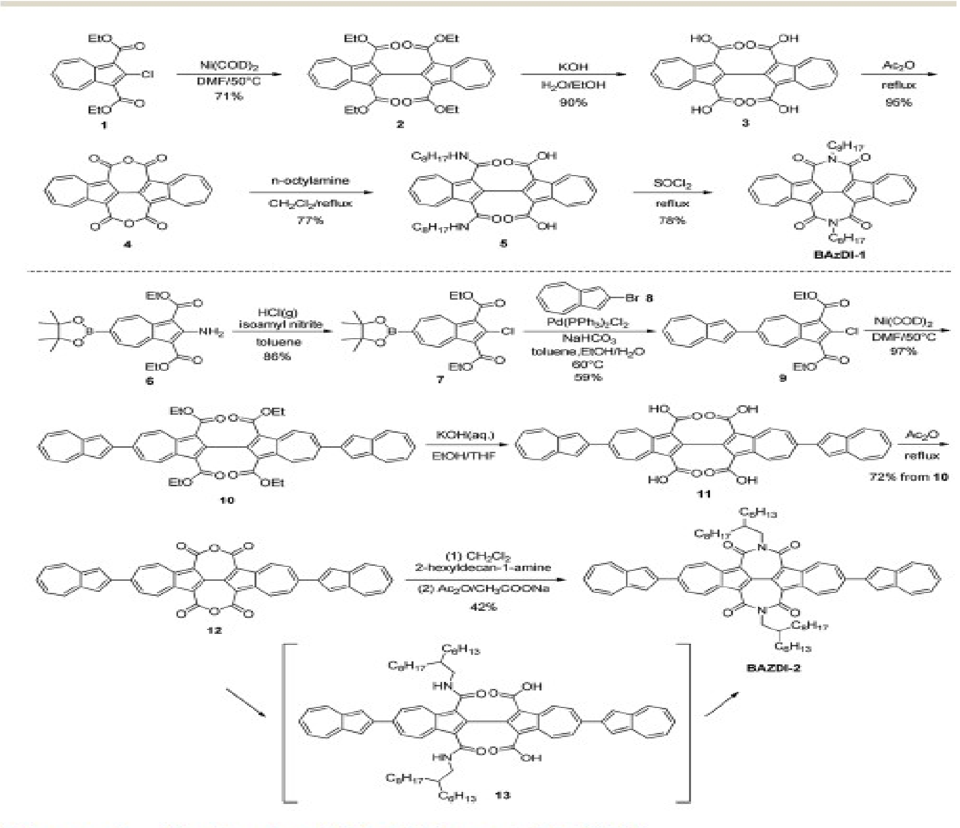
Scheme 4. Synthesis of 1,3,6-Trisubstituted Azulenes Utilizing Iodine and a Formyl Group As Synthetic Handles



Scheme 5. Synthesis of 1,3,6-Trisubstituted Azulenes Exploiting the Chloromethylketone Functionality

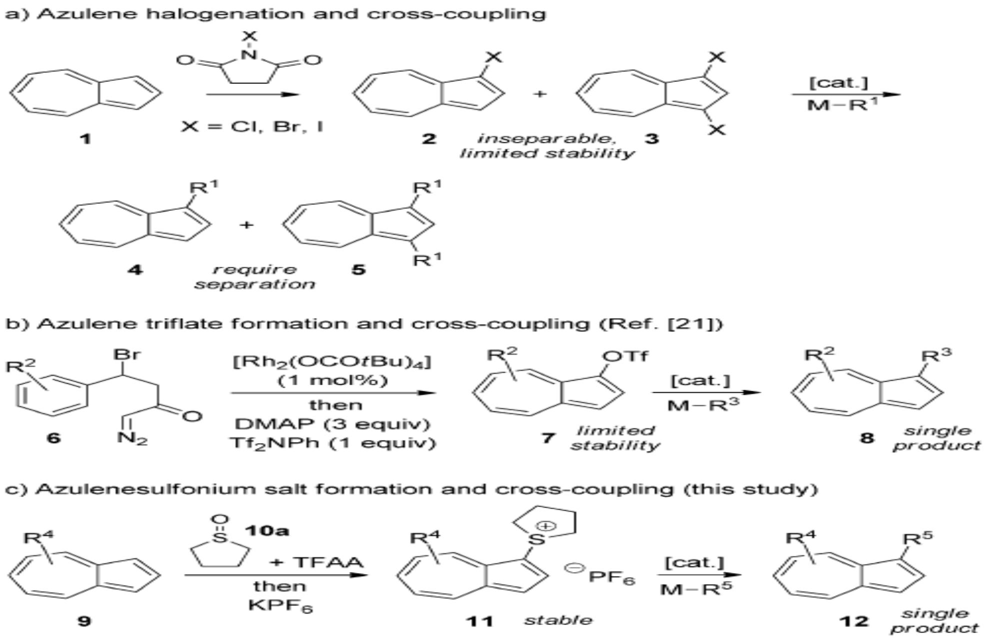


Leino, T. O., Baumann, M., Yli-Kauhaluoma, J., Baxendale, I. R., & Wallén, E. A. (2015). Synthesis of 1, 3, 6-Trisubstituted Azulenes. *The Journal of organic chemistry*, *80*(22), 11513-11520.



Scheme 1 Synthesis of BAzDI-1 and BAzDI-2.

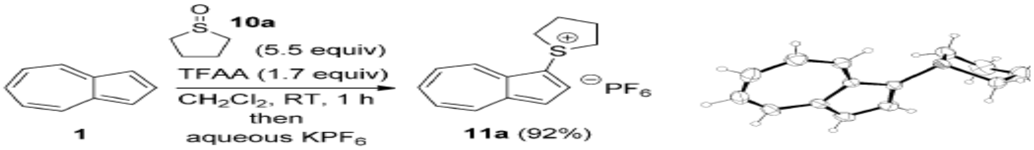
Xin, H., Ge, C., Yang, X., Gao, H., Yang, X., & Gao, X. (2016). Biazulene diimides: a new building block for organic electronic materials. *Chemical science*,*7*(11), 6701-6705.


a) Azulene halogenation and cross-coupling

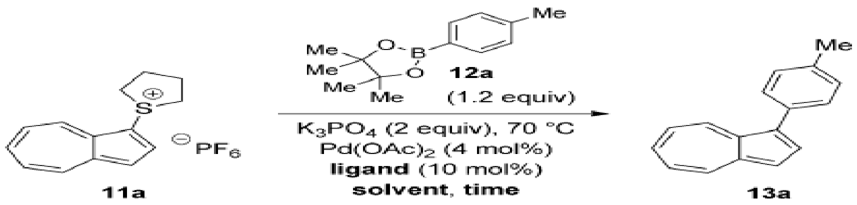
b) Azulene triflate formation and cross-coupling (Ref. [21])

c) Azulenesulfonium salt formation and cross-coupling (this study)

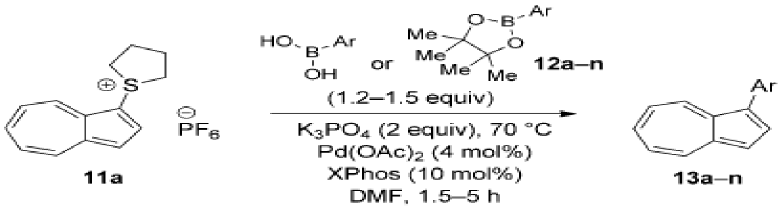
Scheme 1. Strategies for azulene cross-coupling. DMAP = 4-dimethylaminopyridine, Tf = trifluoromethanesulfonyl.



Scheme 2. Synthesis of the parent sulfonium salt **11a** and its X-ray crystal structure.

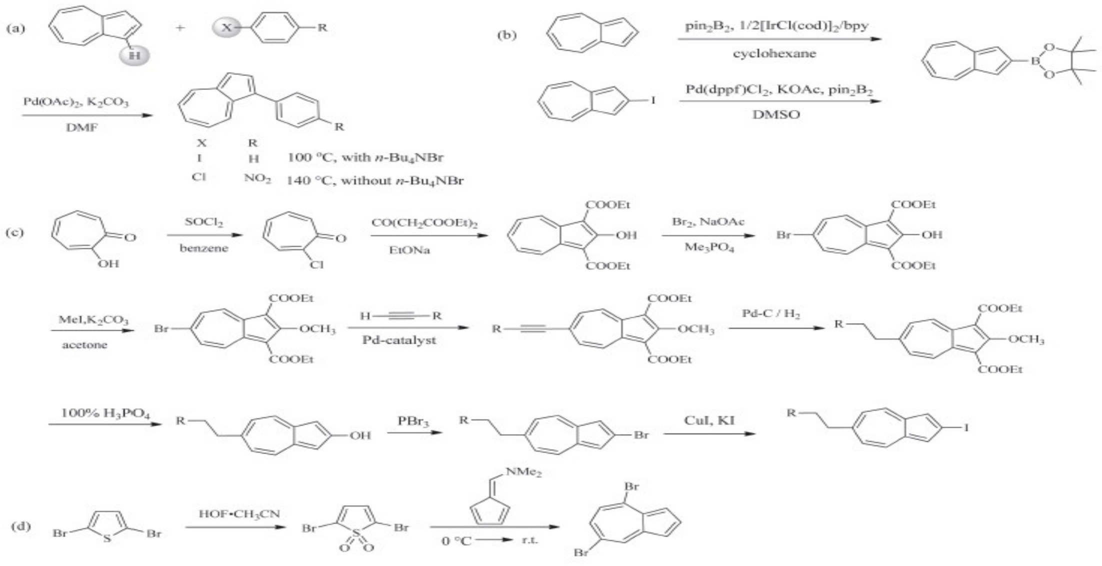


Scheme 3. Optimization of cross-coupling parameters.



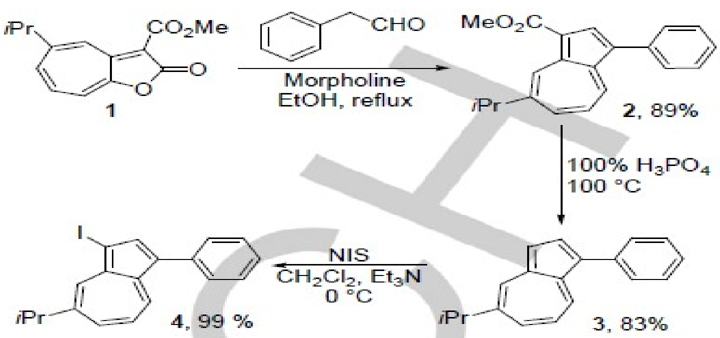
Scheme 4. Variation of the organoboron coupling partner.

Cowper, P., Jin, Y., Turton, M. D., Kociok-Köhn, G., & Lewis, S. E. (2016). Azulenesulfonium Salts: accessible, stable, and versatile reagents for cross-coupling. *Angewandte Chemie International Edition*, *55*(7), 2564-2568.

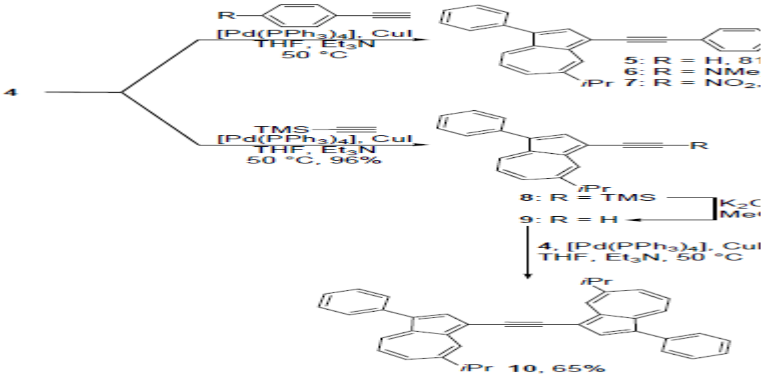


Scheme 1. Synthetic route to azulene derivatives substituted at (a) 1-position; (b) 2-position; (c) 2,6-postions; (d) 5,8-positions.

Dong, J. X., & Zhang, H. L. (2016). Azulene-based organic functional molecules for optoelectronics. *Chinese Chemical Letters*, *27*(8), 1097-1104.

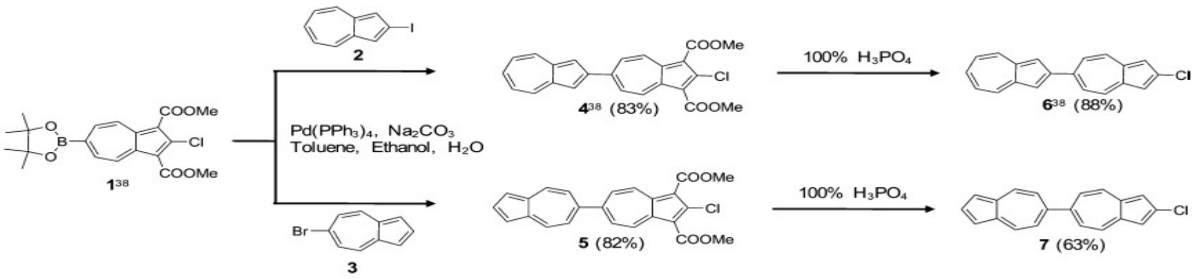


Scheme 1. Synthesis of 1-iodoazulene derivative 4.



Scheme 2. Synthesis of the alkyne precursors 5–7 and 10.

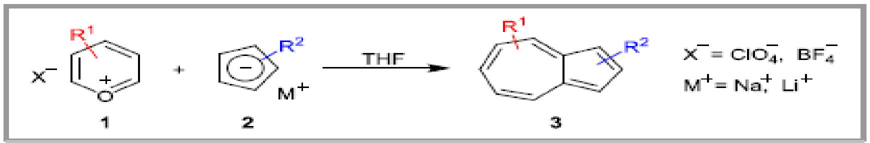
Shoji, T., Maruyama, A., Tanaka, M., Nagai, D., Shimomura, E., Fujimori, K., ... & Yasunami, M. (2016). Synthesis and Properties of (3-Phenyl-1-azulenyl) tetracyanobetadienes and Tris (aryltetracyanobetadiene) s Connected with 1, 3, 5-Tri (1-azulenyl) benzene Core. *ChemistrySelect*, *1*(1), 49-57.



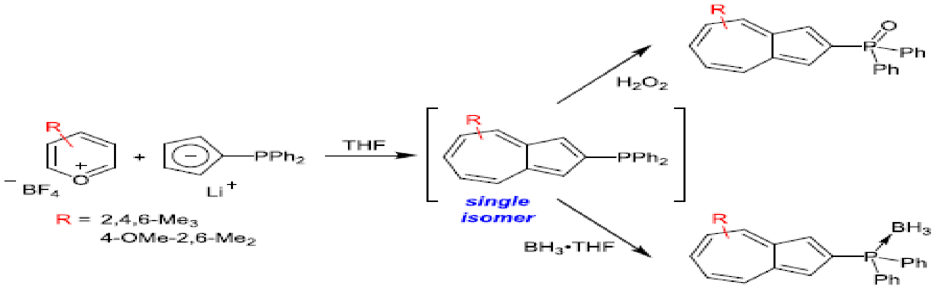
Yamaguchi, Y., Takubo, M., Ogawa, K., Nakayama, K. I., Koganezawa, T., & Katagiri, H. (2016). Terazulene isomers: polarity change of OFETs through molecular orbital distribution contrast. *Journal of the American Chemical Society*, *138*(35), 11335-11343.

See the following review:

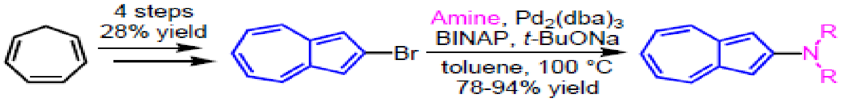
Xin, H., & Gao, X. (2017). Application of azulene in constructing organic optoelectronic materials: new tricks for an old dog. *ChemPlusChem*, *82*(7), 945-956.



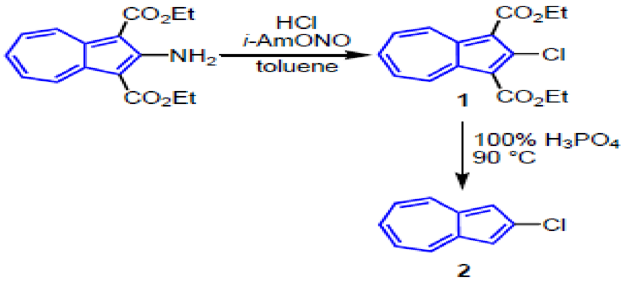
Scheme 1 Hafner's synthesis of substituted azulenes from a pyrylium salt and a metallated Cp.



Gee, A. P., Cosham, S. D., Johnson, A. L., & Lewis, S. E. (2017). Phosphorus-substituted azulenes accessed via direct hafner reaction of a phosphino cyclopentadienide. *Synlett*, *28*(08), 973-975.

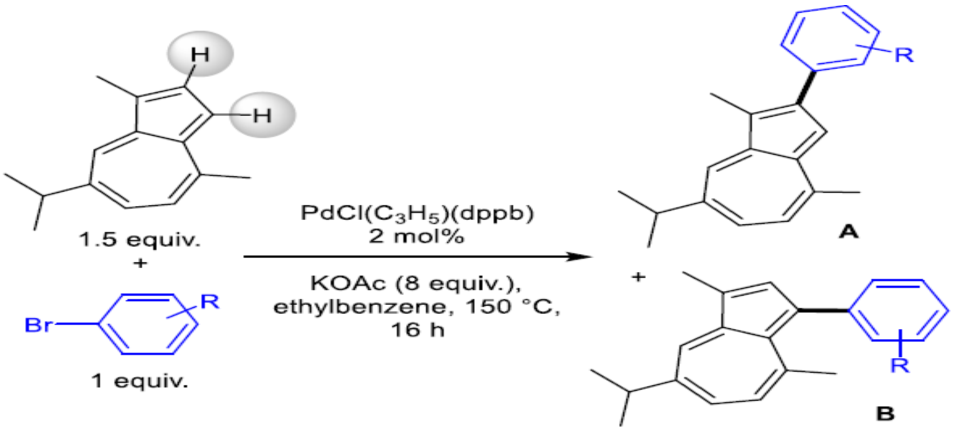


Scheme 1 Synthesis of 2-aminoazulenes by Hartwig-Buchwald reaction.



Scheme 2 Synthesis of 2-chloroazulenes 1 and 2 by Nozoe's procedure.

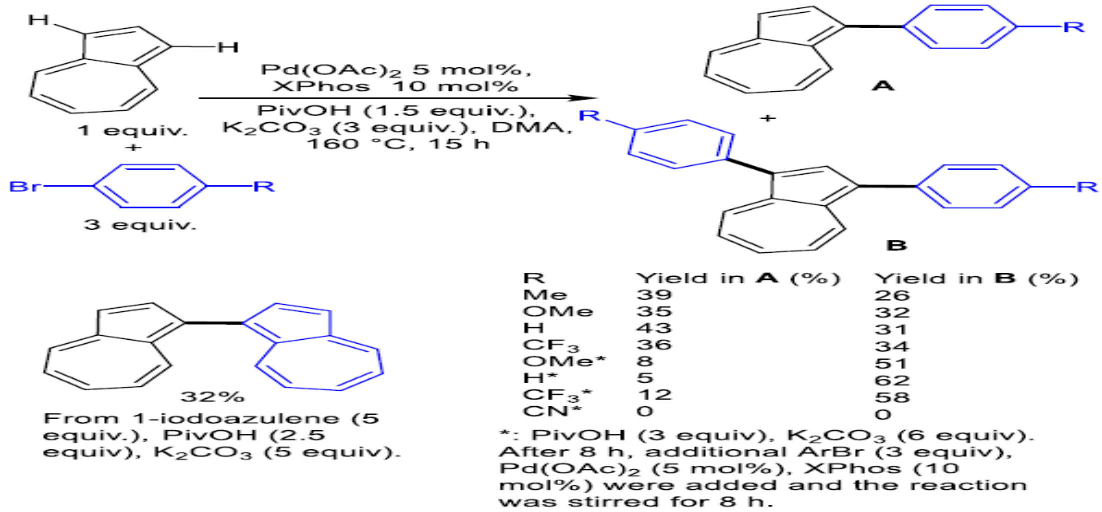
Shoji, T., Sugiyama, S., Araki, T., Ohta, A., Sekiguchi, R., Ito, S., ... & Yasunami, M. (2017). Synthesis of 2-amino- and 2-arylazoazulenes via nucleophilic aromatic substitution of 2-chloroazulenes with amines and arylhydrazines. *Organic & biomolecular chemistry*, *15*(18), 3917-3923.



R	ratio **A**:**B**	Yield of **A** (%)
4-CN	53:47	38
4-CN	15:85	51 of **B***
4-Cl	77:23	53
4-F	77:23	51
4-Me	70:30	56
3-Me	76:24	54
H	75:25	56
3-Me	37:63	38 of **B***

* DMA as the solvent

Scheme 2. Pd-catalyzed arylations C2- or C3- positions of guaiazulene with aryl bromides

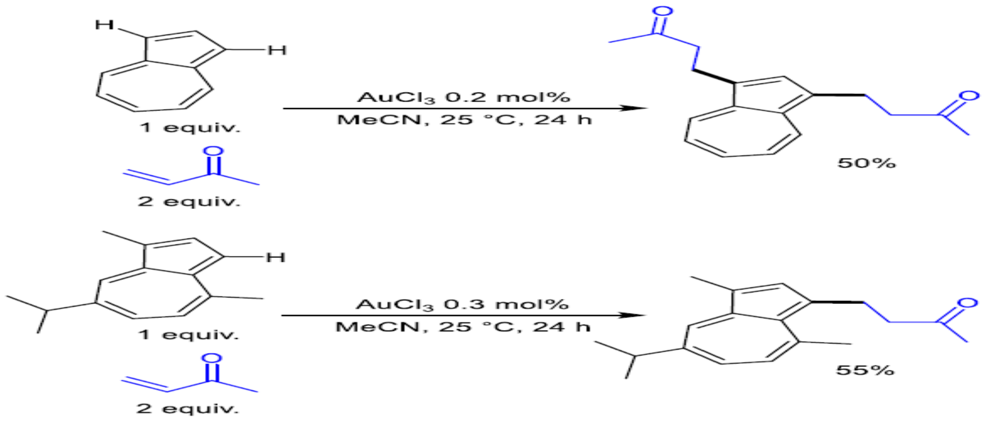


From 1-iodoazulene (5 equiv.), PivOH (2.5 equiv), K$_2$CO$_3$ (5 equiv).

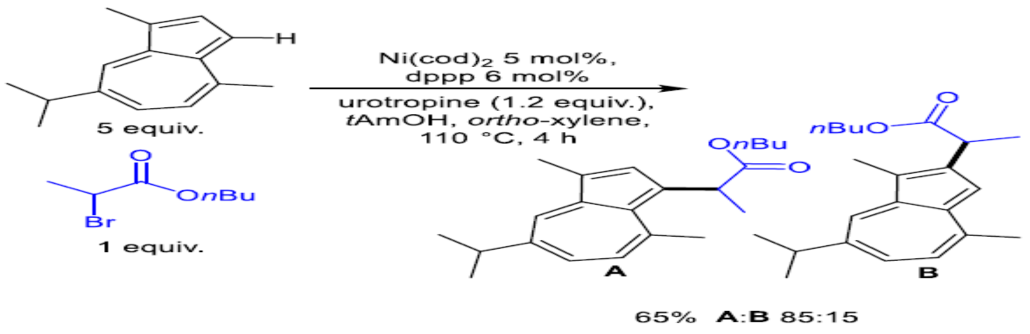
R	Yield in **A** (%)	Yield in **B** (%)
Me	39	26
OMe	35	32
H	43	31
CF$_3$	36	34
OMe*	8	51
H*	5	62
CF$_3$*	12	58
CN*	0	0

*: PivOH (3 equiv), K$_2$CO$_3$ (6 equiv). After 8 h, additional ArBr (3 equiv), Pd(OAc)$_2$ (5 mol%), XPhos (10 mol%) were added and the reaction was stirred for 8 h.

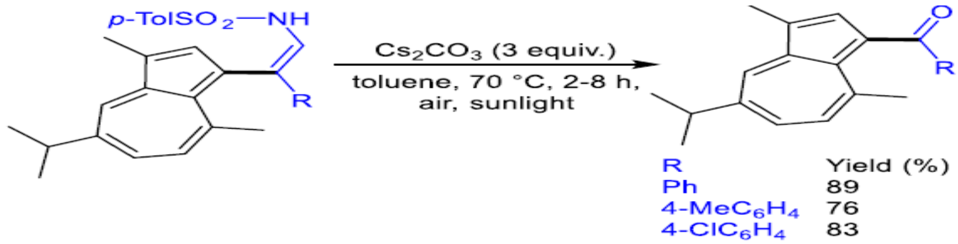
Scheme 4. Pd-catalyzed arylations at C1-position of azulene with aryl bromides



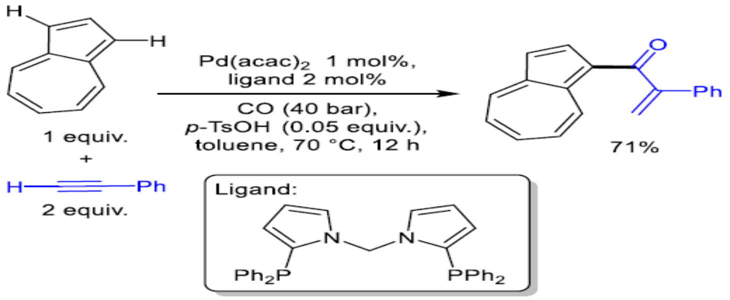
Scheme 7. Au-catalyzed alkylations at C1-position of azulene with methyl vinyl ketone



Scheme 11. Ni-catalyzed alkylation of azulene with a 2-bromopropanoate



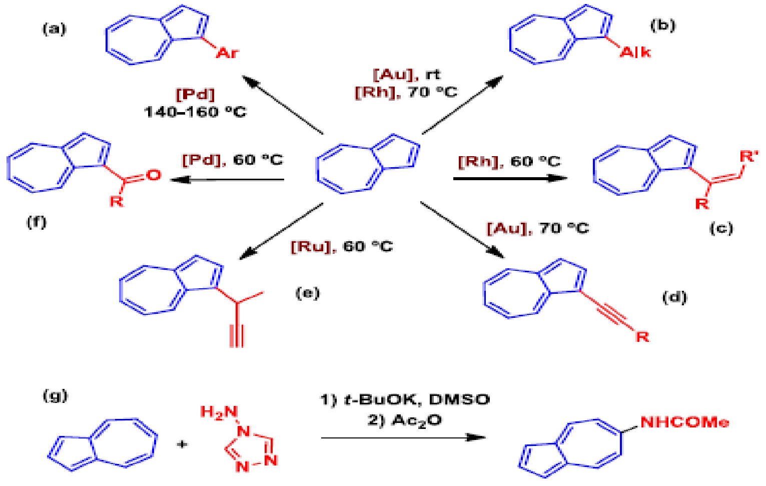
Scheme 13. Rh-catalyzed alkenylations of guaiazulene with *N*-sulfonyl-1,2,3-triazoles



Scheme 17. Pd-catalyzed carbonylation of azulene with phenylacetylene and carbon monoxide

Shi, X., Sasmal, A., Soulé, J. F., & Doucet, H. (2018). Metal-Catalyzed C− H Bond Activation of 5-Membered Carbocyclic Rings: A Powerful Access to Azulene, Acenaphthylene and Fulvene Derivatives. *Chemistry–An Asian Journal*, *13*(2), 143-157.

Scheme 1. Reported metal-catalyzed methods for azulene C-H bond functionalization and C-C bond formation (a-f) and stoichiometric C-N bond generation (g)



Scheme 2. Azulene C-H bond functionalization and C-C and C-N bond formation by carbene or nitrene insertion

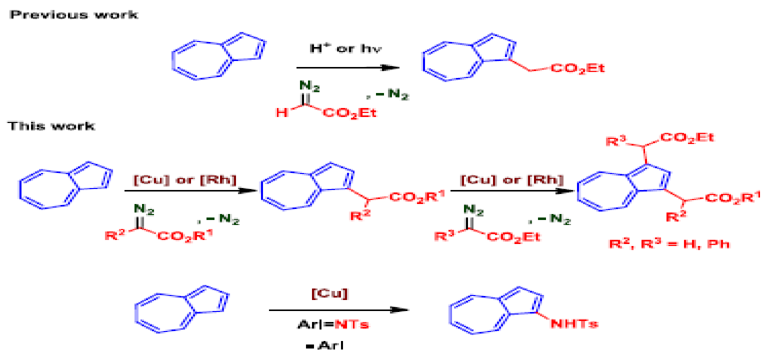
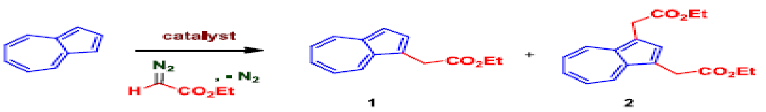


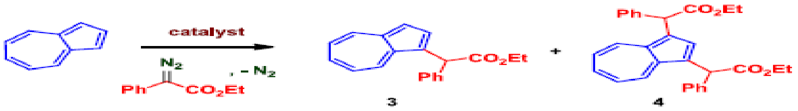
Table 1. Catalytic functionalization of azulene by carbene transfer from ethyl diazoacetate catalyzed by $Tp^{(CF_3)_2,Br}Cu(NCCH_3)$.[a]



entry	cat:EDA:azulene[b]	mmol EDA	1%	2%
1	1:50:100	1.98	37	0
2	1:75:50	0.62	28	6
3	1:120:50	9.4	11	39

[a]Conditions: azulene was dissolved in CH_2Cl_2 along with $Tp^{(CF_3)_2,Br}Cu(NCCH_3)$ and a solution of EDA in the same solvent was added for 14 h with a syringe pump under inert atmosphere. See the Table S1 in the SI for experimental details. [b]Mmol ratio.

Table 2. Catalytic functionalization of azulene with ethyl 2-phenyldiazoacetate.[a]

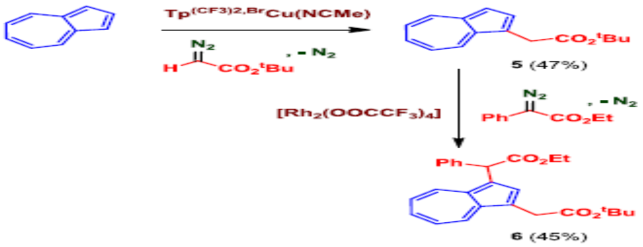


entry	catalyst	cat:PhEDA:azulene[b]	3%	4%
1	$Tp^{(CF_3)_2,Br}Cu(L)$	1:50:100	21	0
2	$Rh_2(OOCCF_3)_4$	1:50:100	40	0
3	$Tp^{(CF_3)_2,Br}Cu(L)$	1:100:50	32	6
4	$Rh_2(OOCCF_3)_4$	1:100:50	0	46

[a]Conditions employed as described Table 1. L = CH_3CN. See Table S2 in the SI for full experimental details. [b]Mmol ratio.

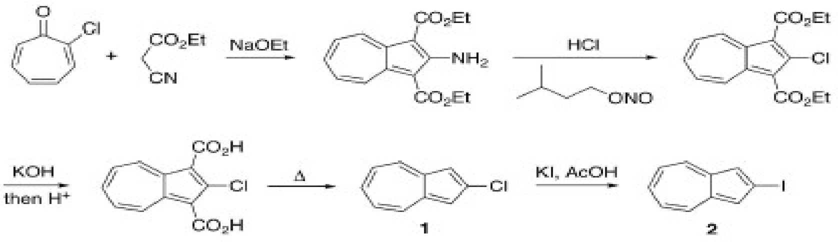
Carreras, J., Popowski, Y., Caballero, A., Amir, E., & Pérez, P. J. (2018). Catalytic Functionalization of C–H Bonds

Scheme 4. Synthesis of asymmetrically disubstituted azulenes.

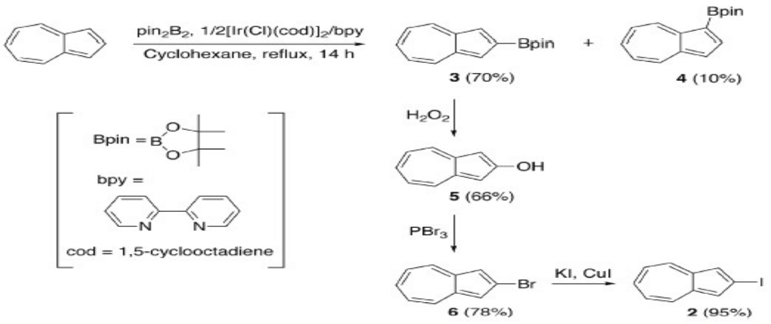


of Azulene by Carbene/Nitrene Incorporation. *The Journal of organic chemistry*, *83*(18), 11125-11132.

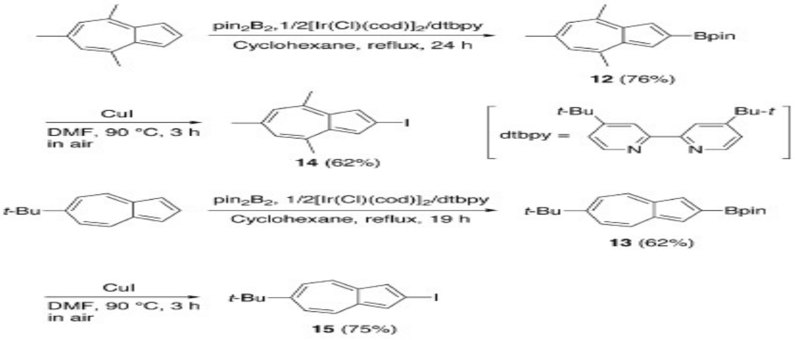
Scheme 1. Traditional Synthetic Route to 2-Haloazulenes



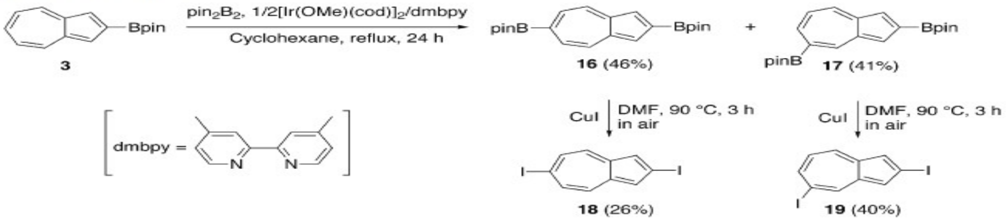
Scheme 2. Synthetic Route to 2-Haloazulenes from Azulene



Scheme 5. Iodination of 12 and 13



Scheme 6. Iodination of 16 and 17

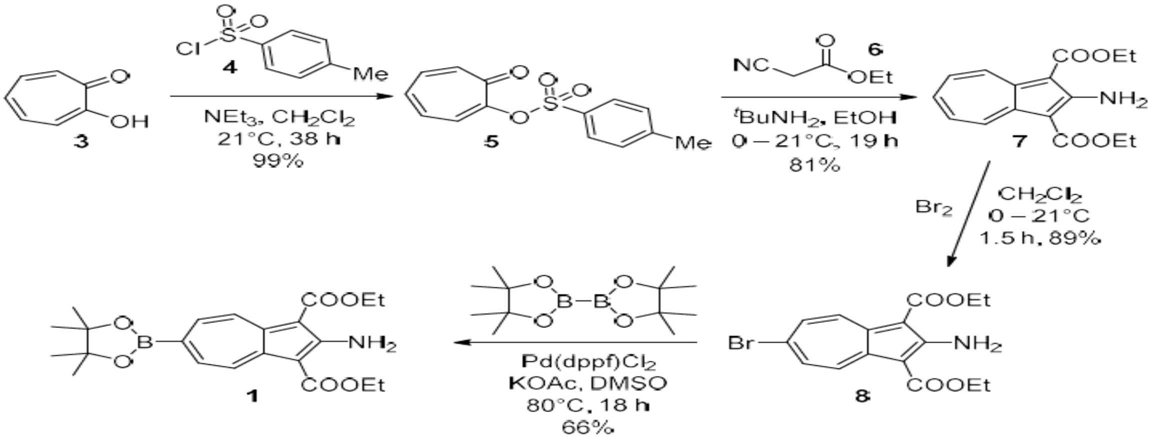


Narita, M., Murafuji, T., Yamashita, S., Fujinaga, M., Hiyama, K., Oka, Y., ... & Ishiguro, K. (2018). Synthesis of 2-iodoazulenes by the iododeboronation of azulen-2-ylboronic acid pinacol esters with copper (I) iodide. *The Journal of organic chemistry*, *83*(3), 1298-1303.

The following thesis have a good reviews worth a look:

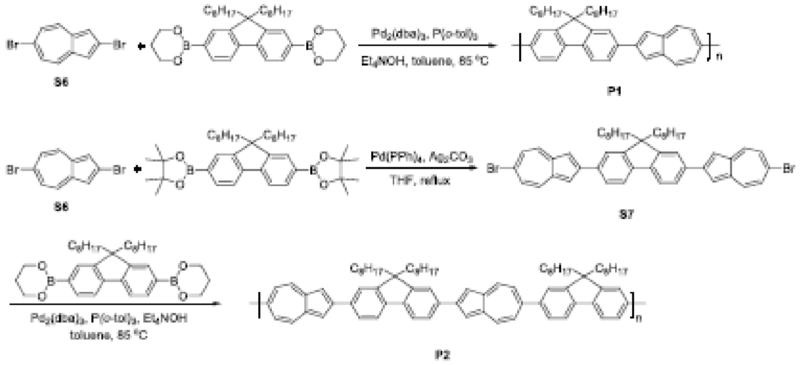
Wells, J. M. (2018).*New Routes to Troponoid Natural Products*(Doctoral dissertation, Curtin University).

Leino, T. (2018). Synthesis of Azulene-Based Compounds for Targeting Orexin Receptors.

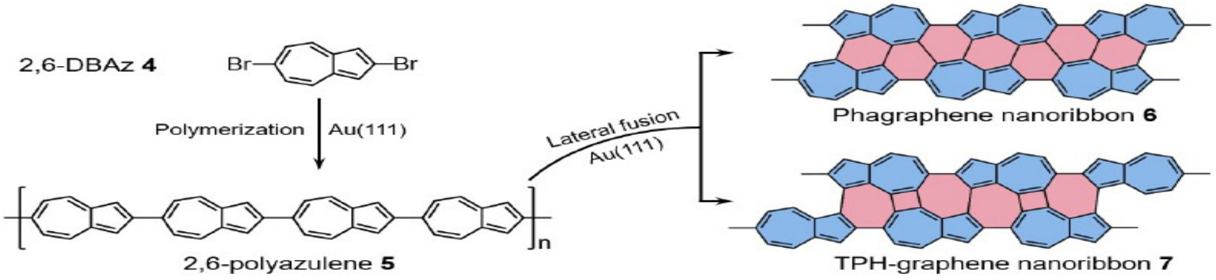


Murfin, L. C., Weber, M., Park, S. J., Kim, W. T., Lopez-Alled, C. M., McMullin, C. L., ... & Bull, S. D. (2019). Azulene-Derived Fluorescent Probe for Bioimaging: Detection of Reactive Oxygen and Nitrogen Species by Two-Photon Microscopy. *Journal of the American Chemical Society*.

Scheme 1. Synthesis of 2,6-Azulene-Based Polymers P1 and P2

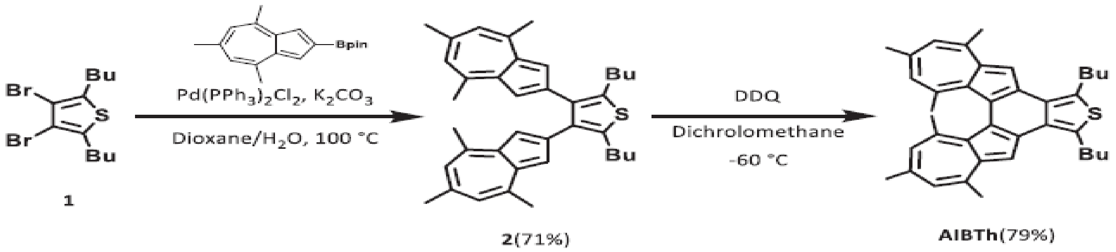


Gao, H., Ge, C., Hou, B., Xin, H., & Gao, X. (2019). Incorporation of 1, 3-free-2, 6-connected azulene units into the backbone of conjugated polymers: Improving proton responsiveness and electrical conductivity. *ACS Macro Letters*, *8*(10), 1360-1364.



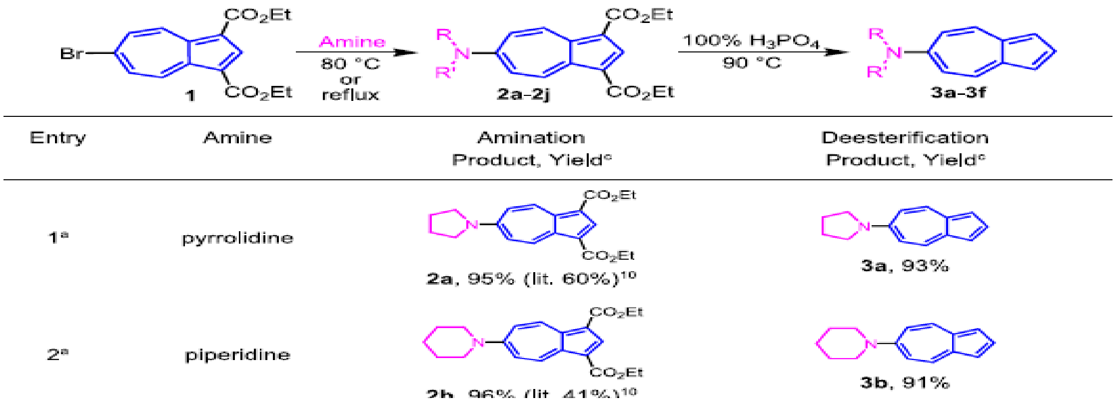
ure 1. Reaction scheme for the synthesis of nanoribbons of non-alternant 2D carbon allotropes. a,

Fan, Q., Martin-Jimenez, D., Ebeling, D., Krug, C. K., Brechmann, L., Kohlmeyer, C., ... & Gottfried, J. M. (2019). Nanoribbons with Nonalternant Topology from Fusion of Polyazulene: Carbon Allotropes beyond Graphene. *Journal* *of the American Chemical Society*, *141*(44), 17713-17720.



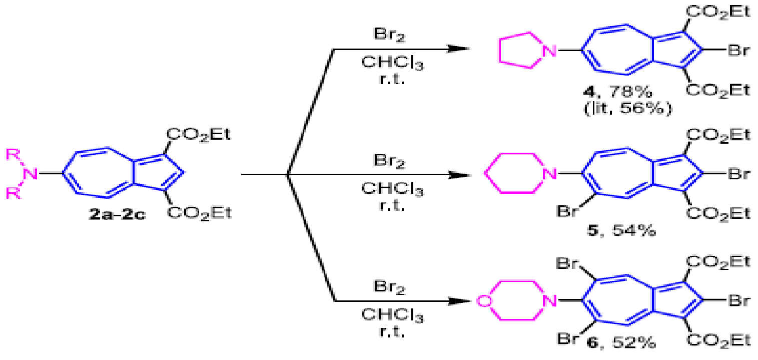
Scheme 1. Synthesis of **AIBTh**.

Narita, M., Teraoka, T., Murafuji, T., Shiota, Y., Yoshizawa, K., Mori, S., ... & Tani, F. (2019). An Azulene-Based Chiral Helicene and Its Air-Stable Cation Radical. *Bulletin of the Chemical Society of Japan*, *92*(11), 1867-1873.

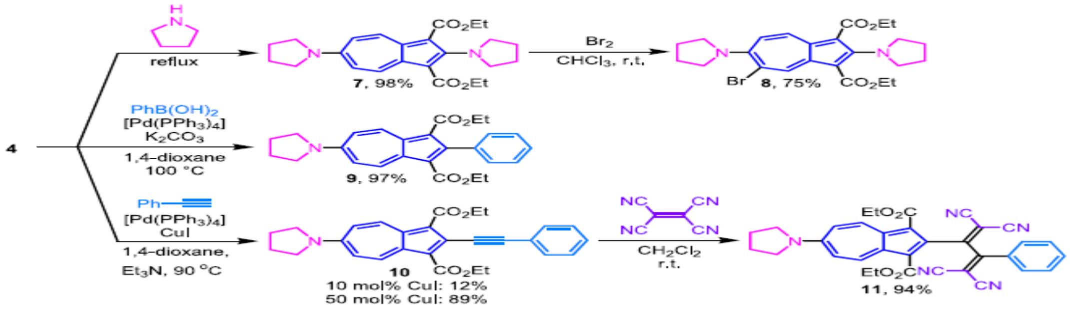


Entry	Amine	Amination Product, Yield^c	Deesterification Product, Yield^c
1^a	pyrrolidine	**2a**, 95% (lit. 60%)^{10}	**3a**, 93%
2^a	piperidine	**2b**, 96% (lit. 41%)^{10}	**3b**, 91%

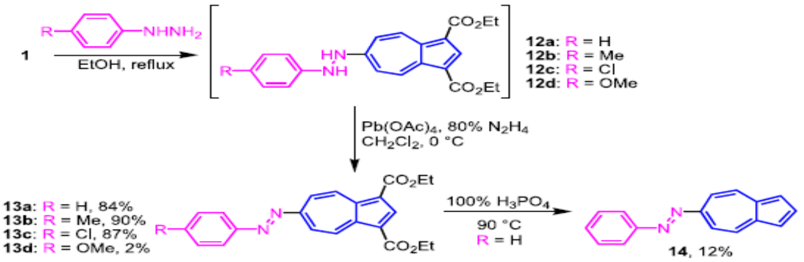
Scheme 1. Synthesis of 6-Amino-2-Bromoazulenes 4−6 by the Bromination of 6-Aminoazulenes 2a−2c



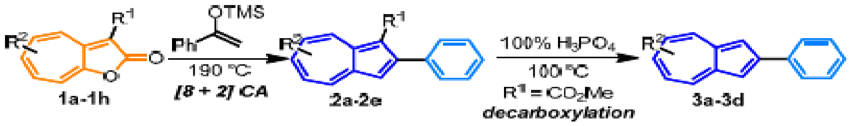
Scheme 2. Molecular Transformation of 2-Bromo-6-Pyrrolidinylazulene 4



Scheme 4. Synthesis of 6-Arylazoazulenes 13a–13d via the S_NAr Reaction of 1 with Arylhydrazines and Conversion to 6-Phenylazoazulene (14)



Shoji, T., Sugiyama, S., Takeuchi, M., Ohta, A., Sekiguchi, R., Ito, S., ... & Yasunami, M. (2019). Synthesis of 6-Amino-and 6-Arylazoazulenes via Nucleophilic Aromatic Substitution and Their Reactivity and Properties. *The Journal of organic chemistry*, *84*(3), 1257-1275.



Entry	Substrate	R¹	R²	[8 + 2] CA Product, Yield [%]ᵇ	decarboxylation Product, Yield [%]ᵇ
1	**1a**	CO_2Me	H	**2a**, 92	**3a**, 95
2	**1b**	CO_2Me	6-*i*-Pr	**2b**, 85	**3b**, 96
3	**1c**	CO_2Me	7-*i*-Pr	**2c**, 84	**3c**, 89
4	**1d**	CO_2Me	6-Me	**2d**, 75	**3d**, 75
5	**1e**	Ph	H	**2e**, 70	–
6	**1f**	H	H	**3a**, 66	–
7	**1g**	H	6-*i*-Pr	**3b**, 63	–
8	**1h**	H	5-*i*-Pr	**3c**, 71	–

[a] 3 equiv. of silyl enol ether was employed. [b] Isolated yield.

Table 2. Reaction of 2*H*-cyclohepta[*b*]furan-2-ones with aryl-substituted silyl enol ethers.

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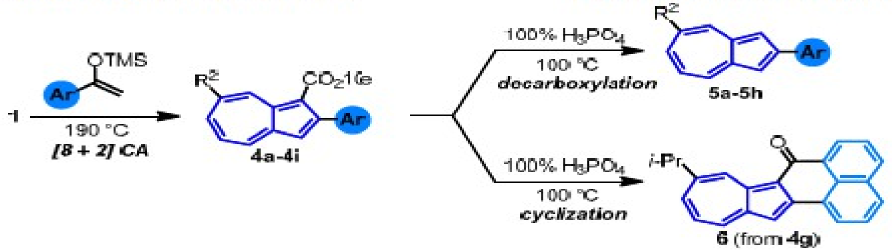
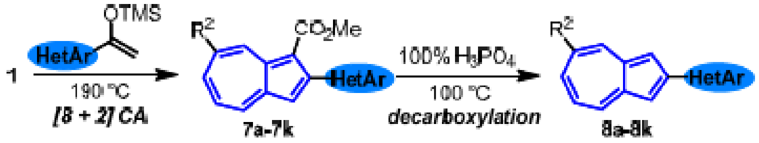


Table 3. Reaction of 2*H*-cyclohepta[*b*]furan-2-ones with heteroaryl-substituted silyl enol ethers.



Shoji, T., Sugiyama, S., Kobayashi, Y., Yamazaki, A., Ariga, Y., Katoh, R., ... & Ito, S. (2020). Direct synthesis of 2-arylazulenes by [8+ 2] cycloaddition of 2H-cyclohepta [b] furan-2-ones with silyl enol ethers. *Chemical Communications*.