Outline

Cathodic Reductions

- Benylic halides
- Unsaturated esters
- Ketones
- Iminiums
- Deoxygenations
- Elimination
- Substitution
- Electrogenerated bases
- Cathodic chain reactions

Anodic oxidations

- Methoxylation of isocyanides
- Oxidative fragmentation of cyclopropanes
- Alkoxylations of ethers
- Oxidative fragmentation
- Non-conjugated alkenes
- Conjugated alkenes
- Enol ethers
- The Shono oxidation
  - Derivatization thereof

Mediated electrolysis

- Alcohol oxidation
- C-H amination
- Amine oxidation to nitriles
- Hoffmann rearrangement

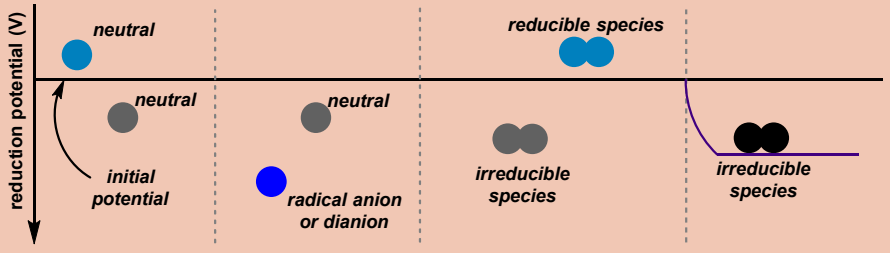
Ph.D with Prof. Ryohei Oda at Kyoto University
Professor at Kyoto University 1963–1992
Professor at Kindai University 1992–1999

As one of the pioneers of organic electrochemistry, it is perplexing – if not completely mind-boggling – that there exists no Wikipedia page for Tatsuya Shono.

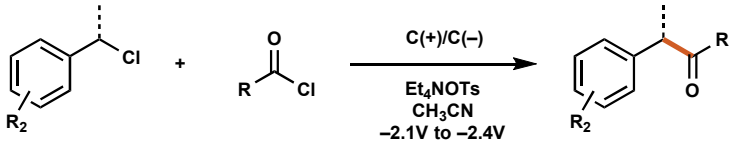
The following topic is not presented in chronological order in an attempt to structure major findings in a systematic manner. The topic is also not an attempt to be comprehensive, but to highlight acheivements in the context of modern organic chemistry

Tatsuya Shono: Cathodic Reductions

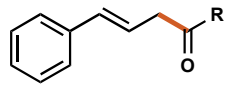
Cathodic reductions overview:

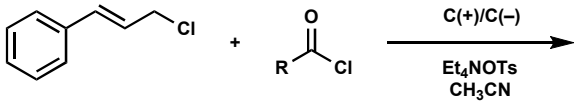


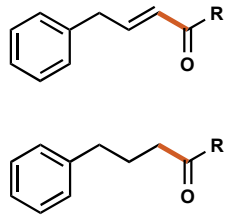
Cathodic reduction of benzylic/allylic halides:



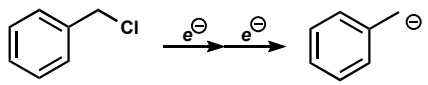
Chem. Lett, **1977**, *1021*





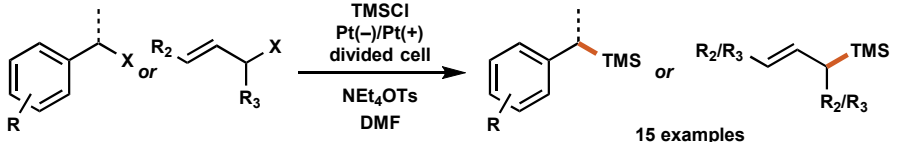


R = Et 65% (1:0.5:0.5)
Pr 50% (1:1:0.6)
*i*Pr 49% (0.6:1:0.6)



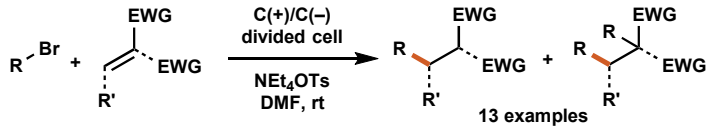
E_{red} < –1.5V
complete recovery of acyl chloride @ –1.5V

productive reactive intermediate

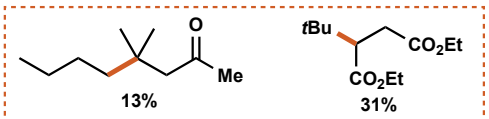


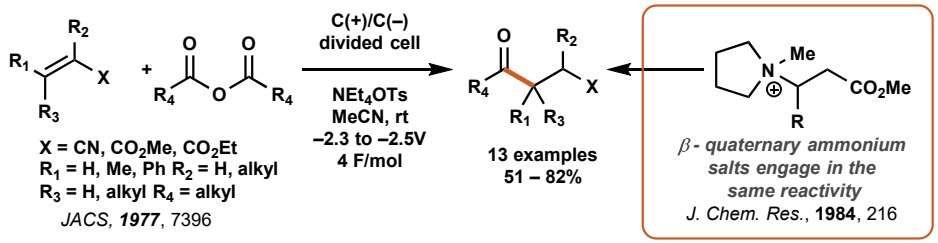
Chem. Lett., **1984**, 463

Cathodic C-C couplings of unsaturated esters/nitriles:



Nippon Kagaku Kaishi, **1972**, 2370

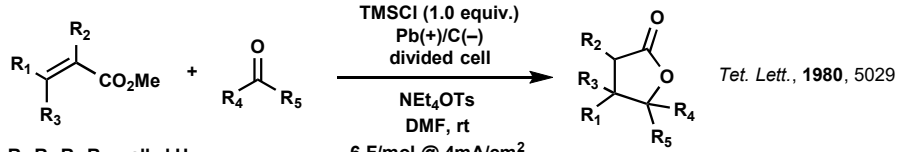




X = CN, CO_2Me, CO_2Et
R_1 = H, Me, Ph R_2 = H, alkyl
R_3 = H, alkyl R_4 = alkyl

JACS, ***1977***, 7396

β - quaternary ammonium salts engage in the same reactivity
J. Chem. Res., **1984**, 216



Tet. Lett., **1980**, 5029

R_1,R_2,R_3,R_4 = alkyl,H
R_5 = alkyl

benzaldehyde benzophenone yield no product

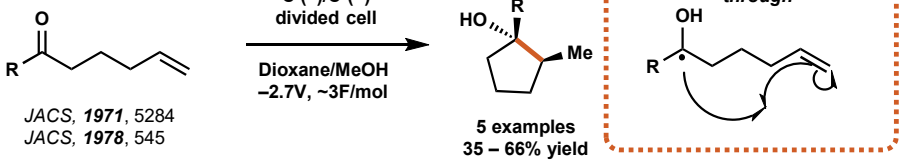
reduction of unsaturated olefin as reactive intermediate

- *role of TMSCl is unclear but critical for reactivity*
- *further studies suggest that TMSCl activates the cathode surface*

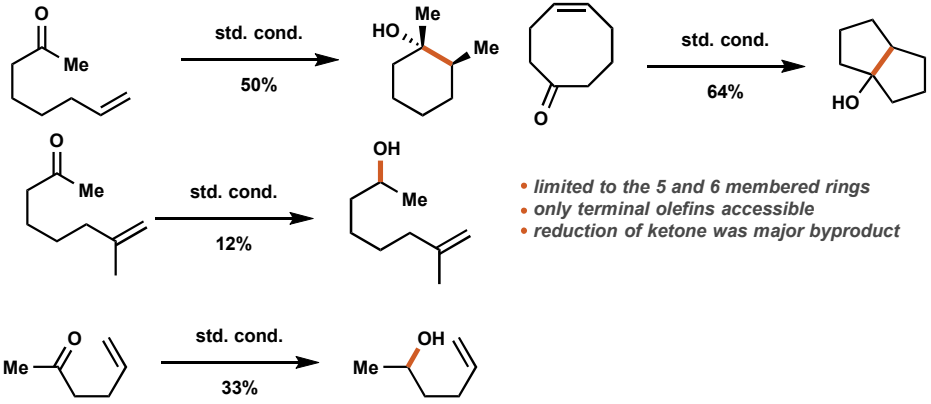
Corey, *Tet. Lett.*, **1983**, 2821

Tatsuya Shono: Cathodic Reductions

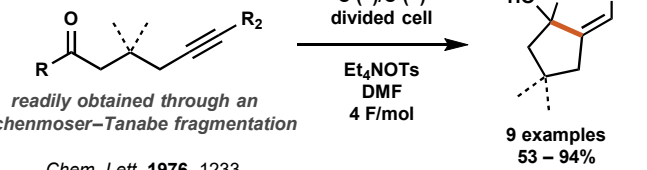
Intramolecular ketyl–olefin couplings:



JACS, ***1971***, 5284
JACS, ***1978***, 545

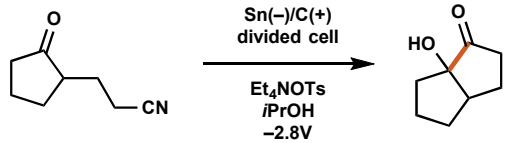


- *limited to the 5 and 6 membered rings*
- *only terminal olefins accessible*
- *reduction of ketone was major byproduct*



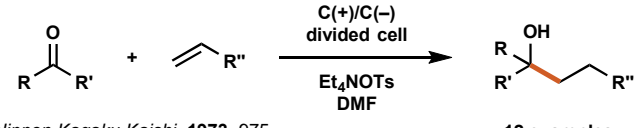
readily obtained through an Eschenmoser–Tanabe fragmentation

Chem. Lett, **1976**, 1233

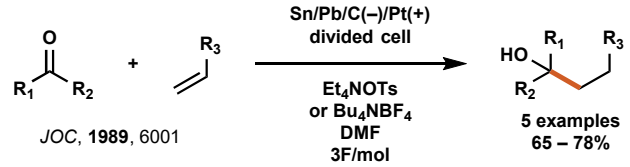


Tet. Lett, **1990**, 1303

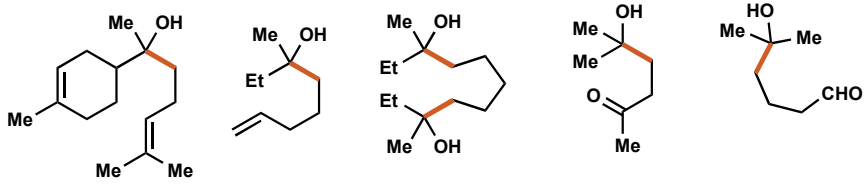
Intermolecular ketyl–olefin couplings:

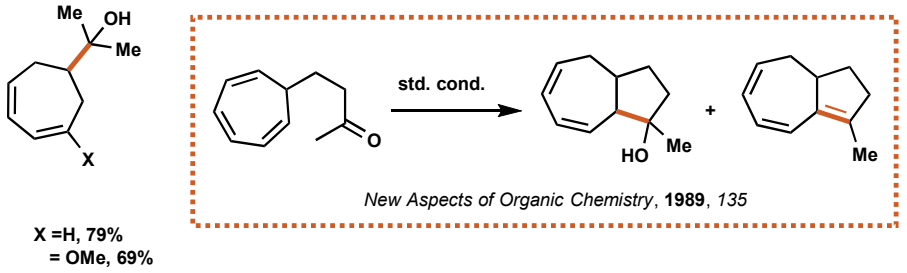


Nippon Kagaku Kaishi, **1973**, 975



JOC, **1989**, 6001



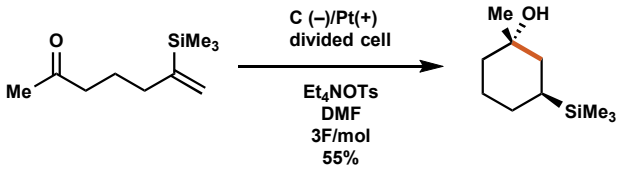


New Aspects of Organic Chemistry, **1989**, *135*

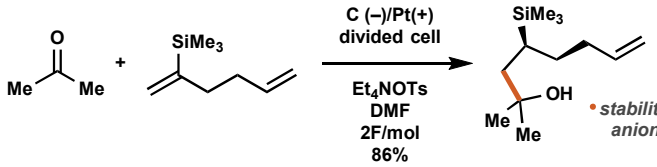
Tet. Lett., **1995**, 5041

- *use of vinylsilanes enables 1,1–disubstituted olefins*

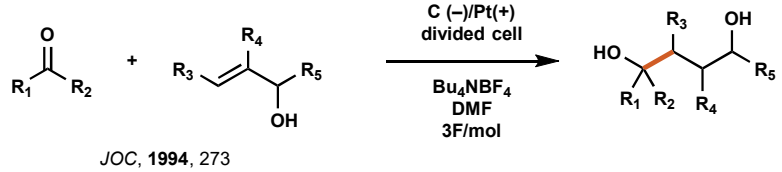
Tatsuya Shono: Cathodic Reductions



- *overrides native intramolecular reactivity*

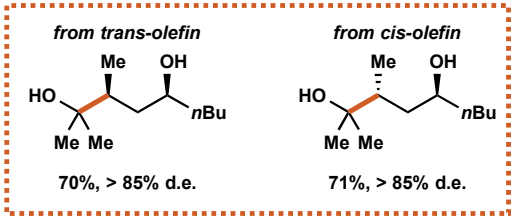


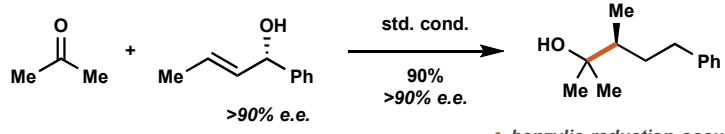
- *stability of intermediate radical and anion lead to a "directing group" effect*



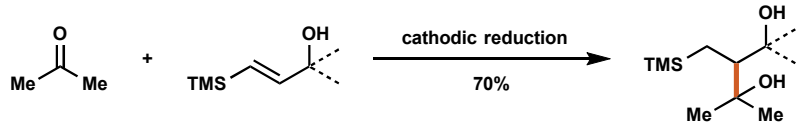
JOC, **1994**, 273

- *allylic alcohols enable internal olefin couplings through a hydrogen bonding effect*
- *chair-type TS rationalizes the high diastereoselectivity from cis and trans olefins*





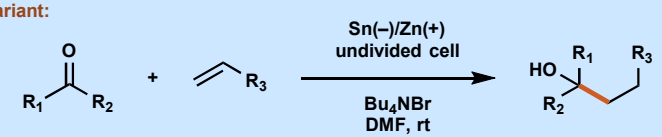
- *benzylic reduction occurs after ketyl-olefin coupling*



Tet. Lett., **1996**, 6737

- *silylallyl alcohols switch selectivity of coupling to the internal position*

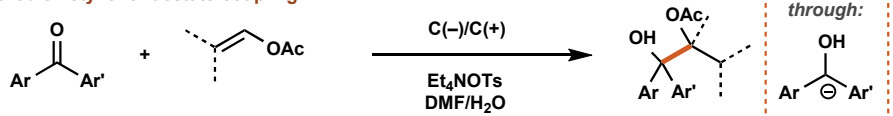
Modern variant:



JACS, **2020**, 20979

>40 examples
synthetically useful yields
high functional group tolerance

Cathodic ketyl-enol acetate coupling:

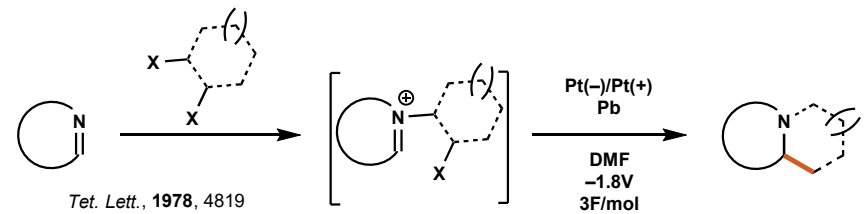


1.0 equiv. 10 equiv

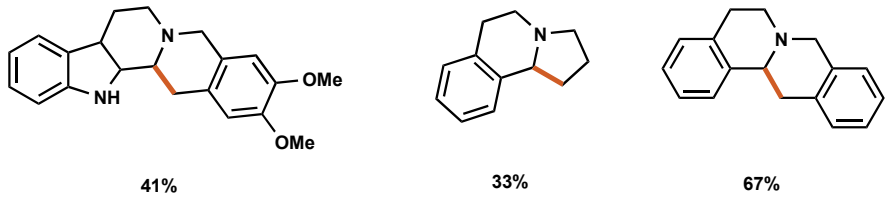
Tet. Lett., **1979**, 4091

11 examples
45 - 76%

Iminium reductive alkylation for alkaloid synthesis:

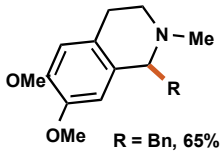


Tet. Lett., **1978**, 4819
Tet. Lett., **1980**, 3073



41% 33% 67%

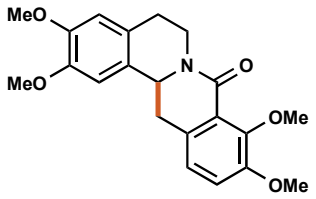
Tatsuya Shono: Cathodic Reductions



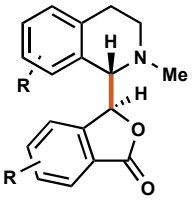
R = Bn, 65%
CH_3, 35%

amenable to intermolecular addition

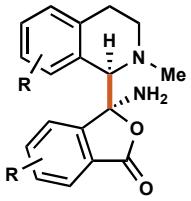
Natural products prepared using this methdology



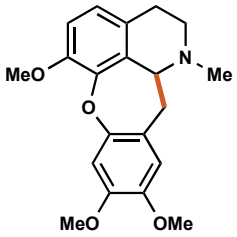
8-oxo-tetrahydropalmatine
Tet. Lett., **1980**, 3073



cordrastine I, dl-noscapine



cordastine II, hydrastine dl-noscapine

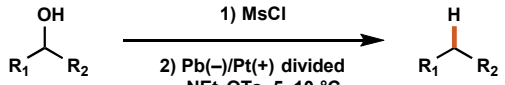


culanine

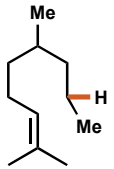
Tet. Lett., **1980**, 1351

Tet. Lett., **1981**, 2385

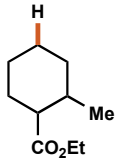
Reductive deoxygenation:



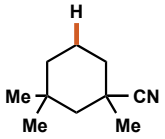
Tet. Lett., **1979**, 2157



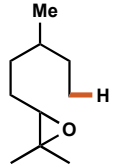
63%



57%



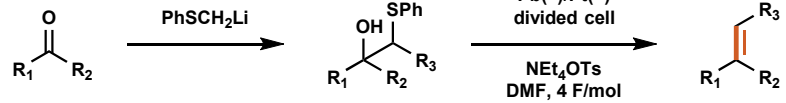
71%



87%

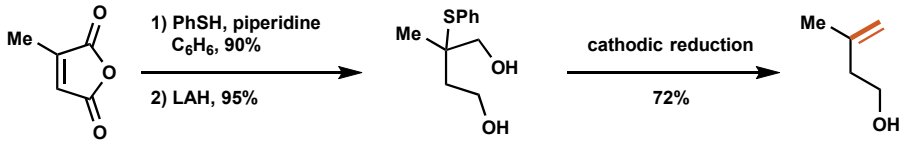
tolerant of hydride-incompatible functionality

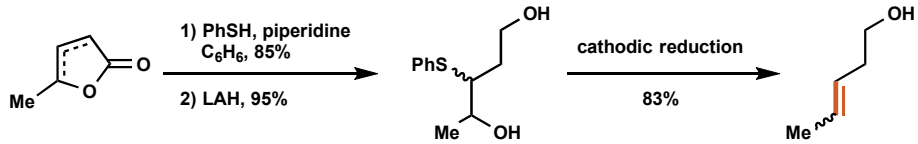
Elimination:

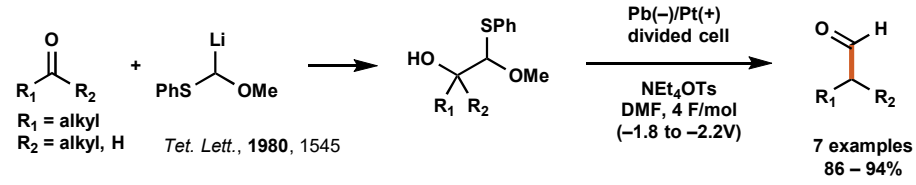


Tet. Lett., **1978**, 2807

8 examples
37–71% over two steps





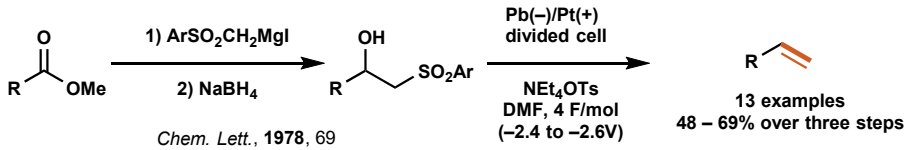


R_1 = alkyl
R_2 = alkyl, H

Tet. Lett., **1980**, 1545

7 examples
86 – 94%

formal homologation of ketones and aldehydes



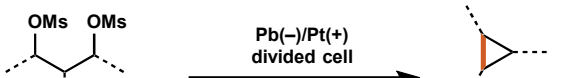
Chem. Lett., **1978**, 69

13 examples
48 – 69% over three steps

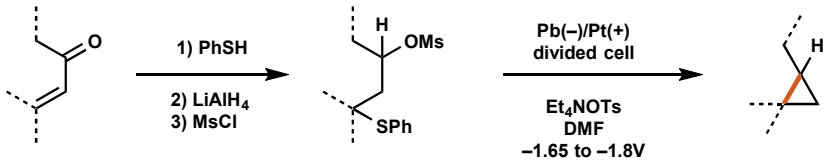
formal olefination of esters

Tatsuya Shono: Cathodic Reductions

Cylopropanes through reductive intramolecular substitution:

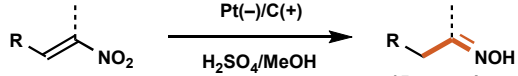


JOC, **1981**, 3090



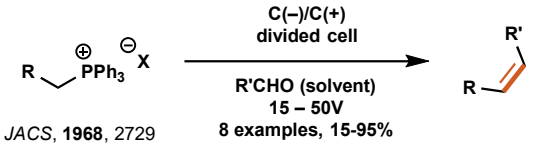
Tet. Lett., **1978**, 1205

Reduction of nitroalkenes to oximes:

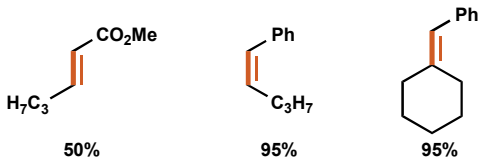


JOC, **1983**, 2103

Electrogenerated bases:

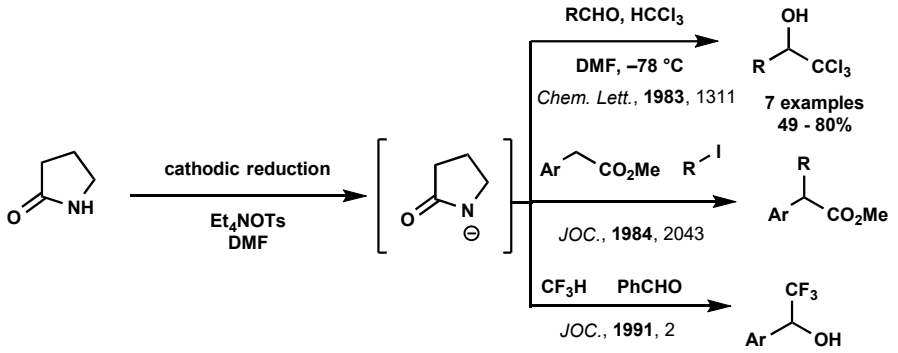


JACS, **1968**, 2729



Electrochemically generated bases bias proximity to the cathode to provide (in some cases) reactivity that diverges significantly from traditional methods

The electrochemical wittig is not one of these cases

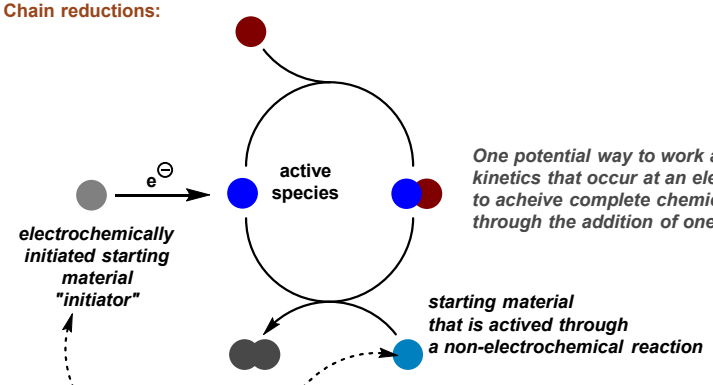


Chem. Lett., **1983**, 1311

JOC., **1984**, 2043

JOC., **1991**, 2

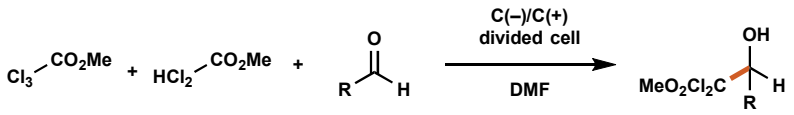
Chain reductions:



One potential way to work around the slow kinetics that occur at an electrode surface is to acheive complete chemical conversion through the addition of one theoretical electron

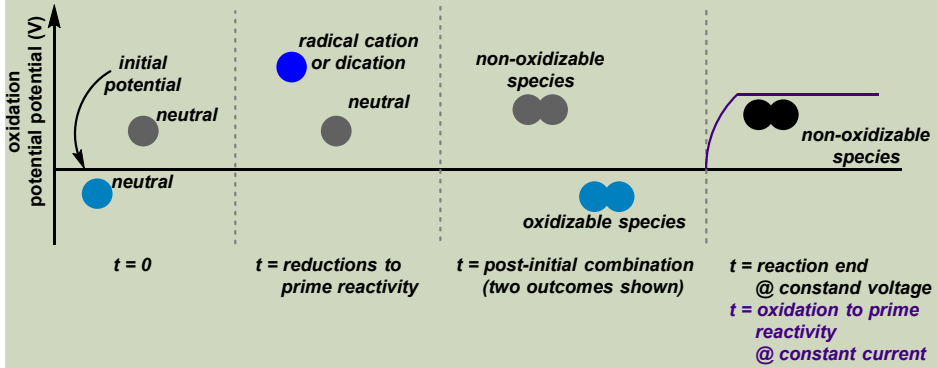
JOC, **1985**, 2527

up to 732% current efficency

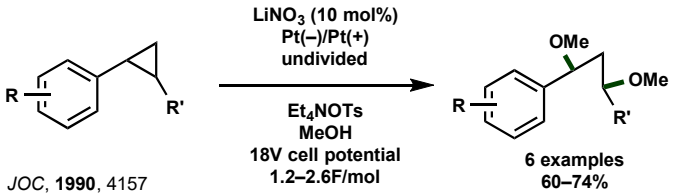


Tatsuya Shono: Anodic Oxidations

Anodic oxidation overview:



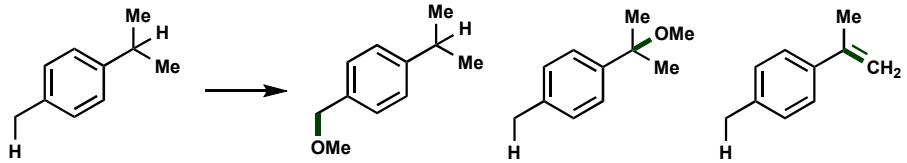
Oxidative fragmentation of cyclopropanes:



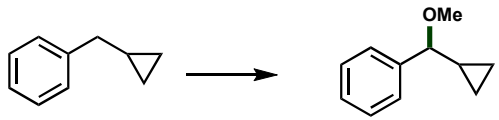
JOC, **1990**, 4157

6 examples
60–74%

- *oxidation is initiated at the aromatic ring*
- *supported by Hammet studies*

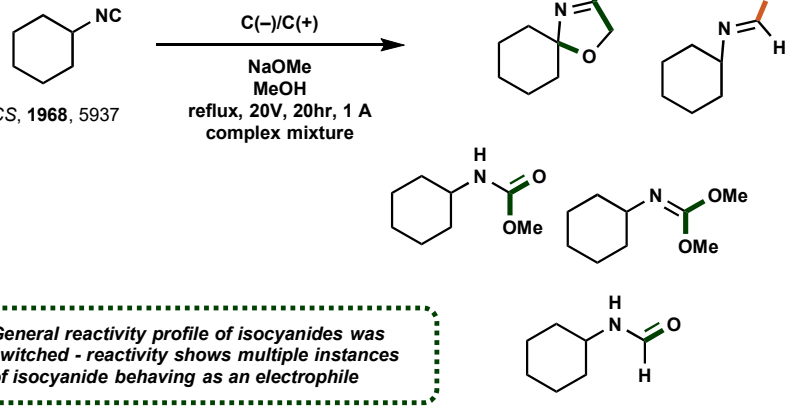


14% 10% 19%



25%

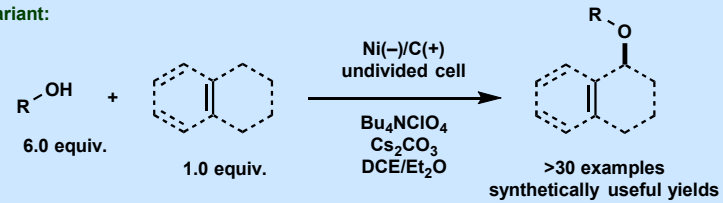
Methoxylation of isocyanide:



JACS, **1968**, 5937

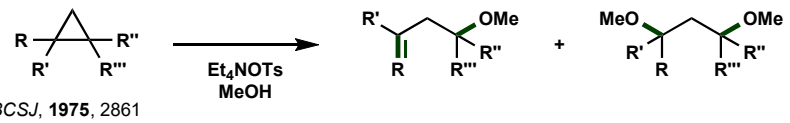
General reactivity profile of isocyanides was switched - reactivity shows multiple instances of isocyanide behaving as an electrophile

Modern variant:



Sci. Adv., **2020**, eaaz0590

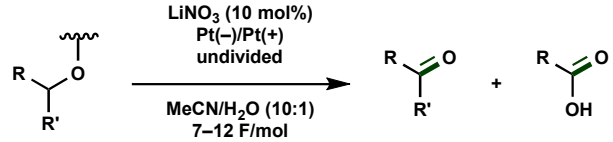
Tatsuya Shono: Anodic Oxidations



BCSJ, **1975**, 2861

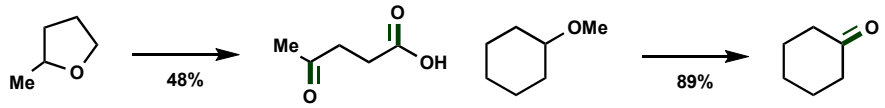
5 examples
6 - 71%

- *each methyl group decreases oxidation potential by around 0.3V*
- *reaction is initiated through electron donation to anode (solvent most likely not involved)*

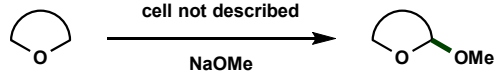


Chem. Lett., **1994**, 1045

9 examples
48–92% yield



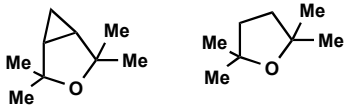
Alkoxylation of cyclic ethers:



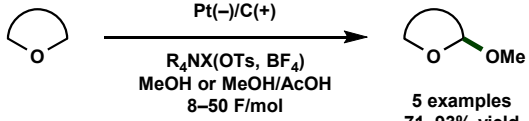
JACS, **1969**, 2803

7 examples
3.9–28% yield

Initial mechanistic investigation:

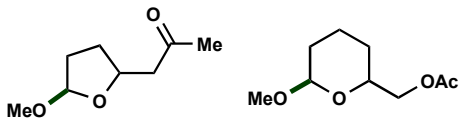


recovered starting material in both cases suggests radical abstraction by electrolyte is the operative mechansim



Synthesis, **1987**, 1099

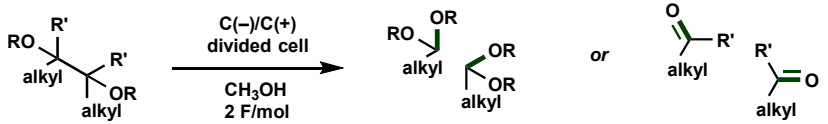
5 examples
71–93% yield



77% (3:1 r.r.)

93% (3.6:1 r.r.)

Oxidative C–C fragmentation



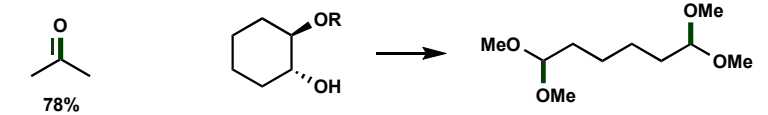
R = H, alkyl
R' = H, alkyl

R' = H
aldehyde oxidation state - mixture of products

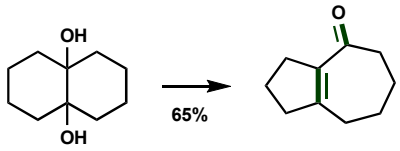
R' = alkyl
ketone or dimethyl acetal

JACS, **1975**, 2546

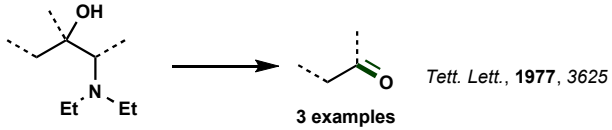
13 examples
47–96%



R= H, 65%
R= Me, 54%
***from cyclohexene-oxide:* 52%**

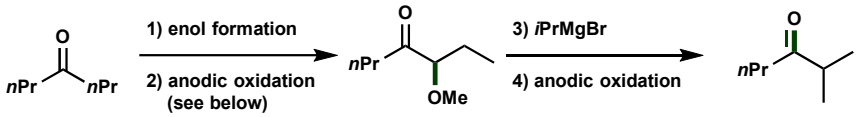


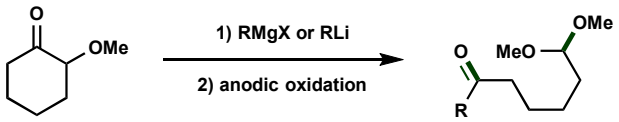
Tatsuya Shono: Anodic Oxidations



3 examples
52–72%

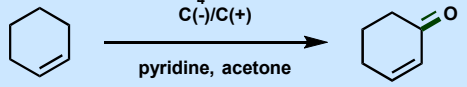
Tett. Lett., **1977**, *3625*





R = Me step 1: 61% step 2: 75%
*n*Bu step 1: 73% step 2: 72%
CH_2CN step 1: 50% step 2: 40%
CH_2CO_2Et step 1: 60% step 2: 44%

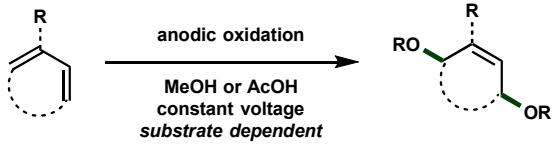
Modern variant:



Nature, **2016**, 77

40 examples
15 natural products
excellent scope and yields

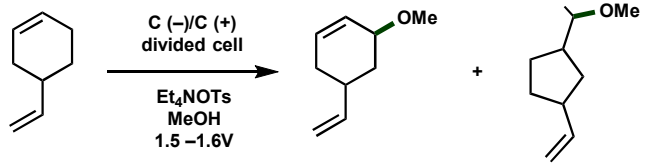
Oxidation of conjugated dienes:



Chem. Lett., **1976**, 311

7 examples
18.6–50.6%

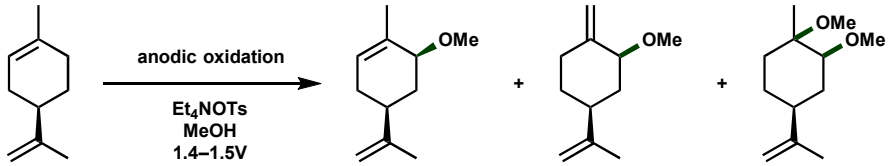
Oxidation of non-conjugated dienes:



JACS, **1972**, 7893
JACS, **1975**, 4261

32.2%

21.3%

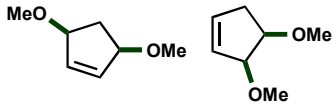


27% (3:1 d.r.)

15.7%

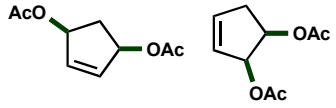
15.7%

From 1,3–cyclopentadiene



50.6%

6.1%



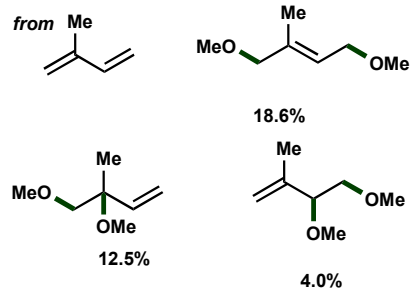
45%

6%

From 1,3–cyclohexadiene

47.2%

11.8%

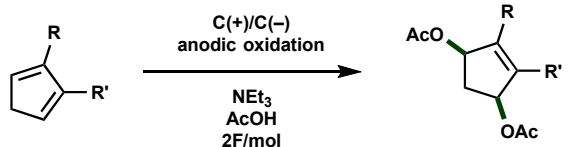


18.6%

12.5%

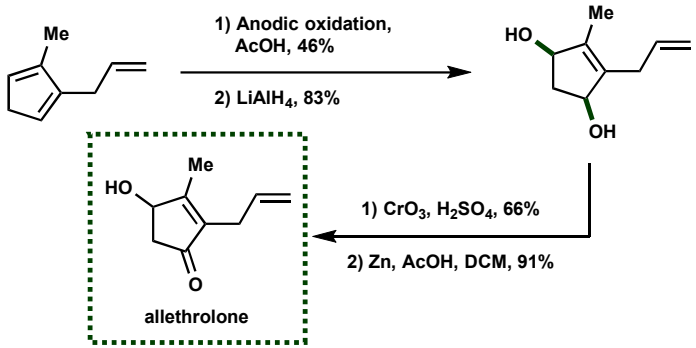
4.0%

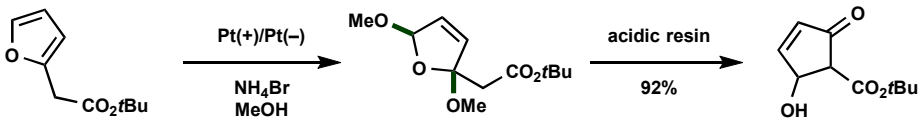
Tatsuya Shono: Anodic Oxidations



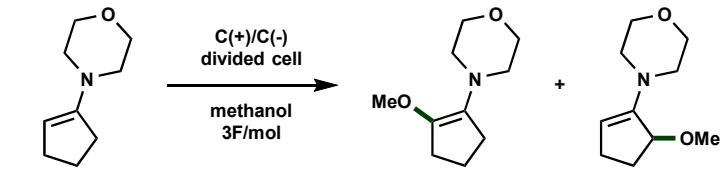
Chem. Lett., **1976**, 574

7 examples
43–61%
1:1 d.r. in all cases



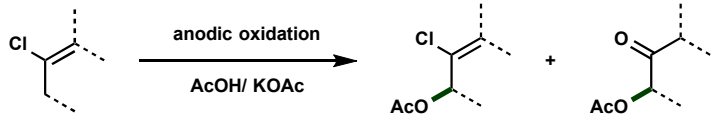


Oxidation of enamines:



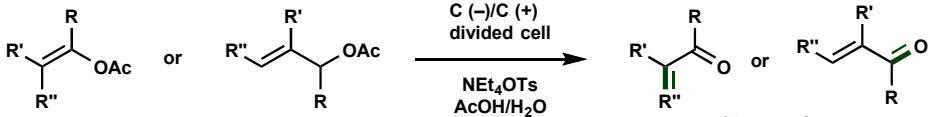
BCSJ, **1978**, 2179

Oxidation of enol ethers:



BCSJ, **1978**, 2179

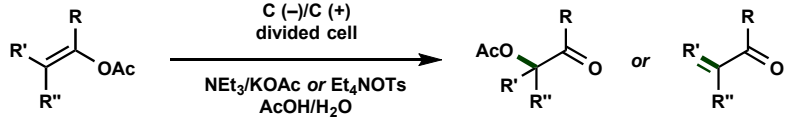
reactions proceed through an allylic cation that is trapped with solvent



JACS, **1973**, 3532

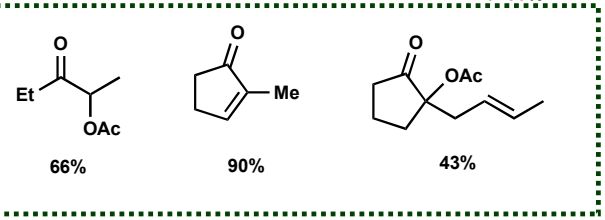
14 examples
8–73% yield

- ***Using Et_4NOTs unsaturated enones are obtained, but KOAc or NEt_3 yielded α–hydroxy ketones***
- ***Some substrates have an insurmountable bias for one or the other***



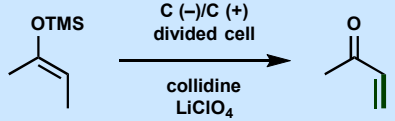
JACS, **1975**, 3532

9 examples
29–90%



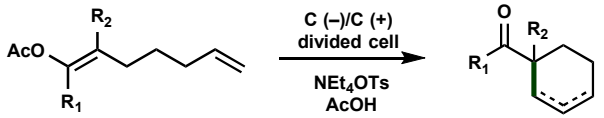
Tatsuya Shono: Anodic Oxidations

Modern variant:

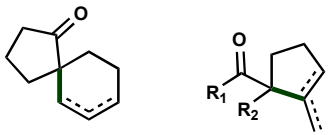


Nat. Chem., **2021**, 367

Oxidative cyclization of enol acetates:



6 examples
18–40%



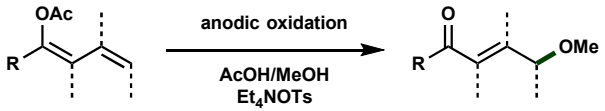
25%

not observed

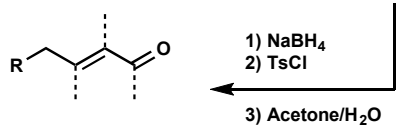
suggests electrophilic attack of the nucleophile of the cationic carbon of the radical cation intermediate

For the eventual utilization of reactions of this type in methods development and synthesis see my MOTW on anodic olefin couplings

1,4–transposition of unsaturated carbonyls:

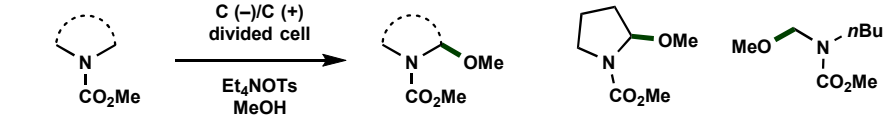


JOC, **1983**, 1983



6 examples
19 – 72% over 4 steps

The Shono oxidation:



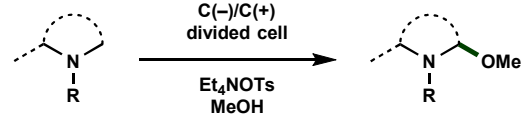
JACS, **1975**, 4264

12 examples
18–78%

65%

53%

carbamate oxidation at anode initiates the reaction process



R = Ts, $PO(OEt)_2$

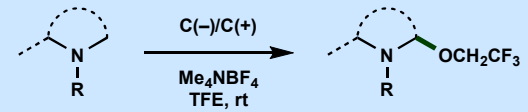
3.5–10.5 F/mol

11 examples
47–98%

oxidation is not limited to carbmates

JOC, **1984**, 3711

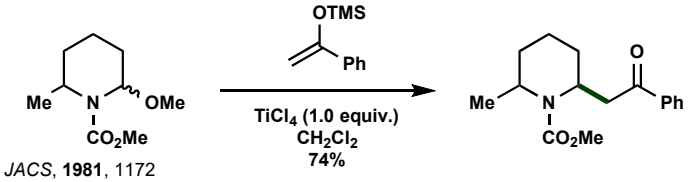
Modern variant:



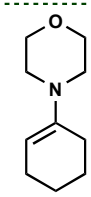
R = SO_2Ar, CO_2R'

JACS, **2022**, 1187

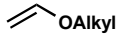
Product derivatization through C-C bond formation:

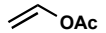


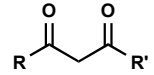
JACS, **1981**, 1172



- *intermolecular nucleophiles demonstrated here*
- *current scope is expanded far beyond this report*

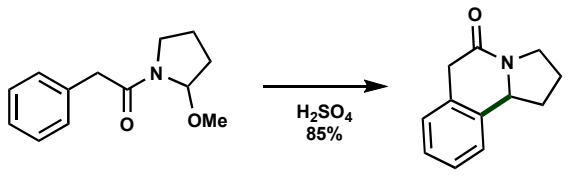




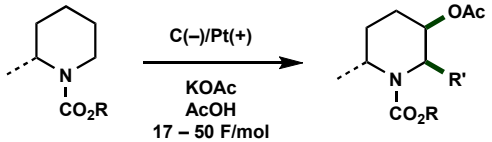


R,R' = Me, OMe

Tatsuya Shono: Anodic Oxidations



Bischler-Napieralski type cyclization



R = Me, Ph, CH_2Ph

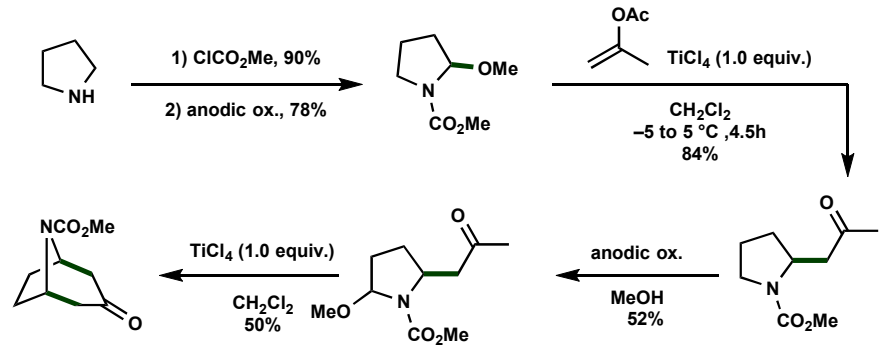
R' = OAc, OH

8 examples

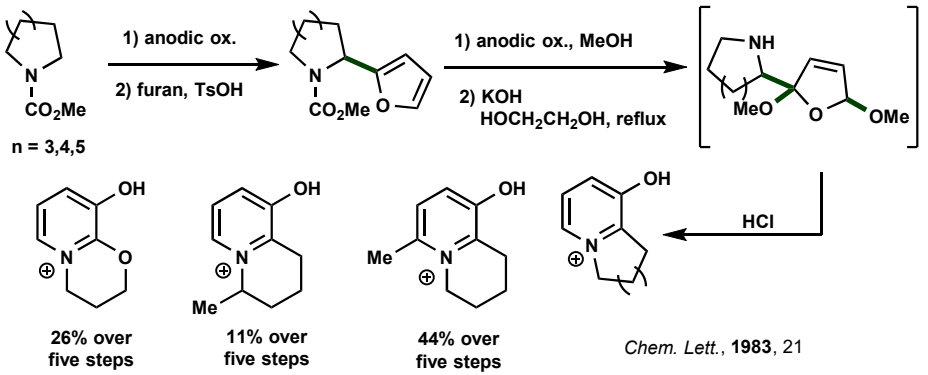
65 – 93%

generally only amenable for piperidines
oxidation - elimination - oxidation protocol is more general

Chem. Lett., **1984**, 1101



tropane alkaloid skeleton



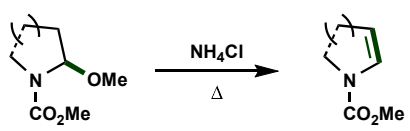
26% over five steps

11% over five steps

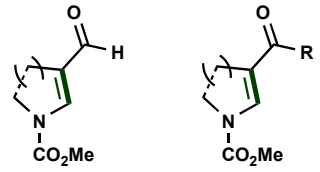
44% over five steps

Chem. Lett., **1983**, 21

products were used to prepare quinolizidines and indolizidines

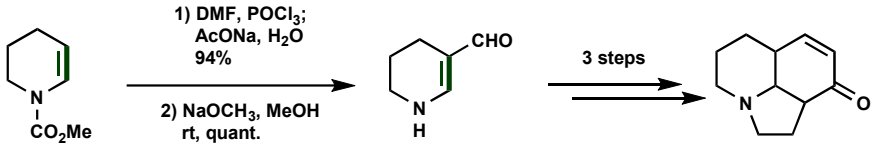


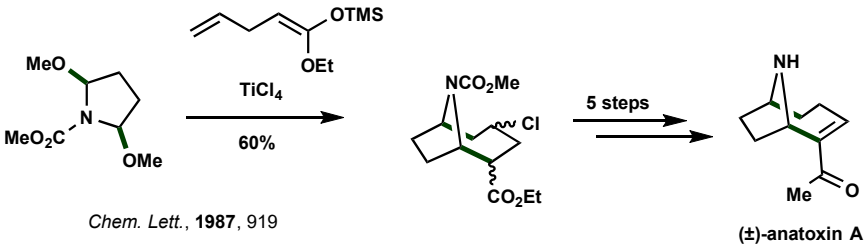
Tett. Lett., **1982**, 1201



through Vilsmeyer formylation

through Friedal-Crafts with acyl chloride and $SnCl_4$



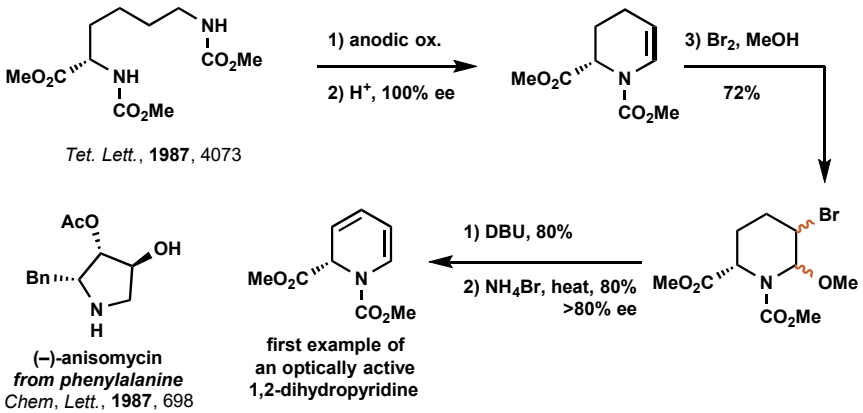


Chem. Lett., **1987**, 919

(±)-anatoxin A

Tatsuya Shono: Anodic Oxidations/Electron Mediators

Chiral pool synthesis of 1,2-dihydropyridines:

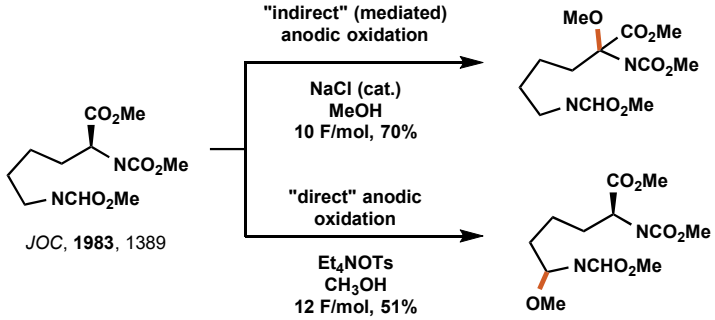


Tet. Lett., **1987**, 4073

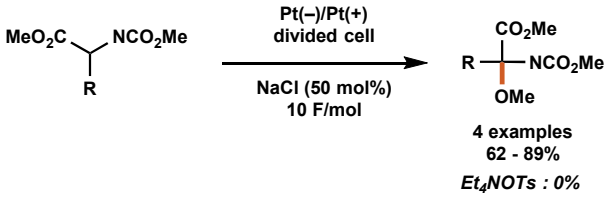
(–)-anisomycin
from phenylalanine
Chem, Lett., **1987**, 698

first example of
an optically active
1,2-dihydropyridine

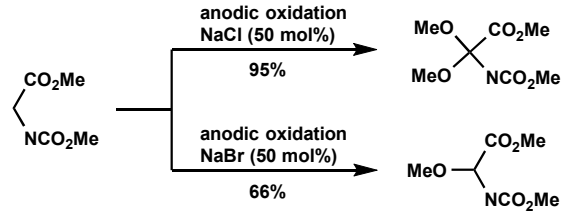
An introduction to electron mediators:

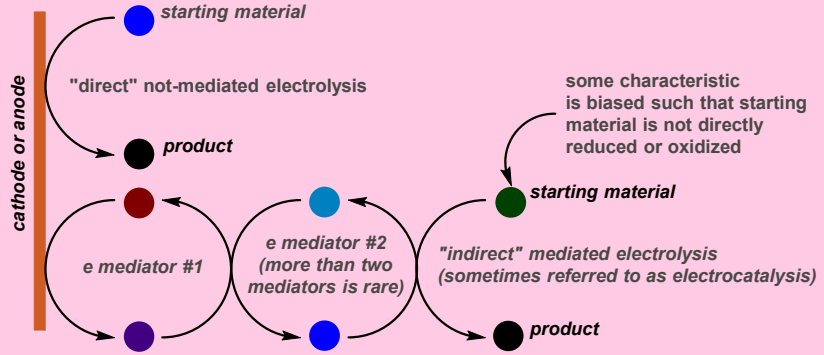


JOC, **1983**, 1389



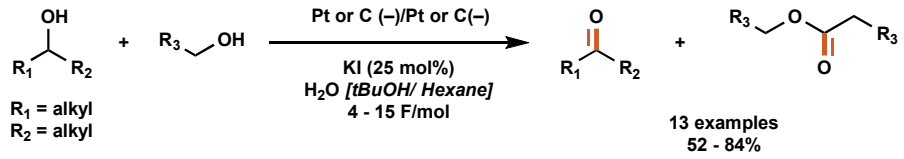
4 examples
62 - 89%
Et4NOTs : 0%





feature is commonly biased in the modern literature to expand scope, couple to other thermodynamic processes (light, heat), and enable catalysis

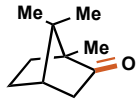
Oxidation of alcohols:



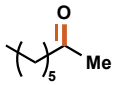
R_1 = alkyl
R_2 = alkyl

13 examples
52 - 84%

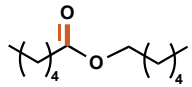
Tet. Lett., **1978**, 165



84%



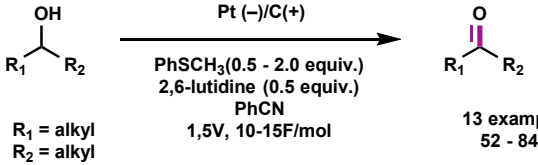
KI (10 mol%)
84%



KI (10 mol%)
83%

Iodonium acts as an electron shuttle from electrode to alcohol

Tatsuya Shono: Electron Mediators



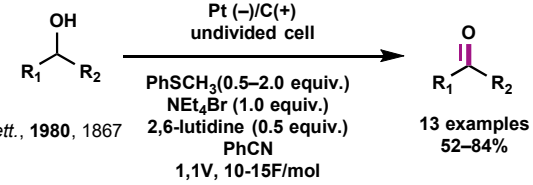
R_1 = alkyl
R_2 = alkyl

13 examples
52 - 84%

Tet. Lett., **1979**, 3861

reaction occurs below the ox. potential of alcohols

A double mediatory system:

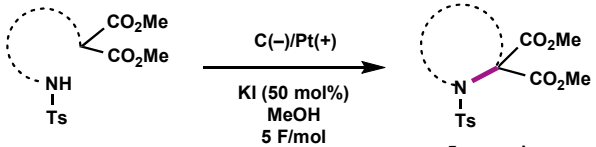


Tet. Lett., **1980**, 1867

13 examples
52–84%

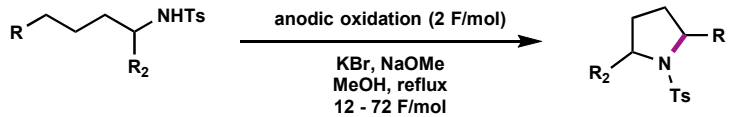
reaction occurs below the ox. potential of thioanisole!

Anodic C–N bond formation:



Chem. Lett., **1988**, 1065

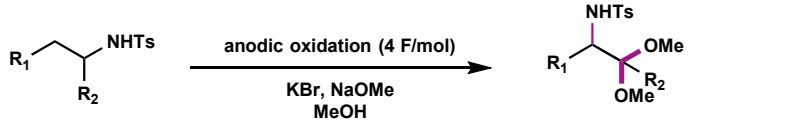
5 examples
46 - 100%



JACS, **1990**, 2368

6 examples
52 - 100%

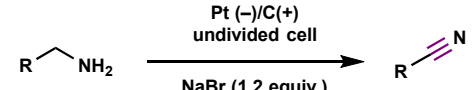
Anodic amine migration:



R_1 = H (59%), Me (61%) ,Et (61%)
R_2 = H

JACS, **1990**, 2368

Anodic amine dehydrogenation to nitriles:



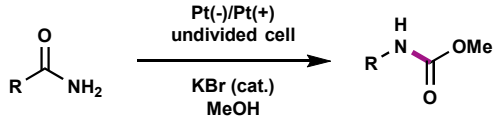
R = alkyl, benzyl aryl

9 examples
60 – 81%

JACS, **1984**, 6075

R = *n*hept LiBr: 73%
KBr: 76%
Et_4NBr: 95%
KI: 28%
NaCl: 26%
Et_4NOTs: not observed

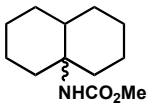
Anodic Hoffman rearrangment:



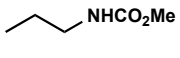
R_1 = alkyl
R_2 = alkyl

Chem. Lett., **1982**, 567

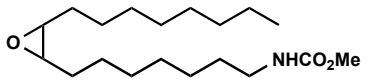
catalytic amount of bromine used (stoichiometric in traditional cases)
KOMe generated is used to trap the isocynate - reaction remains pH netural
also one of the first examples of paired electrolysis



76%



70%



77%

traditional conditions (not described): complex mixtures