Jan-Erling Bäckvall was born in Malung, Sweden, in 1947. He received his PhD from the Royal Institute of Technology, Stockholm, in 1975 under the guidance of Prof. B. Åkerman. After postdoctoral work (1975-1976) with Prof. K. B. Sharpless at Massachusetts Institute of Technology, he joined the faculty at the Royal Institute of Technology (Kungliga Tekniska högskolan). He was appointed Professor of Organic Chemistry at Uppsala University in 1986. In 1997 he moved to Stockholm University where he is currently Professor of Organic Chemistry. He is a member of the Royal Swedish Academy of Sciences and the Finnish Academy of Science and Letters. His current research interests include transition-metal-catalyzed organic transformations, biomimetic oxidations, and enzyme chemistry.

over 330 papers, h-index: 53
ed. of Modern Oxidation Methods (Wiley 2004)

The Essential Backvall
1,2-difunctionalization of alkenes
1,4-difunctionalization of 1,3-diienes
hydrogen transfer
dynamic kinetic resolution
multistep electron transfer
(prep and use of sulfonyl-1,3-diienes)
(copper catalysis)

Backvall's key experiment for elucidating Wacker mechanism:

high [CuCl2] & [LiCl] to get oxidative cleavage (instead of β-elim); since CuCl2 cleavage of Pd-C proceeds with inversion, preceding hydroxypalladation must have been trans

"NuX-Pd-ation" of alkenediene:

\( \begin{align*}
\text{NuX-Pd-ation} & \quad \text{NuX} \quad \text{displacement} \quad \text{overall result} \\
A: \quad \text{trans} & \quad \text{inversion} \quad \text{cis-1,2 or 1,3} \\
\quad \text{trans} & \quad \text{retention} \quad \text{trans-1,2 or 1,3} \\
B: \quad \text{cis} & \quad \text{inversion} \quad \text{trans-1,2 or 1,3} \\
\quad \text{cis} & \quad \text{retention} \quad \text{cis-1,2 or 1,3}
\end{align*} \)

Stereoselectivity in each step from SM to Pdt

transmetallation -- generally with retention
R-Hg to R-Pd (ACSCC 1975)
R-Pd to R-Pb (TL 1975)
Pd(II) complexes with alkenes, 1,3-diienes
Cl, N, O, and stabilized C nucleophiles: external attack (trans "NuX-Pd-ation")

oxidative cleavage of Pd-C sigma bonds
-- generally with inversion: e.g. S_2 displacement by Cl
-- however, retention is possible: e.g. anchimeric assistance of Ph

Illustration of (a) cis-arylpaaladation and (b) anchimeric assistance during oxidative cleavage (giving unusual retention): overall result is cis-1,2

Illustration of (a) cis-arylpaaladation and (b) anchimeric assistance during oxidative cleavage (giving unusual retention): overall result is cis-1,2

p-NO_2Ph gave usual inversion product

a few examples of 1,2-difunctionalization (note azidine emerges from bromoamine)
of course, pre-existing functionality also influences stereochemical outcome:

other types of carbon nucleophiles can be employed, and, if conditions are appropriately tuned, b-hydride elimination can occur:

not surprisingly, tethered heteroatom nucleophiles also work:

**Scheme 1.** Palladium-catalyzed intramolecular 1,4-oxidations
A: no LiCl; B: cat. LiCl; C: 2 equiv. LiCl

Synthesis challenge: In one step, convert butadiene to N-benzoylpyrrole. Go!
Dynamic Kinetic Resolution (DKR) = racemization coupled with KR
KR: max yield 50%; but DKR: max yield 100%
1997: Backvall reported "combo catalysis" (Ru complex & lipase)
Ru -> fast racemization, lipase-compatible
DSM Fine Chemicals produces enantiopure alcohols on ton scale via DKR

Iod donors:
p-CIC6H4OAc for DKR of alcohols; isopropenyl acetate may be used if H₂ source is incorporated
dibenzylo carbamate for DKR of amines

Racemization catalysts:
Shv'o Ru catalyst is a superior racemization catalyst; no need for external base
dissociates into Ru-I16e and Ru-16e, the latter acting as base
Backvall recently introduced new Ru catalysts, enabling DKR of 2° alcohols at RT (fastest to date)

Lipases:
CALB for 2° alcohols, diols, β-OH azides, β-OH nitriles, 1° & 2° amines, α- or β-OH phosphonates
PS-C for 2° α- or β- or γ- or β-OH esters, β-halo alcohols, allylic alcohols

It is now possible to access (R) or (S) enantiomer (choose your lipase!):

here, CALB is used to enhance ee from >95% to >99% via hydrolysis of undesired enantiomer
Catalytic oxidation using environmentally benign terminal oxidants (O₂, H₂O₂) is greatly facilitated by incorporation of electron transfer mediators into a catalytic system. Why?

Direct oxidation of catalyst by O₂ or H₂O₂ is generally not efficient/practical. Squeezing in additional ETMs makes e- transfer from catalyst to O₂/H₂O₂ more kinetically favorable. This translates to enhancements in rate, selectivity, and practicality for oxidation of organic substrates.

For a diene/Pd/quinone/MLnO₂ prototypical “triple-catalytic” system, there are ten (4!) thermodynamically favored redox reactions; however, due to specific interactions, only four are kinetically favored:
- O₂ coord to MLn
- MLn coord to HQ
- BQ coord to Pd(II)
- Pd(II) coord to diene

Bäckvall's chloride-free Wacker process:

(amide and sulfoxides are great ligands for Pd(II), and are compatible with oxidative conditions)

asymmetric induction is possible!

Chiral Banzquinone Ligand:

Hybrid HQ/Co(II)porphyrin accelerates electron transfer between Pd and O₂

modified Co(II)porphyrin → BQ not needed!
Jan-Erling Bäckvall

**Baran Group Meeting**

- **Hybrid HQ/cobalt Schiff base:**
  - Same principle as the hybrid HQ/Cosporphyrin
  - \( \rightarrow \) improve rate of electron transfer

- **"Biomimetic" aerobic oxidation of alcohols** (entire "catalyst soup" in PhMe at 100°C):

- \( \text{also works for amine dehydrogenation, and can be coupled with organocatalytic asymmetric Mannich} \)

- **Modified flavin (robust, efficient)**

- **Chemoselective sulfoxidation:**
  - \( \text{10 (1.8 mol %), H}_2\text{O}_2 (1.5 equiv)} \)
  - \( \text{MeOH, rt, 2.5 - 3 h} \)

- **Significant improvement upon original Upjohn procedure:**

  - Can be asymmetric with Sharpless ligand
  - Can use MTO or VO(acac)_2 instead of flavin

- **A mild prep for NMO:**
  - \( \text{10 (1 mol %), H}_2\text{O}_2 (1.1 equiv)} \)
  - \( \text{MeOH, rt, 8 h} \)
**Baran Group Meeting**

**Jan-Erling Bäckvall**

**Jonathan Lockner**

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**Scheme 1:**

1. **8 steps**
   - **11** → COOH
   - **8** → Paeonilactone A

2. **11 → 12a:**
   - R=PhCO

3. **11 → 12b:**
   - R=H

4. **7 → 13:**
   - Oxidation
   - Ref. 4a

5. **13 → 14:**
   - Paeonilactone A

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**Scheme 2:**

1. **4 → 5:**
   - **b**

2. **5 → 6:**
   - R=Ac

3. **5 → 8:**
   - R=H

4. **4 → 9:**
   - **c**

5. **9 → 10:**
   - TBS

6. **10 → 11:**
   - **b**

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*Reagents and conditions:*

(a) Pd(OAc)$_2$ (cat.), $p$-benzoquinone, PhCO$_2$H, acetone, 70%;
(b) MeOH, K$_2$CO$_3$, 95%;
(c) PPh$_3$, DEAD, $\alpha$-ClC$_6$H$_4$CO$_2$H, 80%;
(d) 2.2 equiv of LDA; (e) Mel, THF, 82%.

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**Note:**

- **Bn = CH$_2$Ph, TBS = SiMe$_3$Bu.**
- Reagents and conditions: (a) Pd(OAc)$_2$, LiOAc, LiCl, benzoquinone, acetone/Ac$_2$OH, 72%; (b) n-Bu$_3$MgBr, CuCN, Et$_3$O, 0 °C, 89%; (c) K$_2$CO$_3$, MeOH/H$_2$O, 98%; (d) TBD, imidazole, DMF, 0 °C to room temperature, 92%; (e) Na, NH$_4$I, -78 °C, 98%; (f) TsCl, pyridine, -20 to 0 °C, 98%; (g) BnNH$_2$, Naf, DMSO, room temperature, 87%; (h) $t$-Bu$_2$N$^-$, CH$_2$Cl$_2$/H$_2$O, 68-74%; (i) H$_2$, Pd(OH)$_2$/C, MeOH; H$^+/$/H$_2$O, 68%.

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**Notes:**

- **8 steps**
  - (thus, a formal TS by Bäckvall)

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*Reagents and conditions:*

(a) $m$-CPBA, CH$_2$Cl$_2$, -6 °C, 70%; (b) NH$_4$I, LiClO$_4$, CH$_3$CN, 78%; (c) Bu$_3$SnH, PhH, rtx, 97%.