

Assigning the Absolute Configuration of Laurenrüstich-4-ol

The Synthesis

Seminar talk presented by
Kai Feuer

September 17th, 2021

Institute of Organic Chemistry
Justus-Liebig University Giessen



PRIOSS

Prinzipien oberflächengestützter Synthesestrategien

Principles of on-surface synthesis

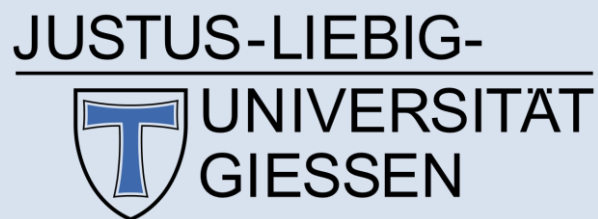


LOEWE

Exzellente Forschung für
Hessens Zukunft



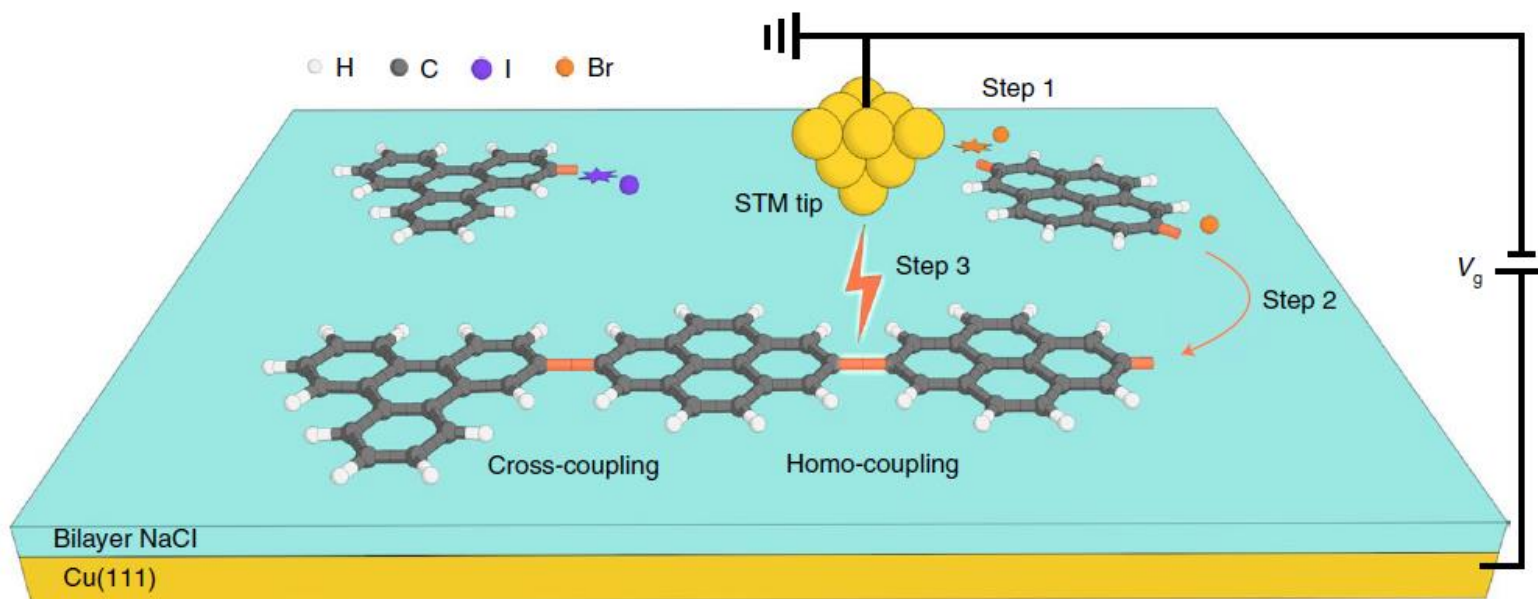
„The objective of the LOEWE focus group is to develop fundamental strategies of on-surface synthesis and to provide a toolset for this new method.“



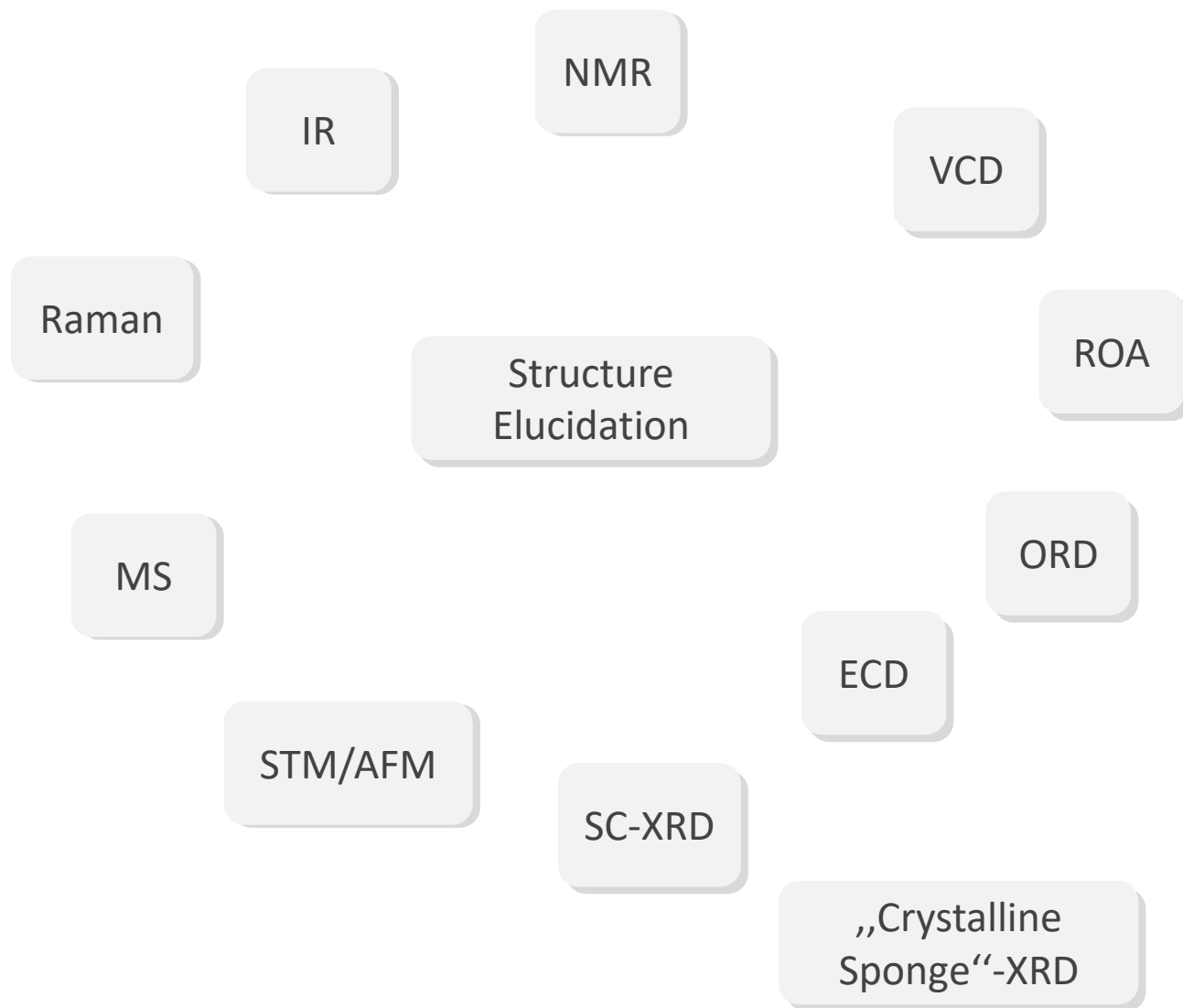


Constructing covalent organic nanoarchitectures molecule by molecule via scanning probe manipulation

Qigang Zhong^{1,2}✉, Alexander Ihle^{1,2}, Sebastian Ahles^{2,3}, Hermann A. Wegner^{2,3},
Andre Schirmeisen^{1,2}✉ and Daniel Ebeling^{1,2}✉

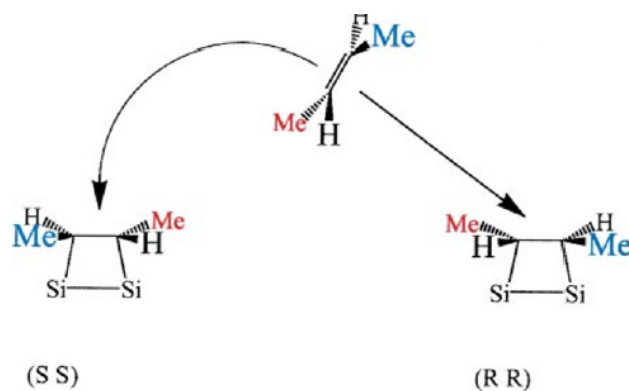
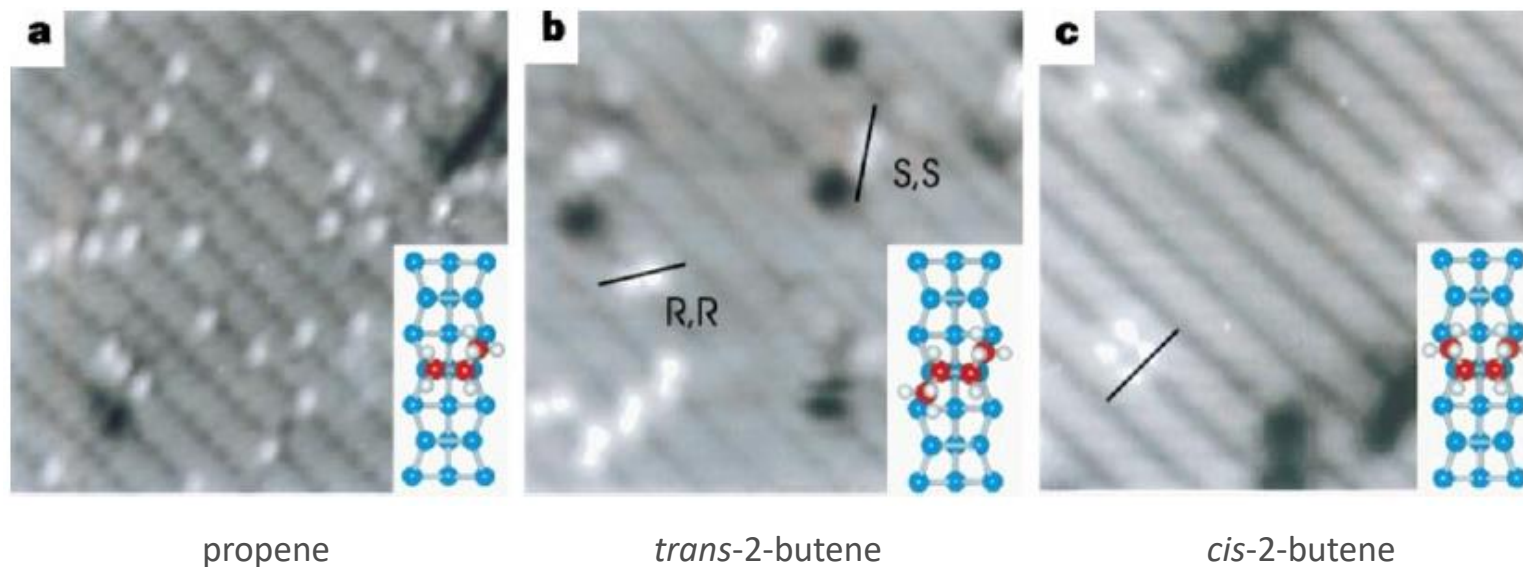


Q. Zhong, A. Ihle, S. Ahles, H. A. Wegner, A. Schirmeisen, D. Ebeling, *Nat. Chem.* **2021**, *2021*, 1–7; Earlier results: S. Zint, D. Ebeling, T. Schlöder, S. Ahles, D. Mollenhauer, H. A. Wegner, A. Schirmeisen, *ACS Nano* **2017**, *11*, 4183–4190; D. Ebeling, Q. Zhong, T. Schlöder, J. Tschakert, P. Henkel, S. Ahles, L. Chi, D. Mollenhauer, H. A. Wegner, A. Schirmeisen, *ACS Nano* **2018**, *13*, 324–336; Q. Fan, D. Martin-Jimenez, S. Werner, D. Ebeling, T. Koehler, T. Vollgraff, J. Sundermeyer, W. Hieringer, A. Schirmeisen, J. M. Gottfried, *J. Am. Chem. Soc.* **2019**, *142*, 894–899; D. Martin-Jimenez, A. Ihle, S. Ahles, H. A. Wegner, A. Schirmeisen, D. Ebeling, *Appl. Phys. Lett.* **2020**, *117*, 131601.



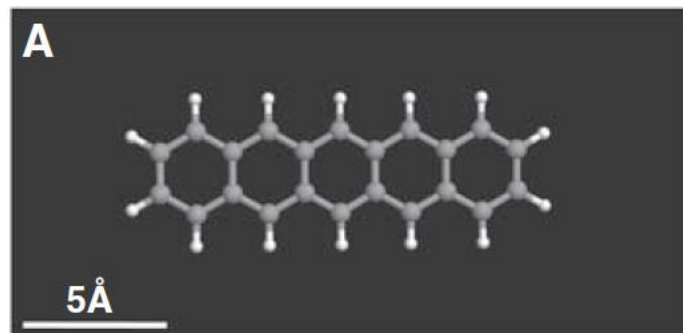
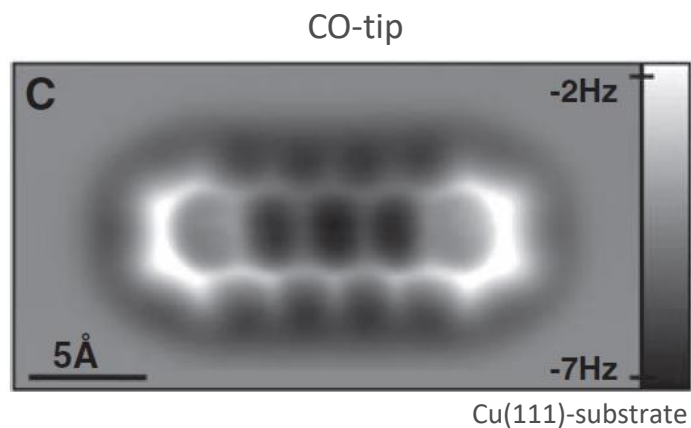
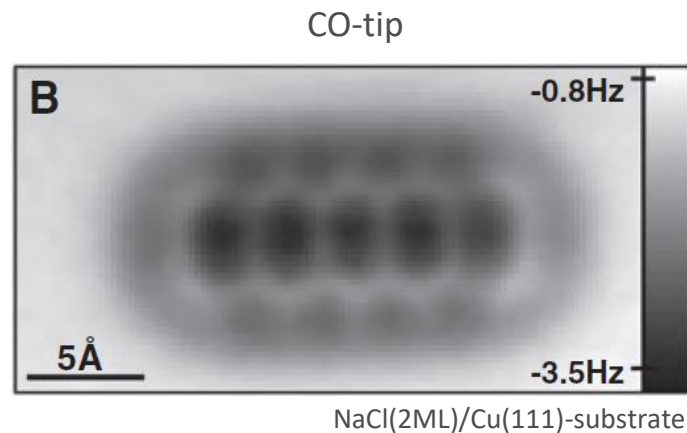
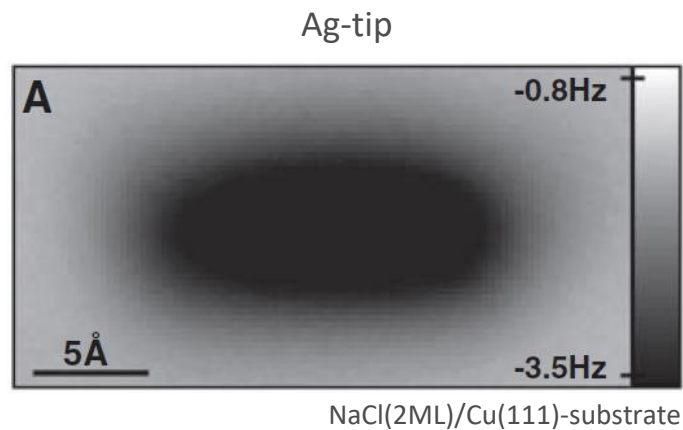


- 1998 Lipinski *et al.*: Determination of the absolute chirality of individual adsorbed molecules





- 2009 Gross *et al.*

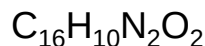




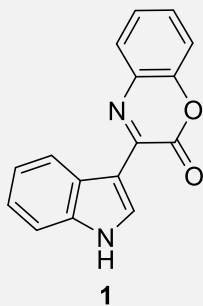
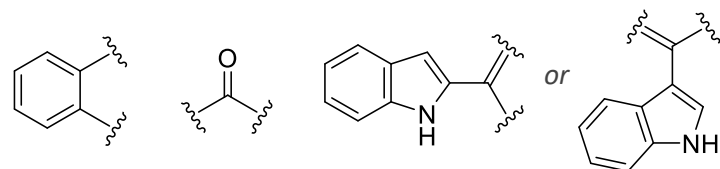
Organic structure determination using atomic-resolution scanning probe microscopy

Leo Gross^{1*}, Fabian Mohn¹, Nikolaj Moll¹, Gerhard Meyer¹, Rainer Ebel², Wael M. Abdel-Mageed^{2,3} and Marcel Jaspars²

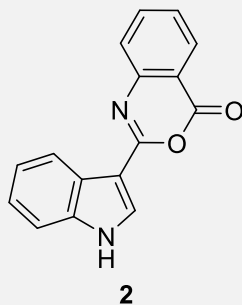
Chemical formula from HRMS



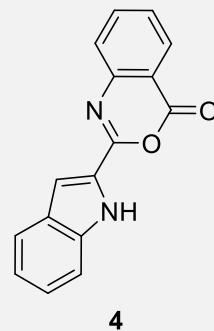
Substructures from NMR data



1



2



4

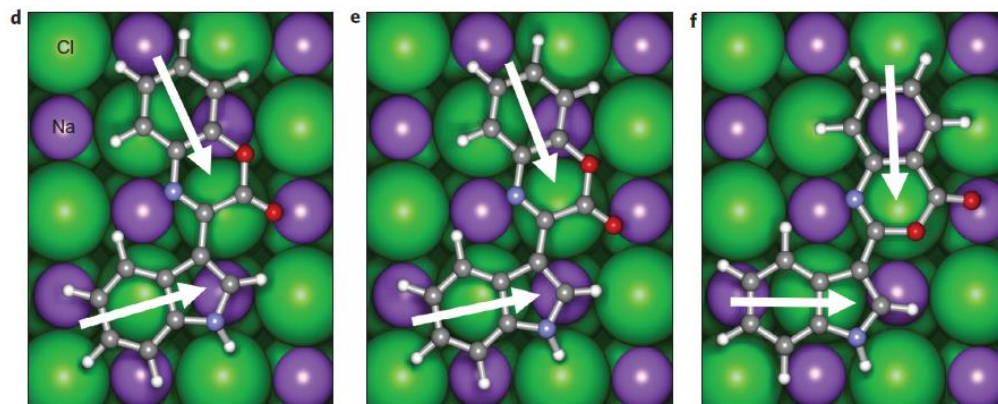
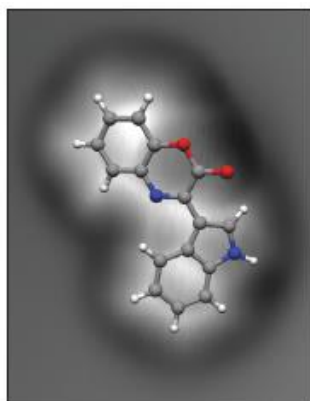
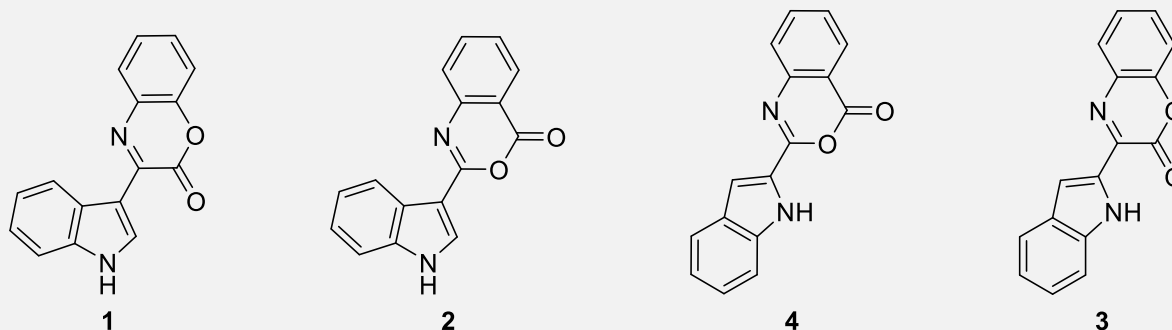


3



Organic structure determination using atomic-resolution scanning probe microscopy

Leo Gross^{1*}, Fabian Mohn¹, Nikolaj Moll¹, Gerhard Meyer¹, Rainer Ebel², Wael M. Abdel-Mageed^{2,3} and Marcel Jaspars²

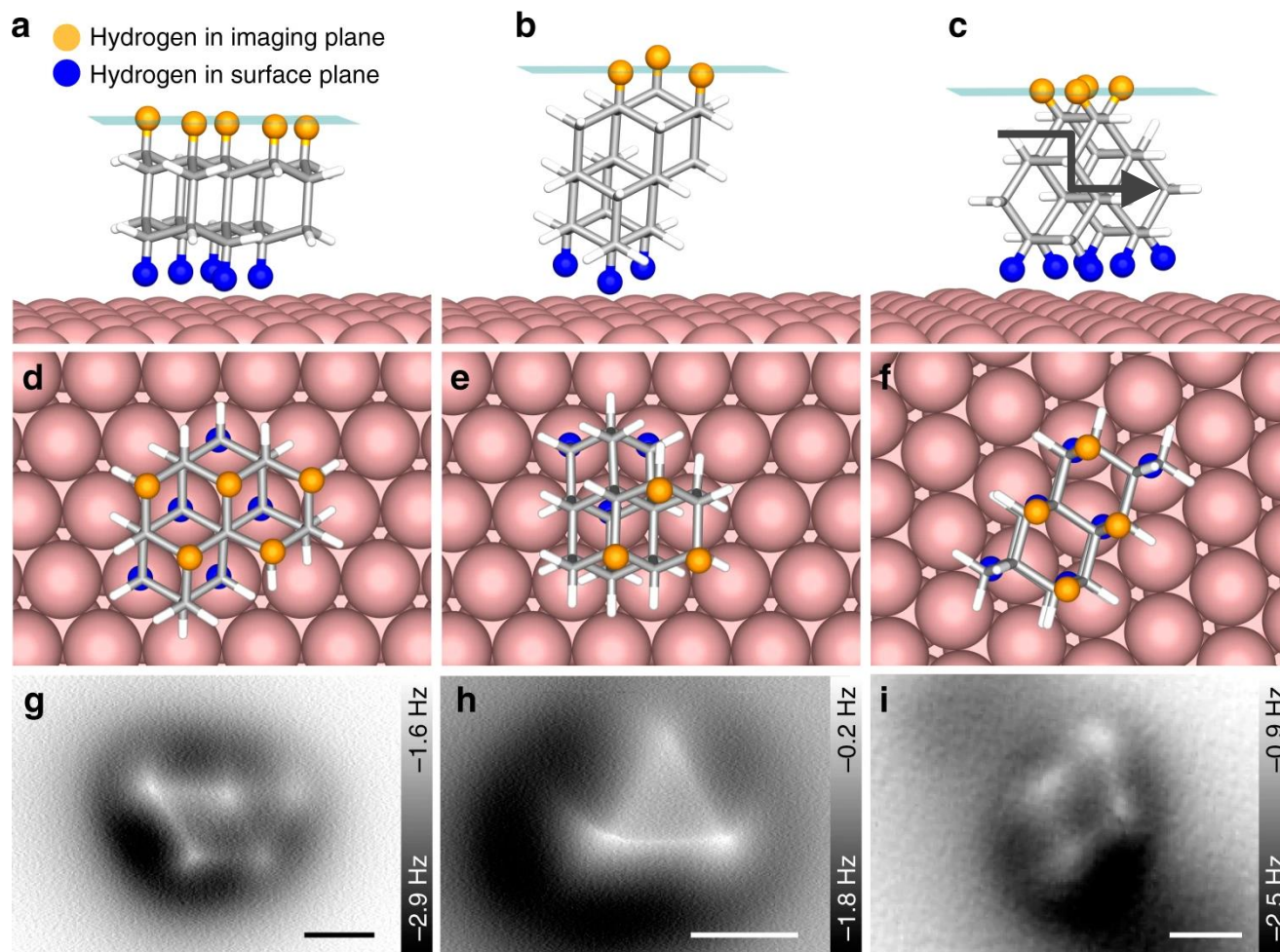


Comparison of experimental adsorption position (left) with DFT-calculated adsorption geometries for **1** (middle) and **2** (right)

L. Gross, F. Mohn, N. Moll, G. Meyer, R. Ebel, W. M. Abdel-Mageed, M. Jaspars, *Nat. Chem.* **2010**, *2*, 821–825. Application in characterization of asphaltenes: B. Schuler, G. Meyer, D. Peña, O. C. Mullins, L. Gross, *J. Am. Chem. Soc.* **2015**, *137*, 9870–9876; B. Schuler, Y. Zhang, S. Collazos, S. Fatayer, G. Meyer, D. Pérez, E. Guitián, M. R. Harper, J. D. Kushnerick, D. Peña, et al., *Chem. Sci.* **2017**, *8*, 2315–2320; B. Schuler, S. Fatayer, G. Meyer, E. Rogel, M. Moir, Y. Zhang, M. R. Harper, A. E. Pomerantz, K. D. Bake, M. Witt, et al., *Energy and Fuels* **2017**, *31*, 6856–6861; L. Zhang, P. Chen, S. Pan, F. Liu, V. Pauchard, A. E. Pomerantz, S. Banerjee, N. Yao, O. C. Mullins, *Energy & Fuels* **2021**, *35*, 13610–13632.

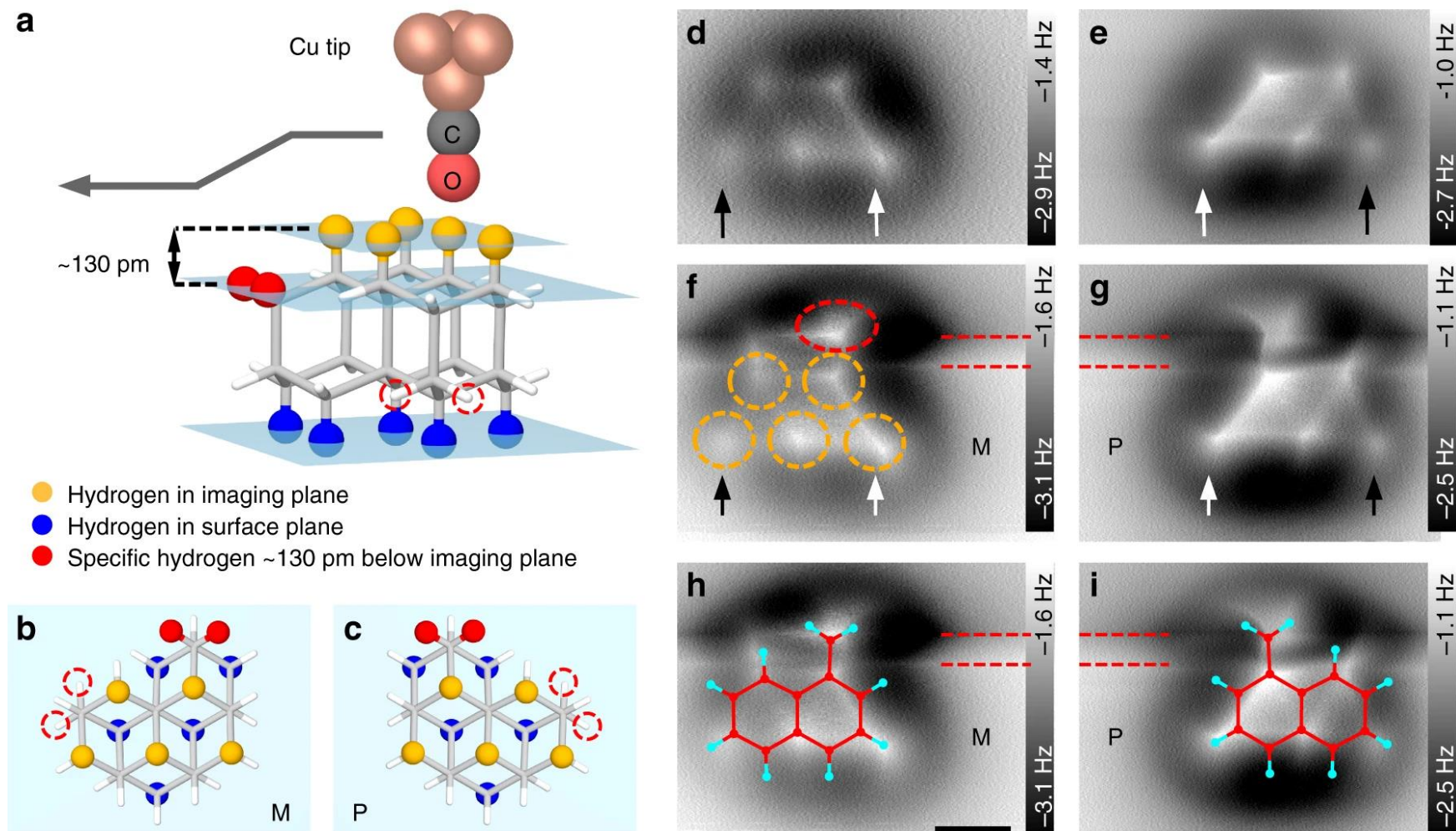


- 2018 Ebeling *et al.* Assigning the absolute Configuration of [123]tetramantane by visual inspection





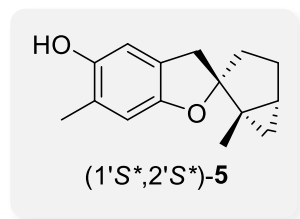
- 2018 Ebeling *et al.* Assigning the absolute Configuration of [123]tetramantane by visual inspection



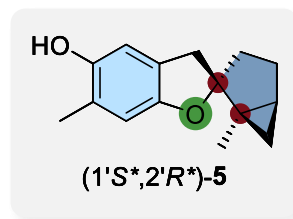
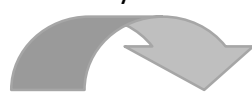


(±)-Laurentristich-4-ol

Sesquiterpene from Red Alga *Laurencia tristicha*



Structure revised
after synthesis



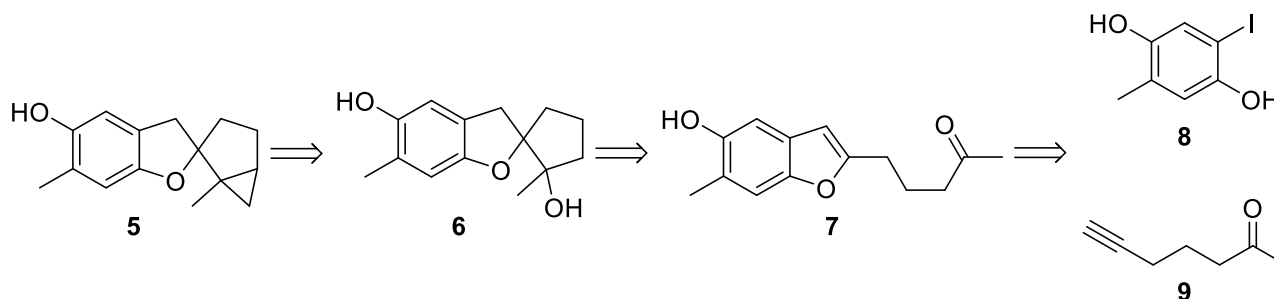
Planar benzyl moiety

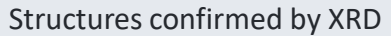
Methyl[3.1.0]bi-
cylcohexyl moiety

Oxygen heteroatom

Spiro center and
quarternary carbon

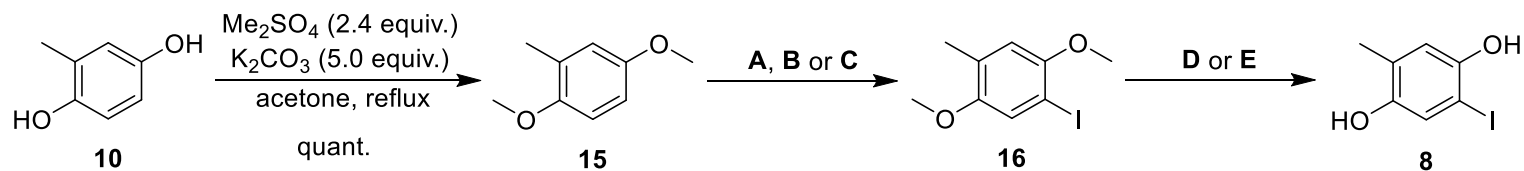
- 2008 Chen *et al.*







- Synthesis of 2-Iodo-5-methylbenzene-1,4-diol **8**:



Iodination:

A: I_2 (0.6 equiv.), HIO_3 (0.1 equiv.);
AcOH, H_2O , H_2SO_4 , 70 °C, o.n.; 53%

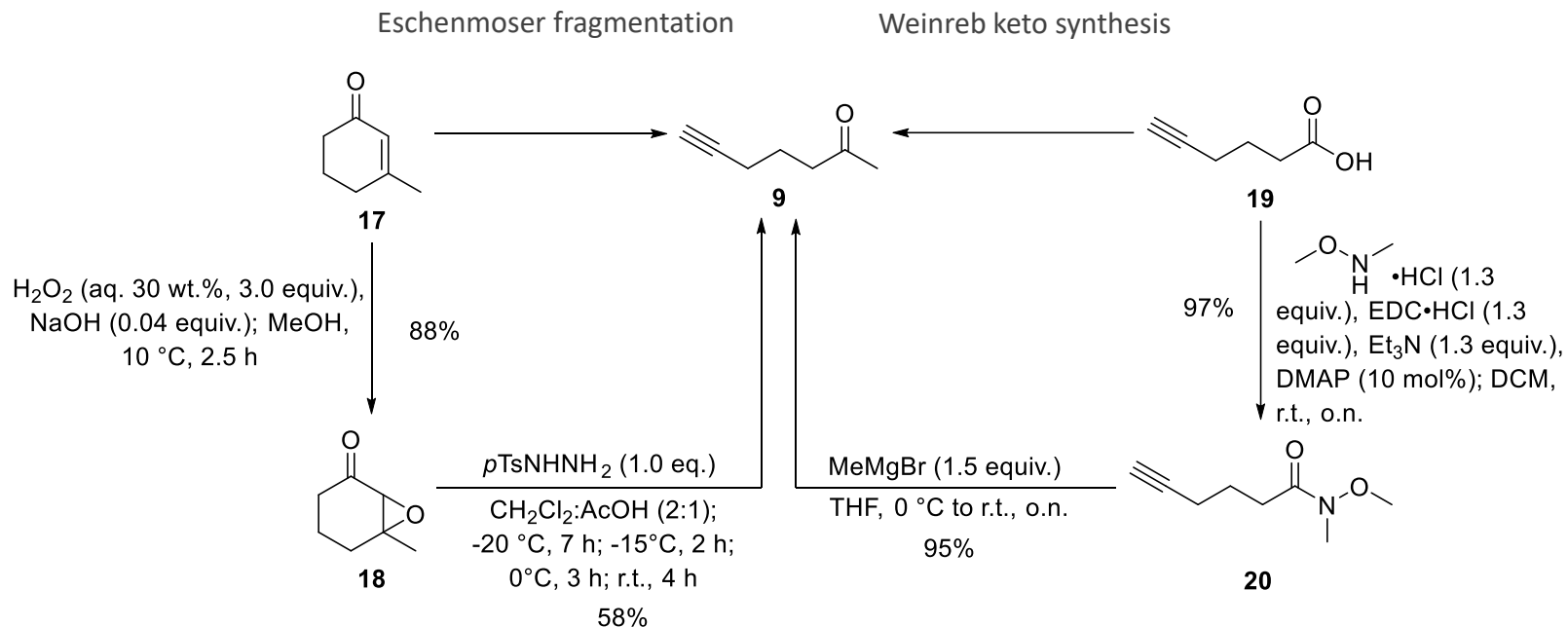
B: I_2 (0.4 equiv.), H_5IO_6 (0.2 equiv.);
MeOH, reflux, o.n.; 49%

C: I_2 (0.5 equiv.), H_5IO_6 (0.2 equiv.);
AcOH, H_2O , H_2SO_4 , 70 °C, o.n.; 84%

Deprotection:

D: BBr (5.0 equiv.);
DCM, -78 °C, 30 min; r.t., o.n.; 62%

E: 1. CAN (2.5 equiv.), AcCN: H_2O (2:1), 0 °C, 30 min;
2. $\text{Na}_2\text{S}_2\text{O}_4$ (20 equiv.), Et_2O : H_2O (2:1), r.t., 1 h; 96%

Synthesis of 6-heptyn-2-one **9**:

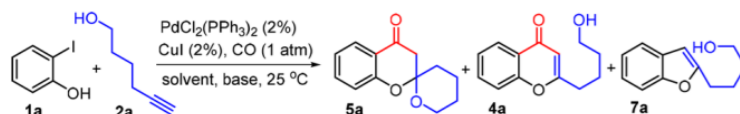
Eschenmoser fragmentation: J. Schreiber, D. Felix, A. Eschenmoser, M. Winter, F. Gautschi, K. H. Schulte-Elte, E. Sundt, G. Ohloff, J. Kalovoda, H. Kaufmann, et al., *Helv. Chim. Acta* **1967**, *50*, 2101–2108; A. Eschenmoser, D. Felix, G. Ohloff, *Helv. Chim. Acta* **1967**, *50*, 708–713; D. Felix, J. Schreiber, G. Ohloff, A. Eschenmoser, *Helv. Chim. Acta* **1971**, *54*, 2896–2912; B. M. Trost, M. J. Bartlett, A. H. Weiss, A. J. von Wangelin, V. S. Chan, *Chem.: Eur. J.* **2012**, *18*, 16498–16509. Weinreb keto synthesis: S. Nahm, S. M. Weinreb, *Tetrahedron Lett.* **1981**, *22*, 3815–3818.



Synthesis of Benzannulated [6,6]-Spiroketal by a One-Pot Carbonylative Sonogashira Coupling/Double Annulation Reaction

 Kuirong Xiang, Pei Tong, Baorun Yan, Lingling Long, Chunbo Zhao, Yuan Zhang,*[✉] and Ying Li*

State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, P. R. China

Table 1. Optimization of Reaction Conditions^a


entry	solvent	base	time (h)	yield (%) ^b 5a: 4a: 7a
1	DMF	DBU	20	0:92:0
2	DMF	Et ₃ N	30	0:79:0
3	DMF	Cs ₂ CO ₃	24	0:73:0
4	CH ₂ Cl ₂	DBU	10	0:0:83
5	CH ₃ CN	DBU	24	0:16:63
6	1,4-dioxane	DBU	24	0:10:61
7	Et ₃ N	Et ₃ N	40	25:48:13
8	Toluene	DBU	48	15:44:25
9	THF	DBU	40	30:58:5
10 ^c	THF	DBU	40	81:7:4
11 ^d	THF	DBU	60	4:38:0
12 ^{c,e}	THF	DBU	40	55:6:17
13 ^{c,f}	THF	DBU	40	35:6:8

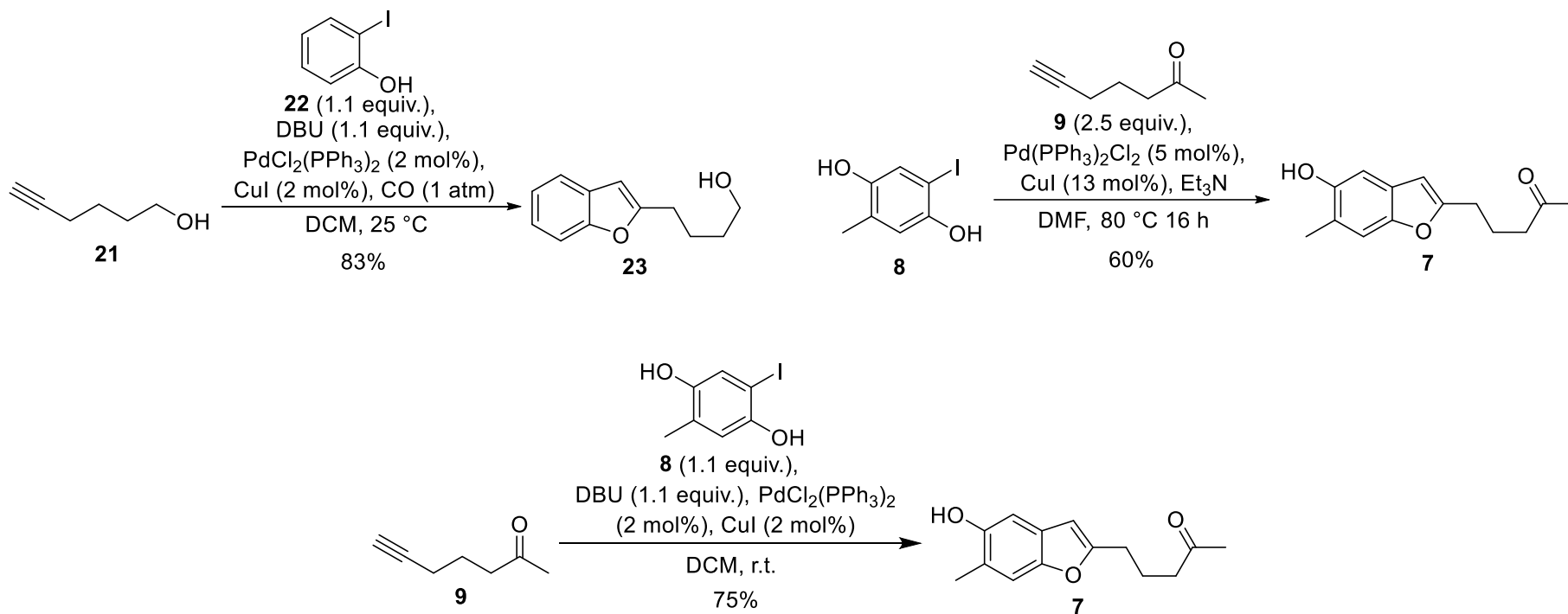
^aAll reactions were carried out by using **1a** (1.1 mmol), **2a** (1.0 mmol), PdCl₂(PPh₃)₂ (0.02 mmol), CuI (0.02 mmol), and solvent (5 mL) under CO (1 atm) at 25 °C, except as noted. ^bIsolated yield.

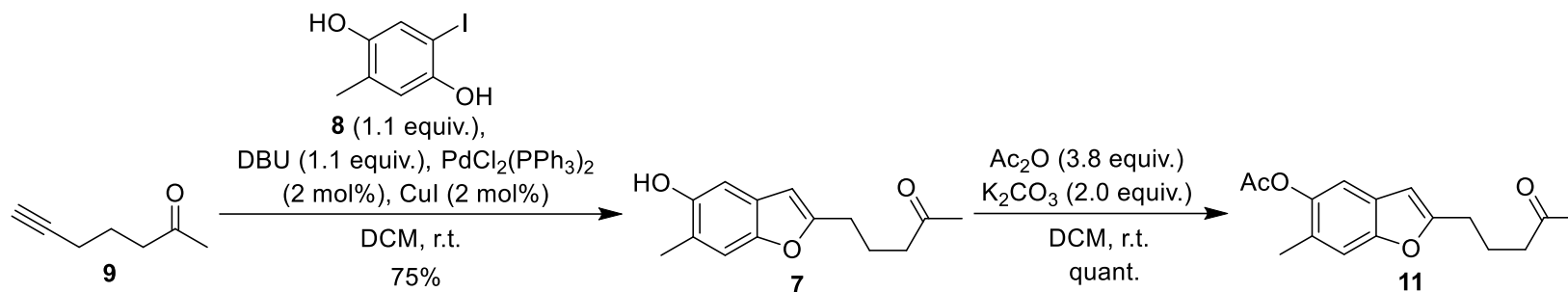


Synthesis of Benzannulated [6,6]-Spiroketal by a One-Pot Carbonylative Sonogashira Coupling/Double Annulation Reaction

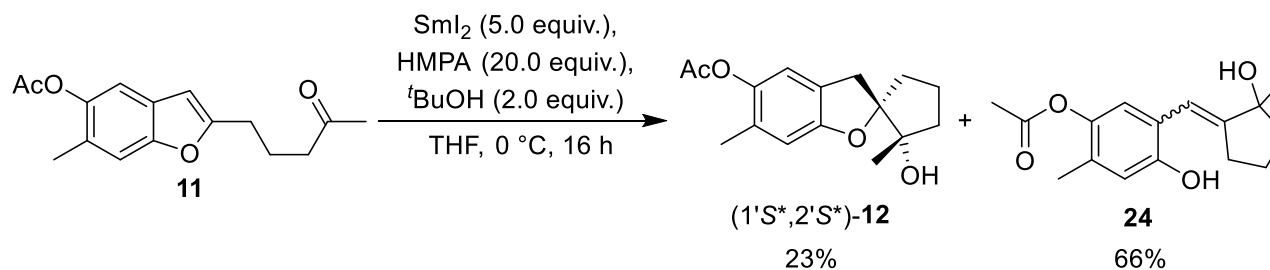
Kuirong Xiang, Pei Tong, Baorun Yan, Lingling Long, Chunbo Zhao, Yuan Zhang,* and Ying Li*

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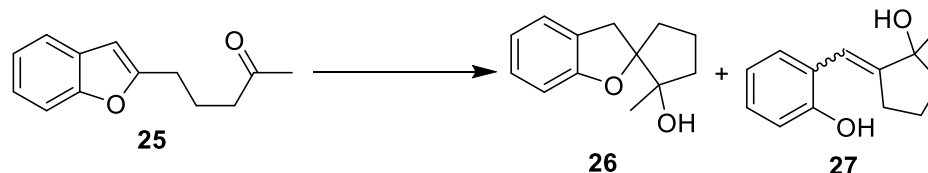
- The key step: Sml₂-mediated ketyl radical cyclization



2:1 ratio of **12**:**24** observed after changes in experimental procedure

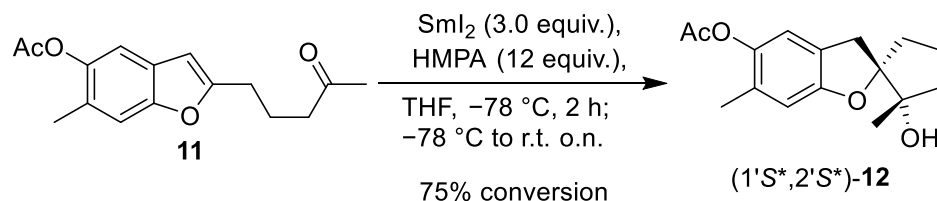


- Testing various conditions on 5-(2-benzofuranyl)-2-pentanone **25**



Entry	Sml ₂ / equiv.	HMPA/ equiv.	Alcohol/ equiv.	T/°C	Conversion ^a /%	26:27 ^a
A	5.0	20	^t BuOH, 2.0	0 to r.t.	100	1:9
B	4.0	0	MeOH, 280	r.t.	0	n.d.
C	4.0	16	none	-78	85	1:0

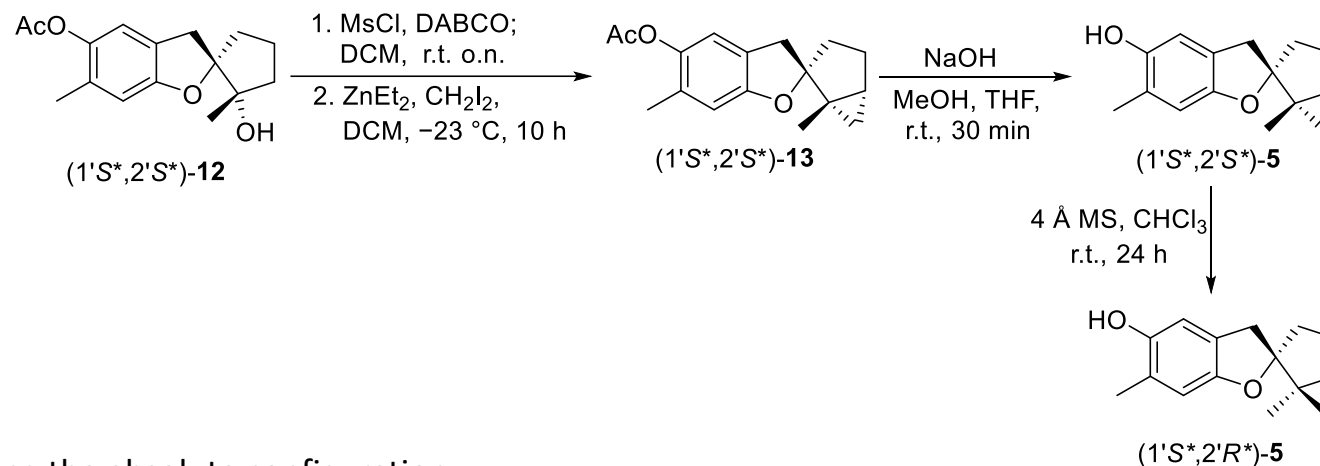
^adetermined by ¹H-NMR spectroscopy



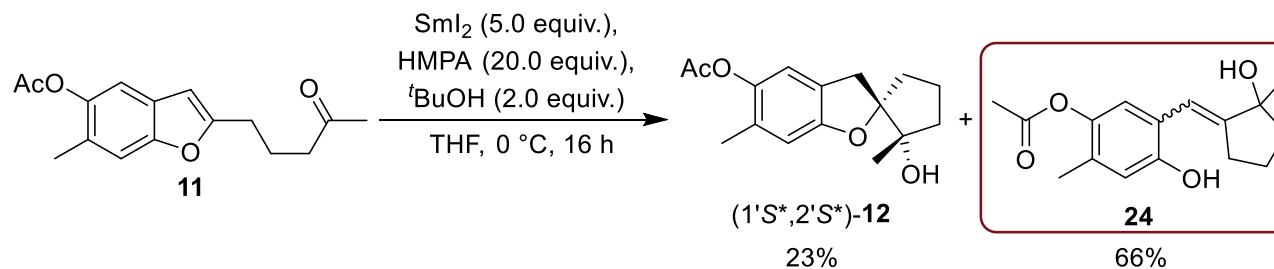
P. Chen, J. Wang, K. Liu, C. Li, *J. Org. Chem.* **2008**, 73, 339–341. Role of HMPA: P. Girard, J. L. Namy, H. B. Kagan, *J. Am. Chem. Soc.* **1980**, 102, 2693–2698; InanagaJunji, Ishikawa Mitsuhiko, Yamaguchi Masaru, *Chem. Lett.* **1987**, 16, 1485–1486; A. Dahlén, G. Hilmersson, *Eur. J. Inorg. Chem.* **2004**, 2004, 3393–3403. Role of proton source: A. Dahlén, G. Hilmersson, *Tetrahedron Lett.* **2001**, 42, 5565–5569; T. K. Hutton, K. W. Muir, D. J. Procter, *Org. Lett.* **2003**, 5, 4811–4814.; P. R. Chopade, E. Prasad, R. A. Flowers, *J. Am. Chem. Soc.* **2003**, 126, 44–45; E. Prasad, R. A. Flowers, *J. Am. Chem. Soc.* **2005**, 127, 18093–18099. Sml₂-mediated cyclizations: H. Y. Harb, D. J. Procter, *Synlett* **2011**, 2012, 6–20; M. Szostak, N. J. Fazakerley, D. Parmar, D. J. Procter, *Chem. Rev.* **2014**, 114, 5959–6039; C. Morrill, C. Jensen, X. Just-Baringo, G. Grogan, N. J. Turner, D. J. Procter, *Angew. Chem. Int. Ed.* **2018**, 57, 3692–3696.



- Optimization of the SmI_2 -mediated cyclization
- Finish the synthesis



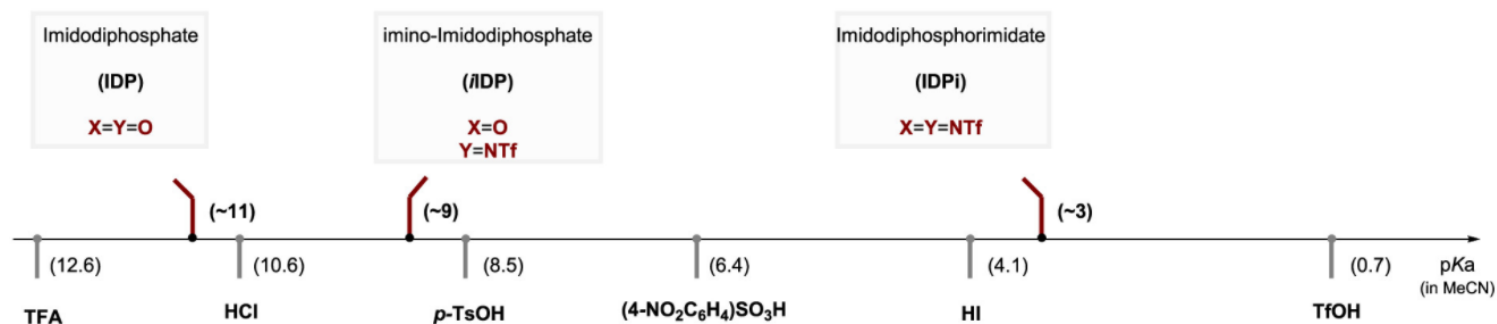
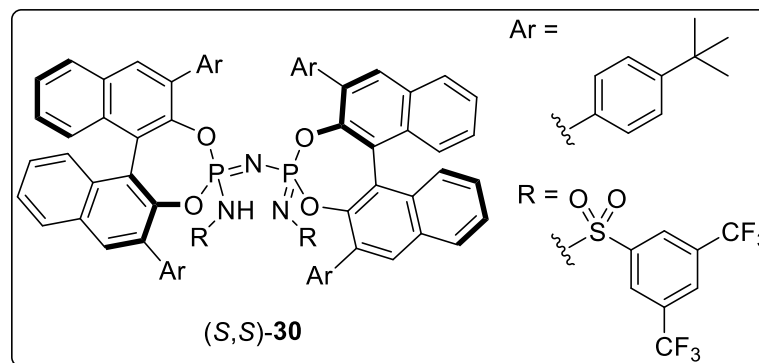
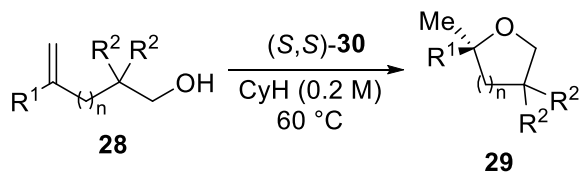
- Assigning the absolute configuration





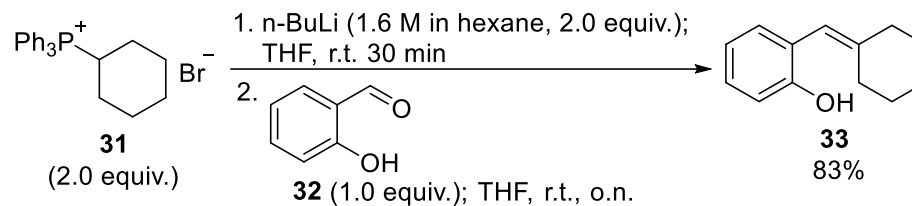
Activation of olefins via asymmetric Brønsted acid catalysis

Nobuya Tsuji,¹ Jennifer L. Kennemur,¹ Thomas Buyck,¹ Sunggi Lee,¹ Sébastien Prévost,¹ Philip S. J. Kaib,¹ Dmytro Bykov,^{2,3} Christophe Farès,¹ Benjamin List^{1*}





Model system for enantioselective acid-catalyzed cyclization to spirocycles



Entry	acid	Catalyst loading/mol%	solvent	T/°C	t/h	33/%	34/%
A	Amberlyst® 15	—	DCM	21	72	98	—
B	Triflic acid	10	DCM	0 to 21	17	—	23
C	(<i>R</i>)-TRIP	5	toluene	80	72	85	3
D	IDPi	1	toluene	80	72	—	89



Prof. Schreiner

Lab B205 & B204

The PRS Group

