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My First Scientific Article

Tips on writing an article for early career researchers

Adam Urban, Barbora Šátková

Our experiences as two Ph.D. candidates

March 19, 2024

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Agenda

1) Scientific communication
2) Take away message
3) Structure and types of scientific articles
4) Choosing a journal
5) Preparation, inspiration, and learning
6) What to keep in mind while writing
7) Publishing process, peer review
8) Tips and tricks

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Why do you write? What is your main reason for wanting to write an article?

Why write academic articles?

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Formal goal: to fulfill requirements for a PhD degree

Career goal: to get a tenure track academic position

Part of academic hiring decisions and ongoing evaluation are based on publication output, with the quality of articles playing an important role.

Research goal: to contribute to existing knowledge in my field (scientific/scholarly communication)

SOURCE: Günter Blöschl - How to write (and publish) a scientific paper in hydrology

What is scientific communication

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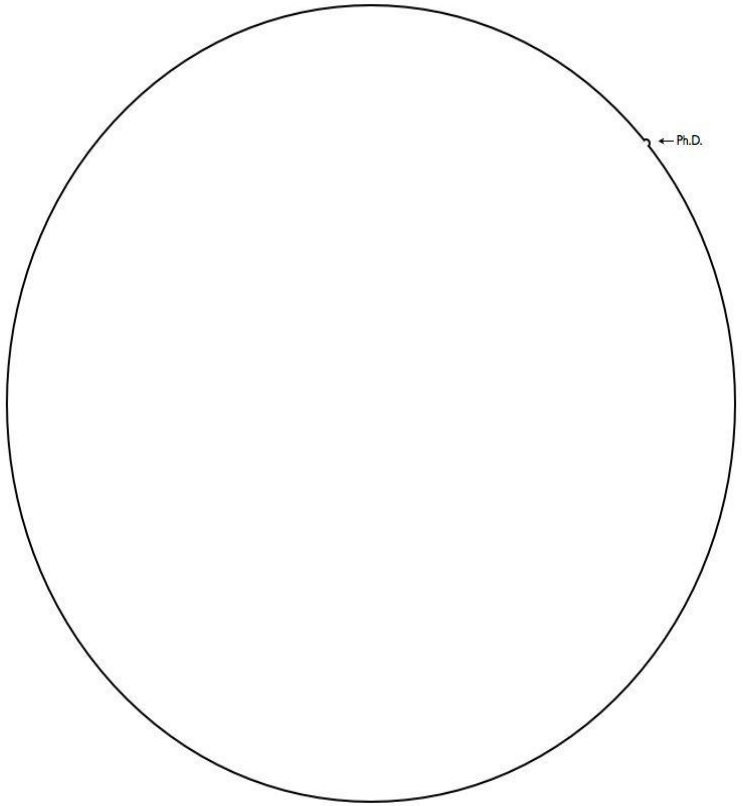
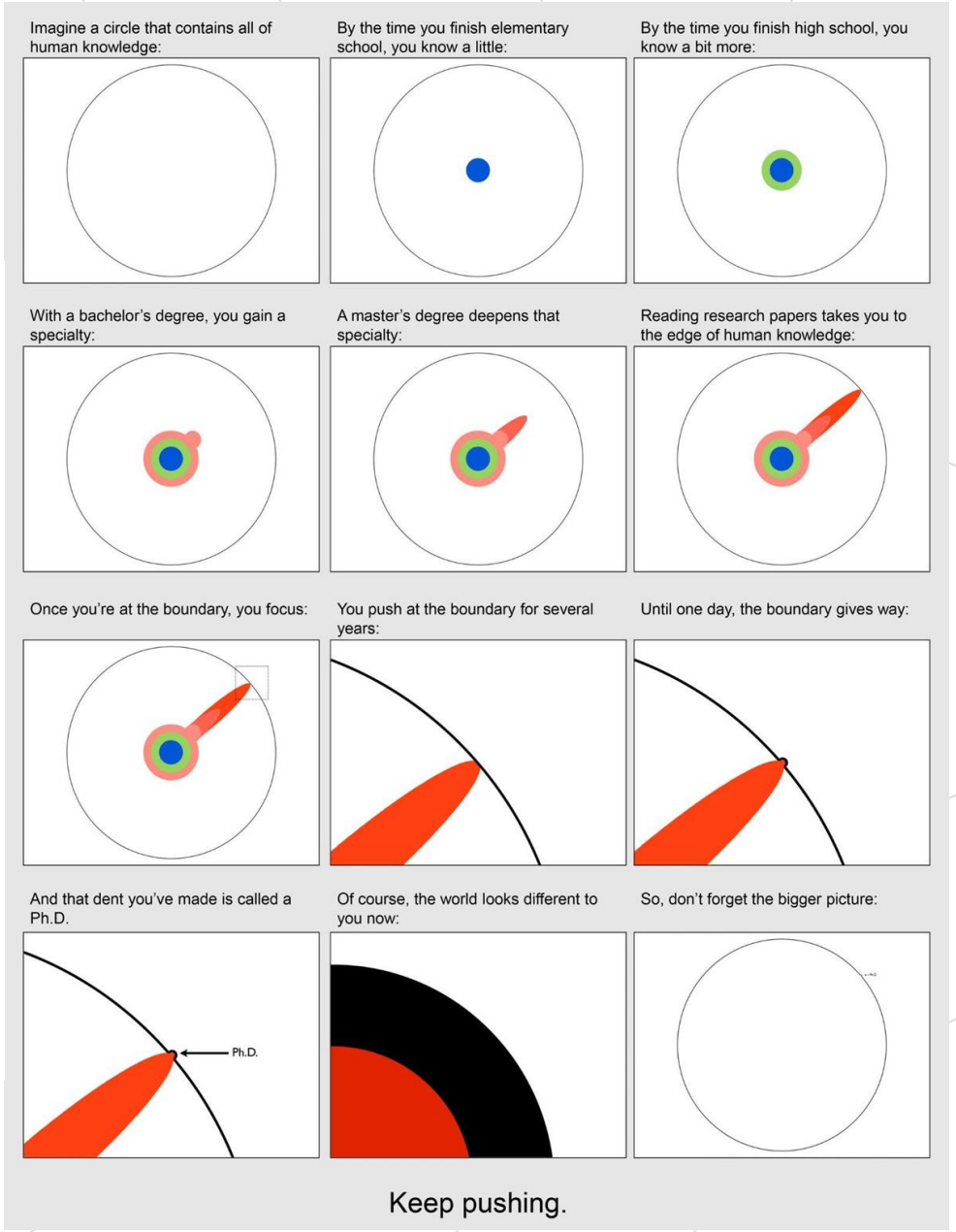
- Ongoing, documented, structured dialogue between researchers (across countries, times, and disciplines)
- The work of one builds upon that of those who came before (“Stand on the shoulders of giants.”)
- **Peer review:** essential for maintaining high academic standards
- Becomes a part of the long-term academic corpus of knowledge
- Contains information obtained by using and applying research methods (qualitative or quantitative)

Your goal can be to make a dent in a circle of human knowledge

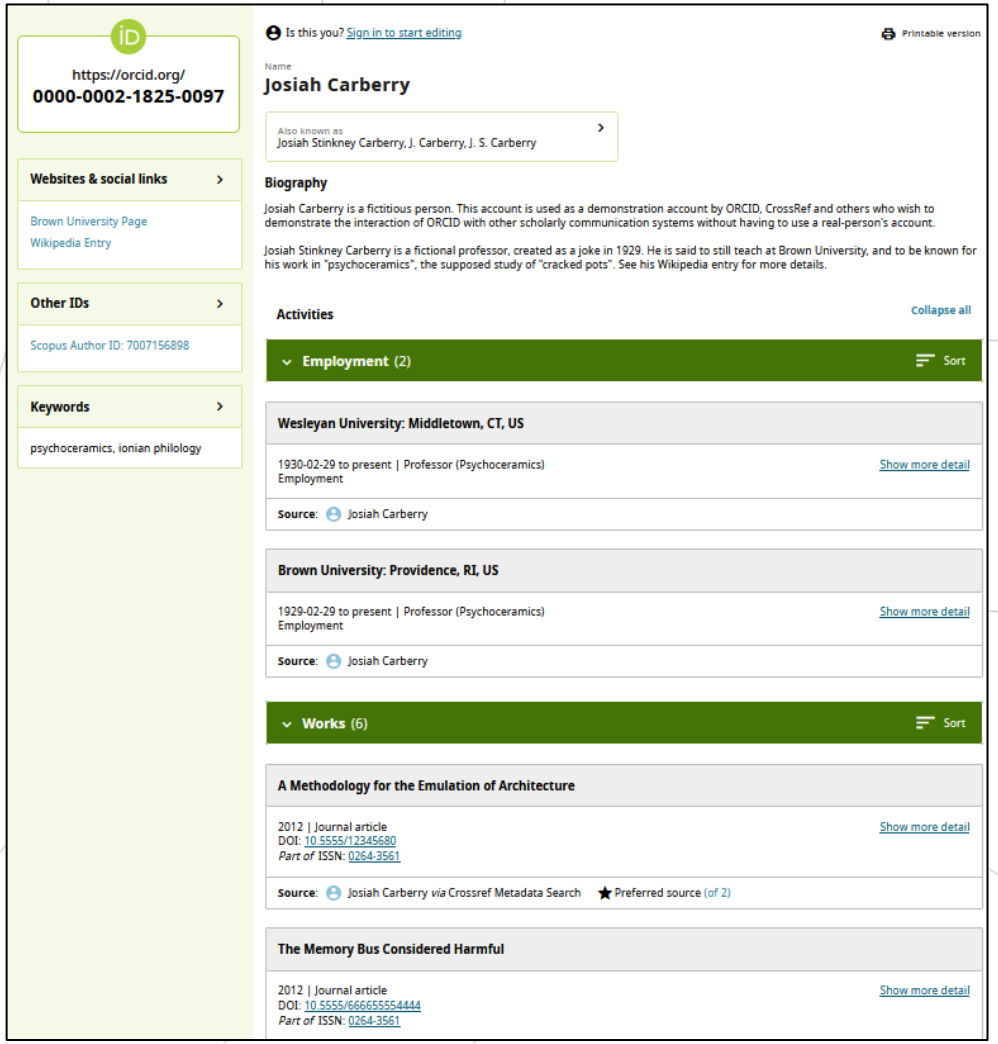


SOURCE: The Illustrated Guide to the Ph.D., created by Matt Might (http://matt.might.net/articles/phd-school-in-pictures/; 2012) and shared under Creative Commons license BY-NC 2.5.



ORCID iD

- Persistent personal identifier used in scientific communication system
  - Required for a grant application or publishing an article
  - 16-digit combination of numbers (example: https://orcid.org/0000-0002-1825-0097)
- ORCID iD provides identifier which is independent of publishers or databases
  - Self-registration and full control over your profile
- Link to the publications, research data and other products of the research process (e.g. research software)
  - Everything at one place



Source: orcid.org

A scientific article is not a thesis or dissertation

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	THESIS OR DISSERTATION	RESEARCH ARTICLE
AUTHOR	Student	Researcher (might be a student)
REVIEWER	Supervisor, consultant, opponent	Reviewers, journal editor
READER	Supervisor, opponent, colleagues, other students, sometimes restricted access …	Primarily other researchers plus interested parties (educators, journalists, decision makers, general public)
CONTENT	Longer in general, usually broader theoretical part, does not necessarily include an experiment	Should contribute an original research study to the field; bringing new insights/knowledge

Scientific article: Take away message

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- Important to formulate for yourself what you are trying to achieve with your research
- Can you explain to yourself and potential readers what you are trying to do in several sentences?
- Be exact and aim at avoiding information that is vague or relevant only to you

"The normalised jack-knife validation error is 0.15 in 37 Austrian catchments for the period 1980-2010."

"The model provided an excellent fit to the data."

Reading tip: chapter Providing proper emphasis (Alley, Michael. *The Craft of Scientific Writing*. New York: Springer, 1996)

Typical structure of a scientific article

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(I.M.R.A.D. structure)

	Title	What is it about?
	Abstract	What was done in a nutshell?
I	**Introduction**	Why did you do it? (previous related research, state-of-the-art/gap this research is filling, theoretical background)
M	**Methods/Theory**	How did you do it?
R, A	**Results, Analysis**	What did you find?
D	**Discussion**	What does it mean? (in relation to previous research efforts)
	Summary and conclusions	What have you learned, what are the major findings?
	Acknowledgements	Who helped you? (include grants for research; check author guidelines)
	References	Upon whose work did you build yours?
	Appendices	Additional information

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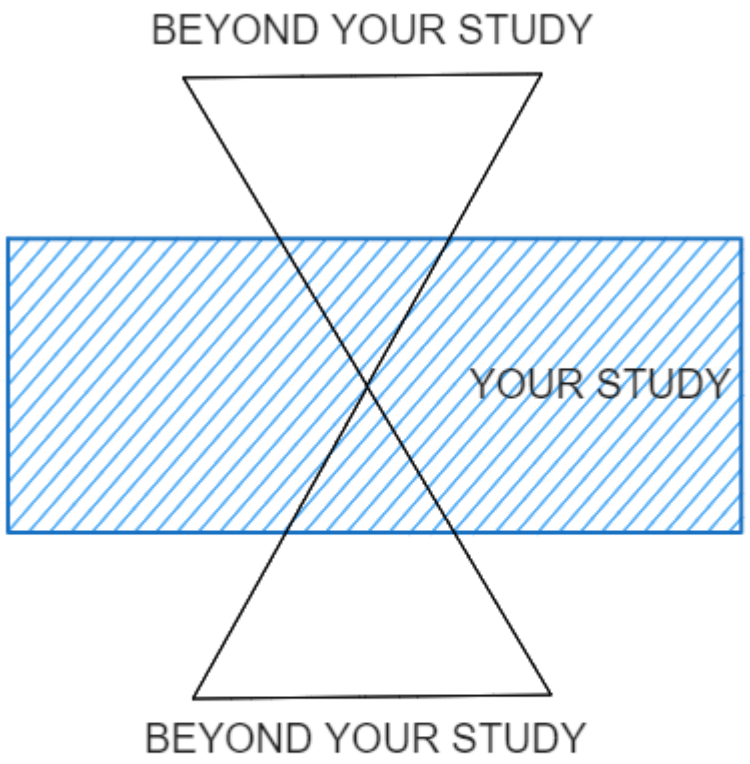
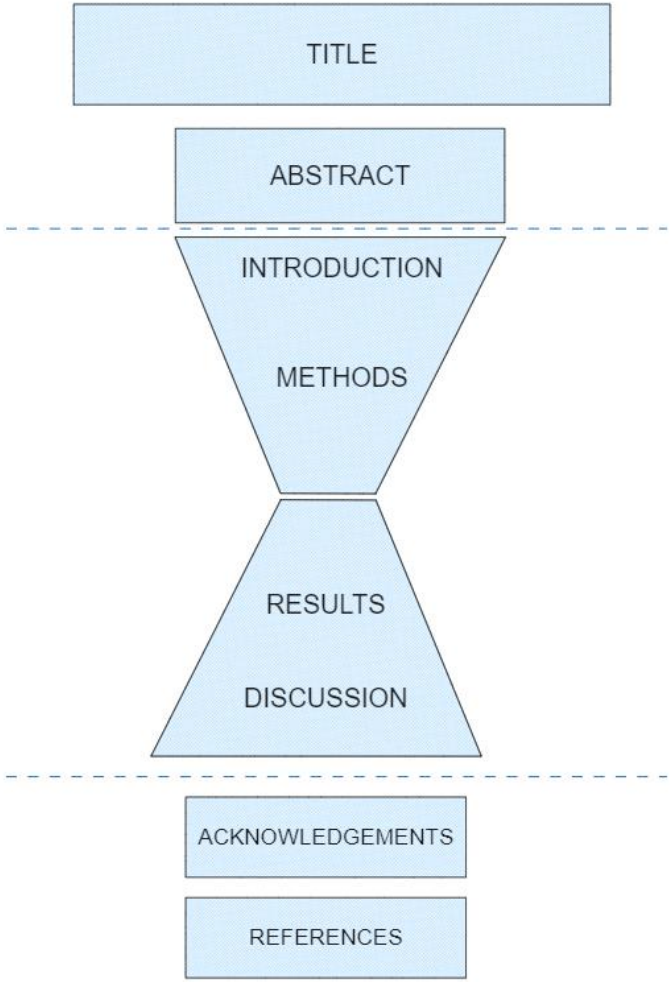
Scope and structure of a scientific article





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ORGANIC CHEMISTRY

Scalable Birch reduction with lithium and ethylenediamine in tetrahydrofuran

James Burrows, Shogo Kamo, Kazunori Koide*

The Birch reduction dearomatizes arenes into 1,4-cyclohexadienes. Despite substantial efforts devoted to avoiding ammonia and cryogenic conditions, the traditional, cumbersome, and dangerous procedure remains the standard. The Benkeser reduction with lithium in ethylenediamine converts arenes to a mixture of cyclohexenes and cyclohexanes; this is operationally easier than the Birch reduction but does not afford 1,4-cyclohexadienes. Here, we report a Birch reduction promoted by lithium and ethylenediamine (or analogs) in tetrahydrofuran at ambient temperature. Our method is easy to set up, inexpensive, scalable, rapid, accessible to any chemical laboratory, and capable of reducing both electron-rich and electron-deficient substrates. Our protocol is also compatible with organocuprate chemistry for further functionalization.

Dearomatization is widely used in chemical synthesis (*1*). The Birch reduction dearomatizes arenes into 1,4-cyclohexadienes with lithium, sodium, or potassium in liquid ammonia at ≤−33°C (Fig. 1A) (*2*, *3*) and has been employed throughout the pharmaceutical industry (*4*, *5*), perfumery industry (*6*, *7*), and academia (*8*–*11*).

Liquid ammonia must be prepared with specialized equipment and carefully dissipated after the reaction is complete. Both steps are time consuming; for example, removal of 1 L of liquid ammonia (850 L as gas) can take up to 12 hours (*12*), and as much as 7.5 L of liquid ammonia per mole of substrate may be needed (*5*, *13*). Even on a 3.5-mmol scale, the Birch process requires 7 hours from setting up equipment to the completion of biphasic extraction (*14*). These logistical challenges make it difficult to perform multiple Birch reductions in parallel. Also, the liquid ammonia solvent has long been deemed necessary to solubilize alkali metals to form the solvated electron.

To overcome these challenges, researchers have developed ammonia-free conditions. For example, the Benkeser group used lithium and neat ethylamine, ethylenediamine, or a mixture of primary and secondary amines, providing a mixture of over-reduced products, and did not use any other solvents (Fig. 1B) (*15*–*17*). Arenes could be reduced to the Birch-type products with lithium in a mixture of methylamine and isopropanol, but overreduction appeared inevitable (*18*). Benzoic acid was reduced to benzaldehyde in 25% yield in the presence of lithium, methylamine, and ammonium nitrate (*19*). The benefit of ethylenediamine as a solvent for dissolving metal reductions was also demonstrated by others (*20*). The Dolby group reduced three substates to the corresponding Birch-type products in 45% to quantitative yield using lithium, ethylenediamine, *n*-propylamine, and *t*-butanol (*4*). This method was moderately successful in one instance (*21*) and was not effective in the *N*-detosylation of a challenging substrate (*22*). Donohoe and House reported the reduction of electron-deficient arenes and heterocycles using di-*tert*-butylbiphenyl ($1000/mol; Sigma-Aldrich) and lithium at −78°C (Fig. 1C) (*23*). Their method was highly oxygen sensitive and as lengthy as the standard Birch procedure (*14*). An's method (Fig. 1D) requires sodium and 3 to 9 equivalents of 15-crown-5 ($1579/mol; Sigma-Aldrich) and is limited to electron-rich or neutral substrates (*24*). The Baran group described an electrochemical reduction of electron-rich arenes (Fig. 1E) with 3.5 to 10 equivalents of tri(pyrrolidin-1-yl)phosphine oxide ($5040/mol; Sigma-Aldrich) and 3 equivalents of 1,3-dimethylurea ($5/mol; Sigma-Aldrich), both of which must be removed from the product by column chromatography (*13*). Their 0.45-mol scale reaction took 3 days in a flow reactor without tri(pyrrolidin-1-yl)phosphine oxide (*13*). The Sugai group treated arenes with lithium and ethylenediamine in tetrahydrofuran (THF) or Et_2O but did not isolate 1,4-cyclohexadiene products (*25*, *26*) and indicated that THF might be a ligand for a lithium ion (*25*).

Despite these efforts, the original, cumbersome, and dangerous Birch protocol remains the current standard (*14*, *27*). Because of the

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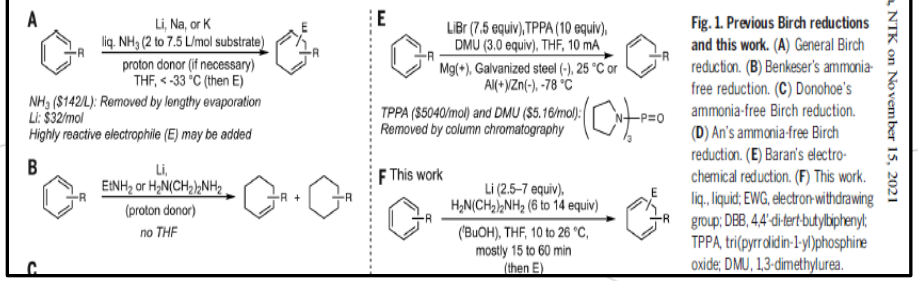

Fig. 1. Previous Birch reductions and this work. (**A**) General Birch reduction. (**B**) Benkeser's ammonia-free reduction. (**C**) Donohoe's ammonia-free Birch reduction. (**D**) An's ammonia-free Birch reduction. (**E**) Baran's electrochemical reduction. (**F**) This work. liq., liquid; EWG, electron-withdrawing group; DBB, 4,4′-di-*tert*-butylbiphenyl; TPPA, tri(pyrrolidin-1-yl)phosphine oxide; DMU, 1,3-dimethylurea.

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Dostupné z: doi:10.1126/science.abk3099

Scalable Preparation of Methylated Ando-Type Horner–Wadsworth–Emmons Reagent

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Supporting Information

ABSTRACT: The Horner–Wadsworth–Emmons (HWE) reactions are vital to the chemical synthesis of complex molecules, forging a carbon–carbon double bond in the generation of α,β-unsaturated enoates from aldehydes or ketones. Despite their frequent use, the *Z*-stereoselective formation of α,β-unsaturated esters from aldehydes have been mostly limited to the use of the commercially available Still–Gennari reagent. Ando developed an alternative reagent to achieve the same formation with less expensive reagents. However, an α-methylated Ando-HWE reagent has remained difficult to prepare, hindering a reliable route to α,β-disubstituted *Z*-enoates. Here, we report the development of a preparative synthesis of a methylated Ando-HWE reagent for the highly *Z*-selective HWE reaction. Costing $0.49/mmol, this synthesis is significantly cheaper than the currently available Still–Gennari reagent ($11/mmol, Millipore Sigma 2018). The purification procedure does not require chromatography, with recrystallization as the only purification method, making it highly amenable to large-scale production.

KEYWORDS: *olefination, Wittig reactions, synthetic methods, alkylation, Horner–Wadsworth–Emmons reaction*

INTRODUCTION

Methods for generating new carbon–carbon bonds are powerful reactions that are widely used in the synthesis of complex molecules. The Horner–Wadsworth–Emmons (HWE) olefination has found widespread use in generating predominantly *E*-α,β-unsaturated esters from aldehydes. The generation of a *Z*-enoate has been more difficult, but two types of reagents have been developed to obtain this selectivity: the Still–Gennari reagent, (2,2,2-trifluoroethyl)phosphonoester **1a**[1] and Ando-type reagents, bis(*O*-aryl)phosphonates **1b**.[2] As shown in Scheme 1, α-alkylation of these types of reagents (step 1) followed by an HWE reaction (step 2) will generate this reagent costs $1.00/mmol, even without including the cost of purification. Alternatively, the Ando group developed reagent **1b** using electron-withdrawing aryloxy groups on the phosphorus atom, which presumably accelerate the formation of a *cis* oxaphosphetane, leading to formation of the *Z*-olefin with high stereoselectivities.[2] These bis(*O*-aryl)phosphonates and their associated reagents cost less to prepare, and the preparation is scalable. Touchard exploited the wide availability of phenols to develop phosphonate **1c**, which could be isolated in a pure form as a solid.[25,26] α-Alkylation of these reagents has been demonstrated with several examples in DMSO using NaH and haloalkanes; however, these reactions typically proceed with modest yields (~65%) and require column chromatography.[27,28] Despite poor synthetic accessibility, these α-alkylated reagents demonstrated similar *Z*-selectivity as the unsubstituted bis(*O*-aryl)phosphonates in the HWE reaction.

To harness the HWE reaction as a reliable route to trisubstituted *Z*-α,β-unsaturated enoates, it is necessary to develop a method to selectively monoalkylate phosphonates such as **1c**. In this manuscript, we report a scalable and inexpensive method for the preparation of the α-substituted phosphonate **2c** for *Z*-selective olefination reactions.

RESULTS AND DISCUSSION

To develop the required monoalkylation method, phosphonate **1c** was prepared according to the literature.[25] The two unsolved problems were the chemoselectivity for the formation of compounds **2c** and **4** and the overall yield of the reaction. A series of bases, solvents, and additives were screened to determine the optimal conditions to maximize formation of **2c**. Treatment of **1c** with MeI and NaH in DMF led to a mixture of the starting material, the desired monomethylated product **2c**, and the undesired dimethylated product **4** as previously noted by Ando (run 1, Table 1).[27] The use of DBU gave a better chemoselectivity between **2c** and **4**, but only with 67% conversion (run 2). To activate MeI, we tested $AgNO_3$ (run 3) and Ag_2O (run 4) and found that the latter was more efficient, providing a mixture of **2c** and **4** in 92% conversion with a ratio of 93:7.

BRESSIN, Robert K., Julia L. DRISCOLL, Yanping WANG a Kazunori KOIDE. Scalable Preparation of Methylated Ando-Type Horner–Wadsworth–Emmons Reagent. *Organic Process Research & Development.* 2019, 23(2), 274-277. ISSN 1083-6160.
Dostupné z: doi:10.1021/acs.oprd.8b00423

the rate should be linearly proportional to the alcohol concentration. Instead, we observed a bell-shaped trend (fig. S4B), which indicates that protonation may occur intramolecularly through LiN-6. The slight preference between related substrates with different steric environments (Fig. 4D) bodes well with this hypothesis. Notably, the reaction mixture containing ^{n}BuOPh turned light blue with 8 equivalents of *t*-butanol, although the desired reduction did not occur. This suggests that excess alcohol may outcompete amino groups on the lithium at an earlier stage of the reaction, forming less-reductive solvated electrons, similar to work with SmI_3 (*51*). A mass effect may have obscured the additional role of *t*-butanol in the past; traditionally, the amine has been used in greater excess than the alcohol, outcompeting the alcohol for coordination to the lithium.

When <1 equivalents of *t*-butanol were present in the reduction of ^{n}BuOPh, the monoolefin was formed in ~20% yield. This is similar to the Benkeser reduction without alcohol (Fig. 1B) (*15*–*17*, *52*–*54*). Although the addition of an alcohol under the Benkeser-type conditions gave Birch-type products (*4*, *18*, *55*), these findings have not garnered widespread use. The alcohol is necessary to synthesize Birch products by protonating both the organolithiated species (LiN-5 or LiN-6) and the lithium amide in the reaction mixture (*18*). The protonation of the lithium amide then hinders the isomerization of the 1,4-diene to the 1,3-diene, which slows the formation of the monoolefin. Potential effects of *t*-butoxide would warrant further investigation.

Literature has shown that more acidic alcohols (e.g., methanol and ethanol) give faster reductions but lower yields than bulkier alcohols (e.g., isopropanol and *t*-butanol) because of an off-reaction with lithium to create H_2 (*45*, *50*). Although our data mostly support such a notion, we wish to consider other factors based on the data with trifluoroethanol (52%), methanol (33%), and ethanol (58%) (table S2) combined with the structural requirements of the amine (Fig. 2A), including optimal bite angle (*56*) (ethylenediamine versus 1,2-diamino-2-methypropane). For example, fig. S5 describes how the equilibrium between a monomer and higher-order aggregates of various ligated lithium intermediates can be affected by the amine ligand among other factors.

The switch of the solvent from an amine to an ethereal solvent (THF) was essential for this work. Altundas's conditions (ammonia gas in a balloon, lithium, and THF) (*30*) suggested that the amine might not be needed as a solvent. 1,2-Dimethoxyethane was ineffective as the solvent, which indicates that only one molecule of THF binds to a lithium ion to form reactive species. The role of THF as a ligand for the alkali metal ion most likely had not been considered before because the ethereal solvent was previously used in smaller amounts than the amine solvent.

The method discussed in this paper could reverse the chemoselectivity for the reduction of $PhCO_2H$ and ^{n}BuOPh by two orders of magnitude with triethylenetetramine (61-fold difference under the standard Birch reduction conditions in favor of $PhCO_2H$ and twofold difference under our conditions in favor of ^{n}BuOPh). More broadly, the structure-reactivity relationship indicates the potential for (reverse) chemoselective reduction in synthesis. To control the selectivity, inner- and outer-sphere electron transfer processes may be considered (*22*, *24*). Our work also suggests a broader role for the alcohol than previously considered, including the product selectivity with naphthalene and indole systems. Also, this study gives a platform to investigate solvated electrons at room temperature.

In addition to the theoretical advancements, the practicality of the technology should render the lithium-mediated reduction and deprotection more accessible to a broader scientific community and more amenable to the time-economic synthesis of complex molecules (*57*). Finally, the scope of the Birch reduction may be expanded by combining the chemistry of organolithium with other organometallic chemistry.

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We thank the Koide group members and L. Burrows (National Energy and Technology Laboratory) for their critical comments science.org/doi/10.1126/science.abk3099 on the manuscript. **Funding:** This study was supported by US National Science Foundation CHE-1955758 (to K.K.) and a Uehara Memorial Foundation postdoctoral fellowship (to S.K.). **Author contributions:** Conceptualization: J.B. and K.K. Investigation: J.B., S.K., and K.K. Funding acquisition: K.K. Supervision: K.K. Writing – original draft: J.B. Writing – review and editing: J.B., S.K., and K.K. **Competing interests:** J.B. and K.K. are inventors on US nonprovisional patent application 63/080,205, submitted by the University of Pittsburgh, which covers the use of lithium and the amines shown in this manuscript in ethereal solvents. **Data and materials availability:** All data are available in the main text or the supplementary materials.

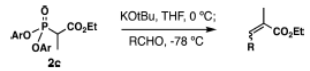
SUPPLEMENTARY MATERIALS

science.org/doi/10.1126/science.abk3099
Materials and Methods
Figs. S1 to S6
Tables S1 and S2
NMR Spectra
References (*58*–*77*)

5 July 2021; accepted 20 September 2021
10.1126/science.abk3099

phosphonate **2c** with various aldehydes commonly used to test similar olefination reagents. These results are summarized in Table 3. Compound **2c** shows comparable *Z*-selectivity to the nonalkylated **1c**[25] and related alkylated reagents[27] with near-perfect selectivity with aromatic (Table 3, run 1) and branched (runs 2 and 3) aldehydes and lower selectivity with conjugated and linear substrates (runs 4 and 5). The yields for the more challenging substrates were lower than those from the literature[25,27] due to the shorter times.

Table 3. HWE Reactions of 2c with Aromatic/Aliphatic Aldehydes in THF



run	RCHO	time (h)	yield (%)[a]	ratio (*Z*/*E*)[a]
1	PhCHO	3	94	97:3
2	$^{c}C_6H_{11}CHO$	3	36	94:6
3	$^{n}BuCH(Et)CHO$	3	60(hrsm)	100:0
4	$^{n}C_7H_{15}CHO$	3	84	86:14
5	$^{i}PrCH{=}CHCHO$	3	69	70:30

[a]Determined by the ^{1}H NMR analyses of the crude mixtures.

In conclusion, we have developed a method to prepare phosphonate **2c** in high yield and chemoselectivity. The procedure is devoid of column chromatography and does not require expensive reagents. The preparation of phosphonate **2c** from PCl_3 costs $0.49/mmol including all reagents and solvents. The use of commercial THF without distillation further simplifies the procedure. This reagent demonstrated high *Z*-selectivity in the HWE reaction with several aldehydes.

EXPERIMENTAL SECTION

Nondistilled THF (250 mL; water <0.008%) was added to a 1-L round-bottom flask under a nitrogen atmosphere. Phosphonate **1c** (105.42 g, 243.76 mmol) was added to the flask, and the resulting reaction mixture was cooled to 0 °C on ice. The mixture was then treated with MeI (15.10 mL, 243.75 mmol) in one portion at 0 °C. The reaction mixture was kept at 0 °C while KO^{t}Bu (27.35 g, 243.75 mmol) was added slowly to the flask in small portions (**Caution: exothermic**). The resulting mixture was allowed to stir for 1 h at 23 °C. The reaction was cooled to 0 °C, and DBU (72.50 mL, 487.50 mmol) was added slowly, followed by MeI (15.10 mL, 243.75 mmol). The resulting slurry was allowed to stir for 1 h at 23 °C. The reaction was cooled to 0 °C and quenched using saturated aqueous NH_4Cl (200 mL), THF was removed under reduced pressure, and the aqueous layer was extracted with EtOAc (2 × 200 mL). The combined organic layers were washed with brine (1 × 200 mL) and dried over Na_2SO_4. The organic layers were then filtered through a cotton plug, and the organic solvents were evaporated under reduce pressure to yield a pale-yellow oil (108.45 g, quantitative yield, 78% purity by ^{1}H NMR analysis). The material was recrystallized from hot hexanes to yield white crystals (72.7 g; 87% purity by ^{1}H NMR).

R_f = 0.34 (20% EtOAc in hexanes); mp = 70–72 °C; IR (film): ν_{max} = 3460, 3083, 2960, 2872, 1741 (C═O), 1488, 1442, 1300 (P═O), 1257, 1182, 1087, 1055, 945, 757 cm^{-1}; ^{1}H NMR (300 MHz, 293 K, $CDCl_3$): δ 7.73 (app d, J = 8.1 Hz, 1H; *Ar*), 7.64 (app d, J = 8.1 Hz, 1H; *Ar*), 7.34–7.31 (app m, 2H; *Ar*), 7.14–7.02 (m, 4H; *Ar*), 4.14 (dq, J = 10.7, 6.9 Hz, 1H; CH_2CH_3), 4.00 (dq, J = 10.7, 6.9 Hz, 1H; CH_2CH_3), 3.47 (dq, J = 24.0, 7.2 Hz, 1H; P(O)C*H*CH_3), 1.68 (dd, J = 19.5, 7.2 Hz, 3H; P(O)CHCH_3), 1.35 (s, 9H; ^{t}*Bu*), 1.31 (s, 9H; ^{t}*Bu*), 1.08 (t, J = 6.9 Hz, 3H; CH_2CH_3); ^{13}C NMR (100 MHz, 293 K, $CDCl_3$): 168.4 (d, J = 4 Hz), 151.0 (d, J = 10 Hz), 150.6 (d, J = 9 Hz), 138.9 (d, J = 4 Hz), 138.8 (d, J = 4 Hz), 127.5, 127.5, 127.3, 127.3, 124.4, 124.3, 119.8 (d, J = 3 Hz), 119.6 (d, J = 3 Hz), 61.9, 41.7 (d, J = 138 Hz), 34.7, 30.2, 30.09, 13.8, 12.0 (d, J = 6 Hz) ppm; HRMS (ES+) calcd for $C_{25}H_{35}O_5P$ $[M + H]^+$: 447.22949, found 447.23151.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.oprd.8b00423.

^{1}H and ^{13}C NMR spectra for compound **2c** (PDF)

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Notes

The authors declare no competing financial interest.

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Org. Process Res. Dev. 2019, 23, 274–277

Common types of academic publications

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Reading tip: More information about reviews

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- Writing well is difficult and is a skill that requires lifelong learning
- **Academic writing involves review by peers and thus, manuscript revisions (minor or major) are almost always needed**

Reduce wordiness:

small ~~in size~~
~~true~~ facts
adequate ~~enough~~
aggregate ~~together~~
near ~~to~~

In the future, corresponding regions of the fear circuit observed in this study could serve as a basis for further study.

x

Corresponding regions of the fear circuit observed in this study could serve as a basis for further study.

Tissue examination was done by light microscopy.

x

Tissues were examined by light microscopy.

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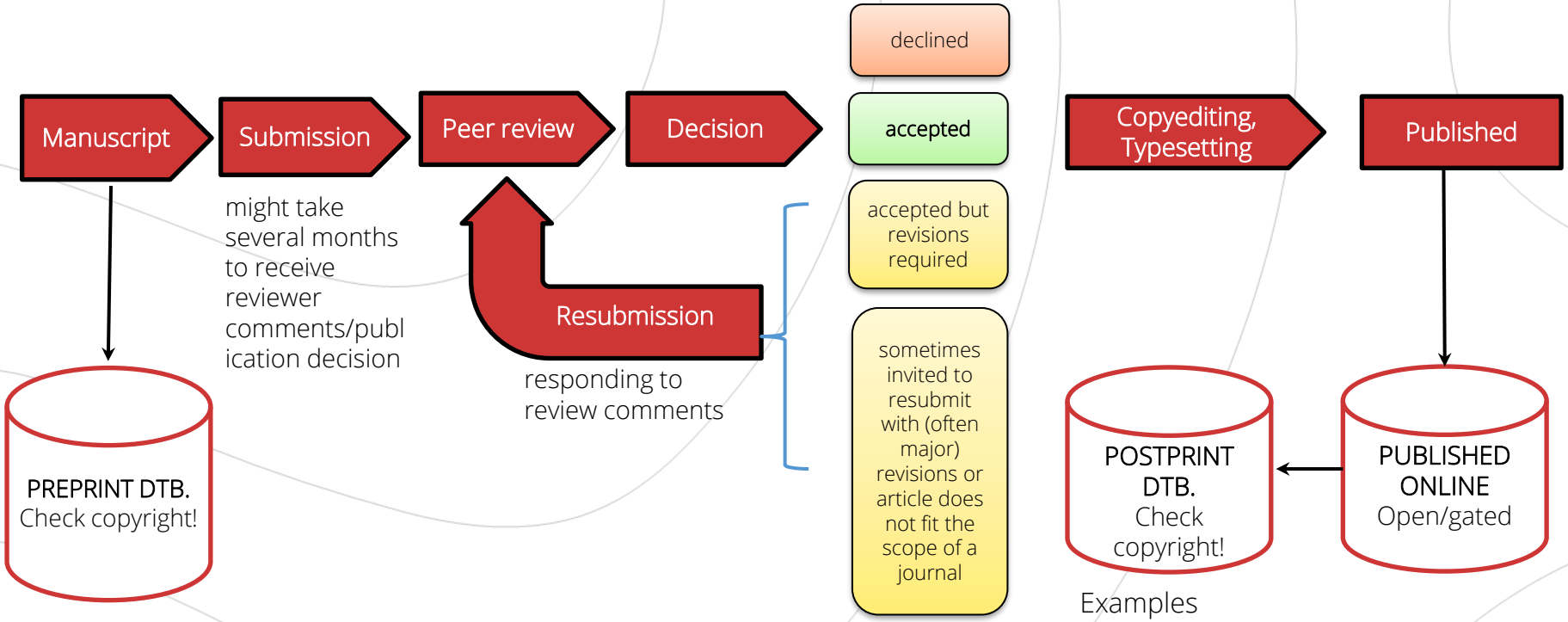

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ARTICLE

Safety, tolerability and viral kinetics during SARS-CoV-2 human challenge

Ben Killingley, Alex Mann, Mariya Kalinova, Alison Boyers, Niluka Goonawardane, Jie Zhou, Kate Lindsell, Samanjit S. Hare, Jonathan Brown, Rebeeca Frise, Emma Smith, Claire Hopkins, Nicolas Noulin, Brandon Londt, Tom Wilkinson, Stephen Harden, Helen McShane, Mark Baillet, Anthony Gilbert, Michael Jacobs, Christine Charman, Priya Mande, Jonathan S. Nguyen-Van-Tam, Malcolm G. Semple, Robert C. Read, Neil M. Ferguson, Peter J. Openshaw, Garth Rapeport, Wendy S. Barclay, Andrew P. Catchpole, Christopher Chiu

DOI: 10.21203/rs.3.rs-1121993/v1 Download PDF

Abstract

To establish a novel SARS-CoV-2 human challenge model, 36 volunteers aged 18-29 years without evidence of previous infection or vaccination were inoculated with 10 $TCID_{50}$ of a wild-type virus (SARS-CoV-2/human/GBR/484861/2020) intranasally. Two participants were excluded from per protocol analysis due to seroconversion between screening and inoculation. Eighteen (~53%) became infected, with viral load (VL) rising steeply and peaking at ~5 days post-inoculation. Virus was first detected in the throat but rose to significantly higher levels in the nose, peaking at ~8.87 log_{10} copies/ml (median, 95% CI [8.41,9.53). Viable virus was recoverable from the nose up to ~10 days post-inoculation, on average. There were no serious adverse events. Mild-to-moderate symptoms were reported by 16 (89%) infected individuals, beginning 2-4 days post-inoculation. Anosmia/dysosmia developed more gradually in 12 (67%) participants. No quantitative correlation was noted between VL and symptoms, with high VLs even in asymptomatic infection, followed by the development of serum spike-specific and neutralising antibodies. However, lateral flow results were strongly associated with viable virus and modelling showed that twice-weekly rapid tests could diagnose infection before 70-80% of viable virus had been generated. Thus, in this first SARS-CoV-2 human challenge study, no serious safety signals were detected and the detailed characteristics of early infection and their public health implications were shown.
ClinicalTrials.gov identifier: NCT04865237.

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Ben Killingley, Alex Mann, Mariya Kalinova et al. Safety, tolerability and viral kinetics during SARS-CoV-2 human challenge, 01 February 2022, PREPRINT (Version 1) available at Research Square [https://doi.org/10.21203/rs.3.rs-1121993/v1]

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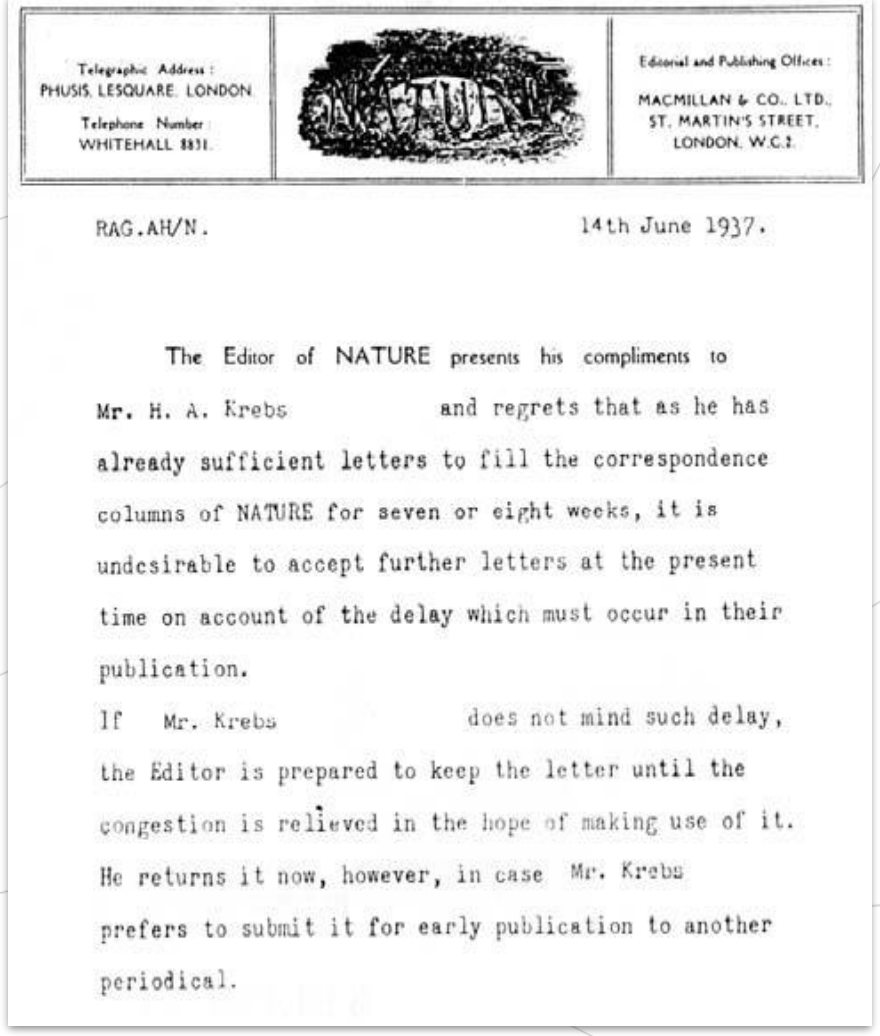

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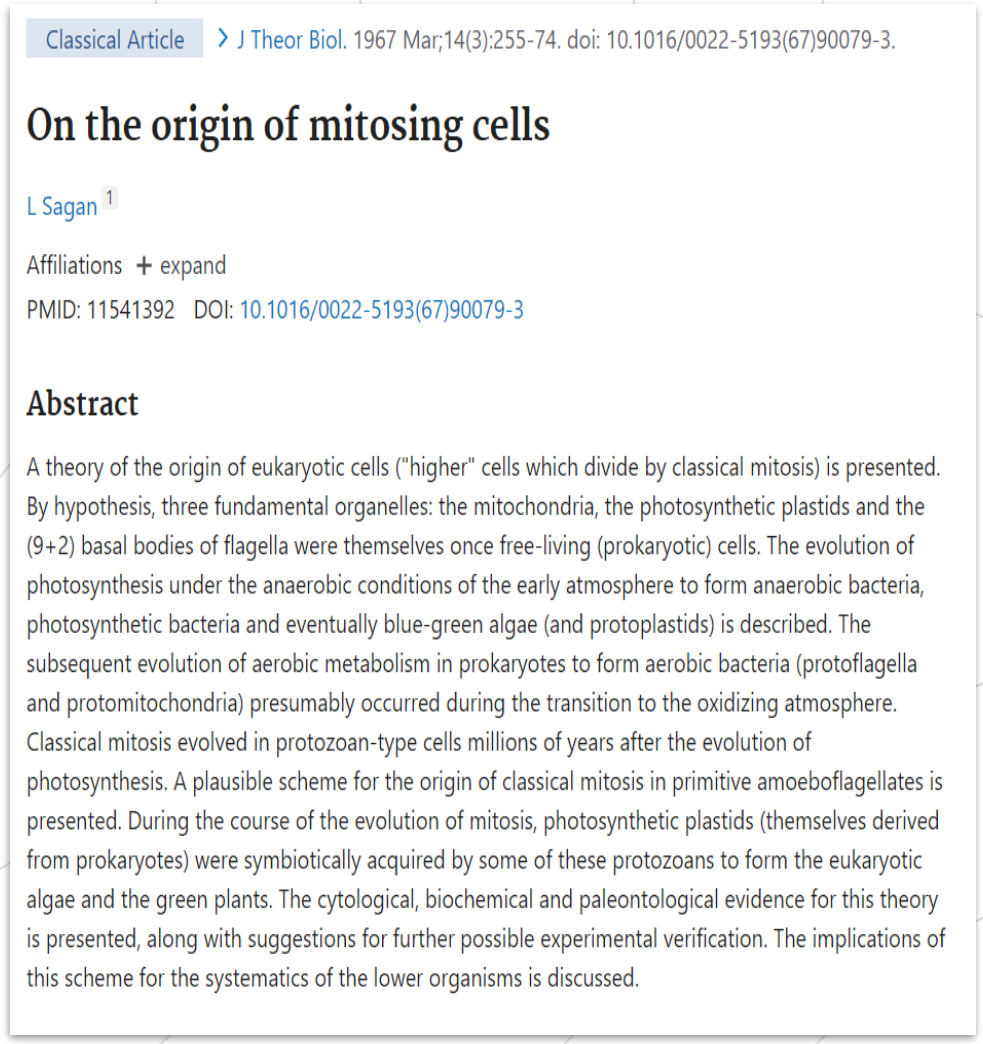
RAG.AH/N. 14th June 1937.

The Editor of NATURE presents his compliments to Mr. H. A. Krebs and regrets that as he has already sufficient letters to fill the correspondence columns of NATURE for seven or eight weeks, it is undesirable to accept further letters at the present time on account of the delay which must occur in their publication.

If Mr. Krebs does not mind such delay, the Editor is prepared to keep the letter until the congestion is relieved in the hope of making use of it. He returns it now, however, in case Mr. Krebs prefers to submit it for early publication to another periodical.

Rejection letter from a *Nature* editor, who didn't accept a letter from Sir Hans Adolf Krebs on the citric acid cycle. Authorea.com



Classical Article › J Theor Biol. 1967 Mar;14(3):255-74. doi: 10.1016/0022-5193(67)90079-3.

On the origin of mitosing cells

L Sagan [1]

Affiliations + expand

PMID: 11541392 DOI: 10.1016/0022-5193(67)90079-3

Abstract

A theory of the origin of eukaryotic cells ("higher" cells which divide by classical mitosis) is presented. By hypothesis, three fundamental organelles: the mitochondria, the photosynthetic plastids and the (9+2) basal bodies of flagella were themselves once free-living (prokaryotic) cells. The evolution of photosynthesis under the anaerobic conditions of the early atmosphere to form anaerobic bacteria, photosynthetic bacteria and eventually blue-green algae (and protoplastids) is described. The subsequent evolution of aerobic metabolism in prokaryotes to form aerobic bacteria (protoflagella and protomitochondria) presumably occurred during the transition to the oxidizing atmosphere. Classical mitosis evolved in protozoan-type cells millions of years after the evolution of photosynthesis. A plausible scheme for the origin of classical mitosis in primitive amoeboflagellates is presented. During the course of the evolution of mitosis, photosynthetic plastids (themselves derived from prokaryotes) were symbiotically acquired by some of these protozoans to form the eukaryotic algae and the green plants. The cytological, biochemical and paleontological evidence for this theory is presented, along with suggestions for further possible experimental verification. The implications of this scheme for the systematics of the lower organisms is discussed.

Groundbreaking article by Lynn Margulis on evolution by endosymbiosis was rejected by 15 journals before finally published, because the topic was too new and nobody could evaluate it.

Sagan L. On the origin of mitosing cells. J Theor Biol. 1967 Mar;14(3):255-74. doi: 10.1016/0022-5193(67)90079-3. PMID: 11541392.

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Final tips & tricks

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- Acknowledge contributions
- Build a network of others over time to review your manuscript prior to review by supervisor/mentor and submission to journal
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Thank you

Questions?