Dihydrolevoglucosenone (Cyrene™) as a bio-based alternative for dipolar aprotic solvents

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Supplementary Information

Modified hydrogenation methods

Low hydrogen pressure

Levoglucosenone (LGO) (100 g, 0.792 mol) was dissolved in ethyl acetate (EtOAc) at a molar EtOAc to LGO ratio of 3. After stirring, 4 g of 10 wt% Pd/C was added and the mixture was purged three times with nitrogen. Hydrogen was administered using special Sigma-Aldrich balloons (~1.1 atm). The reaction was stirred at room temperature for 96 hours. After completion the Pd/C was filtered off and the solvent removed under reduced pressure.

For the solvent-free reaction 1 g of 10 wt% Pd/C was added to LGO (25 g, 0.198 mol). After purging of the reaction mixture with nitrogen (3 times) the hydrogen was administered using special Sigma-Aldrich balloons (~1.1 atm). The reaction was complete after 8 days.

High hydrogen pressure

To a 10 mL high pressure reactor was added 0.8 g LGO (6.3 mmol), 4 mL EtOAc and 0.025 g 10 % Pd/C (0.02 mmol). The vessel was pressurised to the desired pressure (3 to 80 bar) and left to react at room temperature with stirring until a steady pressure was observed (2 to 48 hours). Upon release of any residual pressure, the resulting mixture was removed and filtered through a plug of Celite, which was additionally flushed with 2 x 5 mL EtOAc. The solvent was then removed under reduced pressure

The reaction was repeated at 80 bar as previously described but solvent-free, going to completion in less than 2 hours.

Characterization

The reaction products were characterized using ^{1}H and ^{13}C NMR, GC-MS and ESI (see below).

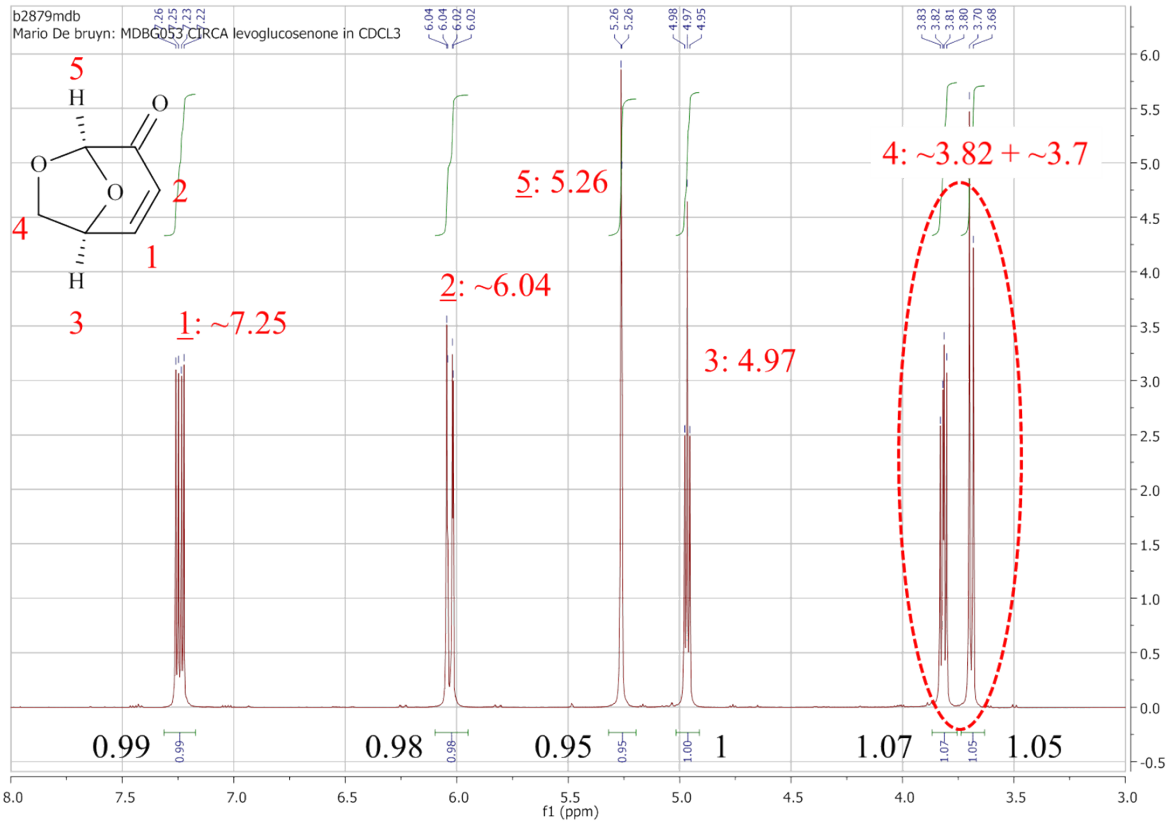


Figure S1: ^{1}H NMR of levoglucosenone in $CDCl_3$.

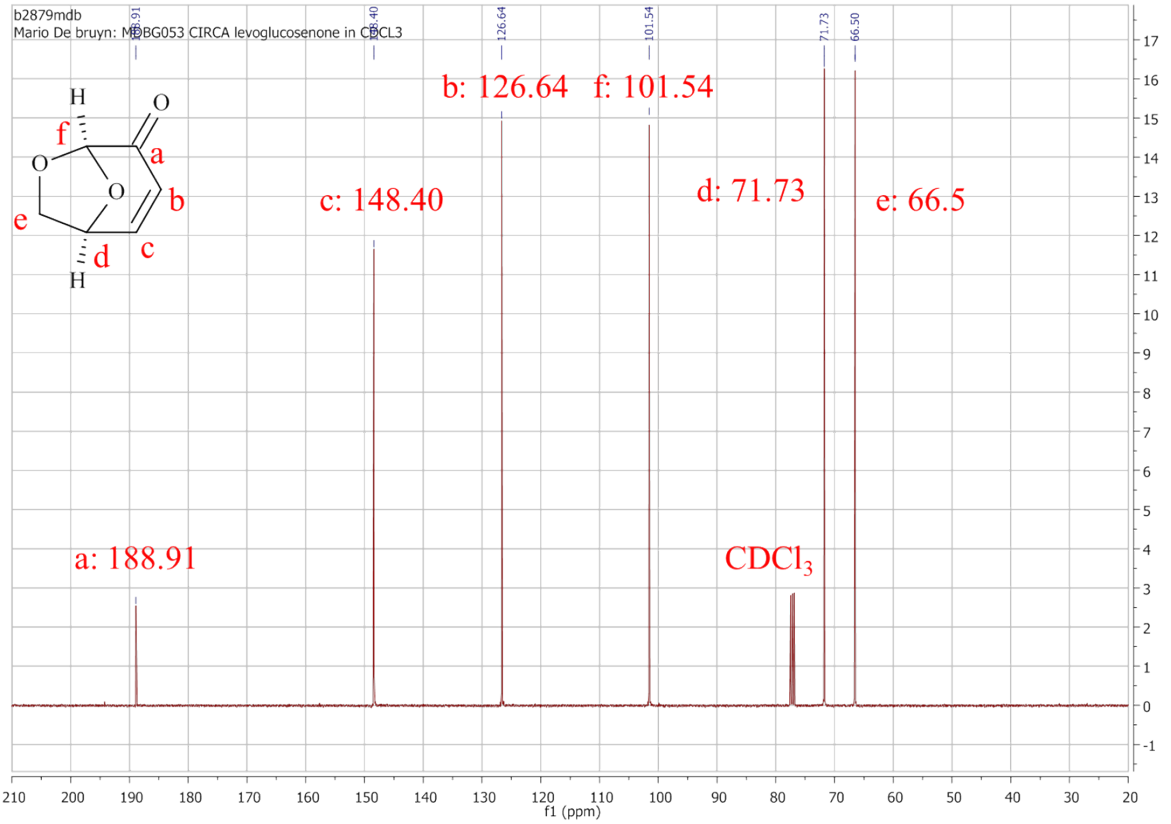


Figure S2: ^{13}C NMR of levoglucosenone in $CDCl_3$.

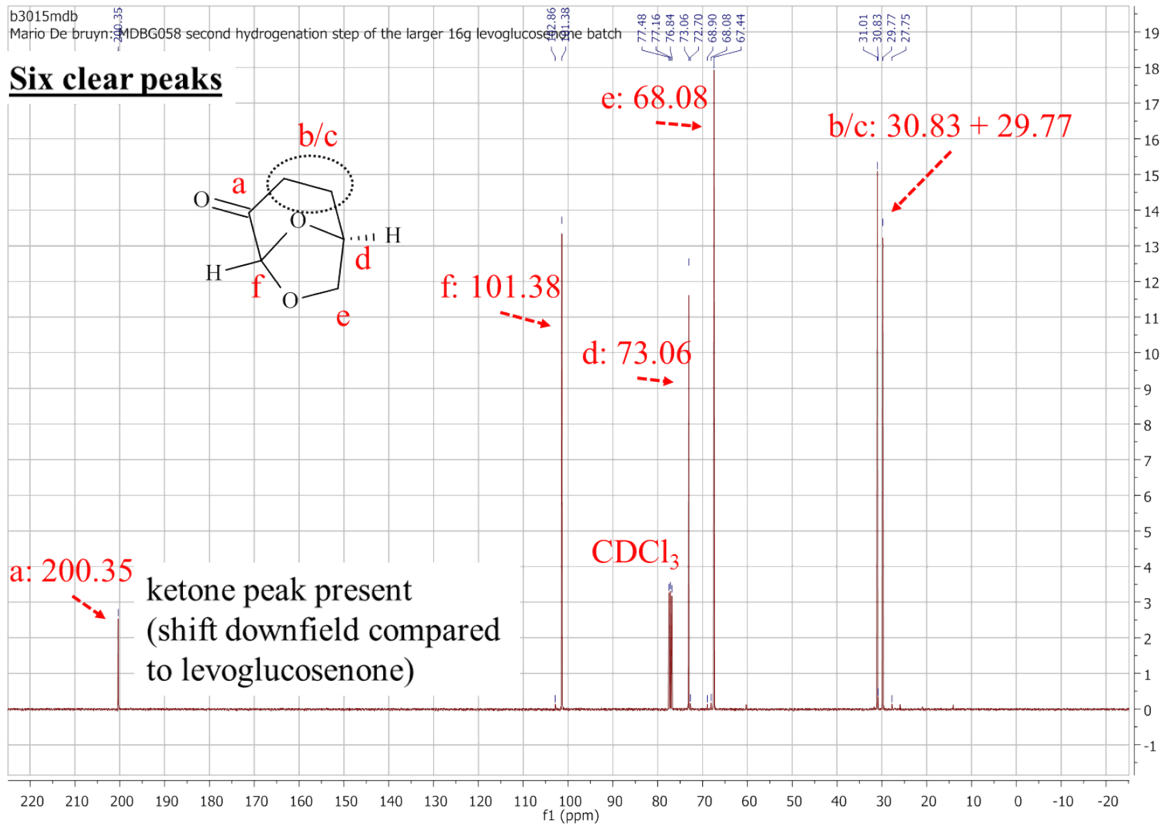


Figure S3: ^{13}C NMR in $CDCl_3$ of the reaction of levoglucosenone to dihydrolevoglucosenone after 6 hours.

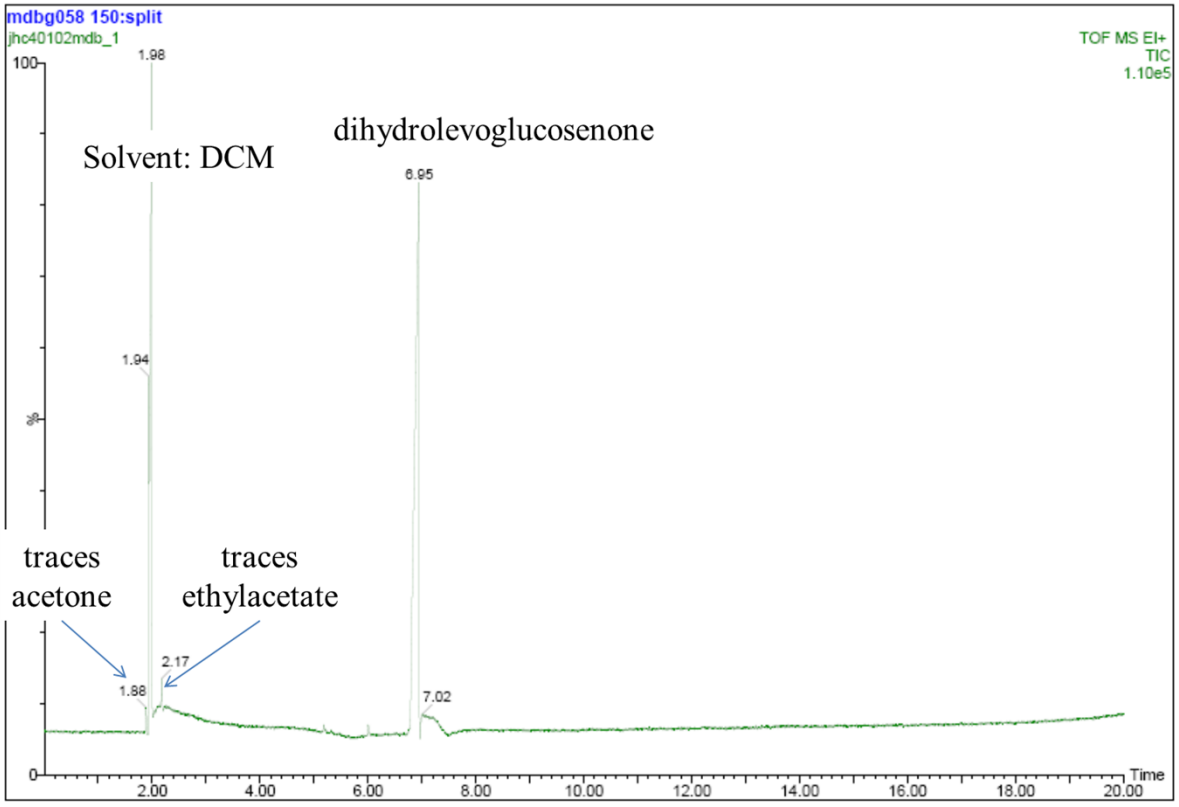


Figure S4: GC-EI of the reaction of levoglucosenone to dihydrolevoglucosenone after 6 hours.

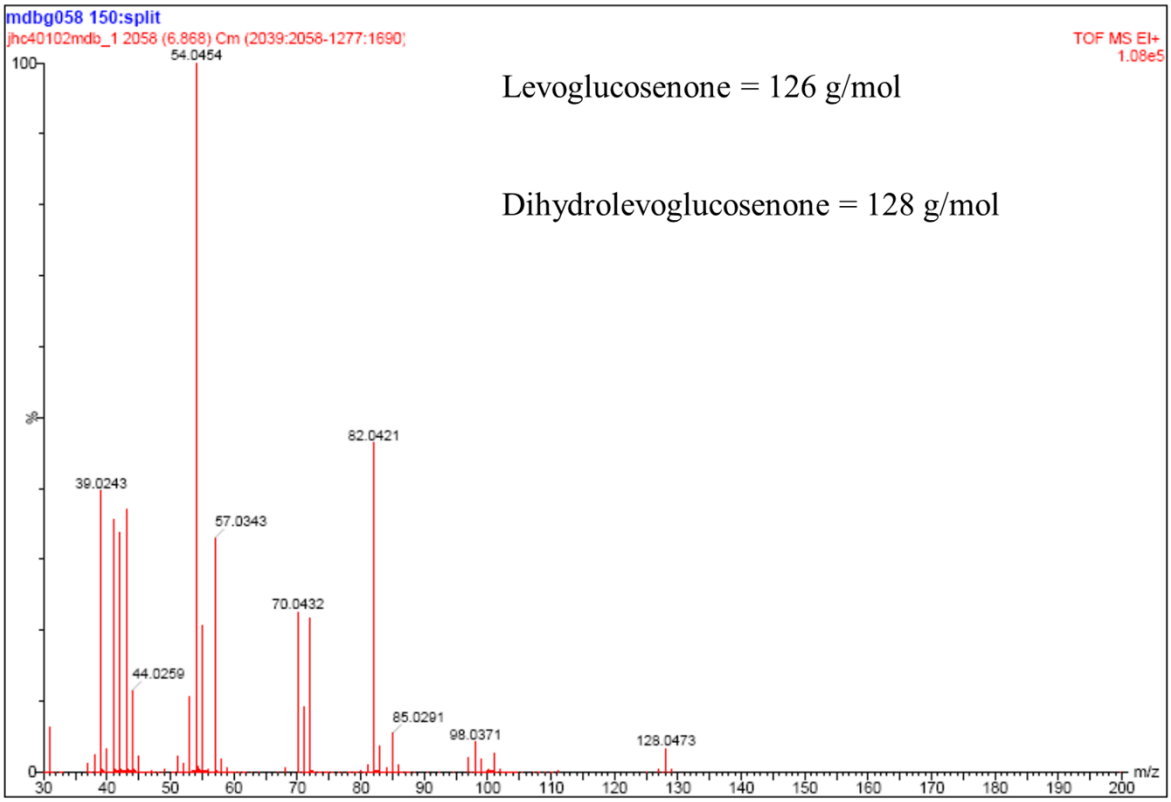
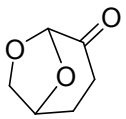


Figure S5: GC-EI of the reaction of levoglucosenone to dihydrolevoglucosenone after 6 hours.

Solvent Predictions

HSPiP

Hansen Solubility Parameters HSP (δ_d, δ_p, δ_h), Boiling point (BP) and density of Cyrene™ have been predicted using the HSPiP software (4th Edition 4.1.04, developed by Abbott, Hansen and Yamamoto) utilising the Y-MB method (Dr. Hiroshi Yamamoto's neural network molecular breaking technique). The following SMILES input has been used:



SMILES O=C1C(OC2)OC2CC1

Figure S6. Cyrene™ structure and SMILES.

Subsequently Cyrene™ was located in the "Hansen space" (see below) and compared to other organic solvents.

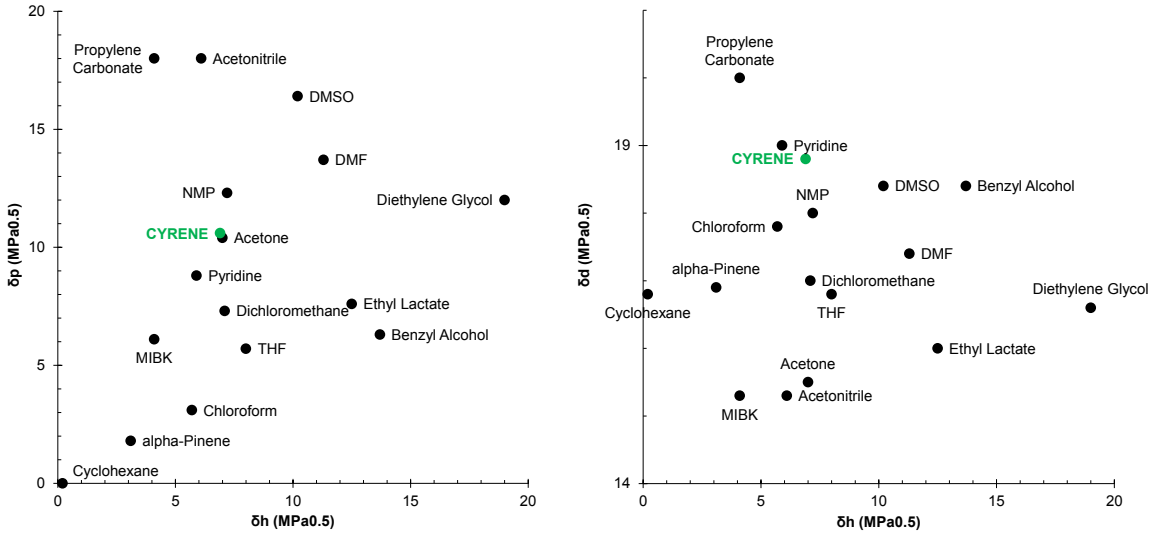


Figure S7. Cyrene™ location in the (δ_p, δ_h) and (δ_d, δ_h) maps. (HSP of Cyrene™ predicted with Y-MB method while HSP of other solvents obtained from the HSPiP database or from reference 1).

The following formula has been used to calculate the distance between Cyrene™ and other solvents (Solvent Optimizer option within HSPiP software):

$$D = \sqrt{\left(4\left(\delta_d^{Cyrene} - \delta_d^{solvent}\right)^2 + \left(\delta_p^{Cyrene} - \delta_p^{solvent}\right)^2 + \left(\delta_h^{Cyrene} - \delta_h^{solvent}\right)^2\right)}$$

COSMOtherm

The 3D molecular geometry of Cyrene™ has been sketched with ArgusLab (version 4.0.1, Mark Thompson and Planaria Software LLC, Seattle, WA). Then conformational analysis has been performed using the COSMOconf program (COSMOconfX Demo Version v3 by COSMOlogic GmbH & Co.KG, Germany) that involves semi-empirical AM1 (Austin Model 1) calculations followed by a more accurate DFT (Density Functional Theory) treatment of the most important AM1 conformers. TURBOMOLE program (TURBOMOLE Demo Version V6.5 2013, a development of University of Karlsruhe and Forschungszentrum Karlsruhe GmbH, 1989-2007, TURBOMOLE GmbH, since 2007 Germany) was used to perform the DFT/COSMO geometry optimizations according to the standard quantum chemical method for COSMO-RS (Becke-Perdew density functional and Triple Zeta Valence Polarized basis set, *i.e.* BP-TZVP).

The σ-surfaces have been generated using the COSMOtherm software (F. Eckert and A. Klamt, COSMOtherm, Demo Version C3.0, Release 14.01; COSMOlogic GmbH & Co. KG, Leverkusen, Germany, 2013).

Solvatochromic parameters

The Kamlet-Taft solvatochromic parameters were obtained from the UV-vis. spectra of Reichardt's dye, 4-nitroaniline, and *N*,*N*-diethyl-4-nitroaniline in solution with a Jasco V-550 UV spectrophotometer. Spectra were recorded in triplicate at absorbances between 0.1 and unity. The observed absorbance wavelengths of the three dyes can be converted to the Kamlet-Abboud-Taft solvatochromic parameters of hydrogen bond donation (α),[2] hydrogen bond accepting ability (β),[3] and dipolarity/polarisability (π*) respectively.[4] Reichardt's dye is also used to determine E_T^N, a complimentary scale of solvent polarity.[5]

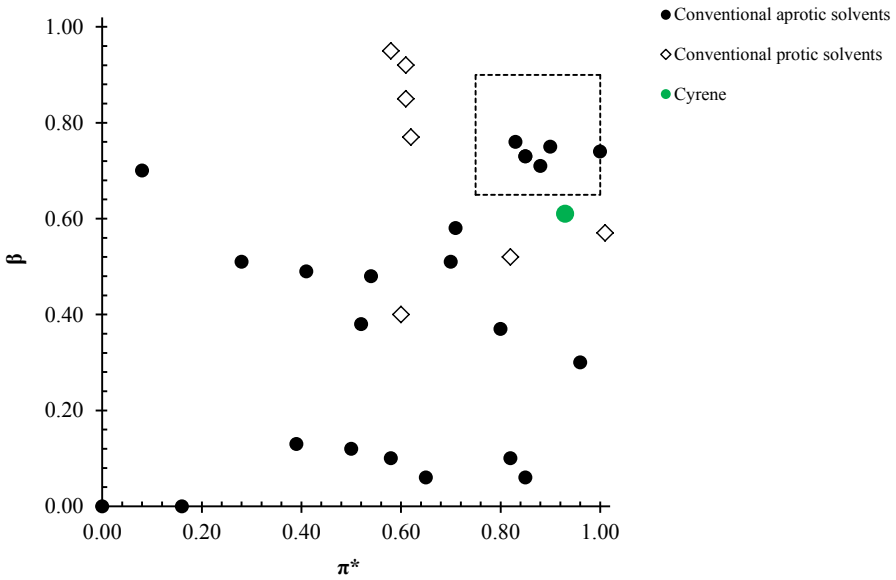


Figure S8. The Kamlet-Abboud-Taft solvatochromic parameters β and π* with the traditional highly dipolar aprotic region (DMF, NMP, DMSO, *etc*.) indicated within the boxed region.

Test reactions

Menschutkin reaction

To a solution of 1,2-dimethylimidazole (0.288 g, 3.00 mmol) preheated to 323 K in the chosen solvent (3 mL) was added 1-bromodecane (0.69 mL, 3.33 mmol) in a single aliquot. The progression of the reaction was monitored by the ^{1}H-NMR spectroscopy signals belonging to the CH_2X moiety of 1-bromodecane and the analogous signal belonging to the product until over 50% conversion had been achieved. The product 1-decyl-2,3-dimethylimidazolium bromide is a known literature compound, and the signals observed in the ^{1}H-NMR spectra corresponded to those previously reported for this compound.[6] A correlation between solvent polarity and the rate constant of the reaction was calculated by linear regression with the Data Analysis tool found in Microsoft Excel. Only π* was found to be statistically significant as an independent variable.

Table S1. Reaction data for the Menschutkin reaction[a]

Solvent	ln(**k** /moldm^{-3}s^{-1})	**α**	**β**	***π****
Cyrene™	-9.27	0.00	0.61	0.93
Acetonitrile	-9.87	0.35	0.37	0.80
Chloroform	-10.93	0.20	0.10	0.58
DMAC	-9.52	0.00	0.73	0.85
DMF	-9.58	0.00	0.71	0.88
DMSO	-9.01	0.00	0.74	1.00
1,4-Dioxane	-11.26	0.00	0.38	0.52
NMP	-9.19	0.00	0.75	0.90
Sulpholane	-8.81	0.00	0.30	0.96

[a]Polarity data describing the additional solvents was sourced from reference 7.

Fluorination

Potassium fluoride (0.0581 g, 1.00 mmol) was dissolved in the chosen solvent (3 mL) and preheated at 403 K for two hours. The temperature was then lowered to 363 K and 2-chloro-5-nitropyridine (0.1057 g, 0.67 mmol) was added as a single dose. The progression of the reaction was monitored by

^{1}H-NMR spectroscopy as previously. The product 2-fluoro-5-nitropyridine is a known literature compound, and the signals observed in the ^{1}H-NMR spectra corresponded to those previously reported for this compound.[8]

Table S2. Reaction data for the fluorination of 2-chloro-5-nitropyridine[a]

Solvent	ln(**k** /moldm^{-3}s^{-1})	**α**	**β**	***π****
Cyrene™	-10.76	0.00	0.61	0.93
DMF	-8.54	0.00	0.71	0.88
DMSO	-6.07	0.00	0.74	1.00
NMP	-10.34	0.00	0.75	0.90
Sulpholane	-9.93	0.00	0.30	0.96
Cyclohexanone	Negligible	0.00	0.58	0.71

[a]Polarity data describing the additional solvents was sourced from reference 7.

References

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3 M. J. Kamlet and R. W. Taft, *J. Am. Chem. Soc.*, 1976, **98**, 377.
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