8.28 (s, 1H, Ade-*H*8), 8.36, 8.37 (s, 1H, Ade-*H*2), 8.37, 8.46 (br s, 2H, Ade-N6H_2), 11.30 (s, 1H, Thy-N3*H*); MS: *m*/*z*: 562.0 [Pd(**1**)Cl]$^+$; elemental analysis (%) calcd for **2**·3H_2O: C 28.99, H 4.12, N 13.92; found: C 28.13, H 3.97, N 13.14. A small quantity of crystals of **2** suitable for single-crystal X-ray diffraction studies were grown by slow cooling of a hot aqueous solution.[9]

3: Same procedure as for Pd analogue **2**, except that $K_2[PtCl_4]$ (0.074 g, 0.182 mmol) in aqueous solution was used as starting material, and to this was added dropwise a hot ethanolic solution of **1** (0.076 g, 0.182 mmol), and the mixture refluxed overnight. The cooled solution was taken to dryness under reduced pressure, and the resultant solid residue dissolved in hot water (50 mL). The mixture was filtered to remove undissolved solids and concentrated to a minimum volume in vacuo. The addition of a saturated aqueous solution of $NaBF_4$ precipitated **3** as a white solid, which was washed with water, ethanol, and diethyl ether and pump dried. Yield 0.093 g, 69.3%. ^{1}H NMR ([D$_6$]DMSO, TMS): δ = 1.78, 1.81 (s, 3H, Thy-CH_3), 2.13, 2.23 (m, 2H, H17), 3.04 (m, 1H, H16), 3.10 (m, 1H, H16), 3.22 (d, 1H, H13′), 3.36 (m, 1H, H14), 3.39 (m, 1H, H14′), 3.62 (d, 1H, H13), 3.73 (m, 1H, H11′), 3.82 (m, 1H, H11), 4.74 (m, 2H, H18), 4.81, 5.07 (d, 1H, H10′), 5.13 (m, 1H, H10), 7.51, 7.53 (s, 1H, Thy-*H*6), 8.28, 8.29 (s, 1H, Ade-*H*8), 8.41, 8.43 (s, 1H, Ade-H2), 8.47, 8.57 (br s, 2H, Ade-N6H_2), 11.29 (s, 1H, Thy-N3*H*); MS: *m*/*z*: 652.0 [Pt(**1**)Cl]$^+$; elemental analysis (%) calcd for **3**·2H_2O: C 26.35, H 3.51, N 12.65; found: C 27.07, H 3.98, N 12.71. Crystallization by slow cooling of a hot aqueous solution of **3** yielded a few single crystals, some of which were suitable for diffraction studies.[9]

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[8] a) Crystal data for **2**: $C_{17}H_{32}ClF_3N_7O_{6.5}PdS_2Si_{0.5}$, M_r = 715.51, monoclinic, space group *I*2/*a*, *a* = 24.3737(16), *b* = 7.9006(5), *c* = 29.2031(19) Å, β = 97.894(2)°, *V* = 5570.3(6) Å^3, *Z* = 8, ρ_{calcd} = 1.706 g cm^{-3}, Mo$_{K\alpha}$ radiation, λ = 0.71073 Å, μ = 1.00 mm^{-1}, *T* = 160 K. 18467 measured reflections were corrected for absorption; 4903 were unique (R_{int} = 0.0451, $\theta \le 25.0°$); *R* = 0.0829 (*F* values, $F^2 > 2\sigma$), R_w = 0.1771 (F^2 values, all data), GOF 1.312 for 350 parameters, max./min. residual electron density 2.58/ – 1.47 e Å^{-3}. b) Crystal data for **3**: $C_{17}H_{32}ClF_3N_7O_{6.5}PtS_2Si_{0.5}$, M_r = 804.20, monoclinic, space group *I*2/*a*, *a* = 24.4619(10), *b* = 7.9190(3), *c* = 29.1288(10) Å, β = 98.073(2)°, *V* = 5586.7(4) Å^3, *Z* = 8, ρ_{calcd} = 1.912 g cm^{-3}, synchrotron radiation at Darebury Laboratory station 9.8, λ = 0.6942 Å, μ = 5.36 mm^{-1}, *T* = 160 K. 18024 measured reflections were corrected for absorption; 6866 were unique (R_{int} = 0.0360, $\theta \le 27.5°$); *R* = 0.0388 (*F* values, $F^2 > 2\sigma$), R_w = 0.1053 (F^2 values, all data), GOF 1.185 for 350 parameters, max./min. residual electron density 2.49/ – 1.19 e Å^3. c) The anion in both crystal structures wass identified as SiF_6^{2-}, generated by etching of the glass by the aqueous BF_4^- ions. Detailed evidence is available from the authors. d) Programs: standard Bruker AXS control and integration software and SHELXTL. CCDC-170471 (**2**) and CCDC-170472 (**3**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

Dearomatizing Disrotatory Electrocyclic Ring Closure of Lithiated *N*-Benzoyloxazolidines**

Jonathan Clayden,* Savroop Purewal, Madeleine Helliwell, and Simon J. Mantell

Aromatic amides—both naphthamides and benzamides—can be dearomatized in a cyclization reaction triggered by a benzylic lithiation α to the amide nitrogen.[1] The reaction has been optimized for the synthesis of functionalized cyclohexadienes **4** and cyclohexenones from amides **1**, and both the benzamide and naphthamide versions of the reaction (Scheme 1) have been employed in the synthesis of important members of the kainoid family of cyclic amino acids.[2]

Superficially, the mechanism of this cyclization appears to be an intramolecular conjugate addition reaction[3] of the benzylic anionic center into the electron-deficient *ortho* position of the aromatic ring, with the product stereochemistry arising from the preference of the phenyl group for the *exo* face of the forming bicyclic ring system. However, under this interpretation, the cyclization of the lithiated benzamide **2** has at least some (Baldwin-disfavored) 5-*endo-trig* character,[4] and the cyclization of a 2-naphthamide **2** (R^1, R^2 = benzo) rather more.

An attractive alternative rationalization, illustrated in the box in Scheme 1, is that the cyclization is pericyclic and

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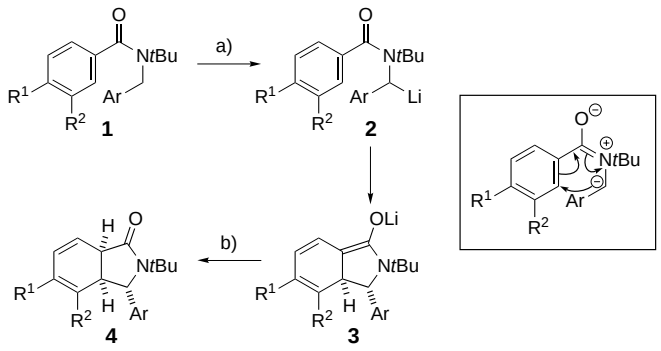
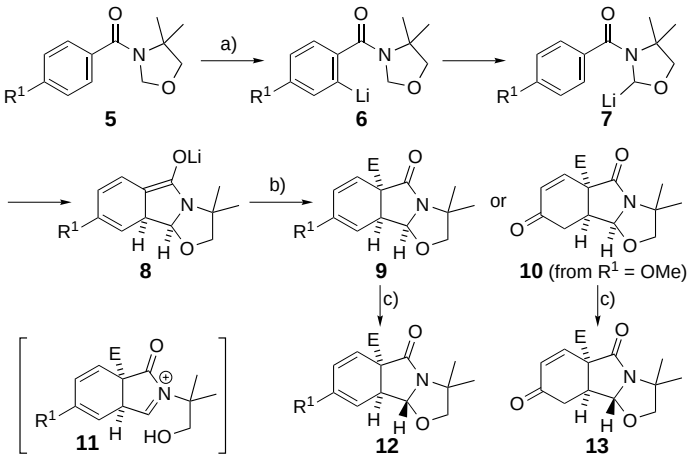


Scheme 1. Dearomatizing cyclization of lithiated *N*-aroyl benzylamines. a) LDA, $-78-+25\,^{\circ}C$; b) NH_4Cl.



Scheme 2. Dearomatizing cyclization of lithiated *N*-benzoyl oxazolidines **5**; a) Method A: *s*BuLi or *t*BuLi (1.5 equiv), DMPU (6 equiv), THF, $-78\,^{\circ}C$, 30 min then $0\,^{\circ}C$, 2 h or Method B: *t*BuLi (1.5 equiv), DMPU (6 equiv), THF, $-78\,^{\circ}C$, 14–16 h; b) E^+; c) 2 M HCl, MeOH or Et_2O.

therefore is not subject to the usual stereoelectronic constraints adumbrated by Baldwin.[4] A disrotatory thermal electrocyclic ring closure of **2** obeys the Woodward–Hoffmann rules,[5] and will lead to the correct stereochemistry of **3**, provided that the aryl ring starts *trans* to the *tert*-butyl group. Stereochemistry alone can therefore not distinguish between the two mechanisms of cyclization in this case.

However, when the nitrogen atom is within a ring, the stereochemistry of the product is diagnostic of the reaction mechanism. Herein, we describe the first dearomatizing anionic cyclization of a non-benzyl substituted benzamide, the stereochemistry of which gives strong evidence that the cyclization is pericyclic.

The *N*-benzoyl oxazolidines **5** ($R^1 = H$ and $R^1 = OMe$)[6] were lithiated with *t*BuLi or *s*BuLi in the presence of 1,3-dimethylhexahydro-2-pyrimidinone (DMPU) at $-78\,^{\circ}C$ (Scheme 2). The resulting deep orange organolithium compounds were either warmed to $0\,^{\circ}C$ over 2 h (method A) or stirred at $-78\,^{\circ}C$ for 14–16 h (method B). From **5** ($R' = H$) a tricyclic product **9** was obtained as a single diastereoisomer in moderate to good yield (Table 1).[7] Enones **10** were obtained from **5** ($R^1 = OMe$) after work up with 1 M HCl. The structure of **9a** was established by X-ray crystallography[8] (Figure 1a), while evidence for the stereochemistry of **9b–d**, **10a** and **10b** (Table 1) was gained from nuclear Overhauser enhancement (NOE) studies (Figure 2 and Table 1).

On stirring **9b–d** or **10b** with acid (2 M HCl in ether), a clean isomerization took place to yield a diastereoisomer **12b–d** quantitatively (or enone **13** from **10b**), presumably via the acyliminium ion **11**. An X-ray crystal structure[8] (Figure 1b) of **12c** confirmed its stereochemistry, and NOE

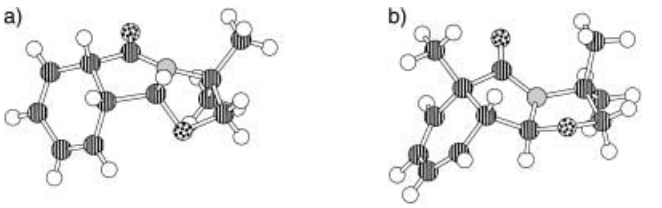


Figure 1. a) X-ray crystal structure of **9a**; b) X-ray crystal structure of **12c**.

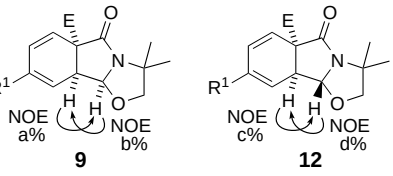


Figure 2. Stereochemistry of **9** and **12**.

studies (Figure 2) confirmed the stereochemistry of **12b–d** and **13**. Evidently the initial cyclization produces a *cis*-fused tricyclic ring system which is significantly less stable than the *trans*-fused system formed after epimerization under thermodynamic control.

While an ionic cyclization of lithiated **5** would be expected to generate directly a more stable *trans* tricyclic enolate *epi*-**8**, and hence **12**, thermal electrocyclic ring closure of lithiated **5** must be disrotatory and therefore has no alternative but to form the enolate **8** with a *cis* tricyclic structure (Scheme 3). The stereochemistry of the product strongly suggests that the

Tabelle 1. Yields and Stereochemistry.

Entry	R^1	E^+	E	Yield **9**[a] or **10**[b] [%]	NOE a %	NOE b %	Yield **12** or **13** [%]	NOE c %	NOE d %
1	H	NH_4Cl	H	**9a** 60	–	–	–	–	–
2	H	CD_3OD	D	**9b** 60	20.0	22.3	**12b** 13[c]	2.2	2.5
3	H	MeI	Me	**9c** 53[d]	13.2	17.3	**12c** 100	2.3	1.8
4	H	BnBr	Bn	**9d** 45	14.6	11.2	**12d** 99	4.1	2.9
5	H	PBB-Br[e]	PBB	**9e** 41	–	–	–	–	–
6	MeO	1 M HCl	H	**10a** 55	14.9	13.5	–	–	–
7	MeO	MeI then 1 M HCl	Me	**10b** 48	12.5	13.8	**13** 100	3.7	2.6

[a] From **5** ($R^1 = H$) by method A. [b] From **5** ($R^1 = OMe$) by method B. [c] Major product is **19** (E = H). [d] By NMR. [e] PBB = *p*-$BrC_6H_4CH_2$.

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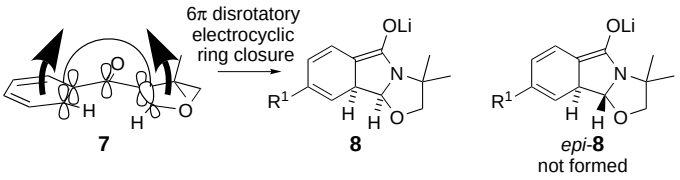
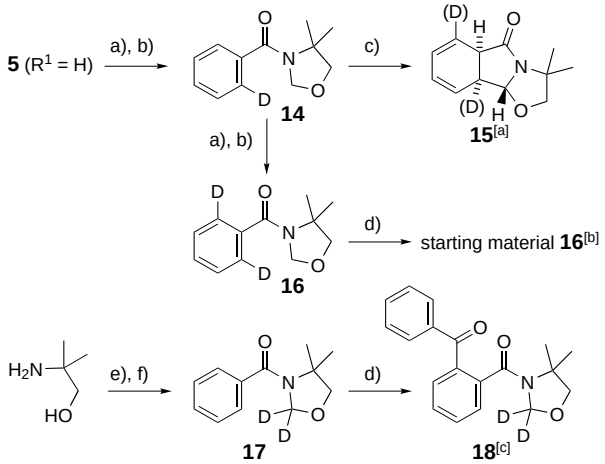


Scheme 3. Mechanisms for ring closure of **7**.

cyclization of **5** is indeed pericyclic, and we presume the same for the cyclization of **1**.

To cyclize, **5** must be lithiated at the position α to the O and to N atoms to give **7**.[9] However, when **5** ($R^1 = H$) was lithiated at $-78\,^{\circ}C$ and quenched after 30 min with an electrophile (CD_3OD), only the *ortho*-deuterated product **14** was obtained, in 95% yield. By repeating this step, both *ortho* protons could be replaced to give **16** (Scheme 4). Presumably, the sequence of events leading to cyclization involves firstly formation of an *ortho*-lithiated compound **6**,[10] which slowly undergoes "anion translocation"[11] to give **7**, which then cyclizes. The powerful kinetic isotope effect typical of low-temperature lithiations[12] can be used to hinder the mechanism at either the **5**→**6** or the **6**→**7** step (Scheme 2). Under the same cyclization conditions, **16** failed to lithiate



Scheme 4. Establishing role of lithium: a) *s*BuLi, THF, $-78\,^{\circ}C$, 30 min; b) CD_3OD; c) method A (Scheme 2); d) method B (Scheme 2); e) CD_2O, Δ; f) PhCOCl, CH_2Cl_2, NaOH, H_2O. [a] 34% **15**, 19% **14** + 20% addition of *s*BuLi to benzamide ring; [b] 60% **16** + 25% addition of *s*BuLi to benzamide ring; [c] 62% **18** + traces of cyclization products.

and predominantly starting material was returned. With **17**, on the other hand, *ortho*-lithiation occurred, but an inability to form **7** meant that, on warming, the *ortho*-lithiated species dimerized by intermolecular nucleophilic substitution to give the ketone **18** in 62% yield. Monodeuterated **14** cyclized to give monodeuterated **15** as a mixture of regioisomers (Scheme 4).

Scheme 2 summarizes all the key steps in the mechanism that leads from **5** to **9** and **12** or **13** via the key electrocyclic ring closure **7**→**8**. The tricyclic products, generated in two steps from simple starting materials and are potentially very versatile synthetic intermediates.

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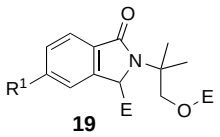
[7] By using method A, the cyclization was accompanied by formation of a by-product **19** in up to 50% yield, which may arise by decomposition of the cyclized product or by an alternative cyclization mechanism involving lithiation α to N, α-elimination of alkoxide to form a carbene, and insertion into an aromatic C–H bond. Formation of this by-product was avoided with method B, but instead up to 50% remaining starting material was recovered.



[8] CCDC-173233 (**9a**) -173234 (**12c**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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