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Converting dipyrrinones to lactim ethers to fluorescent *N,N′*-difluoroboryl derivatives

Suchitra Datta, David A. Lightner

Department of Chemistry, University of Nevada, Reno, Nevada, USA

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Abstract A high-yield straightforward conversion of lactams to lactim ethers is shown by the conversion of (10*H*)-dipyrrin-1-ones to (11*H*)-dipyrrin-1-ol methyl and ethyl ethers in 90% yield from heating in neat trimethyl or triethyl phosphite at 160°C. Unlike the parent dipyrrinones, which form intermolecularly hydrogen-bonded dimers in $CHCl_3$, their lactim ethers are shown to be monomeric by vapor pressure osmometry. The latter react with boron trifluoride etherate to *N,N′*-bridged BF_2 derivatives that exhibit strong fluorescence (ϕ_F 0.6–0.8) near 535 nm. X-Ray crystal structures were obtained of the lactim ethyl ether of kryptopyrromethenone and the BF_2 derivative of the lactim ethyl ether 2,3-diethyl-7,8-dimethyl-(10*H*)-dipyrrin-1-one.

Keywords Dipyrroles; Lactim; Difluoroboryl; Fluorescence; X-Ray crystallography.

Introduction

In formulating constitutional structures of 1-oxygenated dipyrrins, *Hans Fischer* favored the 1-hydroxydipyrrin representation [1] over the tautomeric (10*H*)-dipyrrin-1-one, the lactim over the lactam (Fig. 1). This decision, consistent in *Fischer*'s vast work on pyrrole compounds, whether for mono-, di-, tri-, or linear tetrapyrroles, was largely due to an inability to distinguish between the two tautomeric forms by the then-existing methodology. And it was reinforced particularly by the observations in chemical reactions that one could convert 1-bromodipyrrins by reaction with methanolic potassium hydroxide to the corresponding 1-methoxy derivatives, which were transformed to what were believed to be 1-hydroxydipyrrins by treatment with methanol and a few drops of conc. HCl; or by reaction with potassium acetate, or silver ion-assisted solvolysis in acetic acid to the corresponding 1-acetates, *inter alia*. We now know, unequivocally from ^{15}N NMR studies of *Falk et al.* [2, 3] (lactam N, ~ -250 ppm; lactim N, ~ -140 ppm) that the lactam tautomer, the dipyrrinone of Fig. 1 is the more stable form.

Lactim derivatives, usually methyl or ethyl ethers, have been prepared in recent times by *Falk et al.* [4, 5] from the corresponding lactams using powerful enol trapping alkylation agents such as *Meerwein*'s reagents in 63–78% yields. Thus, trimethoxonium tetrafluoroborate converted methyl xanthobilirubinate to its lactim methyl ether (**1**, Fig. 2), whose X-ray crystal structure determination [2, 6] is apparently the only one of an (11*H*)-dipyrrin-1-ol. In the following

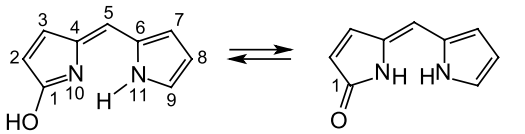
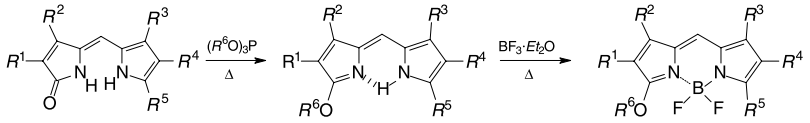


Fig. 1 Lactim-lactam tautomers of dipyrrins

Correspondence: David A. Lightner, Department of Chemistry, University of Nevada, Reno, Nevada 89557-0020 USA. E-mail: lightner@scs.unr.edu



	R^1	R^2	R^3	R^4	R^5	R^6
1	CH_3	CH_2CH_3	CH_3	$(CH_2)_2CO_2CH_3$	CH_3	CH_3
2	CH_3	CH_2CH_3	CH_3	$(CH_2)_2CO_2CH_3$	CH_3	CH_2CH_3
3	CH_3	CH_2CH_3	CH_3	CH_2CH_3	CH_3	CH_3
4	CH_3	CH_2CH_3	CH_3	CH_2CH_3	CH_3	CH_2CH_3
5	CH_2CH_3	CH_2CH_3	CH_3	CH_3	H	CH_3
6	CH_2CH_3	CH_2CH_3	CH_3	CH_3	H	CH_2CH_3
7	CH_3	CH_2CH_3	CH_3	$(CH_2)_2CO_2CH_3$	CH_3	–
8	CH_3	CH_2CH_3	CH_3	CH_2CH_3	CH_3	–
9	CH_2CH_3	CH_2CH_3	CH_3	CH_3	H	–
2B	CH_3	CH_2CH_3	CH_3	$(CH_2)_2CO_2CH_3$	CH_3	CH_2CH_3
4B	CH_3	CH_3	CH_2CH_3	CH_2CH_3	CH_3	CH_2CH_3
6B	CH_2CH_3	CH_2CH_3	CH_3	CH_3	H	CH_2CH_3

Fig. 2 The lactim ethers (**1**–**6**) and selected BF_2-derivatives (**2B**, **4B**, **6B**) of this study, prepared from the corresponding lactams (**7**–**9**)

we describe a new and facile way to convert (10*H*)-dipyrrin-1-ones into their lactim methyl or ethyl ethers (Fig. 2) in 90% yield simply by heating in triethyl- or trimethylphosphite. The conversion works well even with sensitive 9-H dipyrrinones. And the lactim ethers may be converted smoothly to their strongly red-fluorescing *N*,*N*′-difluoroboryl derivatives (Fig. 2) through the action of boron trifluoride etherate [7, 8], thereby adding new members of the *BODIPY* type of fluorescent dyes [9].

Results and discussion

Synthesis aspects

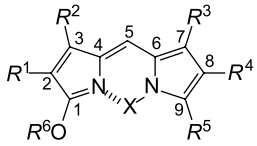
The known dipyrrinones, methyl xanthobilirubinate (**7**) [10], kryptopyrromethenone (**8**) [10a, c] and (4*Z*)-7,8-diethyl-2,3-dimethyl-(10*H*)-dipyrrin-2-one (**9**) [11], available from work in this laboratory, were converted to their lactim ethers simply by heating (sealed tube) to 160°C for 24 h with a 2:1 molar excess of either trimethyl- or triethylphosphite. Following precipitation of the product by quenching with water, it was purified by radial chromatography on silica gel, eluting with 2% (vol.) methanol in dichloromethane. The yields were typically ~90% of purified product.

The first *N*,*N*′-difluoroboryl derivative of a dipyrrinol ether was that from *Falk et al.* [5] derived from methyl ether **3**. Analogously, we converted the lactim ethyl ethers **2**, **4**, and **6** to their *N*,*N*′-difluorylboryl derivatives (**2B**, **4B**, and **6B**) by heating the latter in benzene in the presence of boron trifluoride etherate and triethylamine, as modified from earlier procedures [7, 8]. Purification by radial chromatography gave strongly fluorescent BF_2 derivatives in yields of ~60%.

Structures and NMR spectroscopy

The lactim ether structures follow from the known structures of the starting dipyrrinones and from ^1H and ^{13}C NMR spectroscopy (Table 1). Two (**1** and **3**) were known from earlier work [4, 12, 13]. Lactim methyl ether (**1**) prepared first by *Fischer* and *Adler* [12a], has been synthesized more recently by *Falk et al.* [4]. Lactim methyl ether **3** has been also reported by *Fischer* [12b] and more recently by *Falk et al*. [5]. The earliest reports lacked the full NMR and UV-visible spectral data. The ^{13}C NMR spectra of **1**–**6** may be compared with the parent dipyrrinones (**7**–**9**). As noted previously [2, 3], the ^{13}C NMR chemical shift of C(1) varies little between the lactam and lactim ether forms (Table 1). Similarly, the remaining ring carbons vary little; however, C(5), the carbon to which the two ''pyrrole'' rings are connected is strongly deshielded (~10 ppm) in the lactim relative to the lactam. Since the lactims are all ethers,

Table 1 Comparison of ^{13}C NMR chemical shifts (δ/ppm) of lactim ethers **1**–**6** to the parent lactams (**7**–**9**) and BF_2 derivatives (**2B**, **4B**, and **6B**) determined in $CDCl_3$ at 23°C



	R^1	R^2	R^3	R^4	R^5	R^6	X
1	*Me*	*Et*	*Me*	P^M	*Me*	*Me*	H
2	*Me*	*Et*	*Me*	P^M	*Me*	*Et*	H
3	*Me*	*Et*	*Me*	*Et*	*Me*	*Me*	H
4	*Me*	*Et*	*Me*	*Et*	*Me*	*Et*	H
5	*Et*	*Et*	*Me*	*Me*	H	*Me*	H
6	*Et*	*Et*	*Me*	*Me*	H	*Et*	H
2B	*Me*	*Et*	*Me*	P^M	*Me*	*Et*	BF_2
4B	*Me*	*Et*	*Me*	*Et*	*Me*	*Et*	BF_2
6B	*Et*	*Et*	*Me*	*Me*	H	*Et*	BF_2

Position		**1**	**2**	**3**	**4**	**5**	**6**
1	=C–O/C=O	174.6	173.9	174.2	173.5	174.9	174.3
2	=C–	131.2	131.0	130.7	130.4	128.74	129.0
3	=C–	148.4	148.1	148.3	147.9	148.0	147.8
4	=C–	142.5	142.9	142.2	142.4	143.4	143.7
5	=CH–	111.4	110.9	111.6	111.2	111.8	111.4
6	=C–	126.7	126.8	126.6	126.6	128.78	128.8
7	=C–	125.1	124.7	125.1	124.8	124.5	124.2
8	=C–	119.8	119.7	121.3	121.5	120.0	119.9
9	=C–	121.7	122.0	123.7	123.5	121.5	121.2
2^1	CH_3/CH_2	8.9	9.0	12.5	12.5	17.6	17.6
2^2	$-CH_3$	–	–	–	–	14.8	14.8
3^1	CH_3/CH_2	18.6	18.6	18.6	18.5	18.5	18.5
3^2	CH_3	16.4	16.4	16.4	16.4	17.2	17.2
7^1	CH_3/CH_2	10.1	10.0	10.0	9.9	10.8	10.8
8^1	CH_2/CH_3	20.6	20.6	18.1	18.0	9.8	9.8
8^2	CH_2/CH_3	35.8	35.8	16.1	16.1	–	–
8^3	C=O	174.4	174.4	–	–	–	–
8^5	OCH_3	52.2	52.2	–	–	–	–
9^1	CH_3	12.6	12.5	9.0	8.9	–	–
1^2	CH_3/CH_2	55.9	64.4	55.8	64.3	56.0	64.5
1^3	CH_3	–	15.3	–	15.2	–	15.3

Position		**7**	**8**	**9**	**2B**	**4B**	**6B**
1	=C–O/C=O	174.1	174.1	174.2	166.0	166.4	167.9
2	=C–	122.4	122.2	129.2	115.6	114.8	124.6
3	=C–	148.4	148.2	148.2	147.1	146.3	147.6
4	=C–	127.2	127.0	128.4	128.0	127.4	130.5
5	=CH–	101.4	101.2	101.7	116.7	116.7	116.8
6	=C–	122.4	122.9	124.6	130.2	130.7	129.9
7	=C–	119.1	122.2	119.6	133.8	133.9	131.5
8	=C–	124.9	124.6	124.4	126.0	130.5	124.0
9	=C–	131.1	131.6	121.5	149.2	150.3	133.9
2^1	CH_3/CH_2	9.6	9.5	18.0	8.9	8.8	16.9
2^2	$-CH_3$	–	–	14.1	–	–	15.7
3^1	CH_3/CH_2	18.0	17.5	17.2	18.2	18.2	18.1
3^2	CH_3	15.0	15.4	16.1	15.8	15.9	16.6
7^1	CH_3/CH_2	11.5	11.5	10.4	9.7	9.6	9.6
8^1	CH_2/CH_3	19.9	18.0	9.7	34.7	14.9	10.1
8^2	CH_2/CH_3	35.2	15.1		19.8	17.5	–
8^3	C=O	174.1	–	–	173.6	–	–
8^5	OCH_3	51.2	51.6	–	51.9	–	–
9^1	CH_3	8.5	8.5	–	12.5	12.5	–
1^2	CH_3/CH_2	–	–	–	70.2	70.2	70.6
1^3	CH_3	–	–	–	15.9	15.8	15.7

new carbon signals appear with the expected chemical shifts for the CH_3–O and CH_3CH_2–O groups. These new ether groups were also detected in the ^{1}H NMR spectra, but the protons from the dipyrrole β-substituents are largely unchanged in the lactim ethers relative to the parent dipyrrinones. Consistent with that found in the ^{13}C NMR, the C(5)-H is more deshielded (to ~6.4 ppm) in the former than in the latter (~6.1 ppm). And, significantly, one observes but one NH signal in the former, deshielded to ~11 ppm in $CDCl_3$. Other than the change in number of NHs, and the presence of CH_3O and CH_3CH_2O groups, the most notable difference between lactim and lactams is the strong deshielding of the carbon signal for C(5) in the lactim.

The structures of *N*,*N*′-difluoroboryl derivatives of lactim ethyl ethers **2**, **4**, and **6** follow from the structures of the parent dipyrrinones. The ^{13}C NMR spectra of the lactim ether BF_2 derivatives (**2B**, **4B**, and **6B**) differ in a major way from either the lactim ethers (**2**, **4**, **6**) or dipyrrinones (**7**–**9**). The chemical shift of C(1) is shielded in **2B**, **4B**, and **6B** by 6–8 ppm relative to the lactim ethers; C(5) is deshielded by about 5 ppm; and even more major shifts occur at C(2), C(4), C(7), and, especially, C(9). In the ^{1}H NMR, significantly, the C(5) H of **2B**, **4B**, and **6B** shifts downfield (~6.85 ppm) relative to that of **2**, **4**, and **6** (6.46 ppm).

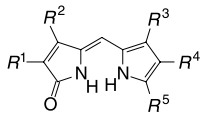
State of aggregation in solution

Dipyrrinones typically form intermolecularly hydrogen-bonded dimers in non-polar solvents, such as $CHCl_3$ [2, 13]. Vapor pressure osmometry (*VPO*) determinations for the first time of the molecular weights in $CHCl_3$ of dipyrrin-(11*H*)-ol ethers and their *N*,*N*′-difluorylboryl derivatives clearly indicate that **1**–**6** are monomers at high (10^{-2} *M*) concentrations (Table 2), as are **2B**, **4B**, and **6B**. Thus, these compounds exhibit no tendency toward self-association. The results stand in strong contrast to the parent dipyrrinones (**7**–**9**), which have been shown to be dimers by *VPO* and to be intermolecularly hydrogen bonded by ^{1}H NMR analysis.

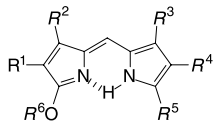
UV-visible spectral data

Lactim ethers **1**–**6** differ in their UV-visible spectral characteristics from those of the parent dipyrrinones **7**–**9** (Table 3). The long wavelength absorption maxima are bathochromically shifted in the former by

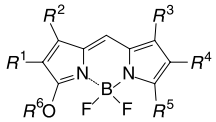
Table 2 Molecular weights (MWs) of lactim ethers **1**–**6** and BF_2 complexes **2B**, **4B**, and **6B** determined by vapor pressure osmometry[a] at 45°C in $CHCl_3$ solution[b]



7–9



1–6



2B, 4B, 6B

Cpd	R^1	R^2	R^3	R^4	R^5	Formula weight (FW)/g mol^{-1}	Measured MW/g mol^{-1}
1	*Me*	*Et*	*Me*	$(CH_2)_2CO_2CH_3$	*Me*	318	334 ± 16
2	*Et*	*Et*	*Me*	$(CH_2)_2CO_2CH_3$	*Me*	334	340 ± 20
3	*Me*	*Et*	*Me*	*Et*	*Me*	272	280 ± 15
4	*Et*	*Et*	*Me*	*Et*	*Me*	286	292 ± 8
5	*Et*	*Et*	*Me*	*Me*	H	258	262 ± 12
6	*Et*	*Et*	*Me*	*Me*	H	272	280 ± 10
2B	*Et*	*Et*	*Me*	$CH_2CH_2CO_2Me$	*Me*	382	400 ± 30
4B	*Et*	*Et*	*Me*	*Et*	*Me*	334	350 ± 28
6B	*Et*	*Me*	*Me*	*Et*	H	320	315 ± 18
7	–	*Et*	*Me*	$(CH_2)_2CO_2Me$	*Me*	304	579[c]
8	–	*Et*	*Me*	*Et*	*Me*	258	509 ± 20[c,d]
9	–	*Me*	*Et*	*Et*	H	244	448 ± 25[d]

[a] Calibrated with benzil (FW = 210 g mol^{-1}, MW = 220 ± 15 g mol^{-1}); [b] Conc. range, 0.8 = 2.1 × 10^{-3} mol kg^{-1}; [c] Data from Refs. [14, 2]; [d] Data from Ref. [12]

Table 3 Comparison of solvent-dependence and influence of methoxyl groups on the UV-visible spectral data of dipyrrinone lactim ethers **1–6**, BF_2 derivatives **2B**, **4B**, **6B**, and dipyrrinones **7–9**

Pigment	λ_{max} (ε)[a]					
	C_6H_6	$CHCl_3$	CH_3CN	CH_3OH	$(CH_3)_2SO$	CF_3CO_2H
1	421 (31400)	419 (28900)	415 (31900)	416 (31500)	412 (30800)	473 (45600)
2	483 (1500)^{sh}	481 (5200)^{sh}	415 (32100)	416 (30800)	421 (30000)	473 (48700)
	423 (30600)	420 (27300)				
3	424 (29300)	421 (28200)	415 (30000)	419 (31300)	423 (31500)	481 (42000)
4	490 (4500)^{sh}	486 (9900)	415 (31000)	420 (31600)	425 (30000)	481 (45600)
	425 (28200)	423 (24300)				
5	468 (4100)^{sh}	468 (27500)	401 (33600)	408 (32800)	403 (32700)	470 (51200)
	409 (31600)	411 (21300)				
6	409 (30000)	405 (27900)	401 (30700)	409 (30000)	404 (30100)	465 (49000)
7	413 (26500)	408 (34000)	402 (28900)	411 (37700)	410 (34000)	419 (17800)
8	412 (39900)	409 (33900)	406 (32000)	416 (39400)	415 (35600)	414 (18500)
9	394 (33900)	392 (29300)	383 (30300)	400 (33900)	400 (32400)	dec
2B	527 (67700)	526 (68900)	520 (70400)	521 (71200)	523 (72300)	dec
4B	530 (59800)	530 (60900)	522 (59300)	524 (59500)	525 (60900)	dec
6B	508 (36700)	505 (31000)	505 (28900)	504 (33000)	511 (35300)	dec

[a] λ_{max} in nm; ε in $dm^3 \cdot mol^{-1} cm^{-1}$ measured at 10^{-5} *M*

~5–10 nm relative to the latter; whereas the ε values are not much changed. As noted previously [7, 8] larger changes are observed between **1–6** (or **7–9**) and **2B**, **4B**, and **6B**. The last show nearly 100 nm bathochromic wavelength shifts, and nearly a doubling of the ε-values – undoubtedly due to the alterations in the electronic structure of the pigments **2B**, **4B**, and **6B** rather than planarization of the chromophore. The ε values and wavelength maxima are similar to those found [8] among dipyrrin · BF_2 derivatives. Interestingly, when C(9) is not substituted by an alkyl group, as in **6B**, the ε-value drops to nearly one-half that of the C(9)–CH_3 analogs, **2B** and **4B**, and the wavelength undergoes a hypsochromic shift. Similar changes are not noticed in comparing **5** and **6** to **1–4**, but have been recorded for a related dipyrrin · BF_2 [8].

Fluorescence

Following the early studies of *Treibs* and *Kreuzer* [15], *Falk et al.* [7], and *Lugtenburg et al.* [8] explored the strong fluorescence of BF_2 derivatives of a wide variety of dipyrrins. Subsequently, such red-emitting highly fluorescent dipyrrin derivatives were modified to commercial importance [9a, 16]. Unlike the dipyrrinones and their lactim ethers, which are not fluorescent, the BF_2 derivatives exhibit strong fluorescence with emission near 530 nm (Table 4), typical of dipyrrin · BF_2 derivatives [7, 8]. Fluores-

Table 4 Solvent dependence of the fluorescence excitation (λ_{ex}/nm) and emission (λ_{em}/nm) wavelengths and quantum yields (ϕ_F)[a] of **2B**, **4B**, and **6B** at 23°C, following excitation at 498 nm

Compound	Cyclohexane		C_6H_6		$CHCl_3$		CH_3OH		$(CH_3)_2SO$	
	λ_{em}	ϕ_F	λ_{em}	ϕ_F	λ_{em}	ϕ_F	λ_{em}	ϕ_F	λ_{em}	ϕ_F
2B[b]	556	0.84	553	0.98	558	0.89	556	0.69	554	0.91
	523		527		526		520		523	
4B	539	0.72	541	0.81	537	0.78	533	0.64	539	0.78
6B[b]	549	0.68	541	0.73	540	0.73	543	0.58	540	0.73
	519		525		524		517		522	

[a] Reference standard: fluorescein, $\phi_F = 0.79$ in ethanol, $\lambda_{exc} = 498$ nm; [b] Fluorescence curves are "double-humped" of equal intensity

cence of **2B**, **4B**, and **6B** was measured, and the fluorescence quantum yields (ϕ_F) were found to be in the range 0.6–0.8, which is comparable to dipyrrin $\cdot BF_2$ derivatives. However **2B**, **4B**, and **6B** exhibit bathochromically-shifted λ_{em} and generally larger ϕ_F relative to dipyrrin $\cdot BF_2$ derivatives [8].

X-Ray crystal structures

Crystals of **4**, suitable for X-ray crystallography, were grown from dichloromethane; crystals of **6B** were grown from *n*-hexane. There is apparently only one other X-ray crystal structure available of a (11*H*)-dipyrrin-1-ol-ether [6], but there are a large number of X-ray structures of *BODIPYs* [9], which almost exclusively have a substituent at C(5). We found only two with a C(5)-H, and these had an amino group or an acetamido group at C(9) [17]. Like

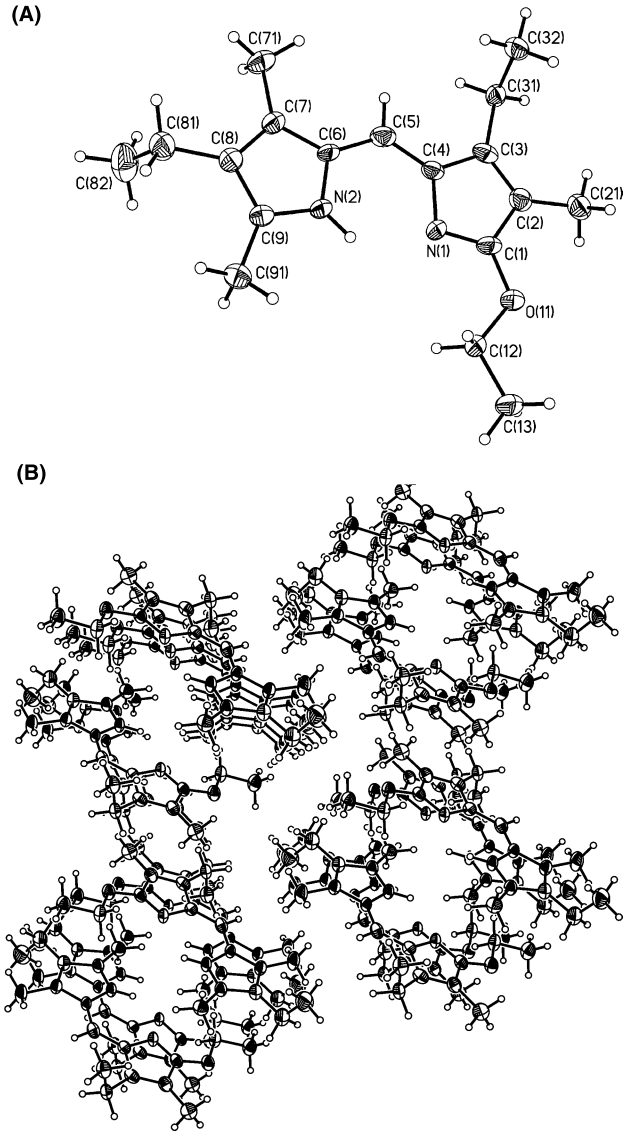


Fig. 3 (A) Crystal drawing structure of lactim **4** showing numbering system of the main atoms. (B) Crystal stacking diagram of **4**

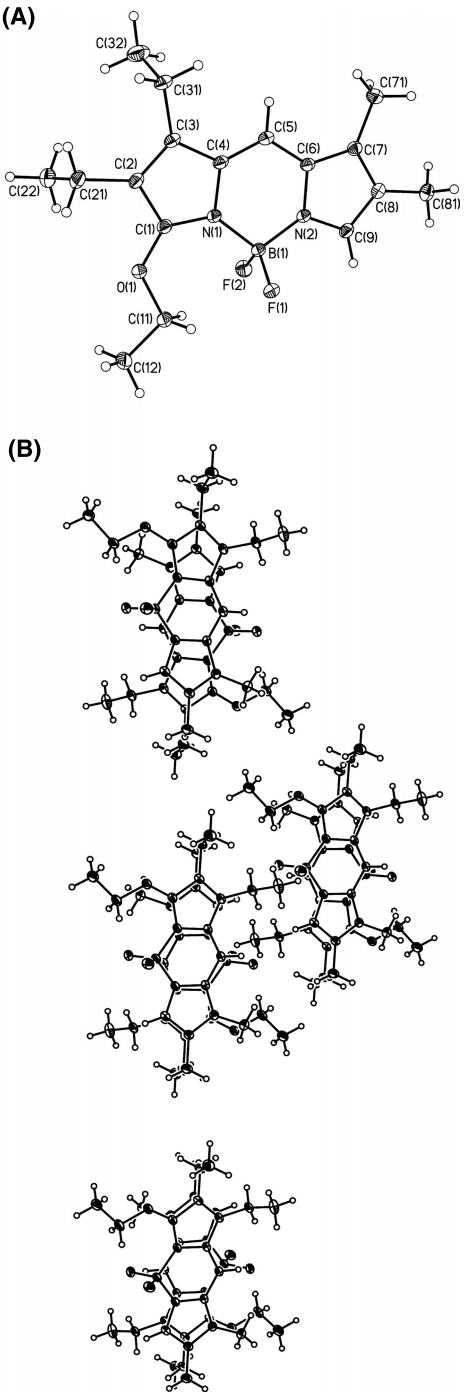


Fig. 4 (A) Crystal structure drawing of lactim ethyl ethers-BF_2 derivative **6B** showing the numbering system of the main atoms. (B) Crystal stacking diagram of **6B**, edge view

that of **1**, **4** showed a *syn*-(4*Z*) configuration (Fig. 3), as did **6B** (Fig. 4), the same as confirmed for solutions of **4** and **6B** in $CDCl_3$ by nuclear *Overhauser* effects NMR spectroscopy. Pigment **4** shows the expected bond alteration pattern (Fig. 4) and molecular dissymmetry in the left half of the molecule as found in the lactim methyl ether (**1**) of methyl xanthobilirubinate (**7**) [7], with very similar bond angles. The core dipyrrins of **4** and **1** do not match up exactly: there are small differences in bond lengths near C(4) and C(6), N(2) and C(9). Yet, the similarities are unmistakably close. As in **1**, the available data suggest that the tautomeric equilibrium shown in Fig. 5A lies to the left. Molecules of **4** lie in parallel sheets and stack in columns (Fig. 3A).

As expected, crystals of **6B** also showed a planar dipyrrin, with planar molecules (torsion angles (C(5)–C(4)–N(1)–B(1) = +0.5°, C(5)–C(6)–N(2)–B(1) = +1.2°, C(3)–C(4)–N(1)–C(1) = 0.7°, and

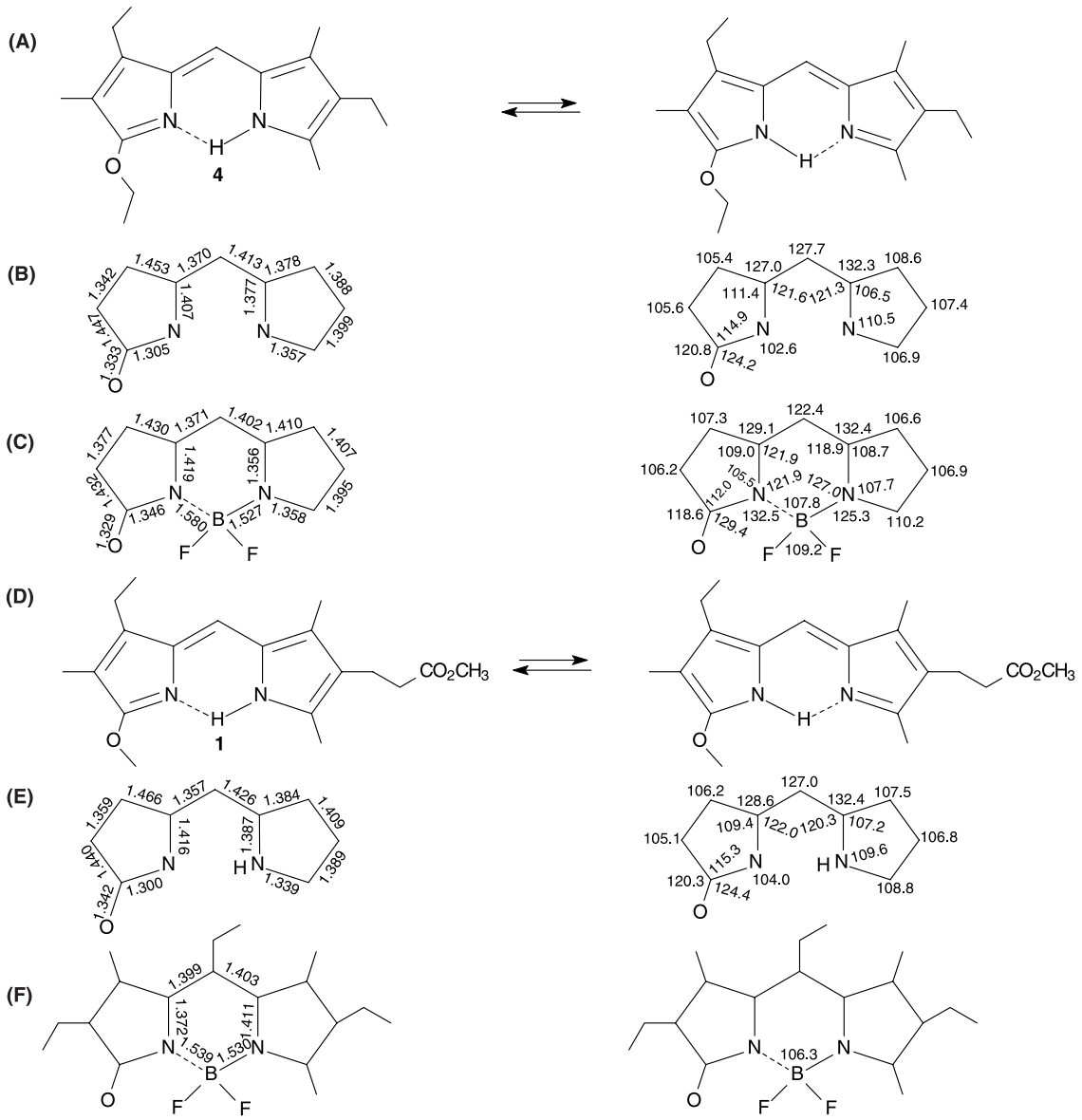


Fig. 5 (A) (Left) Line drawing showing tautomerism of **4** in its stable *syn*-(*Z*) conformation. (B) Bond distances (Å) (left) and bond angles (°) (right) of the dipyrrin core of (B) crystals of **4** and (C) crystals of **6B**. (D) Tautomeric structure drawings of **1** and (E) its bond lengths (left) and bond angles (right) as taken from Ref. [6]. (F) Comparison bond lengths and bond angles of the BF_2 derivative of 2,4,6,9-tetramethyl-3,6,8-triethyldipyrrin [18]; CCD # XUXFOL

C(7)–C(6)–N(1)–C(9) = −0.1°) stacked in columns like plates, some 3.76 Å apart. Bond alternation is exhibited but only in the left half (lactim ether) part of the molecule. The two pyrrole C(6)=C(7) and C(7)–C(8) bonds of **6B** are longer than those of **4**, but the C(8)=C(9) bond is only slightly shorter, while the N(2)–C(9) bond in **6B** is the same as that in **4** and the N(2)–C(6) bond of **6B** is shorter than that in **4**. The BF_2 group exerts a notable effect in closing its ring: notably the C(4)–C(5)–C(6) angle is much smaller in **6B** than in **4** as is the C(5)–C(6)–N(2) angle, but N(1)–C(4)–C(5) remains nearly the same. We could not compare the bond lengths and angles of **6B** to the two known C(5)–H *BODIPYs* [17] as the relevant data were not available from the CCD. However, the bond lengths and angles compared favorably with a 6-ethyl-dipyrrin · BF_2 [18], which is not as planar as **6B**: B(1)–N(1)–C(4)–C(5) = +2.60°, B(1)–N(2)–C(6)–C(5) = −5.4°C.

Concluding comments

A new, high-yield simple method for converting (10*H*)-dipyrrin-1-ones into the (11*H*)-dipyrrin-1-ol methyl and ethyl ethers using neat $(CH_3O)_3P$ and $(CH_3CH_2O)_3P$, respectively, at 160°C is described. The conformation of the lactim ethers is *syn*-(4*Z*), as determined by NMR N*O*E measurements and X-ray crystallography. Three lactim ethyl ethers (**2**, **4**, and **6**) were converted smoothly to their difluoroboryl derivatives (**2B**, **4B**, and **6B**), which are highly fluorescent. As expected, NMR N*O*E studies and an X-ray crystal structures confirm the expected planar *syn*-(4*Z*) conformation. All of the lactim pigments of this work are monomeric in $CHCl_3$, as determined by *VPO* measurements.

Experimental

All nuclear magnetic resonance (NMR) spectra were obtained on a Varian 500 MHz (^{1}H) and 125 MHz (^{13}C) in deuteriochloroform unless otherwise indicated. Chemical shifts were reported in ppm referenced to the residual chloroform proton signal at 7.26 ppm and ^{13}C signal at 77.23 ppm unless otherwise noted. All GC-MS spectra were obtained from a Varian CP-3800 mass spectrometer. Melting points were taken on a Mel-Temp capillary apparatus. Combustion analyses were performed by Desert Analytics, Tucson, AZ and gave results within ±0.4% of theoretical values. For a few compounds FAB HRMS mass determinations of the molecular ion were obtained from the Nebraska Center for Mass Spectrometry. Infrared spectra were recorded on a Perkin-Elmer FT-IR infrared spectrophotometer model SPECTRUM 2000. All ultraviolet-visible spectra were recorded on a Perkin-Elmer λ-12 spectrophotometer. Vapor pressure osmometry (*VPO*) measurements were performed on an OSMOMAT 070-SA instrument (Gonotech GmbH, Germany) in HPLC grade $CHCl_3$ (Fisher) at 45°C. Analytical thin layer chromatography (TLC) was carried out on J.T. Baker silica gel IB-F plates (125 μm layer). For final purification, radial chromatography was carried out on Merck silica gel PF_{254} with calcium sulfate binder, preparative layer grade. All solvents were reagent grade obtained from Fisher-Acros, as were trimethyl- and triethyl-phosphite. Deuterated chloroform, dichloromethane and dimethylsulfoxide were from Cambridge Isotope Laboratories. Trimethylphosphite was from Alfa Aesar; triethylphosphite was from Aldrich. The starting dipyrrinones **7** [10], **8** [10a, c] and **9** [11] were available from previous studies.

General procedure for lactam to lactim ethers

For preparing lactim ethyl ethers, the (10*H*)-dipyrrin-1-one (50 mmol) was mixed with 100 mmol of triethyl phosphite and stirred magnetically while being heated at 160°C for 24 h. After cooling, 500 cm^3 of water was added to the reaction mixture, and the mixture was stirred for one hour during which a yellow solid precipitated. It was collected by filtration and washed with water. It was further purified by radial chromatography on silica gel, eluting with 2% (volume) methanol in dichloromethane to give the desired product, after removing the solvent.

For the preparation of lactim methyl ethers, in the same way heating to 160°C in trimethyl phosphite was carried out in a sealed tube for 24 h for **1** and **3**, 72 h for **5**. The work-up and product isolation were the same as above.

8-(2-Carbomethoxyethyl)-3-ethyl-2,7,9-trimethyl-(11H)-dipyrrin-1-ol methyl ether (**1**, $C_{19}H_{26}N_2O_3$)

Yield 89%, mp 62–64°C (Refs. [4, 11a] 61–62°C); ^{1}H NMR: δ = 1.13 (3H, t, J = 7.5 Hz), 1.87 (3H, s), 2.13 (3H, s), 2.434 (2H, 5, J = 7.5 Hz), 2.26 (3H, s), 2.71 (2H, t, J = 7.5 Hz), 2.59 (2H, q, J = 7.5 Hz), 3.66 (3H, s), 4.03 (3H, s), 6.42 (1H, s), 10.98 (1H, br.s) ppm; ^{13}C NMR in Table 1.

8-(Carbomethoxyethyl)-3-ethyl-2,7,9-trimethyl-(11H)-dipyrrin-1-ol ethyl ether (**2**, $C_{20}H_{28}N_2O_3$)

Yield 87%, mp 63–65°C; ^{1}H NMR: δ = 1.14 (3H, t, J = 7.5 Hz), 1.88 (3H, s), 1.457 (3H, t, J = 7.0 Hz), 2.14 (3H, s), 2.27 (3H, s), 2.45 (2H, t, J = 8.0 Hz), 2.5 2H, q, J = 7.5 Hz), 2.73 (2H, t, J = 8.0 Hz), 3.70 (3H, s), 4.43 (2H, t, J = 7.0 Hz), 6.40 (1H, s), 11.01 (1H, br.s) ppm; ^{13}C NMR in Table 1; HRMS (FAB, 3-*NBA*): calcd for $C_{20}H_{28}N_2O_3$ 344.2100, found 344.2104.

3,8-Diethyl-2,7,9-trimethyl-(11H)-dipyrrin-1-ol methyl ether (**3**, $C_{17}H_{24}N_2O$)

Yield 91%, mp 73–74°C (Refs. [5, 11b] 74, 70°C); ^{1}H NMR: δ = 1.06 (3H, t, J = 7.0 Hz), 1.14 (3H, t, J = 7.0 Hz), 1.88 (3H,

s), 2.14 (3H, s), 2.39 (2H, q, $J = 7.0$ Hz), 2.51 (2H, q, $J = 7.0$ Hz), 2.56 (3H, s), 4.03 (3H, s), 6.44 (1H, s), 10.94 (1H, br.s) ppm; ^{13}C NMR in Table 1.

3,8-Diethyl-2,7,9-trimethyl-(11H)-dipyrrin-1-ol ethyl ether (**4**, $C_{18}H_{26}N_2O$)
Yield 92%, mp 66–68°C; ^{1}H NMR: $\delta = 1.05$ (3H, t, $J = 7.5$ Hz), 1.13 (3H, t, $J = 7.5$ Hz), 1.45 (3H, t, $J = 7.5$ Hz), 1.87 (3H, s), 2.13 (3H, s), 2.25 (3H, s), 2.42 (2H, q, $J = 7.5$ Hz), 2.52 (2H, q, $J = 7.5$ Hz), 4.41 (2H, q, $J = 7.5$ Hz), 6.41 (1H, s), 10.90 (1H, br, s) ppm; ^{13}C NMR in Table 1; HRMS (FAB, 3-*NBA*); calcd for $C_{18}N_{26}N_2O$ 286.2045, found, 286.2036.

2,3-Diethyl-7,8-dimethyl- (11H)-dipyrrin-1-ol methyl ether (**5**, $C_{16}H_{22}N_2O$)
Yield 91%, mp 83–85°C; ^{1}H NMR: $\delta = 1.08$ (3H, t, $J = 7.5$ Hz), 1.16 (3H, t, $J = 7.5$ Hz), 2.03 (3H, s), 2.13 (3H, s), 2.31 (2H, q, $J = 7.5$ Hz), 2.51 (2H, q, $J = 7.5$ Hz), 4.04 (3H, s), 6.45 (1H, s), 6.74 (1H, s), 11.01 (1H, NH, br, s) ppm; ^{13}C NMR in Table 1; HRMS (FAB, 3-*NBA*): calcd for $C_{16}H_{22}N_2O$ 258.17320, found, 258.1740.

2,3-Diethyl-7,8-dimethyl- (11H)-dipyrrin-1-ol ethyl ether (**6**, $C_{17}H_{24}N_2O$)
Yield 93%, mp 80–81°C; ^{1}H NMR: $\delta = 1.44$ (3H, t, $J = 7.0$ Hz), 2.03 (3H, s), 2.14 (3H, s), 2.32 (2H, q, $J = 7.5$ Hz), 2.51 (2H, q, $J = 7.5$ Hz), 4.46 (2H, q, $J = 7.0$ Hz), 6.43 (1H, s), 6.73 (1H, s), 11.03 (1H, br, s) ppm; ^{13}C NMR in Table 1; HRMS (FAB, 3-*NBA*): calcd for $C_{17}H_{24}N_2O$ 272.1889, found, 272.1895.

N,N′-Difluorylboryl-8-(3-carbonylmethoxy-ethyl)-2,7-dimethyl-3-ethyl-(11H)-dipyrrin-1-ol ethyl ether (**2B**, $C_{20}H_{27}N_2O_3$)
Lactim ether (**2**) (40 mg, 0.120 mmol) was dissolved in 10 cm^3 dry benzene, and 0.4 cm^3 triethyl amine and 1 cm^3 boron trifluoride etherate were added. After heating at reflux for 15 min, the reaction mixture was cooled, washed with 20 cm^3 water and extracted with 5×50 cm^3 CH_2Cl_2. The organic extracts were combined, dried over Na_2SO_4 and evaporated. The residue was purified by radial chromatography on silica gel, eluting with CH_2Cl_2 to yield 34 mg of pure **2B**, which was crystallized from *n*-hexane. Yield: 34 mg (74%); mp 88–90°C; ^{1}H NMR: $\delta = 1.16$ (3H, t, $J = 7.5$ Hz), 1.47 (3H, t, $J = 7.5$ Hz), 1.97 (3H, s), 2.16 (3H, s), 2.42 (2H, t, $J = 7.5$ Hz), 2.45 (3H, s), 2.56 (2H, q, $J = 7.5$ Hz), 2.71 (2H, t, $J = 7.5$ Hz), 3.67 (3H, s), 4.61 (2H, q, $J = 7.5$ Hz), 6.85 (1H, s) ppm; ^{13}C NMR in Table 1.

N,N′-Difluoroboryl-3,8-diethyl-2,7,9-trimethyl-(11H)-dipyrrin-1-ol ethyl ether (**4B**, $C_{18}H_{25}N_2OBF_2$)
Lactim ether (**4**) (25 mg, 0.087 mmol) was dissolved in 8 cm^3 dry benzene, and 0.2 cm^3 triethylamine and 0.5 cm^3 boron trifluoride etherate were added. After heating at reflux for 15 min, the reaction mixture was cooled, washed with 2×10 cm^3 water and extracted with CH_2Cl_2 (5×100 cm^3). The organic extracts were combined, dried over Na_2SO_4 and evaporated (rotovap). The residue was purified by radial chromatography on silica gel, eluting with CH_2Cl_2 to yield 21 mg of pure **4B**, which was crystallized from *n*-hexane. Yield: 16 mg, 56%, mp 76–78°C; ^{1}H NMR: $\delta = 1.04$ (3H, t, $J = 8.0$ Hz), 1.15 (3H, t, $J = 8.0$ Hz), 1.46 (3H, t, $J = 7.0$ Hz), 1.97 (3H, s), 2.14 (3H, s), 2.37 (2H, q, $J = 8.0$ Hz), 2.45 (3H, s), 2.55 (2H, q, $J = 8.0$ Hz), 4.56 (2H, q, $J = 7.0$ Hz), 6.85 (1H, s) ppm; ^{13}C NMR in Table 1.

N,N′-Difluoryl-3,4-diethyl-7,8-dimethyl-(11H)-dipyrrin-1-ol ethyl ether (**6B**, $C_{17}H_{23}N_2OBF_2$)
Lactim ether (**6**) (25 mg, 0.922 mmol) was treated as above for the synthesis of **4B** to afford pure product. Yield: 18 mg (62%); mp 86–88°C; ^{1}H NMR: $\delta = 1.11$ (3H, t, $J = 7.5$ Hz), 1.20 (3H, t, $J = 7.5$ Hz), 1.47 (3H, t, $J = 7.0$ Hz), 1.98 (3H, s), 2.01 (3H, s), 2.15 (3H, s) 2.37 (3H, t, $J = 7.5$ Hz), 2.58 (2H, q, $J = 7.5$ Hz), 4.80 (2H, q, $J = 7.0$ Hz), 6.87 (1H, s), 7.21 (1H, s) ppm; ^{13}C NMR in Table 1.

X-Ray structure and solution
Crystals of **4** and **6B** were grown by slow diffusion of *n*-hexane into a solution of CH_2Cl_2. A crystal was placed into the tip of a 0.1 mm diameter glass capillary and mounted on a *Bruker* SMART Apex system for data collection at 100(2) K. A preliminary set of cell constants was calculated from reflections harvested from 3 sets of 20 frames. These initial sets of frames were oriented such that orthogonal wedges of reciprocal space were surveyed (final orientation matrices determined from global least-squares refinement of 2152 reflections for **4** and 4376 reflections for **6B**). The data collection was carried out using MoKα radiation (0.71073 Å graphite monochromator) with a frame time of 20 s and a detector distance of 4.94 cm. A randomly oriented region of reciprocal space was surveyed to the extent of 2 hemispheres and to a resolution of 0.77 Å for **4** and 0.84 Å for **6B**. Four major sections of frames were collected with 0.5° steps in ω at 600 different ϕ settings and a detector position of 27° in 2θ for **4** and for **6B**. The intensity data were corrected for absorption and decay (SADABS) [19]. Final cell constants were calculated from the *xyz* centroids of strong reflections from the actual data collection after integration (SAINT 6.45) [20]. Crystal data and refinement information for may be found in Table 5.

The structure was solved and refined using SHELXL-L [21]. The triclinic space group *P*-1 of **4** and **6B** was determined based on systematic absences and intensity statistics. A direct-methods solution was calculated which provided most non-hydrogen atoms from the *E*-map. Full-matrix least squares/difference *Fourier* cycles were performed for structure refinement. All non-hydrogen atoms were refined with anisotropic displacement parameters unless stated otherwise. Hydrogen atom positions were placed in ideal positions and refined as riding atoms with relative isotropic displacement parameters (A C–H distance fixed at 0.096 Å and a thermal parameter 1.2 times the host carbon atom). Tables of atomic coordinates, bond lengths and angles, anisotropic displacement parameters, hydrogen coordinates and isotropic displacement parameters have been deposited at the Cambridge Crystallographic Data Centre, CCDC No. 680463 for **4** and 680464 for **6B**.

Table 5 Crystal data and structure refinement for **4** and **6B**

Compound	**4**	**6B**
Empirical formula	$C_{18}H_{26}N_2O$	$C_{17}H_{23}N_{2O}BF_2$
Formula Weight	286.4	320.4
Temperature/K	100(2)	100(2)
Wavelength/Å	0.71073	0.71073
Crystal system	Triclinic	Triclinic
Space group	*P*-1	*P*-1
Unit cell dimensions	$a = 7.392(7)$ Å	$a = 8.05621(2)$ Å
	$b = 10.769(9)$ Å	$b = 9.02893(2)$ Å
	$c = 11.766(10)$ Å	$c = 12.3816(3)$ Å
	$\alpha = 108.323(15)^\circ$	$\alpha = 83.234(2)^\circ$
	$\beta = 102.226(18)^\circ$	$\beta = 88.4790(10)^\circ$
	$\gamma = 100.48(2)^\circ$	$\gamma = 66.0620(10)^\circ$
Volume/Å^3	837.2(12)	817.13(3)
Z	2	2
Density (calculated)/Mg m^{-3}	1.132	1.204
Absorption coefficient/mm^{-1}	0.070	0.090
F(000)	310	316
Crystal size/mm^3	$0.57 \times 0.25 \times 0.04$	$0.60 \times 0.15 \times 0.07$
Theta range for data collection/°	1.90–24.60	1.66–32.57
Index ranges	$-8 \le h \le 8$, $-8 \le k \le 12$, $-13 \le l \le 12$	$-9 \le h \le 11$, $-13 \le k \le 13$, $-15 \le e \le 17$
Reflections collected	2758	10203
Independent reflections	2152 [R(int) = 0.0271]	4376 [R(int) = 0.231]
Completeness to theta = 27.60°	76.1%	–
Completeness to theta = 32.57°	–	73.6%
Absorption correction	None	None
Max. and min. transmission	0.9972 and 0.9610	0.9937 and 0.9479
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	2152/0/197	4376/0/214
Goodness-of-fit on F^2	1.053	1.031
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0697$, $wR2 = 0.1967$	$R1 = 0.0435$, $wR2 = 0.1090$
R indices (all data)	$R1 = 0.1064$, $wR2 = 0.2192$	$R1 = 0.0513$, $wR2 = 0.1168$
Extinction coefficient	0.000(5)	0.019(3)
Largest diff. peak and hole/eÅ^{-3}	0.380 and −0.255	0.521 and −0.319

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