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Unexpected Ring Transformation to Pyrrolo[3.2-*b*]pyridine Derivatives. Fused Azolium Salts. 22‡

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2-Arylsulfanyl and 2-benzylsulfanylpyridinium *N*-arylimides (**2**) easily prepared from 3-aryltetrazolopyridinium salts (**1**) with aryl and benzylthiolates, respectively, reacted with various dipolarophiles yielding cycloadducts that underwent transformation to give tetrahydropyrrolo[3,2-*b*]pyridines (**5**, **6**, and **8**) in good yields. A similar rearrangement (formation of **15**) was also observed in the case of parent derivatives being unsubstituted in position 2 (**12**). The abscence of any significant solvent effect, comparison of the sulfur and non-sulfur analogues, as well as the stereoselective nature of the observed ring transformation seem to support a sigmatropic mechanism. Structure elucidation of the products has been carried out by single-crystal X-ray diffraction and ^{1}H NMR experiments.

Introduction

In continuation of our studies on ring-opening reactions of fused azolium salts[1] we have recently found that tetrazolopyridinium salts (**1**) readily react with aryl and benzylthiolates to yield 2-sulfanylpyridinium *N*-arylimides (**2**). These stable red zwitterions can participate in 1,3-dipolar cycloaddition reactions.[2] Thus, **2** reacted with *N*-phenylmaleimide to give cycloadduct **3** (Scheme 1). As the easily available zwitterion **2** is regarded as a valuable starting material for further transformations, continuation of these studies seemed of preparative importance.

We describe now that extension of the cycloaddition reaction of **2** for additional dipolarophiles may result in a dramatic change of the course of the reaction, and an unexpected ring transformation following the earlier experienced cycloaddition can occur.

Results and Discussion

In contrast to the previously reported results[2] we found that reaction of **2** with fumaronitrile did not afford the expected [3+2] cycloadduct **4**; instead, tetrahydropyrrolo-[3,2-*b*]pyridine derivative **5** was obtained in moderate yields (Scheme 2). This finding can be rationalized by the primary formation of the expected cycloadduct **4** followed by a ring transformation involving N−N cleavage—as shown on the structure—and formation of a new bond between aryl-N and C-6 of the pyridine ring providing the isolated product **5**. The structure of this product was supported by ^{1}H NMR data; furthermore, unambiguous proof was provided by the X-ray analysis of **5b** (Figure 1[3]) revealing the cis fusion of the pyrrole and pyridine rings.

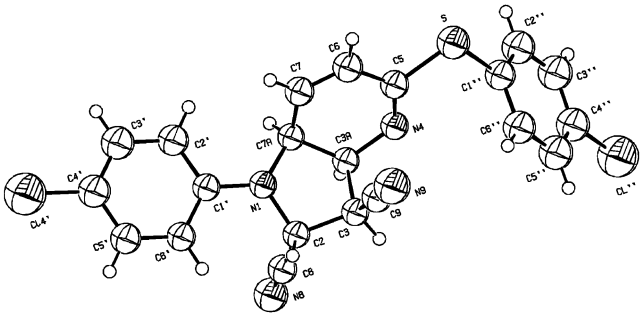

FIGURE 1. ORTEP diagram of **5b**.

Upon this observation the question arose if the observed ring transformation can occur only in the particular case of fumaronitrile as a dipolarophile. To clarify this, cycloadduct **3** obtained from **2** with *N*-phenylmaleimide was refluxed in chloroform for 1 h. We found that under these conditions (and also upon storage of a solution of **2** in chloroform at room temperature for 3 days) the expected rearrangement did occur and the fused tetrahydropyrrolopyridine **6** was obtained in excellent yields (Scheme 3). Also in this case, the structure of one

‡ Part 21: Bátori, S.; Bokotey, S.; Messmer, A. *Tetrahedron*, **2003**, *59*, 4297. For part 20, see ref 2.

(1) (a) Béres, M.; Hajós, Gy.; Riedl, Zs.; Soós, T.; Timári, G.; Messmer, A. *J. Org. Chem*. **1999**, *64*, 5499. (b) Soós, T.; Hajós, Gy.; Messmer, A. *J. Org. Chem*. **1997**, *62*, 1136. (c) Messmer, A.; Gelléri, A.; Hajós, Gy. *Tetrahedron* **1986**, *42*, 4827.

(2) Messmer, A.; Kövér, P.; Riedl, Zs.; Gömöry, Á.; Hajós, Gy. *Tetrahedron* **2002**, *58*, 3613.

(3) Compound **5b**: $C_{21}H_{14}Cl_2N_4S$; M_r 425.32; light yellow prism; size 0.30 × 0.20 × 0.10 mm^3; monoclinic; space group *P*21/*c*; a = 10.904(1) Å, b = 18.298(1) Å, c = 10.284(1) Å, β = 99.305(8)°, V = 2024.9(3) Å^3, Z = 4, r_{calcd} = 1.395 g/cm^3, m = 3.959 mm^{-1}, T = 293(2) K. The final model (254 parameters) was refined to wR_2 = 0.1596 for all data (4217 reflections), R_1 = 0.0510 for reflections with $I > 2\sigma(I)$ (3158), and GOF = 1.066.

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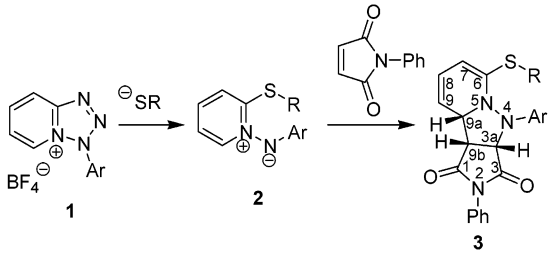
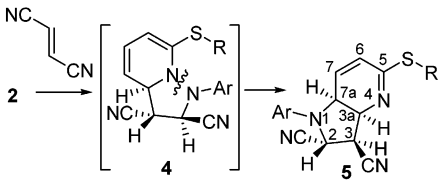
SCHEME 1



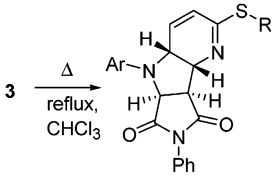
	R	Ar
a	benzyl	4-Cl-C_6H_4
b	4-Cl-C_6H_4	4-Cl-C_6H_4
c	4-CH_3-C_6H_4	4-Cl-C_6H_4
d	4-CH_3-C_6H_4	4-F-C_6H_4
e	4-CH_3-C_6H_4	4-*i*Pr-C_6H_4

SCHEME 2



	R	Ar
a	benzyl	4-Cl-C_6H_4
b	4-Cl-C_6H_4	4-Cl-C_6H_4
c	4-CH_3-C_6H_4	4-Cl-C_6H_4

SCHEME 3



	R	Ar
a	benzyl	4-Cl-C_6H_4
b	4-Cl-C_6H_4	4-Cl-C_6H_4
c	4-CH_3-C_6H_4	4-Cl-C_6H_4
d	4-CH_3-C_6H_4	4-F-C_6H_4
e	4-CH_3I-C_6H_4	4-*i*Pr-C_6H_4

of the products (**6a**) was determined by X-ray diffraction (Figure 2[4]) revealing the cis-fusion of the product.

Upon workup of the reaction mixture obtained with zwitterion **2b** and dimethyl acetylenedicarboxylate (DMAD) the expected cycloadduct **7** was not obtained; instead and in apparent analogy to the formation of **6** (vide supra), the rearranged product **8** was isolated (Scheme 4).

Oxidation of compounds **5**, **6**, and **8** with DDQ readily afforded the corresponding fully unsaturated heterocycles **9**, **10**, and **11**, respectively (Scheme 5).

As discussed above, the obvious key step of the observed rearrangement reaction (i.e. formation of **5**, **6**, and **8**) is the cleavage of the N,N bond, which conceivably

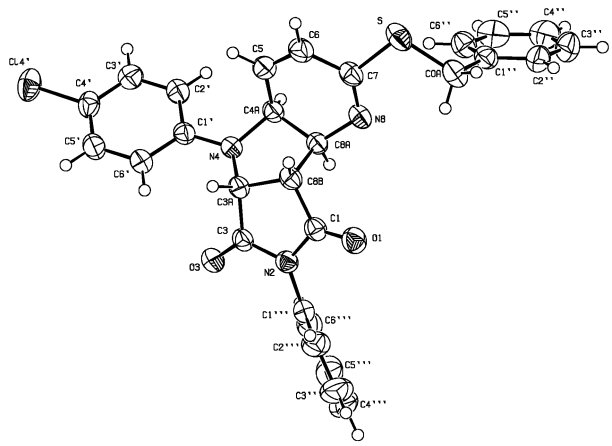


FIGURE 2. ORTEP diagram of **6a**.

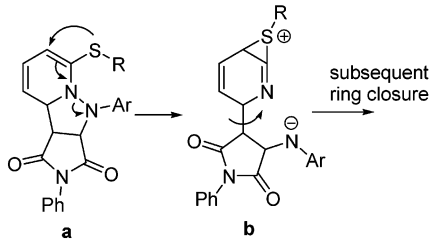


FIGURE 3. A possible mechanism of the N−N bond fission in **a** by neighboring group participation of the sulfanyl group to form intermediate **b**.

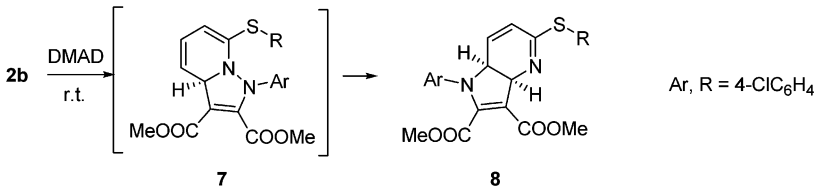
can occur in different ways: Path A, homolytically (radical pathway); Path B, heterolytically, forming an arylnitrenium cation that adds as an electrophile onto the negatively charged dihydropyridine ring; Path C, inverse heterolytic cleavage with formation of an arylimide moiety that undergoes ring closure by nucleophilic attack of the positively charged dihydropyridine ring; and Path D, [1,5]-sigmatropic shift of the *N*-aryl moiety from the dihydropyridine N-atom to C-6 of this ring.

Since the reaction rate did not change in the presence of a radical trap (*N*,*N*-dimethyl-4-nitrosoaniline),[5a] Path

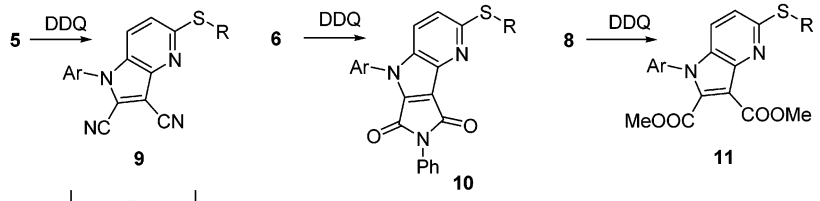
(4) Compound **6a**: $C_{28}H_{22}ClN_3O_2S$; M_r 500.00; colorless prism; size 0.45 × 0.20 × 0.09 mm^3; orthorhombic; space group *P*212121; a = 7.517(1) Å, b = 15.096(2) Å, c = 20.836(2) Å, V = 2364.4(5) Å^3, Z = 4, r_{calcd} = 1.405 g/cm^3, m = 2.515 mm^{-1}, T = 293(2) K. The final model (316 parameters) was refined to wR_2 = 0.1127 for all data (4875 reflections), R_1 = 0.0429 for reflections with $I > 2\sigma(I)$ (4596), and GOF = 1.051.

(5) (a) Two solutions of **3d** (50 mg, 0.1 mmol) in acetone (2 mL)—with and without addition of *N*,*N*-dimethyl-4-nitrosoaniline (5 mL)—were refluxed for 20 min. The reaction mixture was subjected to column chromatography and **6d** was separated; as a result, 21 and 23 mg of product, respectively, were obtained. (b) Transformation of **3d** to **6d** was monitored by ^{1}H NMR spectroscopy. For this purpose, a solution of **3d** (20 mg) in 0.6 mL of DMSO-d_6 and acetone-d_6 was placed into an NMR tube. The progress of the reaction was observed by diappearance of the signal of H-9 in **3d** (at 5.65 ppm in DMSO-d_6 and 5.75 ppm in acetone-d_6) and appearance of the signal of H-5 in **6d** (at 5.32 ppm in DMSO-d_6 and 6.45 ppm in acetone-d_6). The following conversions have been measured at room temperature: in 8 h—DMSO 16%, acetone 16%; in 24 h—DMSO 32%, acetone 33%; in 50 h—DMSO 53%, acetone 56%.

SCHEME 4



SCHEME 5



	R	Ar
a	benzyl	4-Cl-C_6H_4
b	4-Cl-C_6H_4	4-Cl-C_6H_4
c	4-CH_3-C_6H_4	4-Cl-C_6H_4

A seems rather improbable. As to Paths B and C involving heterolytic N,N-bond cleavage, the latter path appears more realistic because of the possibility of neighboring group participation as shown in Figure 3: The sulfur atom of the 2-sulfanyl substituent can attack the adjacent C-3 of the pyridine ring forming a sulfonium cation intermediate, which may induce the N,N-bond fission. Both Paths B and C involve formation of a zwitterion intermediate and, consequently, acceleration of the reaction in more polar solvents is expected. To check this anticipation the reaction was repeated in acetone and in dimethyl sulfoxide solution. No significant difference of the reaction rates in these solvents was found;[5b] thus, Paths B and C are considered improbable as well.

On the other hand, the pericyclic route D (Figure 4) is in line also with the observed stereospecifity of the rearrangement reaction resulting in cis-fused pyridine and pyrrole rings in **5** and **6** as proved by the X-ray analysis. According to the Woodward−Hoffmann rules this [1,5]-sigmatropic rearrangement should take place in a *suprafacial* manner resulting in the cis orientation of 3a-H and 7a-H (H_A and H_B in Tables 1 and 2) as observed.

Detailed investigations have been carried out to determine the configuration of the cycloadducts and rearranged products based on the scalar H−H couplings and NOE measurements on the protons attached to saturated carbon atoms of these compounds. The vicinal couplings in the five-membered ring showed unexpected values, but taking into account the rigid structure of the fused six- and five-membered rings, no deviation from the Karplus rule has been found. In certain cases the dihedral angle between the protons in the trans position was distorted to approximately 70°, resulting in smaller scalar couplings compared to those of cis protons, connected by a dihedral angle close to 30°. It is worth mentioning that measurements of NOE effects proved to be ambiguous in some cases, as small NOEs of the adjacent trans protons could also be observed. To compare these ^{1}H NMR parameters, the *J* values and appearance of the

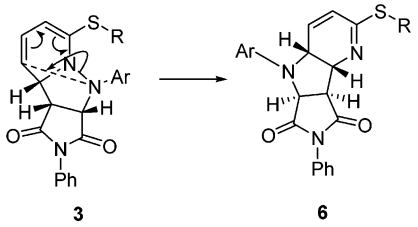


FIGURE 4. [1,5]-Sigmatropic rearrangement of the cycloadduct **3** to **6** with participation of three electron pairs as shown by the arrows.

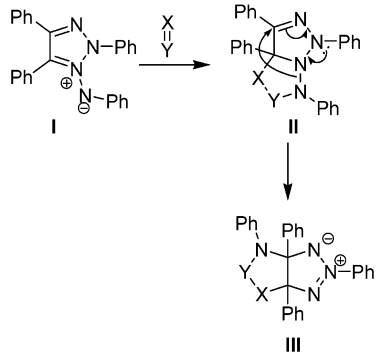


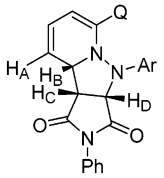
FIGURE 5. 1,3-Dipolar cycloaddition of [1,2,3]triazoliumimide **I** and rearrangement of the resulting cycloadduct **II** with N,N bond breakage forming **III**.[6,7]

NOE effects on the protons in question are compiled in Tables 1 and 2.

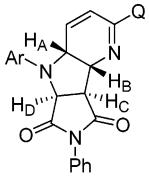
A literature search revealed a report by Butler et al.[6,7] on the [3+2] cycloaddition reaction of 2,4,5-triphenyl-2*H*-[1,2,3]triazol-1-ium-1-phenylimide **I** with dipolarophiles X = Y and the rearrangement reaction of the resulting cycloadducts. Thus, 3a,4,5,6-tetrahydro-1*H*-pyrazolo[1,5-*c*][1,2,3]triazole **II** is converted into 3,3a,4,5,6,6a-hexahy-

(6) Butler, R. N.; Evans, A. M.; Gillan, A. M.; James, J. P.; McNeela, E. M.; Cunningham, D.; McArdle, D. *J. Chem. Soc., Perkins Trans. 1* **1990**, 2537.
(7) Butler, R. N.; O'Shea, D. F. *Heterocycles* **1994**, *37*, 571.

TABLE 1. Comparison of Coupling Constants and NOE Effects of Cycloadducts (3 and 17) and Rearrangement Products (6) Obtained with *N*-Phenylmaleimide



Q=SR, **3**
Q=H, **17**

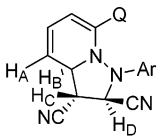


Q=SR, **6**

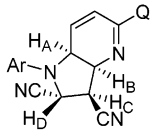
compd	*J* (Hz)	compd	*J* (Hz)
	Q = SR		
3a[a]	$J_{AB} = 5.0$	**6a**[b]	$J_{AB} = 7.8$
	$J_{BC} = 7.5$		$J_{BC} = 6.0$
	$J_{DC} = 8.0$		$J_{DC} = 8.0$
3d	$J_{AB} = 5.0$	**6d**	$J_{AB} = 7.5$
	$J_{BC} = 7.0$		$J_{BC} = 6.0$
	$J_{DC} = 8.0$		$J_{DC} = 8.0$
3e	$J_{AB} = 4.8$	**6e**	J_{AB} = not measured
	$J_{BC} = 7.5$		$J_{BC} = 6.0$
	$J_{DC} = 8.0$		$J_{DC} = 8.5$
	Q = H		
17	$J_{AB} = 5.0$		
	$J_{BC} = 8.2$		
	$J_{DC} = 7.5$		

[a] The irradiation of H_C produced similar NOE effects on H_B and H_D, proving that these three protons are in the cis position to each other. [b] The irradiation of H_B produced a large NOE effect on H_A while the effect on H_C was negligible, proving that H_A and H_B are in the cis relationship while H_B and H_C in the trans relationship.

TABLE 2. Comparison of Coupling Constants and NOE Effects of Cycloadducts (14) and Rearrangement Products (5 and 15) Obtained with Fumaronitrile



Q=H, **14**



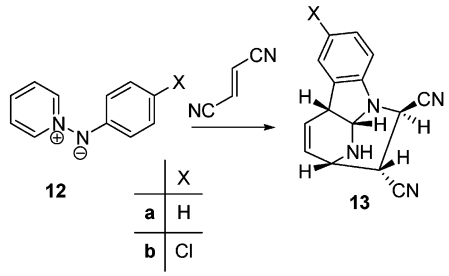
Q=SR, **5**
Q=H, **15**

compd	*J* (Hz)	compd	*J* (Hz)
	Q = SR		
		5a	$J_{AB} = 10$
			$J_{BC} = 7.0$
			$J_{DC} = 2.0$
		5b[a]	$J_{AB} = 10$
			$J_{BC} = 7.0$
			$J_{DC} = 2.0$
		5c	$J_{AB} = 9.0$
			$J_{BC} = 7.0$
			$J_{DC} = 2.5$
	Q = H		
14	$J_{AB} = 4.7$	**15**	J_{AB} =10.5
	$J_{BC} = 9.1$		$J_{BC} = 7.0$
	$J_{DC} = 7.0$		$J_{DC} = 2.5$

[a] The irradiation of H_B produced similar, large NOEs with H_A and H_C, proving that all these protons are in the cis relationship

dropyrrolo[2,3-*d*][1,2,3]triazol-2-ium-1-ide **III** (Scheme 6). The rearrangement reaction of the 5−5-fused ring system **II** is reminiscent of the analogous rearrangement of the

SCHEME 6



5−6-fused ring systems **3**, **4**, and **7** (vide supra): The rearrangement reaction of **II** has been explained by a thermally allowed sigmatropic shift involving N,N-bond cleavage in the pyrazolidine ring and bond formation of the phenyl-substituted N atom at 5-C of the [*d*]-fused dihydro[1,2,3]triazole **III**, in close analogy to the [1,5]-sigmatropic shift discussed above for the isoelectronic [*a*]-fused tetrahydropyrrolopyridine systems (e.g. for **4**).

For reaction Path C the neighboring group effect of the 2-sulfanyl substituent of **2** is essential, and the rearrangement reaction is expected to be impossible in the absence of this group, whereas the pericyclic route D is expected to be indifferent to the absence of the sulfanyl group. Thus, the feasibility of a rearrangement reaction of a cycloadduct derived from pyridinium-*N*-arylimide **12**[8] (lacking C-substituents in the pyridinium ring; prepared in situ from its hydrogen bromide salt[9]) was tackled.

Recently, Huisgen et al.[10−12] have investigated this reaction. Remarkably, these authors have found that the reaction of **12a** with fumaronitrile at room temperature gives rise—via the cycloaddition route—to a bridged ring system **13a** (Scheme 6). This reaction—found to take place also with isoquinolinium arylimides[13,14]—was interpreted as an aza-Cope sigmatropic shift followed by a ring closure step.[15] For structural comparison, we have confirmed this finding by an X-ray structure elucidation (Figure S1).[16]

We repeated the same transformation with our derivative **12b** and also found that the reaction with fumaronitrile at room temperature yields **13b**. Also in accordance with the cited literature we succeeded in isolating the

(8) Tamura, Y.; Tsujimoto, N.; Uchimura, M. *Yakugaku Zasshi* **1971**, *91*, 72.

(9) This salt was prepared according to the procedure elaborated for an analoguous compound: Carceller, R.; Garcia-Navio, J. L.; Izquierdo, M. L.; Alvarez-Builla, J.; Fajardo, M.; Gomez-Sal, P.; Gago, F. *Tetrahedron* **1994**, *50*, 4995.

(10) Huisgen, R.; Temme, R. *Heteroatom Chem*. **1999**, *10*, 79.

(11) Bast, K.; Durst, T.; Huisgen, R.; Lindner, K.; Temme, R. *Tetrahedron* **1998**, *54*, 3745.

(12) Bast, K.; Durst, T.; Huber, H.; Huisgen, R.; Lindner, K.; Stephenson, D. S.; Temme, R. *Tetrahedron* **1998**, *54*, 8451.

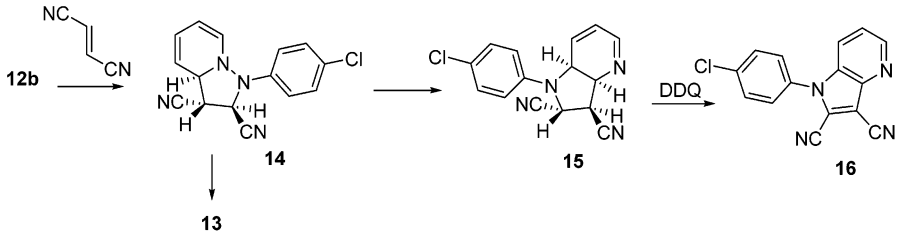
(13) Huber, H.; Huisgen, R.; Polborn, K.; Stephenson, D. S.; Temme, R. *Tetrahedron* **1998**, *54*, 3735.

(14) Huisgen, R.; Grashey, R.; Krishke, R. *Tetrahedron Lett*. **1962**, 387.

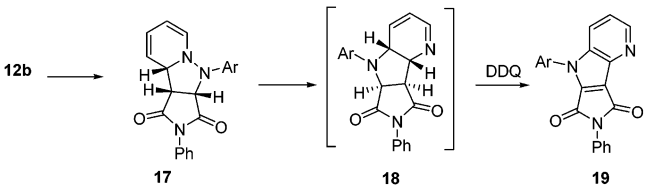
(15) Abramovitch et al. also observed a ring closure of this type with related sulfoxides. These authors discussed the possible mechanism of this transformation and could not decide between the concerted route and heterolytic cleavage: Abramovitch, R. A.; Siani, A. C.; Huttner, G.; Zsolnai, L.; Miller, J. *J. Org. Chem*. **1986**, *51*, 4741.

(16) Compound **13a**: $C_{15}H_{12}N_4$; M_r 248.29; colorless prism; size 0.50 × 0.35 × 0.15 mm^3; monoclinic; space group *P*21/*c*; a = 8.069(1) Å, b = 9.488(1) Å, c = 16.125(1) Å, β = 103.17(1)°, V = 1202.0(2) Å^3, Z = 4, r_{calcd} = 1.372 g/cm^3, m = 0.086 mm^{-1}, T = 293(2) K. The final model (172 parameters) was refined to wR_2 = 0.1542 for all data (5264 reflections), R_1 = 0.0511 for reflections with $I > 2\sigma(I)$ (2791), and GOF = 0.946.

SCHEME 7



SCHEME 8



crystalline primary cycloadduct **14b** at 0 °C. When, however, the same reaction was repeated under reflux conditions, formation of a mixture of **13b** and the expected ring transformation product **15** (in a ratio of approximately 1:1) was experienced (Scheme 7). When, however, the crystalline cycloadduct **14** was added to boiling toluene, the resulting product mixture contained a higher portion of **15** (**13b**:**15** = 1:2). Workup of this reaction mixture allowed the isolation of crystalline **15**; its structure has also been verified by X-ray crystallography (Figure S2).[17] This finding clearly shows that **14** besides rearranging to tetrahydro-1*H*-2,9-ethanopyrido[2,3-*b*]indole (**13b**) also undergoes the rearrangement reaction to tetrahydropyrrolo[3,2-*b*]pyridine (**15**) despite the pyridine ring being devoid of the sulfanyl substituent; this disproves the assumed neighboring group participation involved in Path C. The rearrangement product **15** was also oxidized by DDQ to the heteroaromatic product **16** (Scheme 7).

To answer the question if **13b** is the precursor of **15** the former product was heated in toluene for 24 h but **13b** was recovered unchanged.

Azomethine imine **12b** also reacted with *N*-phenylmaleimide to give cycloadduct **17**. However, this cycloadduct did not rearrange via the aza-Cope reaction to the bridged isomer, presumably because of the high rigidity of the ring system. Applying more forced conditions to induce the rearrangement led only to decomposition. However, the treatment of the crude mixture—obtained from **12b** and *N*-phenylmaleimide—with DDQ and separation of the reaction mixture by chromatography afforded the heteroaromatic product **19**, i.e., the oxidation product of the anticipated fused rearrangement intermediate **18** (Scheme 8).

Conclusion

The rearrangement of pyrazolo[2,3-*a*]pyridines to fused pyrrolo[3,2-*b*]pyridines by a new type of stereospecific ring transformation involving N−N bond fission provides a new method to prepare the latter heterocyclic system. To the best of our knowledge no paper on the *N*-aryl derivative of the pyrrolo[3,2-*b*]pyridine ring system has been published so far. Further studies on the sulfur-containing zwitterions (e.g. **2**) are in progress.

Experimental Section

X-ray Crystallography. The crystals of **5b**, **6a**, **13a**, and **15b** were mounted on glass fibers. Each data set was collected on an Enraf-Nonius CAD4 diffractometer with graphite-monochromated Cu Kα (for **5a**, **6a**, and **15b**) or Mo Kα (for **13a**) radiation at room temperature. Lattice parameters were determined by a least-squares fit for 25 reflections. The intensities of three standard reflections were monitored every hour, and correction was made for the indicated decay. All reflections were corrected for Lorentz and polarization effects.[18] Absorption correction was applied by using ψ-scan data.[19] The space groups were determined from the unit cell parameters and systematic absences. The structures were solved by direct methods (SHELXS-97[20]). All non-hydrogen atoms were modeled anisotropically in the structure refinement (SHELXL-97[21]). Hydrogen atoms were located in difference Fourier maps. Since they were found close to ideal positions, they were refined isotropically in the riding mode, using idealized geometry.

General Methods. IR spectra were obtained on a FT spectrophotometer. NMR spectra were recorded on a spectrometer operating at 400 and 100 MHz for ^{1}H and ^{13}C, respectively. Chemical shifts are reported in ppm downfield from tetramethylsilane. Proton assignments are based on decoupling and homonuclear correlation experiments. NOE ^{1}H NMR enhancements were determined from 1D difference NOE ^{1}H NMR spectra obtained by subtraction of two spectra acquired at identical conditions except for irradiation frequency. The HSQC method was used for the determination of the one-bond proton carbon connectivities, while quaternary carbons were assigned by using the HMBC method (two- and three-bond proton carbon connectivities). HRMS was measered with use of direct inlet spectrometers. All commercial grade reagents were used without further purification.

Synthesis of 2-arylsulfanylpyridinium-*N*-arylimides **2b**,**c** as well as their cycloaddition with *N*-phenylmaleininmide has been published earlier.[1] Derivatives **2a**,**d**,**e** and their cycloaddition products (**3a**,**d**,**e**) have been prepared by these published procedures[2] starting from 6 mmol of the appropriate tetrazolopyridinium salt **1** or 1.5 mmol of the zwitterion **2**, respectively.

2-Benzylsulfanylpyridinium-*N*-(4-chlorophenyl)imide (2a): red crystals, (1.66 g, 85%); mp 168−170 °C; ^{1}H NMR ($CDCl_3$) δ 4.13 (s, 2H, H−CH_2), 6.90 (m, 2H, H-2′, H-6′), 6.92 (ddd, J = 8, 6.5, 1 Hz, 1H, H-5), 7.02 (ddd, J = 8, 8, 1 Hz, 1H,

(17) Compound **15b**: $C_{15}H_{11}ClN_4$; M_r 282.73; colorless prism; size 0.35 × 0.17 × 0.08 mm^3, monoclinic; space group $P2_1/c$; a = 11.913(1) Å, b = 13.827(1) Å, c = 8.300(1) Å, β = 90.51(1)°, V = 1367.1(2) Å^3, Z = 4, ρ_{calc} = 1.374 g/cm^3, μ = 2.425 mm^{-1}, T = 293(2) K. The final model (181 parameters) was refined to wR_2 = 0.1536 for all data (2846 reflections), R_1 = 0.0502 for reflections with $I > 2\sigma(I)$ (2236), and GOF = 1.123.

(18) Harms, K. *XCAD4*, Data Reduction Program for CAD4 Diffractometers; Philipps-Universität: Marburg, Germany, 1996.

(19) Reibenspies, J. *DATCOR*, Program for Empirical Absorption Correction; Texas A & M University: College Station, TX, 1989.

(20) Sheldrick, G. M. *SHELXS-97*, Program for Crystal Structure Solution; University of Göttingen: Göttingen, Germany, 1997.

(21) Sheldrick, G. M. *SHELXL-97*, Program for Crystal Structure Refinement; University of Göttingen: Göttingen, Germany, 1997.

H-4), 7.13 (m, 2H, H-3′, H-5′), 7.18 (dd, J = 8, 1 Hz, 1H, H-3), 7.30 (m, 1H, H-4″), 7.34 (m, 2H, H-3″, H-5″), 7.44 (m, 2H, H-2″, H-6″), 8.57 (dd, J = 6.5, 1 Hz, 1H, H-6); ^{13}C NMR ($CDCl_3$) δ 37.0 (C−CH_2), 118.2 (C-2′, 6′), 120.0 (C-5), 122.7 (C-3), 123.5 (C-4′), 124.8 (C-4), 128.2 (C-1″), 129.3 (C-3′, 5′), 129.5 (C-2″, 6″), 129.9 (C-3″, 5″), 133.9 (C-4″), 135.0 (C-6), 150.3 (C-2), 151.2 (C-1′); HRMS calcd for $C_{18}H_{15}ClN_2S$ 327.0723, found 327.0714. Anal. Calcd for $C_{18}H_{15}ClN_2S$: C, 66.15; H, 4.63; N, 8.57; S, 9.81. Found: C, 66.03; H, 4.40; N, 8.35; S, 9.76.

2-[(4-Methylphenyl)sulfanyl]pyridinium-*N*-(4-fluorophenyl)imide (2d): red crystals (1.52 g, 82%); mp 131−133 °C.

2-[(4-Methylphenyl)sulfanyl]pyridinium-*N*-(4-isopropylphenyl)imide (2e): red crystals (1.48 g, 74%); mp 93−95 °C.

(3a*S*,9a*S*,9b*R*)-*rel*-6-Benzylsulfanyl-4-(4-chlorophenyl)-2-phenyl-3a,4,9a,9b-tetrahydro-1*H*-pyrrolo[3′4′:3,4]pyrazolo[1,5-*a*]pyridine-1,3(2*H*)-dione (3a): colorless crystals, (622 mg, 83%); mp 223−224 °C; ^{1}H NMR ($CDCl_3$) δ 3.60 (dd, J = 8, 7.5 Hz, 1H, H-9b), 3.72 (d, J = 12.5 Hz, 1H, H−CH_2), 3.76 (d, J = 12.5 Hz, 1H, H−CH_2), 4.36 (dd, J = 7.5, 5 Hz, 1H, H-9a), 4.60 (d, J = 8 Hz, 1H, H-3a), 4.88 (dd, J = 6 Hz, 1H, H-7), 5.78 (ddd, J = 9.5, 5, 1 Hz, 1H, H-9), 6.08 (dd, J = 9.5, 6 Hz, 1H, H-8), 7.10−7.30 (m, 11H, H-2′, H-3′, H-5′, H-6′, H-2″, H-3″, H-4″, H-5″, H-6″, H-2‴, H-6‴), 7.36−7.50 (m, 3H, H-3‴, H-4‴, H-5‴); ^{13}C NMR (DMSO-d_6) δ 34.8, 53.8, 60.7, 64.5, 95.7, 114.7, 115.8 (2C), 123.6, 125.1, 126.3 (2C), 127.0, 127.2, 128.4 (2C), 128.8 (2C), 128.9, 129.0 (2C), 129.4 (2C), 132.4, 135.8, 148.2, 172.3, 172.4; HRMS calcd for $C_{28}H_{22}ClN_3O_2S$ 499.1121, found 499.1129. Anal. Calcd for $C_{28}H_{22}ClN_3O_2S$: C, 67.26; H, 4.43; N, 8.40; S, 6.41. Found: C, 67.11; H, 4.26; N, 8.29; S, 6.30.

(3a*S*,9a*S*,9b*R*)-*rel*-4-(4-Fluorophenyl)- 6-[(4-methylphenyl)sulfanyl]-2-phenyl-3a,4,9a,9b-tetrahydro-1*H*-pyrrolo-[3′4′:3,4]pyrazolo[1,5-*a*]pyridine-1,3(2*H*)-dione (3d): colorless crystals (550 mg, 76%); mp 129−131 °C.

(3a*S*,9a*S*,9b*R*)-*rel*-4-(4-Isopropylphenyl)-6-[(4-methylphenyl)sulfanyl]-2-phenyl-3a,4,9a,9b-tetrahydro-1*H*-pyrrolo[3′4′:3,4]pyrazolo[1,5-*a*]pyridine-1,3(2*H*)-dione (3e): colorless crystals (692 mg, 91%); mp 135−137 °C.

General Procedure for the Reaction of Zwitterion 2 with Fumaronitrile to Tetrahydro-Pyrrolo[3,2-*b*]pyridine Derivatives (5). To a solution of the appropriate pyridinium-*N*-arylimide (**2**, 2.97 mmol) in dichloromethane (10 mL) was added fumaronitrile (228 mg, 3.56 mmol). The reaction mixture was stirred at room temperature for 1 day. The solvent was removed, the residue was treated with ether, the solid material was filtered off, and the resulting solid was recrystallized from acetonitrile.

(2*R*,3*R*,3a*S*,7a*S*)-*rel*-5-Benzylsulfanyl-1-(4-chlorophenyl)-2,3,3a,7a-tetrahydro-1*H*-pyrrolo[3,2-*b*]pyridine-2,3-dicarbonitrile (5a): prepared from **2a** as colorless crystals (468 mg, 39%); mp 207−209 °C.

(2*R*,3*R*,3a*S*,7a*S*)-*rel*-1-(4-Chlorophenyl)-5-[(4-chlorophenyl)sulfanyl]-2,3,3a,7a-tetrahydro-1*H*-pyrrolo[3,2-*b*]pyridine-2,3-dicarbonitrile (5b): prepared from **2b** as colorless crystals (358 mg, 29%); mp 189−190 °C; IR (KBr) ν_{max} 2240, 1641, 1594, 1497 cm^{-1}; ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ 4.52 (dd, J = 7, 2 Hz, 1H, H-3), 4.62 (ddd, J = 10, 3, 2 Hz, 1H, H-7a), 4.88 (dd, J = 10, 7 Hz, 1H, H-3a), 5.44 (d, J = 2 Hz, 1H, H-2), 6.00 (dd, J = 10, 2 Hz, 1H, H-6), 6.40 (dd, J = 10, 3 Hz, 1H, H-7), 6.96 (m, 2H, H-2′, H-6′), 7.33 (m, 2H, H-3′, H-5′), 7.45 (m, 2H, H-3″, H-5″), 7.54 (m, 2H, H-2″, H-6″); ^{13}C NMR ($CDCl_3$ + DMSO-d_6) δ 40.1 (C-3), 49.3 (C-7a), 50.4 (C-2), 59.4 (C-3a), 116.4 (CN), 117.0 (CN), 117.4 (C-2′, 6′), 120.7 (C-6), 125.2 (C-4″), 127.2 (C-4′), 129.7 (C-3′, 5′), 129.8 (C-3″, 5″), 131.4 (C-7), 135.3 (C-1″), 136.9 (C-2″, 6″), 142.4 (C-1′), 163.1 (C-5); HRMS calcd for $C_{21}H_{14}Cl_2N_4S$ 424.0316, found 424.0322. Anal. Calcd for $C_{21}H_{14}Cl_2N_4S$: C, 59.30; H, 3.32; N, 13.17; S, 7.54. Found: C, 59.09; H, 3.29; N, 13.11; S, 7.31.

(2*R*,3*R*,3a*S*,7a*S*)-*rel*-1-(4-Chlorophenyl)-5-[(4-methylphenyl)sulfanyl]-2,3,3a,7a-tetrahydro-1*H*-pyrrolo[3,2-*b*]pyridine-2,3-dicarbonitrile (5c): prepared from **2c** as colorless crystals (282 mg, 23%); mp 192−193 °C.

General Procedure for Isomerization of the Cycloadduct 3 to 1*H*-Pyrrolo[3′,4′:4,5]-1*H*-pyrrolo[3,2-*b*]pyridine-1,3(2*H*)-dione Derivatives (6). A solution of cycloadduct **3** (1.5 mmol) in chloroform (5 mL) was refluxed for 1 h. The solvent was removed, the residue was treated with ether, and the resulting solid was filtered off.

(3a*R*,4a*S*,8a*S*,8b*S*)-*rel*-7-Benzylsulfanyl-4-(4-chlorophenyl)-2-phenyl-3b,4a,8a,8b-tetrahydro-1*H*-pyrrolo[3′,4′:4,5]-1*H*-pyrrolo[3,2-*b*]pyridine-1,3(2*H*)-dione (6a): prepared from **3a** as colorless crystals (674 mg, 90%); mp 218−219 °C; ^{1}H NMR (DMSO-d_6) δ 3.70 (dd, 1H, J = 8, 6 Hz, H-8b), 4.29 (d, 1H, J = 14 Hz, H−CH_2), 4.47 (d, 1H, J = 14 Hz, H−CH_2), 4.88 (dd, 1H, J = 7.8, 6 Hz, H-8a), 4.98 (d, 1H, J = 8 Hz, H-3a), 5.01 (dd, 1H, J = 7.8, 2 Hz, H-4a), 6.10 (d, 1H, J = 9.6 Hz, H-6), 6.43 (dd, 1H, J = 9.6, 2 Hz, H-5), 7.16 (m, 2H, H-3′, H-5′), 7.32 (m, 2H, H-2′, H-6′), 7.30−7.44 (m, 5H, H-2″, H-3″, H-4″, H-5″, H-6″), 7.51 (m, 1H, H-4‴), 7.52 (m, 2H, H-2‴, H-6‴), 7.55 (m, 2H, H-3‴, H-5‴); ^{13}C NMR (DMSO-d_6) δ 31.9 C-CH_2), 52.2 (C-8b), 54.9 (C-3a), 59.8 (C-4a), 60.4 (C-8a), 117.6 (C-2′, 6′), 122.5 (C-6), 122.6 (C-4‴), 127.2 (C-4″), 127.4 (C-2‴, 6‴), 128.5 (C-2″, 6″), 128.6 (C-5), 128.7 (C-3″, 5″), 129.0 (C-3‴, 5‴), 129.2 (C-3′, 5′), 131.9 (C-4′), 132.1 (C-1‴), 138.3 (C-1″), 143.7 (C-1′), 160.5 (C-7), 173.8 (C-3), 174.4 (C-1); HRMS calcd for $C_{28}H_{22}ClN_3O_2S$ 499.1121, found 499.1106. Anal. Calcd for $C_{28}H_{22}ClN_3O_2S$: C, 67.26; H, 4.43; N, 8.40; S, 6.41. Found: C, 67.04; H, 4.44; N, 8.22; S, 6.21.

(3a*R*,4a*S*,8a*S*,8b*S*)-*rel*-4-(4-Chlorophenyl)-7-[(4-chlorophenyl)sulfanyl]-2-phenyl-3b,4a,8a,8b-tetrahydro-1*H*-pyrrolo[3′,4′:4,5]-1*H*-pyrrolo[3,2-b]pyridine-1,3(2*H*)-dione (6b): prepared from **3b** as colorless crystals (717 mg, 92%); mp 129−131 °C.

(3a*R*,4a*S*,8a*S*,8b*S*)-*rel*-4-(4-Chlorophenyl)-7-[(4-methylphenyl)sulfanyl]-2-phenyl-3b,4a,8a,8b-tetrahydro-1*H*-pyrrolo[3′,4′:4,5]-1*H*-pyrrolo[3,2-*b*]pyridine-1,3(2*H*)-dione (6c): prepared from **3c** as colorless crystals (603 mg, 86%); mp 140−141 °C.

(3a*R*,4a*S*,8a*S*,8b*S*)-*rel*-4-(4-Fluorophenyl)-7-[(4-methylphenyl)sulfanyl]-2-phenyl-3b,4a,8a,8b-tetrahydro-1*H*-pyrrolo[3′,4′:4,5]-1*H*-pyrrolo[3,2-*b*]pyridine-1,3(2*H*)-dione (6d): prepared from **3d** as colorless crystals (623 mg, 86%); mp 179−181 °C.

(3a*R*,4a*S*,8a*S*,8b*S*)-*rel*-4-(4-Isopropylphenyl)-7-[(4-methylphenyl)sulfanyl]-2-phenyl-3b,4a,8a,8b-tetrahydro-1*H*-pyrrolo[3′,4′:4,5]-1*H*-pyrrolo[3,2-*b*]pyridine-1,3(2*H*)-dione (6e): prepared from **3e** as colorless crystals (638 mg, 84%); mp 178−180 °C.

(3a*S*,7a*S*)-*rel*-Dimethyl 1-(4-chlorophenyl)-5-[(4-chlorophenyl)sulfanyl]-3a,7a-dihydro-1*H*-pyrrolo[3,2-*b*]pyridine 2,3-dicarboxylate (8). Dimethyl acetylenedicarboxylate (0.5 mL, 0.578 g, 4.067 mmol) was added to a solution of **2b** (1 g, 2.88 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was stirred at room temperature for 2 h. The solvent was removed, the residue was treated with ether, and the resulting solid was filtered off to yield the product (380 mg, 27%): mp 159−161 °C; ^{1}H NMR ($CDCl_3$) δ 3.69 (s, 3H, H−Me), 3.78 (s, 3H, H−Me), 4.68 (dd, J = 12, 5, Hz, 1H, H-7a), 5.25 (d, J = 12 Hz, 1H, H-3a), 5.87 (d, J = 9.9 Hz, 1H, H-6), 6.13 (dd, J = 9.9, 5 Hz, 1H, H-7), 7.00−7.48 (m, 8H, H-2′, H-6′, H-3′, H-5′, H-2″, H-6″, H-3″, H-5″); ^{13}C NMR ($CDCl_3$) δ 51.2 (Me), 53.1 (Me), 56.7 (C-7a), 61.7 (C-3a), 107.1 (C-3), 123.2 (C-6), 125.2 (C-2′, 6′), 126.3 (C-7), 127.5 (C-1″), 128.9 (C-3′, 5′), 129.7 (C-3″, 5″), 132.1 (C-4″), 135.0 (C-4′), 135.7 (C-2″, 6″), 137.2 (C-1′), 151.1 (C-2), 157.9 (C-5), 162.9 (C═O), 164.8 (C═O); HRMS calcd for $C_{23}H_{18}Cl_2N_2O_4S$ 488.0341, found 488.0364. Anal. Calcd for $C_{23}H_{18}Cl_2N_2O_4S$: C, 56.45; H, 3.71; N, 5.72; S, 6.55. Found: C, 56.22; H, 3.69; N, 5.62; S, 6.33.

General Procedure for Oxidation of the Ring Transformation Products 5 and 6 to Pyrrolo[3,2-*b*]pyridine-2,3-dicarbonitriles (9) and 1*H*-Pyrrolo[3′,4′:4,5]-1*H*-pyrrolo[3,2-*b*]pyridines (10), Respectively. A suspension of **5**

or **6** (0.47 mmol) and DDQ (293 mg, 1.29 mmol) in toluene (10 mL) was refluxed for 3 h. The solvent was removed, the residue was mixed with CH_2Cl_2 (40 mL), and the impurities were removed by filtration. Alumina (2 g) was added to the filtrate, the mixture was stirred for a few minutes, and the mixture were filtered. The organic solvent was evaporated, and the residue was purified as described below.

5-Benzylsulfanyl-1-(4-chlorophenyl)-1*H*-pyrrolo[3,2-*b*]-pyridine-2,3-dicarbonitrile (9a). The residue was submitted to column chromatography (silica/chloroform) to give yellow crystals (102 mg, 54%): mp 175−177 °C.

1-(4-Chlorophenyl)-5-[(4-chlorophenyl)sulfanyl]-1*H*-pyrrolo[3,2-*b*]pyridine-2,3-dicarbonitrile (9b). The residue was crystallized from acetonitrile (148.4 mg, 75%): mp 233−234 °C; IR(KBr) ν_{max} 2225, 1518, 1496, 1422 cm^{-1}; ^1H NMR ($CDCl_3$ + DMSO-d_6) δ 7.19 (d, J = 9 Hz, 1H, H-6), 7.48 (m, 2H, H-2″, H-6″), 7.59 (m, 2H, H-3″, H-5″), 7.66 (m, 2H, H-2′, H-6′), 7.69 (m, 2H, H-3′, H-5′), 7.71 (d, J = 9 Hz, 1H, H-7); ^{13}C NMR ($CDCl_3$ + DMSO-d_6) δ 97.2 (C-3), 110.3 (CN), 111.6 (CN), 117.8 (C-2), 121.8 (C-6), 122.2 (C-7), 128.6 (C-2′, 6′), 129.3 (C-1″), 129.6 (C-4″), 130.2 (C-3′, 5′), 130.9 (C-3″, 5″), 133.0 (C-4′), 135.5 (C-3a), 136.3 (C-7a), 136.5 (C-2″, 6″) 142.4 (C-1′), 159.6 (C-5); HRMS calcd for $C_{21}H_{10}Cl_2N_4S$ 420.0003, found 419.9991. Anal. Calcd for $C_{21}H_{10}Cl_2N_4S$: C, 59.87; H, 2.39; N, 13.30; S, 7.61. Found: C, 59.77; H, 2.23; N, 13.48; S, 7.44.

1-(4-Chlorophenyl)-5-[(4-methylphenyl)sulfanyl]-1*H*-pyrrolo[3,2-*b*]pyridine-2,3-dicarbonitrile (9c). The residue was crystallized from acetonitrile (146.8 mg, 78%): mp 197−199 °C.

7-Benzylsulfanyl-4-(4-chlorophenyl)-2-phenyl-1*H*-pyrrolo[3′,4′:4,5]-1*H*-pyrrolo[3,2-*b*]pyridine-1,3(2*H*)dione (10a): prepared from **6a** as pale yellow crystals (583 mg, 78%);: mp 191−193 °C.

4-(4-Chlorophenyl)-7-[(4-chlorophenyl)sulfanyl]-2-phenyl-1*H*-pyrrolo[3′,4′:4,5]-1*H*-pyrrolo[3,2-*b*]pyridine-1,3(2*H*)-dione (10b): prepared from **6b** as pale yellow crystals (580 mg, 75%); mp 255−256 °C; ^1H NMR (DMSO-d_6) δ 7.10 (d, J = 9 Hz, 1H, H-6), 7.36 (m, 2H, H-2‴, H-6‴), 7.38 (m, 1H, H-4‴), 7.48 (m, 2H, H-3‴, H-5‴), 7.52 (m, 2H, H-2″, H-6″), 7.58 (m, 2H, H-3″, H-5″), 7.67 (m, 2H, H-3′, H-5′), 7.77 (m, 2H, H-2′, H-6′), 7.92 (d, J = 9 Hz, 1H, H-5); ^{13}C NMR (DMSO-d_6) δ 114.7 (C-8b), 120.4 (C-6), 123.6 (C-5), 128.1 (C-3‴, 5‴), 128.4 (C-2′, 6′), 128.5 (C-4‴), 129.5 (2C), 130.4 (2C), 130.5 (C-2‴, 6‴), 130.7 (C-1″), 132.6 (C-4″), 133.7 (C-4′), 134.4 (C-8a), 134.8 (C-4a), 135.0 (C-1‴), 136.3 (C-2″, 6″), 138.2 (C-3a), 142.1 (C-1′), 157.4 (C-7), 160.0 (C-3), 162.2 (C-1); HRMS calcd for $C_{27}H_{15}Cl_2N_3O_2S$ 515.0262, found 515.0261. Anal. Calcd for $C_{27}H_{15}Cl_2N_3O_2S$: C, 65.25; H, 3.13; N, 5.44; S, 6.22. Found: C, 65.05; H, 3.11; N, 5.25; S, 6.10.

4-(4-Chlorophenyl)-7-[(4-methylphenyl)sulfanyl]-2-phenyl-1*H*-pyrrolo[3′,4′:4,5]-1*H*-pyrrolo[3,2-*b*]pyridine-1,3(2*H*)dione (10c): prepared from **6c** as pale yellow crystals (579 mg, 78%); mp 262−264 °C.

^{1}H-Dimethyl 1-(4-Chlorophenyl)-5-[(4-chlorophenyl)-sulfanyl]-1*H*-pyrrolo[3,2-*b*]pyridine-2,3-dicarboxylate (11). A suspension of **8** (110 mg, 0.255 mmol) and DDQ (100 mg, 0.44 mmol) in toluene (10 mL) was refluxed for 2 h. The solvent was removed, the residue was mixed with CH_2Cl_2 (40 mL), and the impurities were removed by filtration. Alumina (2 g) was added and, the mixture was stirred for a few minutes and then filtered. The organic solvent was evaporated, and the residue was crystallized from petroleum ether to yield yellow crystals (80 mg, 73%): mp 124−125 °C; ^1H NMR ($CDCl_3$) δ 3.82 (s, 3H, H−Me), 3.93 (s, 3H, H−Me), 6.98 (d, J = 9 Hz, 1H, H-6), 7.28 (d, J = 9 Hz, 1H, H-7), 7.29 (m, 2H, H-2″, H-6″), 7.38 (m, 2H, H-2′, H-6′), 7.50 (m, 2H, H-3′, H-5′), 7.58 (m, 2H, H-3″, H-5″); ^{13}C NMR ($CDCl_3$) δ 52.1 (Me), 53.1 (Me), 119.0 (C-6), 119.8 (C-7), 128.3 (C-2′, 6′), 129.1 (C-1″), 129.4 (C-3″, 5″), 130.0 (C-3′, 5′), 130.6 (C-3), 134.2 (C-3a), 134.3 (C-7a), 134.8 (C-4″), 135.5 (C-4′), 135.6 (C-2″, 6″), 136.0 (C-1′), 141.8 (C-2), 156.7 (C-5), 161.4 (C═O), 163.5 (C═O); HRMS calcd for $C_{23}H_{16}Cl_2N_2O_4S$ 486.0208, found 486.0318. Anal. Calcd for $C_{23}H_{16}Cl_2N_2O_4S$: C, 56.68; H, 3.31; N, 5.75; S, 6.58. Found: C, 56.42; H, 3.31; N, 5.75; S, 6.28.

(2*R*,3*R*,4*R*,5*R*,10*S*,10a*R*)-*rel*-8-Chloro-1,2,3,4,10,10a-hexahydro-2,10-ethenopyrimido[1,2-*a*]indole-3,4-dicarbonitrile (13b). Zwitterion[7] **12b** prepared from *N*-(4-chlorophenyl)-pyridinium bromide[8] (700 mg, 2.45 mmol) was dissolved in water (30 mL) and saturated potassium carbonate solution (20 mL) was added. The mixture was then extracted with CH_2Cl_2 (3 × 20 mL). The organic phase was dried over Na_2SO_4 and concentrated to half if its volume, and fumaronitrile was added (210 mg, 2.7 mmol). The mixture was stirred at room temperature for 1 d. The solvent was removed, the residue was treated with ether, and the resulting solid was filtered off to yield colorless crystals (310 mg, 44%): mp 184−185 °C (toluene); ^1H NMR ($CDCl_3$) δ 2.40 (d, J = 4 Hz, 1H, N−H), 3.43 (dd, J = 9.3, 4.8 Hz, 1H, H-3), 3.53 (ddd, J = 4.7, 2.8, 1.5 Hz, 1H, H-10), 4.07 (ddd, J = 5, 4.8, 0.9 Hz, 1H, H-2), 4.12 (d, J = 9.3 Hz, 1H, H-4), 4.94 (dd, J = 4.7, 4 Hz, 1H, H-10a), 6.04 (ddd, J = 10, 5, 1.5 Hz, 1H, H-1′), 6.11 (ddd, J = 10, 2.8, 0.9 Hz, 1H, H-2′), 7.19 (d, J = 8.5 Hz, 1H, H-6), 7.24 (dd, J = 8.5, 2 Hz, 1H, H-7), 7.29 (d, J = 2 Hz, 1H, H-9); ^{13}C NMR ($CDCl_3$) δ 35.3 (C-3), 42.1 (C-10), 45.4 (C-2), 52.1 (C-4), 72.4 (C-10a), 115.8 (C−CN), 117.8 (C−CN), 119.0 (C-6), 123.8 (C-1′), 125.5 (C-9), 129.0 (C-7), 130.5 (C-8), 132.7 (C-2′), 137.2 (C-9a), 149.3 (C-6a); HRMS calcd for $C_{15}H_{11}Cl\ N_4$ 282.0672, found 282.0676. Anal. Calcd for $C_{15}H_{11}ClN_4$: C, 63.72; H, 3.92; N, 19.82. Found: C, 63.52; H, 3.78; N, 19.52.

(2*R*,3*R*,3a*R*)-*rel*-1-(4-Chlorophenyl)-1,2,3,3a-tetrahydropyrazolo[1,5-*a*]pyridine-2,3-dicarbonitrile (14). To a solution of **12b** (480 mg, 2.35 mmol) in diethyl ether (10 mL) was added fumaronitrile (220 mg, 2.82 mmol) at room temperature. The mixture was stirred for 20 min and the precipitated product was filterred off and washed with cold diethyl ether (2 mL) to give gray crystals (0.35 g, 53%): mp 90−91 °C. The product proved to be unstable at room temperature and was stored at − 20 °C for a few days or subjected to further transformations immediately. IR (KBr) ν_{max} 2930, 2252, 1572, 1489, 1243 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.86 (dd, J = 9.1, 7 Hz, 1H, H-3), 4.02 (dd, J = 9.1, 4.7 Hz, 1H, H-3a), 4.38 (d, J = 7 Hz, 1H, H-2), 5.23 (d, J = 6.5, 5.5 Hz, 1H, H-6), 5.88 (dd, J = 5.8, 4.7 Hz, 1H, H-4), 6.17 (d, J = 5.5 Hz, 1H, H-7), 6.20 (dd, J = 6.5, 5.8 Hz, 1H, H-5), 6.90 (m, 2H, H-3′, H-5′), 7.31 (m, 2H, H2′, H6′); ^{13}C NMR ($CDCl_3$) δ 43.4, 54.5, 61.4, 102.6, 115.5 (2C), 116.6, 118.8, 119.0, 125.7, 126.2, 129.8 (2C), 137.5, 146.4.

(2*R*,3*R*,3a*S*,7a*S*)-*rel*-1-(4-Chlorophenyl)-2,3,3a,7a-tetrahydro-1*H*-pyrrolo[3,2-*b*]pyridine-2,3-dicarbonitrile (15). Crystals of **14** (100 mg, 0.35 mmol) were added to boiling toluene (5 mL) and the mixture was stirred at 110 °C under Argon for 2 h. The solvent was evaporated and the residue was treated with diethyl ether (5 mL) to give the crude product (70 mg) containing two main components. The more polar component was separated by colomn chromatography (silica-gel; eluent $CHCl_3$:methanol = 100:4) and recrystallized from MeOH to yield colorless crystals (28 mg, 28%): mp 209−211 °C; IR (KBr) ν_{max} 2944, 2246, 1595, 1497, 1330 cm^{-1}; ^1H NMR (DMSO-d_6) δ 4.63 (ddd, J = 10.5, 3, 1.5 Hz, 1H, H-7a), 4.77 (dd, J = 7, 2.5 Hz, 1H, H-3), 4.89 (ddd, J = 10.5, 7, 2 Hz, 1H, H-3a), 5.50 (d, J = 2.5 Hz, 1H, H-2), 6.09 (ddd, J = 10, 5, 1.5 Hz, 1H, H-6), 6.39 (dd, J = 10, 3 Hz, 1H, H-7), 7.00 (m, 2H, H-2′, H-6′), 7.40 (m. 2H, H-3′, H-5′), 8.04 (dd, J = 5, 2 Hz, 1H, H-5); ^{13}C NMR (DMSO-d_6) δ 38.8 (C-3), 47.9 (C-2), 49.2 (C-7a), 57.1 (C-3a), 115.6 (CN), 116.2 (CN), 116.6 (C-2′, 6′), 119.1 (C-6), 123.5 (C-4′), 128.6 (C-3′, 5′), 129.6 (C-7), 141.6 (C-1′), 156.5 (C-5); HRMS calcd for $C_{15}H_{11}ClN_4$ 282.0672, found 282.0676. Anal. Calcd for $C_{15}H_{11}ClN_4$: C, 63.72; H, 3.92; N, 19.82. Found: C, 63.54; H, 3.89; N, 19.62.

1-(4-Chlorophenyl)-1*H*-pyrrolo[3,2-*b*]pyridine-2,3-dicarbonitrile (16). A suspension of **15** (100 mg, 0.35 mmol) and DDQ (193 mg, 0.85 mmol) in toluene (10 mL) was refluxed for 2 h. The solvent was removed, the residue was mixed with dichloromethane (40 mL), and the impurities were removed

by filtration. Alumina (2 g) was added to the filtrate, and the mixture was stirred for 10 min and filtered. The solvent was evaporated, and the residue was crystallized from acetonitrile to afford colorless crystals (85 mg, 86%): mp 235−237 °C; ^{1}H NMR (DMSO-d_6) δ 7.58 (dd, J = 8, 4 Hz, 1H, H-6), 7.75−7.85 (m, 4H, H-2′, H-3′, H-4′, H-5′), 7.95 (d, J = 8 Hz, 1H, H-7), 8.78 (d, J = 4 Hz, 1H, H-5); ^{13}C NMR (DMSO-d_6) δ 97.4 (C-3), 110.9 (CN), 112.6 (CN), 118.9 (C-2), 121.7 (C-6), 123.6 (C-7), 129.5 (C-3′, 5′), 131.0 (C-2′, 6′), 131.6 (C-4′), 133.6 (C-1′), 135.8 (C-7a), 142.5 (C-3a), 149.6 (C-5); HRMS calcd for $C_{15}H_7ClN_4$ 278.0359, found 278.0349. Anal. Calcd for $C_{15}H_7ClN_4$: C, 64.64; H, 2.53; N, 20.10. Found: C, 64.34; H, 2.38; N, 19.91.

(3a*S*,9a*S*,9b*R*)-*rel*-4-(4-Chlorophenyl)-2-phenyl-3a,4,-9a,9b-tetrahydro-1*H*-pyrrolo[3′4′:3,4]pyrazolo[1,5-*a*]pyridine-1,3(2*H*)-dione (17). To a solution of **12b**[7] obtained from *N*-(4-chlorophenyl)pyridinium bromide[8] (700 mg, 2.45 mmol) in water (30 mL) was added saturated potassium carbonate solution (20 mL) to give a red suspension. The mixture was extracted with CH_2Cl_2 (3 × 20 mL). The organic phase was dried and concentrated to half of its volume. To this solution was added *N*-phenylmaleimide (450 mg, 2.6 mmol). The mixture was stirred at room temperature for 15 min. A fast reaction occurred indicated by the disappearance of the red color. The solvent was removed, the residue was treated with ether, and the resulting solid was filtered off (783 mg, 83%): mp 174−176 °C; ^{1}H NMR (DMSO-d_6) δ 3.83 (dd, J = 8.2, 7.5 Hz, 1H, H-9b), 4.34 (dd, J = 8.2, 5 Hz, 1H, H-9a), 4.92 (dd, J = 7.5, 5 Hz, 1H, H-7), 5.07 (d, J = 7.5 Hz, 1H, H-3a), 5.75 (dd, J = 9.5, 5 Hz, 1H, H-9), 6.00 (dd, J = 9.5, 5 Hz, 1H, H-8), 6.12 (d, J = 7.5 Hz, 1H, H-6), 7.13 (m, 2H, H-3′, H-5′), 7.17 (m, 2H, H-2″, H-6″), 7.37 (m, 2H, H-2′, H-6′), 7.44 (m, 1H, H-4″), 7.51 (m, 2H, H-3″, H-5″); ^{13}C NMR (DMSO-d_6) δ 55.6 (C-9b), 58.9 (C-9a), 66.6 (C-3a), 100.3 (C-7), 116.8 (C-3″, 5″), 118.5 (C-9), 123.8 (C-8), 126.0 (C-4′), 127.1(C-3′, 5′), 129.1 (C-4″), 129.7 (C-2′, 6′), 129.8 (C-2″, 6″), 132.9 (C-1″), 138.8 (C-6), 148.5 (C-1′), 173.6 (C-1), 174.4 (C-3); HRMS calcd for $C_{21}H_{16}ClN_3O_2$ 377.0931, found 377.0917. Anal. Calcd for $C_{21}H_{16}ClN_3O_2$: C, 66.76; H, 4.27; N, 11.12. Found: C, 66.54; H, 4.19; N, 10.97.

4-(4-Chlorophenyl)-2-phenyl-1*H*-pyrrolo[3′4′:3,4]pyrazolo[1,5-*a*]pyridine-1,3(2*H*)-dione (19). A suspension of **17** (330 mg, 0.87 mmol) and DDQ (440 mg, 1.9 mmol) in toluene (10 mL) was refluxed for 1 h. The solvent was removed, the residue was mixed with CH_2Cl_2 (40 mL), and the mixture was filtered. Alumina (2 g) was added to the filtrateand the mixture was stirred for 10 min and filtered. The organic solvent was evaporated, and the residue was crystallized from 2-propanol: yellow crystals (79 mg, 24%); mp 248−250 °C; ^{1}H NMR ($CDCl_3$) δ 7.36 (dd, J = 8.5, 4.5 Hz, 1H, H-6), 7.37 (m, 1H, H-4″), 7.40 (m, 2H, H-2″, H-6″), 7.47 (m, 2H, H-3″, H-5″), 7.58 (m, 4H, H-2′, H-3′, H-5′, H-6′), 7.86 (dd, J = 8.5, 1 Hz, 1H, H-5), 8.78 (dd, J = 4.5, 1 Hz, 1H, H-7); ^{13}C NMR ($CDCl_3$) δ 116.7 (C-8b), 120.5 (C-6), 120.8 (C-5), 126.7 (C-3′, 5′), 126.8 (C-3″, 5″), 127.9 (C-4″), 129.0 (C-2′, 6′), 130.1 (C-2″, 6″), 131.7 (C-8a), 132.8 (C-4a), 135.3 (C-4′), 136.5 (C-3a), 138.4 (C-1″), 140.3 (C-1′), 148.3 (C-7), 160.0 (C-3), 161.5 (C-1); HRMS calcd for $C_{21}H_{12}ClN_3O_2$ 373.0618, found 373.0628. Anal. Calcd for $C_{21}H_{12}ClN_3O_2$: C, 67.48; H, 3.24; N, 11.24. Found: C, 67.22; H, 3.24; N, 11.04.

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Supporting Information Available: ORTEP diagrams of **13a** and **15**, analytical data for **2b**,**e**, **3d**,**e**, **5a**,**c**, **6b**,**d**,**e**, **9a**,**c**, and **10 a**,**c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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