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# Unexpected Behavior of the Reaction between 1,2-Diaza-1,3-Butadienes and 3-Dimethylaminopropenoates: A Useful Entry to New Pyrrolines, Pyrroles, and Oxazolines

Orazio A. Attanasi,[†] Gianfranco Favi,[†] Paolino Filippone,*[,†] Amalija Golobič,[‡] Branko Stanovnik,*[,‡] and Jurij Svete[‡]

*Istituto di Chimica Organica, Università degli Studi di Urbino "Carlo Bo", Via Sasso 75, 61029 Urbino, Italy, and Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, 1000 Ljubljana, Slovenia*

*filippone@uniurb.it; branko.stanovnik@uni-lj.si*

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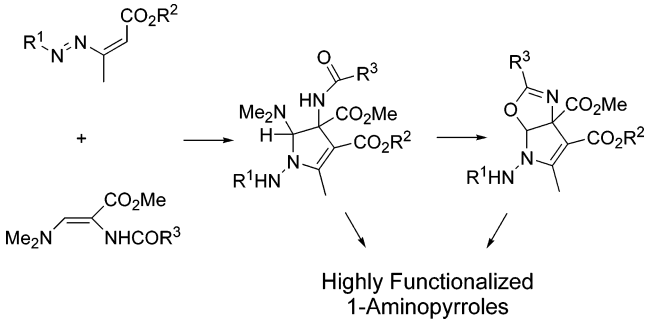


We observed a nucleophilic attack by the ene-amino carbon of 3-dimethylaminopropenoates at the terminal carbon of the azo-ene system of 1,2-diaza-1,3-butadienes. In tetrahydrofuran at 65 °C, this attack produced 1-aminopyrrolines with a high degree of *cis*-stereoselectivity by means of an unusual zwitterionic adduct intermediate followed by intramolecular ring closure. In toluene under reflux, 1-aminopyrrolines produced oxazoline-fused 1-aminopyrrolines. Oxazoline-fused 1-aminopyrrolines were directly obtained by reaction of 1,2-diaza-1,3-butadienes with 3-dimethylaminopropenoates in toluene under reflux. The ring opening of oxazoline-fused 1-aminopyrrolines in acidic or basic media provides highly substituted 1-aminopyrroles. 5-Unsubstituted 1-aminopyrrole derivatives were obtained from 1-aminopyrrolines under basic conditions by loss of dimethylamino and ester groups. We discuss the plausible mechanisms of the ring closure and opening.

## Introduction

The chemistry of 3-dimethylaminopropenoates[1] and 1,2-diaza-1,3-butadienes[2] has been studied separately in the authors' laboratories. These investigations demonstrated that both these compounds are powerful tools in organic chemistry.[1−3] In particular, 3-dimethylaminopropenoates show both electrophilic and nucleophilic aptitudes and 1,2-diaza-1,3-butadienes exhibit both diene and dienophile roles in Diels−Alder reactions and act as Michael acceptors leading to heterocycle derivatives.

* To whom correspondence should be addressed. (P.F.) Phone: +39-0722-303443. Fax: +39-0722-303441. (B.S.) Phone: +386-1-2419-100. Fax: +386-1-2419-220.

† University of Urbino.

‡ University of Ljubljana.

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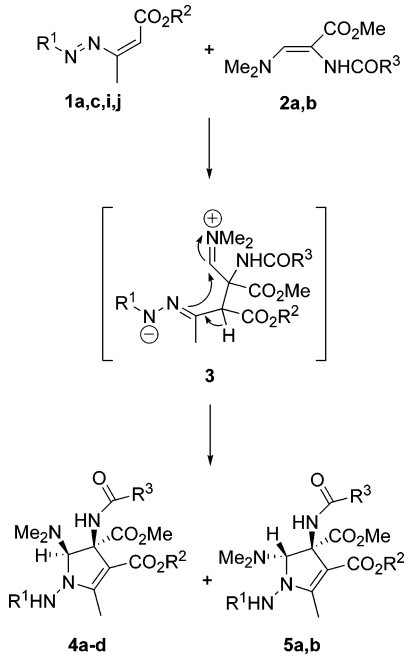
Based on these facts and our continuing investigations, we decided to explore a possible nucleophilic attack of 3-dimethylaminopropenoates at the azo-ene system of 1,2-diaza-1,3-butadienes in an attempt to obtain pyrrolines and pyrroles by subsequent intramolecular cyclization of the preliminary 1,4-adduct intermediates. Surprisingly, we first isolated new highly substituted oxazolines. The mechanisms of formation of pyrrolines, pyrroles, and oxazolines, as well as the behaviors of ring closure and opening, have been elucidated and are reported in this paper.

The synthesis of pyrroles is an attractive area of heterocyclic chemistry,[4] primarily because many pyrroles are subunits of natural products[5] and some are the building blocks for porphyrin synthesis.[6] In particular, 1-aminopyrroles are used as precursors in the synthesis of biologically active compounds such as analgesics[7] and NMDA-receptor antagonists.[8] Despite these applications, the limited number of papers on 1-aminopyrroles in the literature can be ascribed to the few procedures available for their preparation.[9] Direct synthetic routes to 1-aminopyrroles are relatively few, and these derivatives seem to be quite difficult to prepare by both classic[10] and recent methods,[11] especially because of the severe reaction conditions, formation of byproducts, reiterate reaction steps, and workup manipulations.

**SCHEME 1**




This paper reports a simple one-pot protocol for the synthesis of variously functionalized 1-aminopyrrolines and oxazoline-fused 1-aminopyrrolines from which can be readily obtained substituted and (4 or 5)-unsubstituted 1-aminopyrroles.

The presence of different functional groups in many positions of these systems merits particular emphasis. In fact, such compounds may be, in turn, useful for further interesting structural modifications producing more complex compounds.

## Results and Discussion

1,2-Diaza-1,3-butadienes **1a**,**c**,**i**,**j** easily reacted with methyl 2-substituted-3-dimethylaminopropenoates **2a**,**b** under various conditions (Scheme 1, Table 1). When the reactions between 1,2-diaza-1,3-butadienes **1a**,**c** and methyl 2-benzoylamino-3-dimethylaminopropenoate **2a** were carried out in tetrahydrofuran at 65 °C (10−30 h), the *cis*-1-aminopyrroline intermediates **4a**,**b** were obtained almost exclusively and in excellent yields (75−92%). Trace amounts of *trans* diastereomeric products **5a**,**b** were also isolated from the crude reaction mixture (Scheme 1, Table 1). Moreover, when 1,2-diaza-1,3-butadienes **1i**,**j** reacted with methyl 2-benzyloxycarbonylamino-3-dimethylaminopropenoate **2b** in toluene under reflux, only *cis*-1-aminopyrrolines **4c**,**d** were recovered.

The exact stereochemistry of 1-aminopyrroline derivatives **4a**−**d** was assigned by X-ray analysis of compound **4b**. $^1$H NMR spectra of the compounds **4a**, **5a** and **4b**, **5b** did not allow the exhaustive identification of these two diastereomers. The high yield of these products may be ascribed to the favorable intramolecular hydrogen bond between O(1) and N(3) of substituted carbonylamino and dimethylamino residues, respectively, in *cis* isomers

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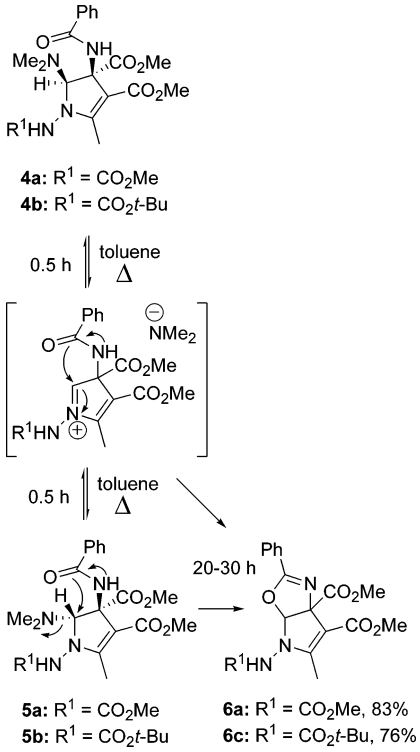
**TABLE 1. Reaction Times and Yields of 1-Aminopyrrolines 4a–d and 5a,b**

| 1 | $R^1$ | $R^2$ | 2 | $R^3$ | 4 | yield[a] (%) | 5 | yield[a] (%) | solvent, *T* (°C) | time (h) |
|---|---|---|---|---|---|---|---|---|---|---|
| **1a** | $CO_2Me$ | Me | **2a** | Ph | **4a** | 92 | **5a** | 2 | THF, 65 | 10 |
| **1c** | $CO_2t$-Bu | Me | **2a** | Ph | **4b** | 75 | **5b** | 9 | THF, 65 | 30 |
| **1i** | $CONH_2$ | Me | **2b** | OBn | **4c** | 44 | | | toluene, reflux | 6 |
| **1j** | $CONH_2$ | Et | **2b** | OBn | **4d** | 38 | | | toluene, reflux | 6 |

[a] Yield of pure isolated products.

**SCHEME 2**




**4a**–**d**. Furthermore, an equimolar mixture of the isomeric couples **4a**, **5a** and **4b**, **5b** was achieved when the single diastereomers **4a**,**b** or **5a**,**b** were treated for 0.5 h in toluene under reflux (Scheme 2).

An analogous equimolar mixture was also obtained when diastereomers **4a**,**b** or **5a**,**b** were treated in chloroform or methanol under reflux. Different reaction times and temperatures considerably influenced the behavior of the reaction. Higher temperatures led to an increase in the percentage of the minor isomeric (*trans*) intermediate. On the basis of these results, it seems reasonable to conclude that the reaction takes place by means of a preliminary 1,4-addition of methyl 2-benzoylamino-3-dimethylaminopropenoate to 1,2-diaza-1,3-butadienes as a consequence of the nucleophilic attack of the ene-amino carbon in the heterodiene system. This attack produces the zwitterionic hydrazone adduct intermediate and then a mixture of *cis*/*trans* pyrroline derivatives by subsequent intramolecular cyclization (Scheme 1).

The *trans* diastereomer is in thermal equilibrium with the *cis* form via the opened zwitterionic hydrazone intermediate **3** (Scheme 1) or via the formation of an azomethine imine by $Me_2N^-$ elimination (Scheme 2). A more reasonable could be a mechanism in which the dimethylamino group picks up a proton as it leaves. Either the hydrazine N–H or the amide N–H can do this intramolecularly through a five-membered transition state. Alternatively, intermolecular protonation could precede the elimination, allowing loss of $Me_2NH$ instead of $Me_2N^-$.

**SCHEME 3**

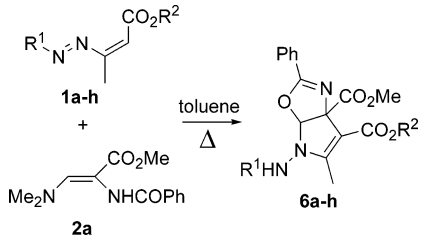



**TABLE 2. Reaction Times and Yields of Oxazolines 6a–h**

| 1 | $R^1$ | $R^2$ | 6 | yield[a] (%) | time[b] (h) |
|---|---|---|---|---|---|
| **1a** | $CO_2Me$ | Me | **6a** | 70 | 20 |
| **1b** | $CO_2Et$ | Et | **6b** | 56 | 26 |
| **1c** | $CO_2t$-Bu | Me | **6c** | 65 | 30 |
| **1d** | $CO_2t$-Bu | Bn | **6d** | 51 | 30 |
| **1e** | $CO_2Bn$ | Me | **6e** | 56 | 27 |
| **1f** | $CO_2Bn$ | Et | **6f** | 54 | 20 |
| **1g** | $CO_2p$-MeO-Bn | Me | **6g** | 61 | 30 |
| **1h** | $CO_2p$-MeO-Bn | Et | **6h** | 66 | 25 |

[a] Yield of pure isolated products. [b] Time of reflux.

The treatment of **4a**,**b** and/or **5a**,**b** in toluene under reflux for 20 h yielded unexpected oxazoline-fused 1-aminopyrrolines **6a**,**c** (Scheme 2). It is likely that, once the 1-aminopyrroline stereoisomers are formed, they undergo isomerization affording the oxazoline-fused 1-aminopyrroline via five-membered ring closure by internal nucleophilic attack of oxygen of the benzoylamino residue with dimethylamine elimination or by attack of the same oxygen atom at the iminium moiety of an azomethine imine intermediate (Scheme 2).

Oxazoline-fused 1-aminopyrrolines **6a**–**h** were directly synthesized in one pot and produced good yields by reaction of 1,2-diaza-1,3-butadienes **1a**–**h** with 3-dimethylaminopropenoate **2a** in toluene under reflux (20–30 h; Scheme 3, Table 2). Contrary to what has been reported in a previous paper,[12] we observed the formation of oxazoline-fused 1-aminopyrrolines instead of aziridine-fused 1-aminopyrrolines. Unfortunately, the coupling constant value for the carbon at approximately 98.1 ppm ($J_{CH}$ = 179.5 Hz) that allowed us to attribute the aziridine system falls in a range that does not unequivocally assign the real structure. Indeed, the X-ray structure of compound **6a** has confirmed the exact oxazoline structure. To the best of our knowledge, this is the first time that these oxazoline-fused 1-aminopyrrolines have been synthesized. The only structure that has an oxazoline ring

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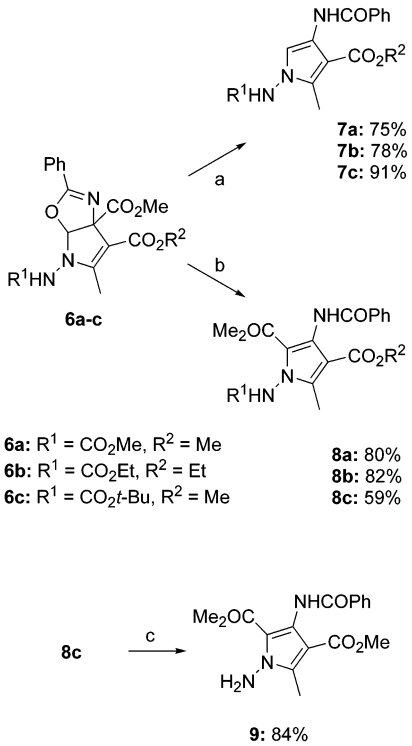
**SCHEME 4**[a]




[a] Reagents and conditions: (a) NaOH(aq) 0.2 M, MeOH, rt,16 h; (b) Montmorillonite KSF, toluene, reflux, 6 h; (c) Amberlyst 15 (H), MeOH, reflux, 15 h.

fused with a five-membered heterocycle reported in the literature is a hydrogenated furan fused with oxazoline.[13]

The substituted oxazolines fused with pyrroline rings are both interesting products and useful intermediates for the preparation of various functionalized 1-aminopyrroles. It was observed that the reactivity of this heterocyclic ring system[14] is strongly dependent on the reaction medium. Two possible pathways to pyrrole derivatives from the relevant oxazolines that result in exclusive opening of the oxazoline ring at the C(1)−O(1) bond were detected. The behavior of these bicyclic oxazolines under basic and acidic conditions is illustrated in Schemes 4 and 5. Oxazoline-fused 1-aminopyrrolines **6a**−**c** were converted into 5-unsubstituted-1-aminopyrrole-3-carboxylic acid derivatives **7a**−**c** in methanol in the presence of an aqueous NaOH (0.2 M) solution at room temperature for 16 h. These products result from the base-induced hydrolysis and decarboxylation of the ester group on the oxazoline ring with consequent aromatization. In the presence of Montmorillonite KSF in toluene under reflux for 6 h, the same compounds **6a**−**c** yielded 1-aminopyrrole derivatives **8a**−**c**. The treatment of the 1-aminopyrrole derivative **8c** with Amberlyst 15 (H) in methanol under reflux for 15 h led to the corresponding 1-aminopyrrole **9** by the hydrolytic cleavage of the *tert*-butoxycarbonyl group (Scheme 4).

The 4-unsubstituted-1-aminopyrrole-2-carboxylic acid derivative **10a** was obtained from oxazoline-fused 1-aminopyrroline **6a** by treatment with trifluoroacetic acid under reflux for 2 h (Scheme 5). In this case, selective hydrolysis, decarboxylation, and transposition of the ester group with a final aromatization process took place. The exact structures of 4-unsubstituted-1-aminopyrrole-2-carboxylic acid derivatives **8a**−**c** were established by X-ray crystallography of compound **8b**. Presumably, the protonation of nitrogen atom of oxazoline ring facilitates the formation of the azomethine imine intermediate and the subsequent 1,2-carboxyl shift to give a more stable intermediate. In the case of the reaction with **6b**, the 1-aminopyrrole derivative **8b** was isolated. The conversion of compound **8b** into the corresponding 4-unsubstituted-1-aminopyrrole-2-carboxylic acid derivative **10b** was achieved after a longer reaction time (an additional 10 h). The presence of different alkyl groups on the carbamoyl moiety remarkably influenced this acidic process. In fact, under the same reaction conditions, the oxazoline-fused 1-aminopyrroline **6c**, containing a *tert*-butyl group instead of methyl or ethyl, was converted into 1-trifluoroacetylaminopyrrole derivative **11** (Scheme 5). No hydrolysis of the ester group in position 4 was observed, even after several additional hours.

5-Unsubstituted 1-aminopyrroles **7a**,**c**−**e** and **13** were also obtained from 1-aminopyrrolines **4a**−**d** and **5a,b** under basic conditions (Scheme 6, Table 3).

Treatment of these substrates in methanol at room temperature with an aqueous 1 M NaOH solution yielded exclusively $H_4$−$H_5$-*trans*-5-(dimethylamino)-4-substituted-1-aminopyrroline-3-carboxylic acid derivatives **12a**−**d**. The stereochemical results were supported by the results of $^1$H NMR analysis. In compound **12b** for $H_5$, a coupling constant of $J_{4,5} = 6.0$ Hz was observed, which is typical for two protons in the anti-position in the pyrroline ring,[15] whereas for $H_4$ only a broad singlet was detected, probably due to the presence of the benzoylamino group. In toluene under reflux, 1-aminopyrroline derivatives **12a**−**d** provided 5-unsubstituted-1-aminopyrrole-3-carboxylic acid derivatives **7a**,**c**−**e** as the main products. These latter compounds arise from the loss of a dimethylamine molecule, with consequent aromatization. Analogous compound **13** was also obtained from 1-aminopyrrolines **4a**,**b** and **5a**,**b** by the same basic treatment under reflux (Scheme 6).

## Conclusion

Our detailed investigation of the reaction between 1,2-diaza-1,3-butadienes and 3-dimethylaminopropenoates demonstrated that a final [3 + 2] cycloaddition reaction takes places by a stepwise pathway via zwitterionic intermediates to produce 1-aminopyrrolines with a high degree of *cis*-stereoselectivity. In toluene under reflux, 1-aminopyrrolines were easily converted into unexpected oxazoline-fused 1-aminopyrrolines. Oxazoline-fused 1-aminopyrrolines were directly obtained by reaction of 1,2-diaza-1,3-butadienes with 3-dimethylaminopropenoates in toluene under reflux. We also developed an efficient protocol for the preparation of variously functionalized

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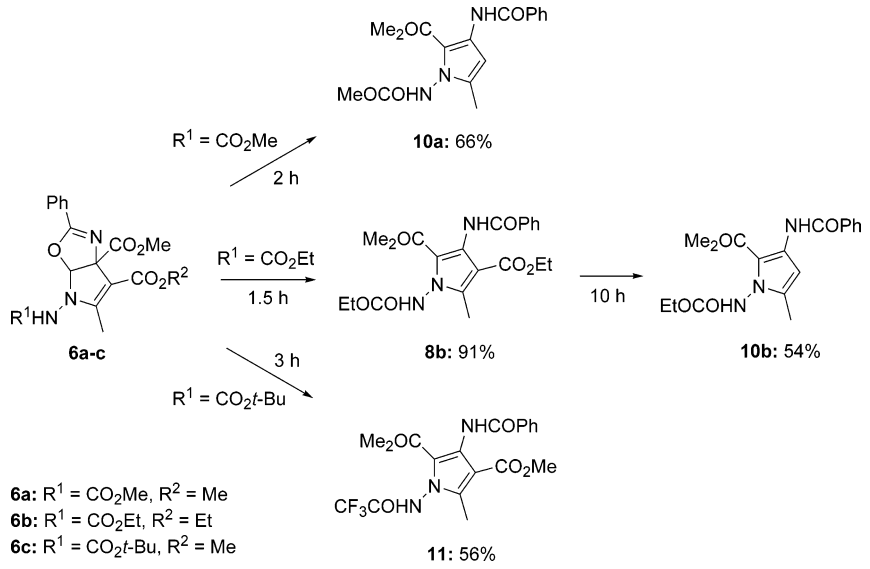
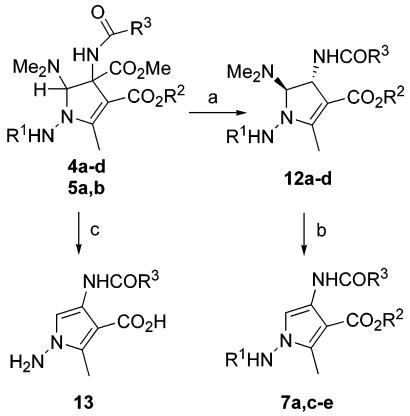
**SCHEME 5**[a]




[a] Reagents and conditions: TFA, reflux.

**SCHEME 6**[a]




[a] Reagents and conditions: (a) NaOH(aq) 1 M, MeOH, rt; (b) toluene, reflux; (c) NaOH(aq) 1 M, MeOH, reflux.

1-aminopyrroles either through the regioselective ring opening of these bicyclic oxazolines or through treatment of 1-aminopyrrolines under basic conditions. Thus, the present work offers a simple and convenient entry to new classes of 1-aminopyrrolines, 1-aminopyrroles, and oxazolines fused with pyrroline rings from easily accessible starting materials. These compounds are of great interest as both products and intermediates in organic, biological, pharmaceutical, analytical, and agricultural chemistry.[16]

## Experimental Section

**General Procedure for the Synthesis of 1-Aminopyrrolines 4a−d and 5a,b from 1a,c,i,j and 2a,b.** 1,2-Diaza-1,3-butadienes **1a**,**c**,**i**,**j** (1.5 mmol) and methyl 2-substituted-3-dimethylaminopropenoates **2a**,**b** (1 mmol) were dissolved in toluene (30 mL) or THF (30 mL) and were stirred under the conditions shown in Table 1 until the disappearance of the methyl 2-substituted-3-dimethylaminopropenoates **2a**,**b** (6−30 h, monitored by TLC). The reaction mixture was concentrated under reduced pressure. Products **4a−d** and **5a**,**b** were isolated by chromatography on silica gel column with cyclohexane−ethyl acetate (70:30 v/v).

**Dimethyl (2*R**,3*S**)-3-benzoylamino-2-(dimethylamino)-1-[(methoxycarbonyl)amino]-5-methyl-2,3-dihydro-1*H*-pyrrole-3,4-dicarboxylate (4a):** mp 95−98 °C; $^1$H NMR (DMSO-$d_6$) $\delta$ 2.15 (s, 3H), 2.30 (s, 6H), 3.52 (s, 3H), 3.57 (s, 3H), 3.67 (s, 3H), 5.22 (brs, 1H), 7.40−7.55 (m, 3H), 7.80−7.85 (m, 2H), 8.46 (brs, 1H), 9.64 (brs, 1H); $^{13}$C NMR (DMSO-$d_6$) $\delta$ 11.9, 40.0, 50.1, 52.0, 52.1, 65.4, 86.2, 90.5, 127.0, 128.2, 131.1, 133.8, 155.5, 160.6, 164.8, 169.5, 170.3; IR 3277, 1739, 1673 cm$^{-1}$; EIMS *m*/*z* 389 (M$^+$ − 45, 10), 360 (8), 343 (12), 330 (10), 313 (100). Anal. Calcd for $C_{20}H_{26}N_4O_7$: C, 55.29; H, 6.03; N, 12.90. Found: 55.41; H, 6.22; N, 13.04.

**Dimethyl (2*R**,3*R**)-3-benzoylamino-2-(dimethylamino)-1-[(methoxycarbonyl)amino]-5-methyl-2,3-dihydro-1*H*-pyrrole-3,4-dicarboxylate (5a):** mp 55−59 °C; $^1$H NMR (DMSO-$d_6$) $\delta$ 2.13 (s, 3H), 2.38 (s, 3H), 2.47 (s, 3H), 3.49 (s, 3H), 3.59 (s, 6H), 5.24 (brs, 1H), 7.40−7.55 (m, 3H), 7.70−7.80 (m, 2H), 7.77 (brs, 1H), 9.56 (brs, 1H); $^{13}$C NMR (DMSO-$d_6$) $\delta$ 11.8, 40.9, 50.3, 52.1, 52.3, 69.4, 87.3, 98.2, 127.0, 128.1, 131.1, 134.9, 155.6, 161.6, 164.3, 164.9, 169.8; IR 3419, 3231, 1749, 1695 cm$^{-1}$; EIMS *m*/*z* 389 (M$^+$ − 45, 35), 360 (15), 347 (3), 320 (22), 313 (100). Anal. Calcd for $C_{20}H_{26}N_4O_7$: C, 55.29; H, 6.03; N, 12.90. Found: 55.11; H, 6.15; N, 13.02.

**General Procedure for the Synthesis of Oxazolines 6a−h from 1a−h and 2a.** 1,2-Diaza-1,3-butadienes **1a**−**h** (1 mmol) and methyl 2-benzoylamino-3-dimethylaminopropenoate **2a** (1 mmol) were dissolved in 30 mL of toluene and refluxed until the disappearance of the reagents (20−30 h, monitored by TLC). The reaction mixture was concentrated under reduced pressure. Products **6a**−**h** were isolated by chromatography on silica gel column with cyclohexane−ethyl acetate (70:30 v/v) and then purified by crystallization from diethyl ether.

**Dimethyl 4-[(methoxycarbonyl)amino]-5-methyl-2-phenyl-4,6a-dihydro-3a*H*-pyrrolo[3,2-*d*][1,3]oxazole-6,6a-dicarboxylate (6a):** mp 106−110 °C; $^1$H NMR (DMSO-$d_6$) $\delta$ 2.07 (s, 3H), 3.60 (s, 3H), 3.66 (s, 6H), 6.17 (s, 1H), 7.45−7.91 (m, 5H), 9.94 (brs, 1H); $^{13}$C NMR (DMSO-$d_6$) $\delta$ 11.3, 50.6, 52.5, 83.8, 98.2, 100.7, 126.0, 128.1, 128.5, 132.1, 156.0, 161.5, 163.3, 163.8, 169.4; IR 3287, 2765, 1704, 1658 cm$^{-1}$; EIMS *m*/*z* 389 (M$^+$, 76), 360 (32), 330 (88), 254 (32), 222 (35), 167 (100).

(16) (a) Sundberg, R. J. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. 4, p 314. (b) Gribble, G. W. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven E. F. V., Eds.; Pergamon-Elsevier Science: Amsterdam, 1996; Vol. 2, Chapter 4.

**TABLE 3. Reaction Times and Yields of 1-Aminopyrrolines 12a−d and 1-Aminopyrroles 7a,c−e and 13**

| 4 (5) | $R^1$ | $R^2$ | $R^3$ | 12 | yield[a] (%) | time (h) | 7 | yield[a] (%) | time (h) | 13 | yield[a] (%) | time (h) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **4a** | $CO_2Me$ | Me | Ph | **12a** | 61 | 12 | **7a** | 93 | 2 | **13** | 63 | 9 |
| **5a** | $CO_2Me$ | Me | Ph | **12a** | 65 | 12 | **7a** | 93 | 2.5 | **13** | 59 | 10 |
| **4b** | $CO_2t$-Bu | Me | Ph | **12b** | 53 | 12 | **7c** | 95 | 4 | **13** | 47 | 6 |
| **5b** | $CO_2t$-Bu | Me | Ph | **12b** | 69 | 12 | **7c** | 95 | 4 | **13** | 56 | 7 |
| **4c** | $CONH_2$ | Me | OBn | **12c** | 58 | 12 | **7d** | 83 | 4 | | | |
| **4d** | $CONH_2$ | Et | OBn | **12d** | 52 | 18 | **7e** | 79 | 4 | | | |

[a] Yield of pure isolated products.

Anal.Calcd for $C_{18}H_{19}N_3O_7$: C, 55.53; H, 4.92; N, 10.79. Found: C, 55.69; H, 5.04; N, 10.94.

**General Procedure for the Synthesis of 1-Aminopyrroles 7a−c from 6a−c.** To appropriate oxazolines **6a**−**c** (1 mmol) in MeOH (5 mL) was added aqueous 0.2 M NaOH (10 mL). The reaction mixture was magnetically stirred at room temperature for 16 h. The crude mixture was neutralized with aqueous 1 M HCl solution and concentrated under reduced pressure. Products **7a**−**c** were isolated by chromatography on silica gel column with cyclohexane−ethyl acetate (50:50 v/v).

**General Procedure for the Synthesis of 1-Aminopyrroles 7a,c−e from 12a−d.** 1-Aminopyrrolines **12a**−**d** (1 mmol) in toluene (15 mL) were allowed under reflux until the disappearance of the starting material (2−4 h, monitored by TLC). The reaction mixture was concentrated under reduced pressure. Products **7a,c**−**e** were isolated by chromatography on silica gel column with cyclohexane−ethyl acetate (50:50 v/v).

**Methyl 4-benzoylamino-1-[(methoxycarbonyl)amino]-2-methyl-1*H*-pyrrole-3-carboxylate (7a):** mp 162−167 °C; $^1$H NMR ($CDCl_3$) $\delta$ 2.36 (s, 3H), 3.74 (s, 3H), 3.87 (s, 3H), 7.45−7.55 (m, 4H), 7.91−7.95 (m, 2H), 8.68 (brs, 1H), 10.53 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 10.8, 51.3, 53.4, 100.5, 111.6, 122.8, 126.9, 128.6, 131.6, 133.7, 135.0, 155.6, 164.2, 167.0; IR 3358, 3149, 1751, 1677 cm$^{-1}$; EIMS *m/z* 331 ($M^+$, 100). Anal. Calcd for $C_{16}H_{17}N_3O_5$: C, 58.04; H, 5.17; N, 12.68. Found: 57.91; H, 5.09; N, 12.63.

**General Procedure for the Synthesis of 1-Aminopyrroles 8a−c from 6a−c.** To oxazolines **6a**−**c** (1 mmol) in toluene (30 mL) was added Montmorillonite KSF (0.53 g), and the mixture was refluxed until the reaction was complete (6 h, monitored by TLC). The reaction mixture was filtered and the solution was concentrated under reduced pressure. Products **8a**−**c** were isolated by chromatography on silica gel column with cyclohexane−ethyl acetate (50:50 v/v).

**Dimethyl 3-benzoylamino-1-[(methoxycarbonyl)amino]-5-methyl-1*H*-pyrrole-2,4-dicarboxylate (8a):** mp 169−172 °C; $^1$H NMR ($CDCl_3$) $\delta$ 2.42 (s, 3H), 3.64 (s, 3H), 3.80 (s, 6H), 7.45−7.58 (m, 3H), 7.92−7.96 (m, 2H), 8.36 (brs, 1H), 9.48 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 10.8, 51.4, 51.6, 53.6, 105.0, 112.3, 127.3, 127.5, 128.6, 132.0, 133.7, 140.8, 156.1, 160.7, 165.0, 165.2; IR 3374, 3175, 1754, 1724, 1670 cm$^{-1}$; EIMS *m/z* 389 ($M^+$, 100). Anal. Calcd for $C_{18}H_{19}N_3O_7$: C, 55.53; H, 4.92; N, 10.79. Found: 55.38; H, 4.81; N, 10.61.

**General Procedure for the Synthesis of 1-Aminopyrrole 9 from 8c.** To 1-aminopyrrole **8c** (1 mmol) in MeOH (30 mL) was added Amberlyst 15(H) (1.55 g), and the mixture was allowed under reflux (15 h). The reaction mixture was filtered off and the solution was concentrated under reduced pressure. Product **9** was isolated by chromatography on silica gel column with cyclohexane−ethyl acetate (50:50 v/v).

**Dimethyl 1-amino-3-benzoylamino-5-methyl-1*H*-pyrrole-2,4-dicarboxylate (9):** mp 151−154 °C; $^1$H NMR ($CDCl_3$) $\delta$ 2.54 (s, 3H), 3.80 (s, 6H), 5.28 (brs, 2H), 7.42−7.56 (m, 3H), 7.91−7.96 (m, 2H), 9.35 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 11.2, 51.3, 51.5, 103.1, 113.5, 127.0, 127.3, 128.6, 131.7, 134.3, 139.6, 162.0, 165.0, 165.4; IR 3343, 3262, 1709, 1668 cm$^{-1}$; EIMS *m/z* 331 ($M^+$, 57), 229 (19), 267 (46), 226 (26), 210 (72), 194 (33), 105 (100). Anal. Calcd for $C_{16}H_{17}N_3O_5$: C, 58.00; H, 5.17; N, 12.68. Found: 57.87; H, 5.03; N, 12.81.

**General Procedure for the Synthesis of 1-Aminopyrroles 8b, 10a,b, and 11 from 6a−c.** The appropriate oxazolines **6a**−**c** (1 mmol) in TFA (3 mL) was refluxed until the disappearance of the reagents (1.5−10 h). The reaction mixture was neutralized with saturated aqueous $NaHCO_3$ solution and concentrated under reduced pressure. Products **8b**, **10a**,**b**, and **11** were isolated by chromatography on silica gel column with cyclohexane−ethyl acetate (50:50 v/v).

**Methyl 3-benzoylamino-1-[(methoxycarbonyl)amino]-5-methyl-1*H*-pyrrole-2-carboxylate (10a):** mp 170−174 °C; $^1$H NMR ($CDCl_3$) $\delta$ 2.21 (s, 3H), 3.74 (s, 3H), 3.79 (s, 3H), 6.89 (s, 1H), 7.45−7.55 (m, 3H), 7.62 (brs, 1H), 7.89−7.94 (m, 2H), 10.22 (brs, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 11.5, 51.2, 53.5, 99.7, 106.7, 127.0, 128.7, 131.8, 133.3, 133.8, 138.4, 156.5, 161.1, 164.7; IR 3333, 3226, 1754, 1663 cm$^{-1}$; EIMS *m/z* 331 ($M^+$, 100). Anal. Calcd for $C_{16}H_{17}N_3O_5$: C, 58.00; H, 5.17; N, 12.68. Found: 58.13; H, 5.28; N, 12.53.

**Dimethyl 3-benzoylamino-5-methyl-1-[(2,2,2-trifluoroacetyl)amino]-1*H*-pyrrole-2,4-dicarboxylate (11):** mp 193−196 °C; $^1$H NMR ($CDCl_3$) $\delta$ 2.36 (s, 3H), 3.36 (s, 3H), 3.77 (s, 3H), 7.50−7.67 (m, 3H), 7.90−8.05 (m, 2H), 9.62 (brs, 1H), 11.18 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 10.0, 51.6, 51.7, 107.4, 110.5, 115.4 ($^1J_{CF}$ = 285.6 Hz), 127.5, 128.3, 128.9, 132.5, 132.9, 140.2, 156.8 ($^2J_{CF}$ = 38.6 Hz), 159.7, 164.5, 165.9; IR 3361, 3195, 3140, 1761, 1727, 1655 cm$^{-1}$; EIMS *m/z* 427 ($M^+$, 27), 105 (100). Anal. gCalcd for $C_{18}H_{16}N_3O_6F_3$: C, 50.59; H, 3.77; N, 9.83. Found: 50.47; H, 3.88; N, 9.72.

**General Procedure for the Synthesis of 1-Aminopyrrolines 12a−d from 4a−d or 5a,b.** To 1-aminopyrrolines **4a**−**d** or **5a**,**b** (1 mmol) in MeOH (5 mL) was added aqueous 1 M NaOH (10 mL). The reaction mixture was stirred at room temperature (12−18 h), neutralized with aqueous 1 M HCl, and concentrated under reduced pressure. Products **12a**−**d** were isolated by chromatography on silica gel column with ethyl acetate−methanol (95:5 v/v).

**Methyl (4*R**,5*R**)-4-benzoylamino-5-(dimethylamino)-1-[(methoxycarbonyl)amino]-2-methyl-4,5-dihydro-1*H*-pyrrole-3-carboxylate (12a):** mp 61−65 °C; $^1$H NMR ($CDCl_3$) $\delta$ 2.26 (s, 3H), 2.38 (s, 6H), 3.63 (s, 3H), 3.70 (s, 3H), 4.25 (brs, 1H), 5.35 (brs, 1H), 6.57 (brs, 1H), 7.38−7.50 (m, 3H), 7.76−7.80 (m 2H), 8.77 (brs, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 12.1, 38.5, 48.2, 50.8, 53.0, 90.3, 98.8, 126.9, 128.3, 131.4, 134.1, 156.7, 162.6, 165.5, 166.6; IR 3547, 3267, 1745, 1660 cm$^{-1}$; EIMS *m/z* 376 ($M^+$, 1), 331 (80), 302 (78), 270 (61), 255 (100). Anal. Calcd for $C_{18}H_{24}N_4O_5$: C, 57.44; H, 6.43; N, 14.88. Found: 57.53; H, 6.29; N, 14.70.

**General Procedure for the Synthesis of 1-Aminopyrroles 13 from 4a,b or 5a,b.** To 1-aminopyrrolines **4a**,**b** or **5a**,**b** (1 mmol) in MeOH (5 mL) was added aqueous 1 M NaOH (10 mL), and the mixture was allowed to stir under reflux (2−4 h). The reaction mixture was neutralized with aqueous 1 M HCl and concentrated under reduced pressure. Product **13** was isolated by chromatography on silica gel column with cyclohexane−ethyl acetate (50:50 v/v).

**1-Amino-4-benzoylamino-2-methyl-1*H*-pyrrole-3-carboxylic acid (13):** mp 195−198 °C; $^1$H NMR (DMSO-$d_6$) $\delta$ 2.40 (s, 3H), 5.88 (brs, 2H), 7.32 (s, 1H), 7.50−7.60 (m, 3H), 7.78−7.90 (m, 2H), 10.59 (s, 1H), 12.39 (brs, 1H); $^{13}$C NMR (DMSO-$d_6$) $\delta$ 10.6, 98.3, 111.6, 121.6, 126.3, 128.7, 131.4, 132.7, 133.7, 161.9, 167.7; IR 3422, 3314, 3233, 1659 cm$^{-1}$; EIMS *m/z* 259

($M^+$, 100). Anal. Calcd for $C_{13}H_{13}N_3O_3$: C, 60.22; H, 5.05; N, 16.21. Found: 60.08; H, 4.89; N, 16.12.

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**Supporting Information Available:** General experimental information, product characterization data, and $^1H$ and $^{13}C$ NMR peak listings for **4b**−**d**, **5b**, **6b**−**h**, **7b**−**e**, **8b**,**c**, **10b**, and **12b**−**d**. X-ray crystallographic data (CIF) and ORTEP drawings of compounds **4b**, **6a**, and **8b**. The authors have deposited atomic coordinates for these structures with the Cambridge Crystallographic Data Centre. This material is available free of charge via the Internet at http://pubs.acs.org.

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