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Reactions of 1,2,5-thiadiazole 1,1-dioxide derivatives with nitrogenated nucleophiles. Part 1—Addition of amines and amides to 3,4-diphenyl-1,2,5-thiadiazole 1,1-dioxide

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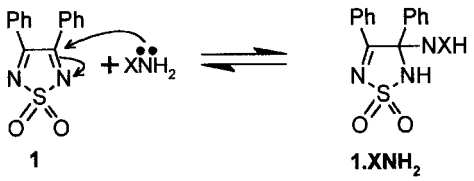
ABSTRACT: The addition reactions of some amides and aromatic amines to a C═N double bond of 3,4-diphenyl-1,2,5-thiadiazole 1,1-dioxide (**1**) were studied in aprotic solvent solutions [*N,N*-dimethylformamide (DMF) and acetonitrile (MeCN)]. Equilibrium constants for the reactions of **1** with acetamide, 2-fluoroacetamide, butyramide, benzamide, aniline and 3-aminopyridine were measured using a previously reported cyclic voltammetric (CV) method. Aliphatic amines gave unstable solutions, probably owing to reactions of anionic species derived from **1**. Other N nucleophiles tested (formamide, succinimide, thioacetamide and cyanamide) yielded different products that have not yet been characterized. DMF, *N,N*-dimethylacetamide (DMA) and *N*-methylacetamide did not react. The addition thiadiazoline produced in the reaction of acetamide with **1** was characterized by IR and ^{1}H and ^{13}C RMN NMR spectroscopy as a prototype compound. For this system, the equilibrium constant could also be measured by a standard UV–VIS method and was found to be in agreement with the value obtained by CV. The reaction of **1** with urea produced a bicyclic product, identified as 3a,6a-diphenyltetrahydroimidazo[4,5-*c*]-1,2,5-thiadiazol-5-one 2,2-dioxide. Copyright © 2003 John Wiley & Sons, Ltd.

KEYWORDS: 1,2,5-thiadiazoline derivatives; nucleophilic addition; aromatic amines; amides; 1,2,5-thiadiazole derivatives

INTRODUCTION

We report here a study of the reactions of several nitrogen nucleophiles with 3,4-diphenyl-1,2,5-thiadiazole 1,1-dioxide (**1**), mainly in acetonitrile (MeCN) or *N,N*-dimethylformamide (DMF) solutions.

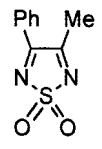
For a group of nucleophiles [acetamide (ACM), 2-fluoroacetamide, butyramide, benzamide, aniline and 3-aminopyridine), the equilibrium reaction (1) (Scheme 1), was experimentally observed:



(1)

Scheme 1

Reaction (1) represents the equilibrium addition reaction of the nucleophile to only one of the two identical C═N double bonds of **1**. This is the behavior that we have previously observed in the reaction of alcohols (ROH) and thiols (RSH), i.e. nucleophiles with **1** or with 3-methyl-4-phenyl-1,2,5-thiadiazole 1,1-dioxide (**2**, Scheme 2):[1]



Scheme 2

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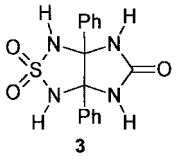
The nucleophilic attack occurred at only one of any of the identical electron-deficient heterocyclic carbon atoms of **1**, or at the methyl-substituted heterocyclic carbon atom of **2**. A rationale for the practical lack of diaddition has been given,[1d] based on the structure of **1**[2a] and its thiadiazoline derivatives.[2b]

The initial reaction between 1 and aliphatic amines, as followed by spectroscopy and cyclic voltammetry (CV), was also an addition to a C═N double bond of **1**. However, further reactions, that were not studied, took place in that more basic medium. The formation of the anion of **2** and its dimerization and tautomerization reactions have been reported in the reaction of **2** with sterically hindered aliphatic amines under similar conditions.[3]

Other nucleophiles (formamide, succinimide, thioacetamide and cyanamide) yielded different products which have not yet been characterized. DMF, *N,N*-dimethylacetamide (DMA) and *N*-methylacetamide did not react, but urea, perhaps surprisingly, added almost quantitatively to both C═N double bonds of **1**, producing the interesting bicyclic compound 6a-diphenyltetrahydroimidazo[4,5-*c*]-1,2,5-thiadiazol-5-one 2,2-dioxide (**3**, Scheme 3). This new compound is closely related to biotin and combines moieties that, independently, are important structural parts in several molecules that have found many different applications (e.g. 1,2,5-thiadiazolidine 1,1-dioxides,[4–7] 2-imidazolone[8–12]).



3

Scheme 3

The equilibrium constants for the addition reactions were measured using CV by our reported method.[1b] The use of the classical spectrophotometric method[13] was restricted because almost all nucleophiles, and the DMF solvent absorb UV radiation in the spectral zone of interest. The **1**–ACM–MeCN system could be probed by both methods, giving equilibrium constant values in good agreement.

EXPERIMENTAL

Compound **1** was synthesized, purified and characterized according to Wright.[14] Standard methods[15–17] were used for the purification of commercial solvents, amides and amines. The solvents were dried on molecular sieves and stored under a dry nitrogen atmosphere. Their water content, as measured by Karl Fischer titration, was <50 ppm.

UV spectral measurements were performed with a Cary 3 spectrophotometer equipped with thermostated cell holders. Teflon-stoppered quartz cells of 1 cm optical pathlength were used. Molar absorptivities (ε) reported are accurate to $\pm 2.5\%$. The experimental measurement procedures were similar to those used previously for alcohol nucleophiles.[1d]

^{1}H and ^{13}C NMR spectra were recorded with a Bruker 200 MHz instrument and IR spectra with a Shimadzu IR-435 spectrophotometer.

CV experiments were performed in a conventional undivided gas-tight glass cell with a dry nitrogen gas inlet and outlet. The working electrode was a 3 mm diameter vitreous carbon disk encapsulated in Teflon, the counter-electrode was a 2 cm^2 Pt foil and an Ag^+ (0.1 M, MeCN)/Ag reference electrode (to which all potentials reported are referred) was used. The supporting electrolyte was 0.1 M $NaClO_4$ in the aprotic solvent used (MeCN or DMF; see Results and Discussion). An LYP-M2 potentiostat, a three-module LYP sweep generator and a Houston Omnigraphic 2000 pen recorder or, for sweep rates >0.5 V s^{-1}, a Leader LBO-5825 oscilloscope was employed.

Solutions preparation, CV experiments and other manipulations were made in a glove-box under a dry nitrogen atmosphere.

Synthesis and characterization of 1·XNH$_2$ thiadiazolines

The title compounds were obtained in solution by adding XNH_2 nucleophile to a solution of **1** in an aprotic solvent. A sample of reasonably pure solid **1**·ACM could be obtained by the following procedure: **1** (0.133 g, 0.492 mmol) and ACM (0.812 g, 13.8 mmol) were mixed with 1 ml of dry DMF or DMSO at room temperature (the reaction was slower in MeCN). In 1 day a completely homogeneous solution was obtained. The reaction was monitored by TLC and CV and was terminated (after a lapse of ca 1 month) when only a small, residual CV signal of **1** remained unchanged over time. The addition of ca 6 ml of water caused the formation of a white precipitate, while the very soluble ACM was kept in solution. The solid was filtered, washed with water and vacuum dried at room temperature (crude yield 90%). TLC analysis showed traces of **1**. Attempts to purify the solid by recrystallization were unsuccessful because of its decomposition to the reagents, as revealed by TLC.

IR spectrum (KBr) of **1**·ACM: 3250 (N—H, two bands), 3050, 3025 (C_{Ar}–H), 1665 (C═O), 1595 (Ph), 1565 (C═N), 1310 and 1180 cm^{-1} (SO_2).

NMR (^{1}H and ^{13}C) spectra of **1**·ACM were obtained by dissolving **1** (0.135 g, 0.499 mmol) and ACM (0.030 g, 0.510 mmol) in 1 ml of DMSO-d_6. Spectra were recorded at different reaction times until the system reached equilibrium. A small proportion of unreacted ACM was observed in the ^{1}H NMR spectrum.

^{1}H NMR (δ, TMS): 9.48 (singlet, 1H, heterocyclic N—

H), 8.45 (singlet, 1H, CH_3—CO—N*H*—), 8.05–7.30 (multiplet, 10H, Ph) and 1.81 (singlet, 3H, C*H*$_3$—CO—NH—). The signals of residual ACM observed were 6.70 (singlet, N—H) and 2.03 (singlet, CH_3—). ^{13}C NMR (δ, TMS): 176.6 (C═N), 172.0 (CH_3—*C*O—NH—), 139.7–125.3 (Ph, 13 signals), 93.8 ($C_{heteroc}$—N), and 22.3 (CH_3—).

Synthesis and characterization of 3

Compound **1** (0.155 g, 0.574 mmol) and urea (0.110 g, 1.831 mmol) were dissolved in 1 ml of DMF or DMSO. The reaction was monitored by TLC until the disappearance of the TLC spot corresponding to **1**. Compound **3** was precipitated from the solution by water addition and washed as indicated for **1**·ACM. The solid was chromatographically pure **3** (yield: 90%).

3: mp. 310–312 °C (decomp.). IR (KBr): 3380 (N—H) and 3320 (N—H), 3030 (C_{Ar}—H), 1690 (C═O), 1440, 1410, 1365, 1320 (SO_2), 1220, 1180 cm^{-1} (SO_2). ^{1}H NMR (δ, TMS) in DMSO-d_6 solution: 8.50 (singlet, 2H, N—H of 2-imidazolidone moiety), 7.97 (singlet, 2H, N—H of 1,2,5 thiadiazolidine moiety) and 7.76–7.06 (multiplet, 10H, 5 signals, Ph). ^{13}C NMR (same solution) (δ, TMS): 159.6 (C═O, multiplet, four signals), 137.5–127.2 (Ph), and 83.8 (Ph—*C*—*C*—Ph).

Anal. Calcd for $C_{15}N_{14}N_4O_3S$: C, 54.54; H, 4.24; N, 16.97; S, 9.70. Found: C, 54.60; H, 4.17; N, 18.18; S, 10.01%.

RESULTS AND DISCUSSION

N-Substituted amides

As already mentioned, *N,N*-disubstituted and *N*-monosubstituted amides did not react with **1**. Solutions of **1** in DMF or DMA produced cyclic voltammograms corresponding to the successive and reversible transfer of two electrons to **1** [Figure 1(a): lc/la couple: **1/1**$^{-\cdot}$, at ca − 0.8 V vs RE: Ag^+ (0.1 M, MeCN)/Ag; llc/lla couple: **1**$^{-\cdot}$/**1**$^{2-}$, at ca − 1.4 V vs RE: Ag^+ (0.1 M, MeCN)/Ag], that remained unchanged over a lapse of several months. Since low concentrations of residual water cause the appearance of an irreversible cathodic peak (IVc at ca − 2.0 V, assigned to the thiadiazoline **1**·H_2O, formed by the nucleophilic addition of water to **1**[1d]), the constancy of the voltammetric response indicated that the concentration of residual water (50 ppm or less; see Experimental) was low enough to prevent **1**·H_2O formation.

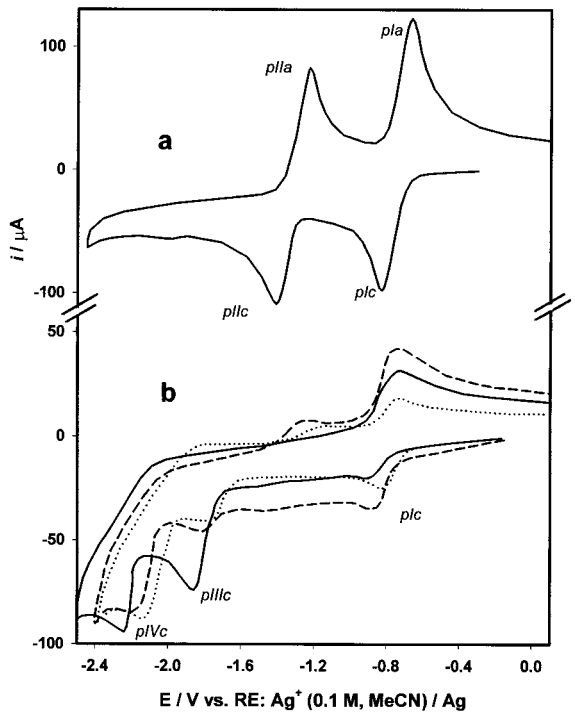


Figure 1. Cyclic voltammograms of **1** with and without added amide nucleophiles. Solvent, DMF; supporting electrolyte, 0.5 M $NaClO_4$; sweep rate, 0.2 V s^{-1}; vitreous carbon working electrode. (a) Initial solution of [**1**]: 4.1 mM; (b) equilibrium CVs of initial solution in the presence of (solid lines) 3.12 M acetamide, (dashed lines) 2.80 M benzamide and (dotted lines) 2.73 M fluoroacetamide

Reaction of 1 with *N*-unsubstituted amides or aromatic amines

Voltammetric experiments. The addition of ACM, butyramide, benzamide, 2-fluoroacetamide, aniline or 3-aminopyridine to a solution of **1** in MeCN or DMF caused a sequence of changes in the initial CV of the solution [Fig. 1(a)]. The rate of change increased with increase in the concentration of nucleophile added and a final equilibrium CV was obtained in all cases. The observed sequence was as follows: the current intensity of both cathodic peaks (Ic and IIc) decreased simultaneously. Peak IIc disappeared from the final equilibrium CV for all experimental nucleophile concentrations used, but the current intensity of peak Ic decreased and reached a final equilibrium intensity that was inversely proportional to the nucleophile concentration. Two cathodic peaks (IIIc and IVc) at more negative potentials appeared and increased in current successively: peak IVc, when peak IIc started to decrease, and peak IIIc, after the disappearance of peak IIc.

Figure 1(b) shows the equilibrium CV obtained after the addition of ACM, benzamide or 2-fluoroacetamide to a solution of **1** in DMF.

The changes described above are similar to those observed for the addition reaction of ROH nucleophiles

to **1** or **2**. Thus, the voltammetric electroreduction mechanism derived from the analysis of those changes[1b–d] should also apply for this case.

The mechanism indicates that, in the equilibrium CV, equal quantities of **1** and of the addition thiadiazoline $\mathbf{1}\cdot XNH_2$ are consumed at peak Ic by the following reactions:

$$\text{E1} \quad \mathbf{1} + e^- \rightleftharpoons \mathbf{1}^{-\cdot}$$

$$\text{C1} \quad \mathbf{1}^{-\cdot} + \mathbf{1}\cdot XNH_2 \rightleftharpoons \mathbf{1}H^{\cdot} + \mathbf{1}\cdot X\ddot{N}H^-$$

$$\text{E2} \quad \mathbf{1}H^{\cdot} + e^- \rightleftharpoons \mathbf{1}H\,{:}^-$$

Thus, peak IIc, associated with the electroreduction of $\mathbf{1}^{-\cdot}$ to $\mathbf{1}^{2-}$, is no longer present (under the experimental conditions chosen; see below) because $\mathbf{1}^{-\cdot}$ is completely consumed by reaction C1. Cathodic peak IIIc is associated with the electroreduction of the addition thiadiazoline that has not been consumed at peak Ic by reaction C1:

$$\text{E3} \quad \mathbf{1}\cdot XNH_2 + e^- \rightleftharpoons \mathbf{1}\cdot XNH_2{}^{-\cdot}$$

$$\text{C2} \quad \mathbf{1}\cdot XNH_2{}^{-\cdot} \rightleftharpoons \mathbf{1}H^{\cdot} + XNH^-$$

followed immediately by the electroreduction of $\mathbf{1}H^{\cdot}$ to $\mathbf{1}H^-$ (E2). The anions $\mathbf{1}H^-$ and $\mathbf{1}\cdot XNH^-$ are further reduced at peak IVc.

In the presence of a sufficient excess of the nucleophile (i.e. $[XNH_2]_{equilibrium} \approx [XNH_2]_0$), and if peak IIc is absent from the equilibrium CV (i.e. peak Ic corresponds to the E1C1E2 mechanism above), a function [Eqn. (2)[1b]] of the current intensity of peaks Ic and IIIc in the equilibrium CV and the voltage sweep rate (v) can be used to estimate the equilibrium constant, $K_1{}^{XNH_2}$, of the addition reaction.

$$K_1{}^{XNH_2} \times [XNH_2]_0 = \frac{2 \times \left[\frac{i(\text{IIIc})}{\nu^{1/2}} + \frac{i(\text{Ic})}{2\times\nu^{1/2}}\right]}{\frac{i(\text{Ic})}{\nu^{1/2}}} \qquad (2)$$

Equation (2) implies that the current functions, $i_p/v^{1/2} \times C$, for all species have similar values. This is reasonable for the closely related species involved. It is also necessary, for the validity of Eqn. (2), that peaks Ic and IIIc are diffusion controlled. The linear dependence of the current intensities of peaks Ic and IIIc on $v^{1/2}$ was experimentally verified for all **1**-unsubstituted amide–solvent systems in the 0.05–0.3 V s^{-1} sweep rate range [Fig. 2(a) and (b)].

For aromatic amine nucleophiles, the i_p vs $v^{1/2}$ plots were not linear at sweep rates below ca 0.1 V s^{-1}. It was also observed that the equilibrium CV was attained much faster (of the order of minutes) for aromatic amines relative to aliphatic or aromatic amides or alcohols (of the order of hours or days). These faster equilibria required faster voltammetric sweep rates (v >0.1 V s^{-1}, in the present case) in order to measure the unperturbed (equilibrium) concentrations by means of the voltammetric peak currents. Consequently, the equilibrium

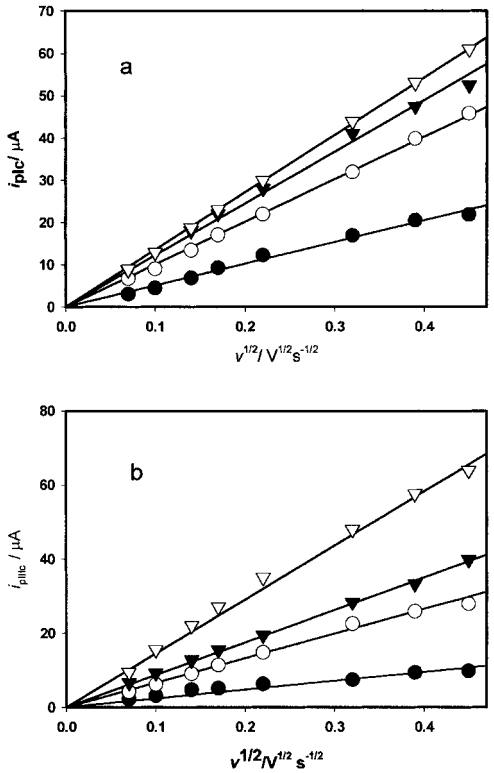


Figure 2. Voltammetric peak intensities as a function of $v^{1/2}$ for peaks (a) Ic and (b) IIIc in the equilibrium cyclic voltammogram of a 4.10 mM solution of **1** in DMF, in the presence different butyramide concentrations. Supporting electrolyte: 0.5 M $NaClO_4$. Butyramide concentration: (○) 0.787; (●) 1.225; (▽) 1.750; (▼) 2.493 M. Straight lines are least-squares adjustments. Correlation coeficients obtained are 0.993 or better

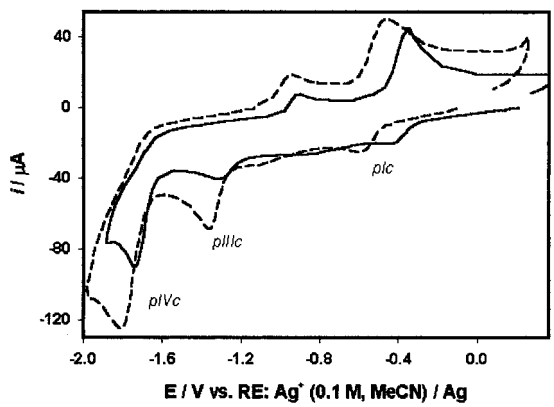


Figure 3. Equilibrium cyclic voltammograms of **1** in the presence of aromatic amine nucleophiles. Supporting electrolyte, 0.5 M $NaClO_4$ in DMF; sweep rate, 0.2 V s^{-1}; vitreous carbon working electrode; [**1**], 4.1 mM. (solid line) 2.40 M 3-aminopyridine; (dashed line) 1.61 M aniline

Table 1. Equilibrium constants for reaction (**1**): addition of amides and aromatic amines to **1**[a]

Solvent	Nucleophile (XNH_2)	Nucleophile concentration range/M	$K_1^{XNH_2}/M^{-1}$
MeCN	ACM (CV method)	2.3–4.0	0.55 ± 0.04
	ACM (U.V. method)	0.2–2.0	0.6 ± 0.1
DMF	ACM	1.2–3.1	2.59 ± 0.06
DMF	fluoracetamide	1.8–3.1	0.70 ± 0.02
DMF	butyramide	0.8–2.4	1.92 ± 0.05
DMF	benzamide	1.5–2.8	0.62 ± 0.04
MeCN	aniline	0.5–2.0	0.52 ± 0.03
DMF	aniline	2.0–4.0	3.8 ± 0.1
DMF	3-aminopyridine	0.5–3.0	2.3 ± 0.1

[a] Cyclic voltammetric method: [**1**], ca 4 mM; reported uncertainties are standard deviations for four independent measurements in the nucleophile concentration range indicated. UV method: [**1**], ca 0.2 mM; reported uncertainty is the standard deviation for seven measurements in the concentration range indicated.

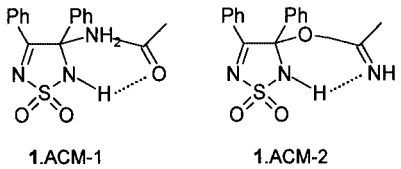
constant values for the addition of aromatic amines were calculated using the peak current data obtained at sweep rates between 0.1 and 20 V s^{-1}. A linear dependence of i_p vs $v^{1/2}$ was found experimentally for Ic and IIIc peaks in that range. Typical experimental equilibrium CVs for solutions of **1** in DMF containing 3-aminopyridine or aniline are shown in Fig. 3.

Calculated equilibrium constant values for the addition reaction of amides and aromatic amines to **1** are given in Table 1. The spectrophotometric results (see below) for the **1**–ACM–MeCN system are also included.

Spectrophotometric measurements. The addition of ACM to solutions of **1** in MeCN caused a gradual decrease in intensity of the 328 nm band of **1**. Simultaneously, a growing band was observed at 275 nm, which was assigned to the addition product **1**·ACM, appeared and grew. An isosbestic point was found at 290 nm. Even in this favorable case, the ACM cut-off made measurements below 245 nm impossible and lowered the accuracy of the measurements of the **1**·ACM absorption band at 275 nm. The absorption intensity of the UV bands in the final equilibrium spectra were recorded for several initial concentrations of ACM and fitted to a Benessi–Hildebrand-type equation to calculate K_1^{ACM} (BH) = 0.6 ± 0.1 M^{-1}, and the molar absorptivity of **1**·ACM, $\varepsilon_{1.ACM}^{275} = (1.4 \pm 0.1) = \times 10^4$ M^{-1} cm^{-1}. We consider the spectrophotometrically calculated equilibrium constant to be in reasonable agreement with the value derived from CV experiments.

Structure of the amide addition compounds

The thiadiazoline-type structure of the **1**·ACM compound is supported by all spectroscopic evidence, such as the ^{13}C NMR resonances at 176.6 and 93.8 ppm (C-sp^3), the UV absorption band at 275 nm of **1**·ACM and the IR spectrum of the solid (NH bands at 3250, C═O band at 1665 and C═N band at 1565 cm^{-1}). However, these spectroscopic measurements cannot distinguish between



1.ACM-1 **1**.ACM-2

Scheme 4

the two possible structures of the addition compounds, illustrated by **1**·ACM-1 or **1**·ACM-2, in Scheme 4.

X-ray diffraction analysis could not be used to settle the question because, as already mentioned (see Experimental), the compound could not be obtained in monocrystalline form.

To the best of our knowledge, no examples of the nucleophilic properties of amides in neutral aprotic media have been reported. In our experiments, the addition reaction might be favored by an increase in the partial charge of the heterocyclic carbon atom, due to the presence of the group. Also, one should consider the stabilization of the product by the closure of a six-atom ring through an H-bond with the N atom of the heterocycle (Scheme 4).

We favor the structure **1**·ACM-1 (Scheme 4). Despite the known larger electron density of the oxygen atom relative to the nitrogen atom in amides, our choice is supported by the lack of reactivity of *N*-substituted amides, which possess an unhindered and similarly reactive oxygen atom as the unsubstituted amides. Furthermore, the IR absorption at 1665 cm^{-1} is more likely a carbonyl band than a —C═NH band, since it is very strong and its frequency is close to the ACM carbonyl absorption (1681 cm^{-1}). Additional support for this choice is provided by semi-empirical (PM3) total energy calculations for geometrically optimized configurations: the calculated energies were −4133 and −4112 a.u. for **1**·ACM-1 and **1**·ACM-2, respectively.

The equilibrium constant for reaction (**1**) with amides becomes lower (compared with $K_1^{XNH_2}$) for fluoroacetamide, because of the effect of the electron-withdrawing

group, and for butyramide or benzamide, because of increasing steric hindrance.

As found in the case of the addition reaction of EtOH to **1**,[1d] the equilibrium constant values correlate with the empirical bond acceptor β parameter of the solvent.

Reaction of 1 with urea

When the reaction between **1** and urea (molar ratio [urea]/[**1**] $\approx$ 30; see Experimental) in DMF solvent was followed by CV, the initial CV scan of **1** evolved to a final CV that did not present cathodic peaks. This is indirect evidence of the formation of a thiadiazolidine (addition to both C=N double bonds of **1**), since they are not voltammetrically reducible.

Further evidence in the same direction was obtained when the reaction was monitored by UV spectrophotometry: the time evolution of the UV spectrum of a solution of **1** (0.2 mM) and urea (2 mM) in a 1:3 DMF–MeCN solvent mixture was measured. The mixed solvent was chosen as a compromise: the reaction was very slow in MeCN, and the cutoff of the DMF–urea system hindered the observance of the spectrum at low wavelengths. The spectrum showed initially only the absorption band of **1**, at 325 nm. This absorption decreased over time and finally vanished, indicating the complete consumption of **1**. A much weaker absorption band at 266 nm developed during the experiment; its final intensity was $\sim$1/10 of the initial absorption band of **1** at 325 nm. Thiadiazoline 1,1-dioxides absorb typically at ca 260 nm, but their molar absorptivity is about 50% greater than that of the corresponding thiadiazoles, while the UV band of the thiadiazolidines is also near 260 nm, but very weak [λ_{max} (nm), ε (M^{-1} cm^{-1}) in MeCN solvent are[1a] for **1** 328, 8860, for 3,4-diphenyl-1,2,5-thiadiazoline 1,1-dioxide 260, 15 850 and for 3,4-diphenyl-1,2,5-thiadiazolidine 1,1-dioxide 260, 350].

IR, ^{13}C NMR and ^{1}H NMR spectroscopy and elemental analysis of the reaction product indicate that its structure corresponds to the bicyclic thiadiazolidine **3**. The synthesis of a series of similar compounds and their structural characterization will be described in Part 2.

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REFERENCES

1. Mirífico MV, Vasini EJ, Sicre JE. *J. Phys. Org. Chem.* 1993; **6**: 341–346; (b) Caram JA, Mirífico MV, Vasini EJ. *Electrochim. Acta* 1994; **39**: 939–945; (c) Caram JA, Mirífico MV, Aimone SL, Vasini EJ. *Can. J. Chem.* 1996; **74**: 1564–1571; (d) Aimone SL, Caram JA, Mirífico MV, Vasini EJ. *J. Phys. Org. Chem.* 2000; **13**: 272–282.
2. Castellano EE, Piro OE, Caram JA, Mirífico MV, Aimone SL, Vasini EJ, Glossman MD. *J. Phys. Org. Chem.* 1998; **11**: 489–494; (b) Castellano EE, Piro OE, Caram JA, Aimone SL, Mirífico MV, Vasini EJ, Marquez-Lucero A, Glossman-Mitnik MD. *J. Mol. Struct.* 2001; **597**: 163–175.
3. Aimone SL, Caram JA, Mirífico MV, Vasini EJ. *J. Phys. Org. Chem.* 2001; **14**: 217–223.
4. Campbell SF, Roberts DA, Stubbs JK. Eur. Pat. 94 766, 1983; 4*Chem. Abstr.* 1984; **100**: 121105.
5. Arya VP, Nagarajan K, Shenoy SJ. *Indian J. Chem., Sect. B.* 1982; **21**: 941–945.
6. Nagarajan K, Arya VP, George T, Nair MD, Sudarsanam V, Ray DK, Shrivastava VB. *Indian J. Chem., Sect. B.* 1984; **23**: 342–246.
7. Preiss M, Metzger KG. Ger. Pat. 2 658 906, 1978; 7*Chem. Abstr.* 1978; **89**: 146919.
8. Parmee ER, Naylor EM, Perkins L, Colandrea VJ, Ok HO, Candelore MR, Cascieri MA, Deng L, Feeney WP, Forrest MJ, Hom GJ, Euan MacIntyre J, Miller RR, Steams RA, Strader CD, Tota L, Wyvratt MJ, Fisher MH, Weber AE. *Bioorg. Med. Chem. Lett.* 1999; **9**: 749–754.
9. Naylor EM, Parmee ER, Colandrea VJ, Perkins L, Brockunier L, Candelore MR, Cascieri MA, Colwell Jr. MF, Deng L, Feeney WP, Forrest MJ, Euan MacIntyre GJ, Strader CD, Tota L, Pei-Ran Wang, Wyvratt MJ, Fisher MH, Weber AE. *Bioorg. Med. Chem. Lett.* 1999; **9**: 755–758.
10. Reitz DB, Garland DJ, Olins GM, Markos CS, Greak CJ, Litschgi JW, McKimnis BR. *Bioorg. Med. Chem. Lett.* 1994; **4**: 111–114.
11. Reitz DB, Garland DJ, Norton MB, Collins JT, Reinhard EJ, Manning RE, Olins GM, Chen ST, Palomo MA, McMahon EG, Koecher KF. *Bioorg. Med. Chem. Lett.* 1999; **3**: 1055–1060.
12. Carling RW, Moore KW, Meyes CR, Jones EA, Bonner K, Emms F, Marwood R, Patel S, Fletcher EA, Beer M, Cchal B, Pike A, Leeson PD. *J. Med. Chem.* 1999; **42**: 2706–2715.
13. Muliken RS, Person WB. *Molecular Complexes*. Wiley–Interscience: New York, 1969.
14. Wright JB. *J. Org. Chem.* 1964; **29**: 1905.
15. Riddick JA, Bunger WB. In *Techniques of Chemistry*, vol. **II**, Weissberger A (ed). Wiley–Interscience: New York, 1970; 201.
16. Perrin DD, Armarego WLF. *Purification of Laboratory Chemicals*. Pergamon Press: Oxford, 1988.
17. Coetzee JF. *Recommended Methods for Purification of Solvents and Tests for Impurities*. Pergamon Press: Oxford, 1982.