JOC*Article*

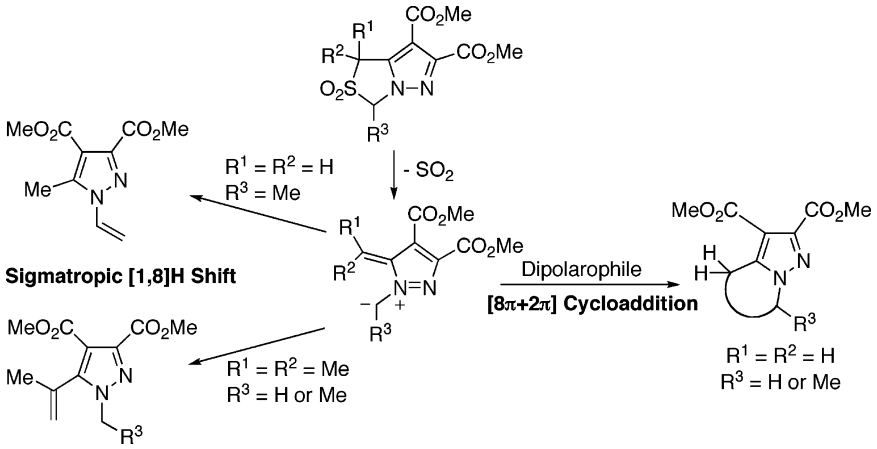
Chemistry of Diazafulvenium Methides in the Synthesis of Functionalized Pyrazoles

Teresa M. V. D. Pinho e Melo,*[,†] Cláudio M. Nunes,[†] Maria I. L. Soares,[†] José A. Paixão,[‡] Ana Matos Beja,[‡] and Manuela Ramos Silva[‡]

Department of Chemistry, University of Coimbra, 3004-535 Coimbra, Portugal, and Department of Physics, University of Coimbra, 3004-516 Coimbra, Portugal

tmelo@ci.uc.pt

Received February 7, 2007



The chemistry of diazafulvenium methides generated by the thermal extrusion of sulfur dioxide from 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*] [1,3]thiazoles is described. The diazafulvenium methides unsubstituted at C-7 participate in [$8\pi + 2\pi$] cycloadditions giving pyrazolo-annulated heterocycles resulting from the addition across the 1,7-position. 1-Methyl-diazafulvenium methides and 7,7-dimethyl-diazafulvenium methides undergo intramolecular sigmatropic [1,8]H shifts giving vinyl-1*H*-pyrazoles.

Introduction

The study of pericyclic reactions of extended dipoles (with more than 4π electrons) is one of our current research interests.[1−4] Storr and co-workers have shown that 2,2-dioxo-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazoles and 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazoles are masked aza- and diazafulvenium methides (**1** and **2**). These 8π 1,7-dipoles can be considered "higher-order" azomethine ylides and azomethine imines, respectively. In fact, the authors described the thermal extrusion of sulfur dioxide from 2,2-dioxo-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]-thiazoles under flash vacuum pyrolysis (FVP) to give transient 1-azafulvenium methide systems (**1**) that can be trapped in pericyclic reactions. The dipolar systems **1a**−**1c** undergo sigmatropic [1,8]H shifts giving vinylpyrroles, and the acyl derivatives **1d** electrocyclize to give pyrrolo[1,2-*c*][1,3]oxazines.[5] On the other hand, the SO_2 extrusion of the studied 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole led to 1,2-diazafulvenium methide **2**, which could be intercepted in [$8\pi + 2\pi$] cycloaddition with silylated acetylenes giving adducts resulting from the addition across the 1,7-position (Scheme 1).[5]

[†] Department of Chemistry.
[‡] Department of Physics.

(1) (a) Pinho e Melo, T. M. V. D.; Soares, M. I. L.; Rocha Gonsalves, A. M. d'A.; McNab, H. *Tetrahedron Lett.* **2004**, *45*, 3889−3893. (b) Pinho e Melo, T. M. V. D.; Soares, Maria I. L.; Rocha Gonsalves, A. M. d'A.; Paixão, J. A.; Matos Beja, A.; Ramos Silva, M. *J. Org. Chem.* **2005**, *70*, 6629−6638.

(2) Pinho e Melo, T. M. V. D.; Soares, M. I. L.; Nunes, C. M. *Tetrahedron* **2007**, *63*, 1833−1841.

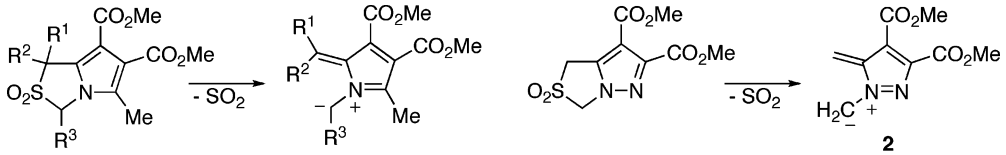
(3) Pinho e Melo, T. M. V. D.; Soares, M. I. L.; Rocha Gonsalves, A. M. d'A. *Tetrahedron Lett.* **2006**, *47*, 791−794.

(4) Pinho e Melo, T. M. V. D. *Eur. J. Org. Chem.* **2006**, 2873−2888.

(5) (a) Sutcliffe, O. B.; Storr, R. C.; Gilchrist, T. L.; Rafferty, P.; Crew, A. P. A. *Chem. Commun.* **2000**, 675−676. (b) Sutcliffe, O. B.; Storr, R. C.; Gilchrist, T. L.; Rafferty, P. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1795−1806.

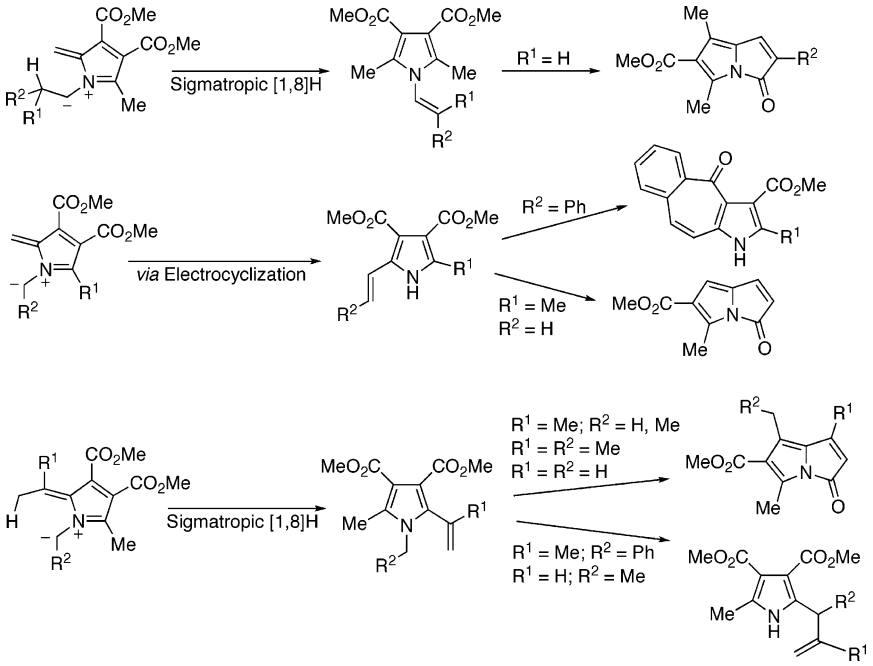
10.1021/jo070265x CCC: $37.00
Published on Web 05/10/2007

SCHEME 1



1a $R^1 = R^2 = H$; $R^3 = CH_3$
1b $R^1 = H$; $R^2 = CH_3$; $R^3 = H$
1c $R^1 = R^2 = CH_3$; $R^3 = H$
1d $R^1 = H$; $R^2 = COR$; $R^3 = H$

SCHEME 2



Our own contribution allowed for the definition of a reactivity pattern of azafulvenium methides (Scheme 2).[1,2] The intramolecular trapping of the transient 8π 1,7-dipoles derived from 1-unsubstitued-2,2-dioxo-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazoles in pericyclic reactions, namely, sigmatropic [1,8]H shifts and 1,7-electrocyclization, affords *N*-vinylpyrroles and *C*-vinylpyrroles, which under flash vacuum pyrolysis conditions are converted into 5-oxo-5*H*-pyrrolizines or 4-oxo-1,4-dihydro-1-aza-benzo-[*f*]azulenes. 7-Methyl- and 7,7-dimethyl-azafulvenium methides undergo sigmatropic [1,8]H shifts to give *C*-vinylpyrroles even in cases where an alternative pericyclic reaction could in principle occur. Azafulvenium methides generated from C-3 unsubstituted 1-methyl-2,2-dioxo-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]-thiazole can only undergo the same type of [1,8]H shift to the corresponding *C*-vinylpyrrole. However, from the reaction of the 1,3-dimethyl-2,2-dioxo-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole derivative the corresponding azafulvenium methide undergoes the two possible sigmatropic [1,8]H shifts. Rearrangements of these *C*-vinylpyrroles afford 5-oxo-5*H*-pyrrolizines or functionalized *C*-allyl-1*H*-pyrroles.

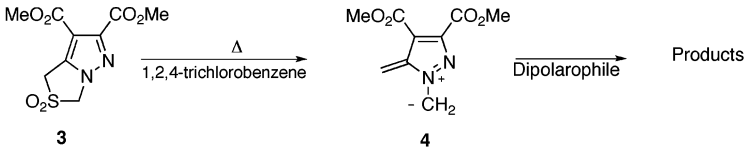
The chemistry of 1,2-diazafulvenium methides has also attracted our attention, and our preliminary results have been described.[3] In this paper, we describe full details of an extensive study on the generation and reactivity of 1,2-diazafulvenium methides.

Results and Discussion

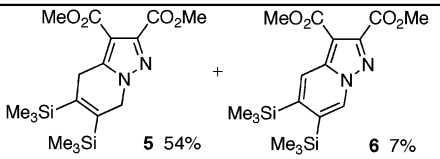
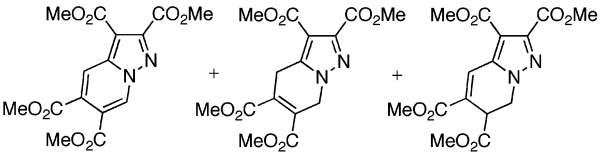
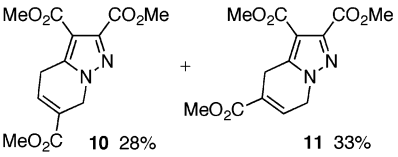
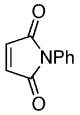
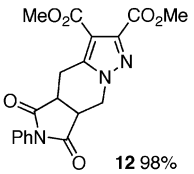
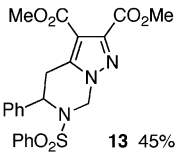
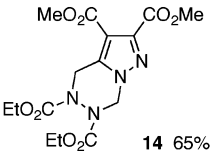
We prepared the 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole **3**[5,6] and observed that it undergoes SO_2 extrusion in refluxing 1,2,4-trichlorobenzene to give 1,2-diazafulvenium methide **4**, which could be trapped by reacting with bis(trimethylsilyl)-acetylene, confirming the result reported by Storr et al.[5] In our hands, the dimethyl 5,6-bis(trimethylsilyl)-4,7-dihydropyrazolo-[1,5-*a*]pyridine-2,3-dicarboxylate **5** was obtained in 54% yield together with the formation of the aromatized derivative **6** in 7% yield (Table 1). However, the dipolar system **4** also participates in the cycloaddition with electron-deficient dipolarophiles. Diazafulvenium methide **4** reacts with DMAD to give a mixture of dihydropyrazolo[1,5-*a*]pyridines (**8** and **9**) in 45% yield and pyrazolo[1,5-*a*]pyridine **7** in 10% yield. The mixture of **8** and **9** can be converted into **7** in 44% yield by treatment with DDQ. The [8π + 2π] cycloaddition of diazafulvenium methide **4** with methyl propiolate affords regioisomers **10** (28%) and **11** (33%). The thermolysis of 2,2-dioxo-1*H*,3*H*-pyrazolo-[1,5-*c*][1,3]thiazole **3** in refluxing 1,2,4-trichlorobenzene for 7 h in the presence of *N*-phenylmaleimide gave hexahydro-5*H*-pyrrolo[3′,4′:5,6]pyrazolo[1,5-*a*]pyridine **12** in 87% yield. This cycloadduct could be obtained in 98% yield by increasing the reaction time to 11 h. The dipole **4** can also be trapped by

(6) Sutcliffe, O. B.; Storr, R. C.; Gilchrist, T. L.; Rafferty, P. *Tetrahedron* **2000**, *56*, 10011−10021.

TABLE 1. Solution Pyrolysis of 2,2-Dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole 3 in the Presence of Dipolarophiles



3 4

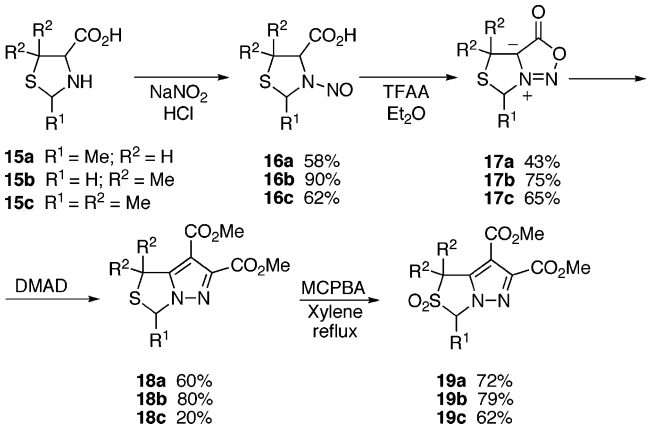
Reaction time	Dipolarophile	Products
6 h	$Me_3Si{-}{\equiv}{-}SiMe_3$	 **5** 54% + **6** 7%
7 h	$MeO_2C{-}{\equiv}{-}CO_2Me$	 **7** 10% + **8** 45% (28:72) + **9**
7 h	${\equiv}{-}CO_2Me$	 **10** 28% + **11** 33%
11 h		 **12** 98%
7 h	$PhO_2SN{=}CHPh$	 **13** 45%
7 h	$EtO_2CN{=}NCO_2Et$	 **14** 65%

$[8\pi + 2\pi]$ cycloaddition with heterodipolarophiles. In fact, the reaction with *N*-benzylidenebenzenesulfonamide[7] gives the corresponding cycloadduct **13** in 45% yield as the only regioisomer. On the other hand, pyrazolo[1,5-*d*][1,2,4]triazine **14** could be obtained in 65% yield from the cycloaddition of 1,2-diazafulvenium methide **4** with diethyl diazene-1,2-dicarboxylate (Table 1). These results contradict the previously described experimental observation where cycloaddition of 1,2-diazafulvenium methide **4** could only be observed with silylated acetylenes and attempts to carry out the reaction with electron-deficient dipolarophiles were not successful.[5] However, the reactivity of 1,7-dipole **4** toward $[8\pi + 2\pi]$ cycloaddition hereby described, characterized by the participation in the reaction with both electron-rich and electron-deficient dipolarophiles, is in agreement with the reported MO calculations.[5]

The work was extended to diazafulvenium methide systems generated from 3-methyl-, 1,1-dimethyl-, and 1,1,3-trimethyl-2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazoles **19**. The 3-methyl-2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole **19a**[3] was prepared from thiazolidine **15a** as outlined in Scheme 3. The sydnone **17a** is a stable mesoionic species, which can be isolated and undergoes 1,3-dipolar cycloaddition with DMAD to give 3-methyl-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole **18a** in 60% yield. 1*H*,3*H*-Pyrazolo[1,5-*c*][1,3]thiazoles **18b** and **18c** were obtained using a similar synthetic strategy. Thiazolidines **15b** and **15c** were prepared from the condensation of DL-penicillamine with

(7) Vishwakarma, L. C.; Stringer, O. D.; Davis, F. A. *Organic Syntheses*; Wiley: New York, 1993; Collect. Vol. VIII, pp 546−550.

SCHEME 3



formaldehyde and acetaldehyde, respectively, and converted into the corresponding sydnone via nitrosation followed by treatment with TFAA. Sydnones **17b** and **17c** are also stable and could be isolated and fully characterized. The reaction of **17b** with DMAD gave the expected 1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole in 80% yield. However, carrying out the 1,3-dipolar cycloaddition of **17c** under the same reaction conditions affords 1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole **18c** in only 10% yield. The yield could be improved to 20% by reducing the reaction time from 3 h to 1 h. The oxidation of 1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazoles **18** with MCPBA afforded sulfones **19** in good yield.

The ^{1}H NMR spectra of *N*-nitrosothiazolidine-4-carboxylic acids **16a**−**16c** showed two sets of signals indicating the existence of isomers. Thiazolidine **15a** is obtained from L-cysteine as a (2*S*,4*R*) and (2*R*,4*R*) diastereoisomeric mixture, but the corresponding *N*-nitroso derivative (**16a**) can be obtained as a single stereoisomer. In fact, it is known that the acylation of a mixture of (2*S*,4*R*)- and (2*R*,4*R*)-2-substituted-1,3-thiazolidine-4-carboxylates can lead to the selective synthesis of *N*-acyl-2-substituted-1,3-thiazolidine-4-carboxylates as pure stereoisomers with (2*R*,4*R*) or (2*S*,4*R*) stereochemistry depending on the reaction conditions. 2-Substituted-1,3-thiazolidine-4-carboxylates can undergo selective inversion at C-2 through a mechanism involving the opening of the ring, but the protection with the acyl group prevents this epimerization and allows the isolation of pure diastereoisomers.[8] A similar chemical behavior was observed in the one-pot synthesis of the chiral hexahydropyrrolo[1′,2′,5′:3,4,5]thiazolo[3,4-*c*]oxazol-1-one ring system from α-amino acids (L-cysteine and D-penicillamine).[9] Therefore, the ^{1}H NMR spectrum of **16a** could be explained considering the existence of two rotamers. This interpretation is reinforced by the fact that *N*-nitrosothiazolidine-4-carboxylic acid **16b**, which has only one chiral center, also shows two sets of signals corresponding to two rotamers. Thiazolidine **15c** was prepared from DL-penicillamine. Thus, **15c** was obtained as a mixture of (2*R*,4*R*), (2*S*,4*R*), (2*S*,4*S*), and (2*R*,4*S*) stereoisomers. However, after the nitrosation reaction *N*-nitrosothiazolidine-4-carboxylic acid **16c** can be obtained as an enantiomeric mixture. Therefore, again in this case two rotamers would be observed in the ^{1}H NMR spectrum of **16c**. Evidence of restricted rotation of *N*-nitroso compounds is well documented, and equilibrium between rotational isomers at room temperature has been encountered for several *N*-nitrosoamines, including five-membered cyclic derivatives such as pyrrolidine, thiazolidine, and oxazoline.[10]

The 3-methyl-2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole **19a** also undergoes SO_2 extrusion in solution to give **20**, which can be intercepted in [8π + 2π] cycloadditions with electron-deficient dipolarophiles giving the corresponding adducts resulting from the addition across the 1,7-positions in high yields (Table 2). The reaction with DMAD gives a mixture of dihydropyrazolo[1,5-*a*]pyridines (**21** and **22**) in 85% yield. This mixture can be oxidized with DDQ to give tetramethyl 7-methylpyrazolo[1,5-*a*]pyridine-2,3,5,6-tetracarboxylate (**23**) in 40% yield. The thermolysis of **19a** in the presence of methyl propiolate afforded a mixture of regioisomers 4,7-dihydropyrazolo[1,5-*a*]-pyridine-2,3,6-tricarboxylate **24** (30%) and 4,7-dihydropyrazolo-[1,5-*a*]pyridine-2,3,5-tricarboxylate **25** (38%).

The 1,7-dipolar cycloaddition of 1,2-diazafulvenium methide **20** with *N*-phenylmaleimide gave two racemic diastereoisomeric products, cycloadducts **26** (81%) and **27** (13%). The structure of the major product (**26**) was determined by X-ray crystallography (see Supporting Information). The crystal structure showed that the unit cell contains four molecules that are two pairs of enantiomers. The stereochemistry of the enantiomers was established as beeing (4a*S*,7a*S*,8*S*) and (4a*R*,7a*R*,8*R*). The formation of cycloadducts **26** and **27** can be explained considering a cycloaddition with *endo* selectivity but with the involvement of the two possible configurations of diazafulvenium methide **20** (see Scheme 7). The lower stability of the configuration having the inward methyl group explains the formation of heterocycle **27** in a lower yield.

An efficient cycloaddition was observed when sulfone **19a** was heated in the presence of *N*-benzylidenebenzenesulfonamide (Table 2). A single cycloadduct **28** was obtained in 81% yield. The structure of compound **28** was unambiguously established on the basis of its ^{1}H NMR spectrum. It shows an ABX system corresponding to H-4 and H-5 protons and a quartet assigned to proton H-7. The cycloaddition of 1,2-diazafulvenium methide **20** with diethyl diazene-1,2-dicarboxylate gave 7-methyl-4*H*,7*H*-pyrazolo[1,5-*d*][1,2,4]triazine-2,3,5,6-tetracarboxylate **29** in 79% yield. In the ^{1}H NMR spectrum of **29** the presence of two conformational isomers could be clearly identified, whereas in the case of derivative **14**, unsubstituted at C-7, the six-membered ring protons are observed as broad signals.

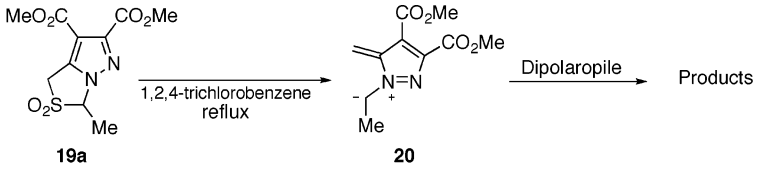
It is noteworthy that the thermolysis of 3-methyl-2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole **19a** in the presence of electron-deficient dipolarophiles requires shorter reaction time than the thermolysis of 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]-thiazole **3** (Tables 1 and 2). However, an attempt to react **19a**

(8) (a) Szilágyi, L.; Györgydeák, Z. *J. Am. Chem. Soc.* **1979**, *101*, 427−432. (b) Györgydeák, Z.; Kajtár-Peredy, M.; Kajtár, J.; Kajtár, M. *Liebigs Ann. Chem.* **1987**, 927−934. (c) Benedini, F.; Ferrario, F.; Sala, A.; Sala, L.; Soresinetti, P. A. *J. Heterocycl. Chem.* **1994**, *31*, 1343−1347. (d) Fülöp, F.; Mattinen, J.; Pihlaja, K. *Tetrahedron* **1990**, *46*, 6545−6552. (e) Lázár, L.; Fülöp, F. *Eur. J. Org. Chem.* **2003**, 3025−3042. (f) Pinho e Melo, T. M. V. D. 1,3-Thiazolidine-4-carboxylic Acids as Building Blocks in Organic Synthesis. In *Targets in Heterocyclic Systems−Chemistry and Properties*; Attanasi, O. A., Spinelli, D., Eds.; Italian Society of Chemistry: Rome, 2004; Vol. 8, pp 288−329.

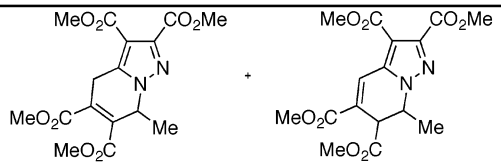
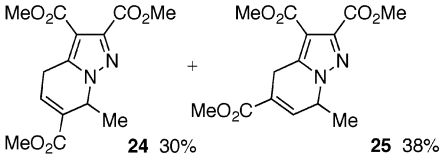
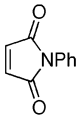
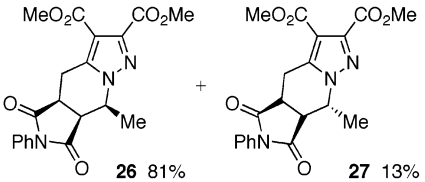
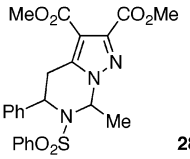
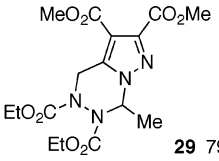
(9) Pinho e Melo, T. M. V. D.; Lopes, S. M. M.; Rocha, Gonsalves, A. M. d'A.; Kaczor, A. Fausto, R.; Paixão, J. A.; Matos Beja, A.; Ramos Silva, M. *Lett. Org. Chem.* **2006**, *3*, 820−826.

(10) (a) Anet, F. A. L.; Muchowski, J. M. *Chem. Ind.* **1963**, 81−82. (b) Jeyaraman, R.; Senthilkumar, U. P. *J. Org. Chem.* **1995**, *60*, 7461−7470. (c) Polonski, T.; Milewska, M. J.; Katrusiak, A. *J. Am. Chem. Soc.* **1993**, *115*, 11410−11417. (d) Roohi, H.; Deyhimi, F.; Ebrahimi, A. *J. Mol. Struct. (Theochem)* **2001**, *543*, 299−308. (e) Wu, H.; Loeppky, N.; Glaser, R. *J. Org. Chem.* **2005**, *70*, 6790−6801. (f) Haky, J. E.; Saavedra, J. E.; Hilton, B. D. *Org. Magn. Reson.* **1983**, *21*, 79−82. (g) Luinsky, W.; Keefer, L.; Loo, J. *Tetrahedron* **1970**, *26*, 5137−5153.

TABLE 2. Solution Pyrolysis of 3-Methyl-2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole 19a in the Presence of Dipolarophiles



19a **20**

Reaction time	Dipolarophile	Products
3h	$MeO_2C—\equiv—CO_2Me$	 **21**:**22** 85% (40:60)
4h	$\equiv—CO_2Me$	 **24** 30% **25** 38%
3h		 **26** 81% **27** 13%
3h	$PhO_2SN=CHPh$	 **28** 81%
4h	$EtO_2CN=NCO_2Et$	 **29** 79%

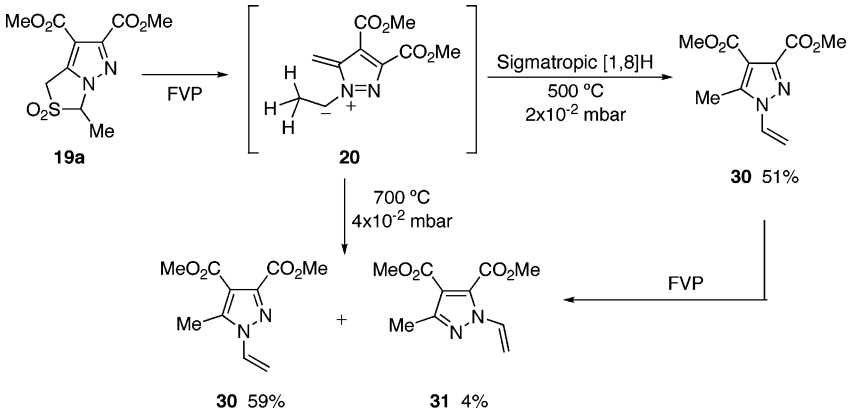
with bis(trimethylsilyl)acetylene led only to the synthesis of the corresponding 1-vinyl-1*H*-pyrazole **30** in 16% yield (see Scheme 4).

As previously mentioned the experimentally observed reactivity of 1,7-dipole **4** toward [8π + 2π] cycloaddition is characterized by the participation in the reaction with both electron-rich and electron-deficient dipolarophiles. This is in agreement with the reported semiempirical molecular orbital calculations.[5] The HOMO and LUMO energies were calculated for 1,2-diazafulvenium methide **4** (HO = −8.5 eV and LU = −1.9 eV), allowing prediction that the addition to electron-deficient dipolarophiles should be dipole-HOMO controlled while the addition to electron-rich dipolarophiles should be dipole-LUMO controlled. The 1,2-diazafulvenium methide **20** has an extra methyl group at C-1 leading to an increase of the HOMO and LUMO energies. Therefore, cycloaddition of **20** with electron-deficient dipolarophiles should be easier than with dipole **4** but the process should be less favorable with electron-rich dipolarophiles. This was confirmed experimentally, and in fact dipole **20** does not even react with electron-rich dipolarophiles.

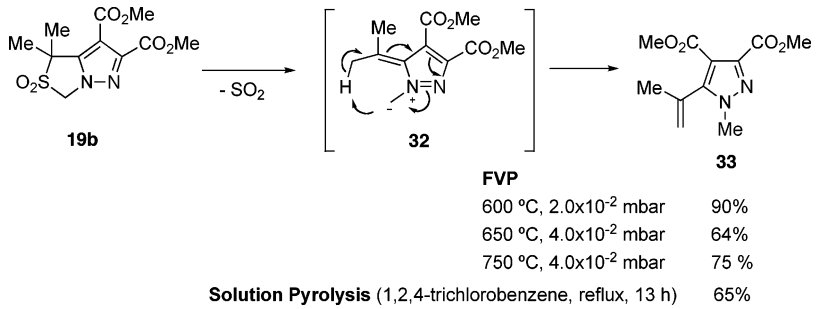
Calculations predict a larger atomic orbital coefficient on C-1 than on C-7 in the HOMO of 1,2-diazafulvenium methide **4.**[5] On the other hand, MNDO and CNDO/2 calculations show a larger atomic orbital coefficient on C-3 than on C-2 in the LUMO of methyl propiolate.[11] One would therefore expect the selective synthesis of trimethyl 4,7-dihydropyrazolo[1,5-*a*]-pyridine-2,3,5-tricarboxylate **11** from the reaction of dipole **4** with methyl propiolate (Table 1). The experimental result confirmed that regioisomer **11** is the major product, although it is obtained with low selectivity. The same regioselectivity was observed in the reaction of diazafulvenium methide **20** with methyl propiolate (Table 2). In contrast with this result, only one regioisomer was obtained from the [8π + 2π] cycloaddition of dipoles **4** and **20** with *N*-benzylidenebenzenesulfonamide

(11) Dieter, R. K.; Balke, W. H.; Fishpaugh, J. R. *Tetrahedron* **1988**, *44*, 1915−1924.

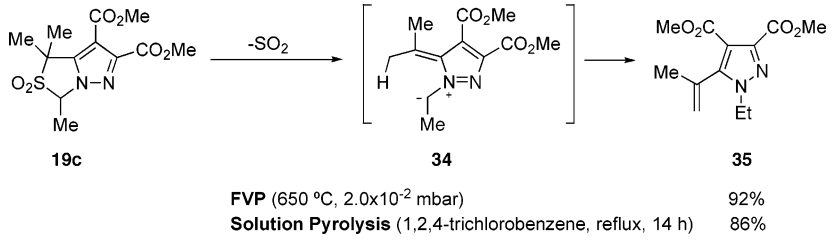
SCHEME 4



SCHEME 5



SCHEME 6



(Tables 1 and 2). A similar regioselectivity pattern is observed in the 1,3-dipolar cycloaddition of mesoionic *N*-methyl-1,3-oxazolium-5-olates, dipoles that give only one regioisomer from the reaction with *N*-benzylidenebenzenesulfonamide but lead to a ca. 1:1 mixture of regioisomers on reacting with ethyl propiolate.[12]

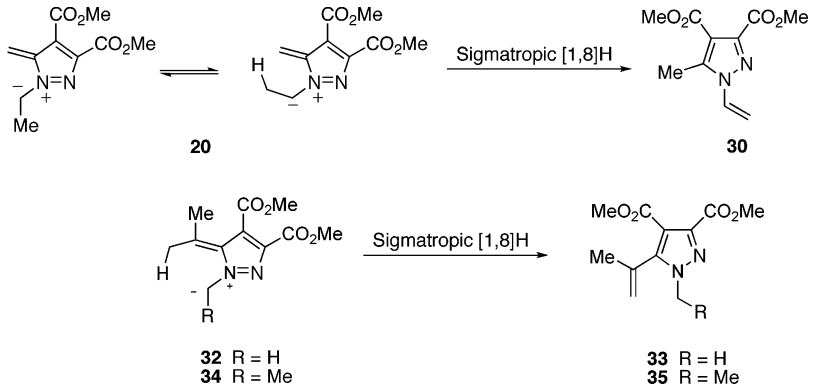
The generation and reactivity of diazafulvenium methide systems in the absence of dipolarophiles were studied. By carrying out flash vacuum pyrolysis (FVP) of sulfone **19a** at 500 °C, 1-vinyl-1*H*-pyrazole **30** was obtained selectively via the diazafulvenium methide **20**, which was trapped in an intramolecular sigmatropic [1,8]H shift. When the FVP was carried out at 700 °C, the same 1-vinyl-1*H*-pyrazole **30** was obtained, together with 2-vinyl-2*H*-pyrazole **31**. Pyrazole **31** is formed by thermal rearrangement of 1-vinyl-1*H*-pyrazole **30** since the FVP of this compound leads to a mixture of **30** and **31** (Scheme 4).

The thermolysis of pyrazole **19b** bearing two methyl groups at C-1 was also studied. Under FVP reaction conditions compound **19b** affords *C*-vinylpyrazole **33**. The optimized conditions (600 °C, 2.0×10^{-2} mbar) allowed the synthesis of heterocycle **33** in 90% yield (Scheme 5). Attempts to promote a rearrangement of **33** under FVP led only to sublimation of the pyrazole. On the other hand, the solution pyrolysis of sulfone **19b** in the presence of electron-deficient dipolarophiles (*N*-phenylmaleimide or DMAD) or bis(trimethylsilyl)acetylene also gave *C*-vinylpyrazole **33** in yields ranging from 40% to 50%, and no $[8\pi + 2\pi]$ cycloadducts were detected. This result can be explained considering the ease with which diazafulvenium methide **32** undergoes sigmatropic [1,8]H shift, although steric effects can also play an important role making the cycloaddition less favorable. In the absence of dipolorophiles, the optimized solution pyrolysis of sulfone **19b** (reflux in 1,2,4-trichlorobenzene for 13 h) gave *C*-vinylpyrazole **33** in 65% yield.

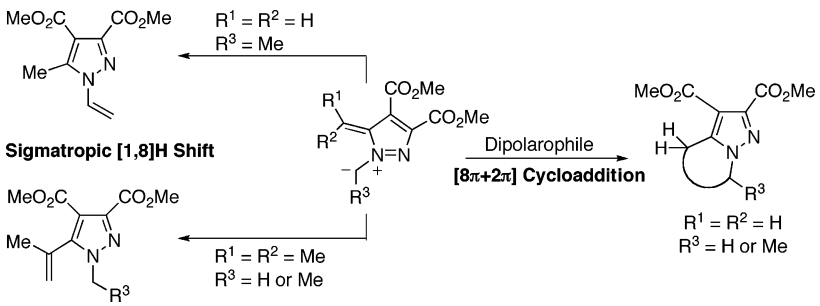
Flash vacuum pyrolysis 1,1,3-trimethyl-2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole **19c** also leads to the corresponding *C*-vinylpyrazole **35** in high yield (Scheme 6). In this particular case, the SO_2 extrusion leads to diazafulvenium methide **34** where two potential [1,8]H sigmatropic shifts could in principle occur. However, the FVP of **19c** did not afford *N*-vinylpyrazole, giving instead *C*-vinylpyrazole **35** exclusively. The same type of selectivity was previously observed for sigmatropic [1,8]H shifts of azafulvenium methides generated from 1,1,3-trimethyl-2,2-dioxo-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazoles.[2] The solution pyrolysis of **19c** in the presence of *N*-phenylmaleimide gave

(12) Bonati, L.; Ferraccioli, R.; Moro, G. *J. Phys. Org. Chem.* **1995**, *8*, 452−462.

SCHEME 7



SCHEME 8



C-vinylpyrazole **35** as the only product. By heating at reflux a solution of sulfone **19c** in 1,2,4-trichlorobenzene for 14 h, *C*-vinylpyrazole **35** could be obtained in high yield (86%).

The difference in reactivity observed between diazafulvenium methide **20** and diazafulvenium methides **32** and **34** may reflect the different ease with which the dipoles can attain the configuration required for the sigmatropic shift. In fact, the 7,7-dimethyl-diazafulvenium methides (**32** and **34**) always have a methyl group in the correct position, whereas in the case of diazafulvenium methide **20** only the configuration having the inward methyl group undergoes the pericyclic reaction (Scheme 7).

The reactivity pattern of the studied diazafulvenium methides is shown in Scheme 8. Thus, diazafulvenium methides unsubstituted at C-7 generated from the solution pyrolysis of 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazoles participate in [8π + 2π] cycloadditions, giving pyrazolo[1,5-*a*]pyridine derivatives. The diazafulvenium methide derivatives bearing methyl groups at C-1 or C-7 undergo intramolecular sigmatropic [1,8]H shifts, giving vinyl-1*H*-pyrazoles.

Conclusions

We described new chemistry of diazafulvenium methides, generated by the thermal extrusion of sulfur dioxide from 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazoles.

The diazafulvenium methides unsubstituted at C-7 can be intercepted in [8π + 2π] cycloadditions giving pyrazolo[1,5-*a*]pyridine derivatives resulting from the addition across the 1,7-position. A range of pyrazolo-annulated heterocycles was obtained, namely, pyrazolo[1,5-*a*]pyridines, hexahydro-5*H*-pyrrolo[3′,4′:5,6]pyrazolo[1,5-*a*]pyridines, tetrahydropyrazolo-[1,5-*c*]pyrimidines, and tetrahydropyrazolo[1,5-*d*][1,2,4]triazines, some of which have potential biological activity.[13]

In the absence of dipolarophiles, 1-methyl-diazafulvenium methide and 7,7-dimethyl-diazafulvenium methides undergo intramolecular sigmatropic [1,8]H shifts giving *N*-vinyl-1*H*-pyrazoles and *C*-vinyl-1*H*-pyrazoles, respectively.

Therefore, it has been demonstrated that diazafulvenium methides are valuable intermediates for the synthesis of functionalized pyrazoles.

Experimental Section

General Procedure for [8 + 2] Cycloadditions. A suspension of the appropriate 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole-6,7-dicarboxylate (0.87 mmol) and dipolarophile (1.74 mmol) in 1,2,4-trichlorobenzene (2.5 mL) was heated at reflux under dry nitrogen (for 6−7 h, starting from **3**; for 3−4 h starting from **19a**) for 6−11 h. After cooling to room temperature, the mixture was purified by flash chromatography [hexane] to remove 1,2,4-trichlorobenzene followed by elution with ethyl acetate−hexane.

Dimethyl 5,6-Bis(trimethylsilyl)-4,7-dihydro-pyrazolo[1,5-*a*]-pyridine-2,3-dicarboxylate[3,5] **5 and Dimethyl 5,6-Bis(trimethylsilyl)-pyrazolo[1,5-*a*]pyridine-2,3-dicarboxylate**[3,5] **6**. The reaction of **3** with bis(trimethylsilyl)acetylene gave a mixture, which was purified by flash chromatography [hexane, ethyl acetate−hexane (1:4), then ethyl acetate−hexane (1:2)] to give **5** as a solid (54%) and **6** as an oil (7%). **Data for 5**: mp 86.1−87.9 °C (from ethyl ether−hexane) (compound previously described as a yellowish oil[5b]). ^{1}H NMR 0.28 (9H, s), 0.30 (9H, s), 3.78 (2H, approximately

(13) (a) Allen, S. H.; Johns, B. A.; Gudmundsson, K. S.; Freeman, G. A.; Boyd, F. L., Jr.; Sexton, C. J.; Selleseth, D. W.; Creech, K. L.; Moniri, K. R. *Biorg. Med. Chem.* **2006**, *14*, 944−954. (b) Elgemeie, G. H.; Zaghary, W. A.; Amin, K. M.; Nasr, T. M. *Nucleosodes, Nucleotides, Nucleic Acids* **2005**, *24*, 1227−1247. (c) Jones, P.; Atack, J. R.; Braun, M. P.; Cato, B. P.; Chambers, M. S.; O'Connor, D.; Cook. S. M.; Hobbs, S. C.; Maxey, R.; Szekeres, H. J.; Szeto, N.; Wafford, K. A.; MacLeod, A. M. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 872−875.

t, J = 4.7 Hz), 3.86 (3H, s), 3.95 (3H, s), 4.76 (2H, approximately t, J = 4.7 Hz); MS (EI) *m/z* 380 (M^+, 11%), 365 (30), 348 (48), 275 (100), 73 (36). **Data for 6**: ^{1}H NMR 0.42 (9H, s), 0.44 (9H, s), 3.94 (3H, s), 4.03 (3H, s), 8.45 (1H, d, J = 0.8 Hz), 8.58 (1H, d, J = 0.8 Hz); MS (EI) *m/z* 378 (M^+, 100%), 363 (18), 347 (43), 331 (75), 259 (34), 73 (24).

Tetramethyl Pyrazolo[1,5-*a*]pyridine-2,3,5,6-tetracarboxylate 7, Tetramethyl 4,7-Dihydro-pyrazolo[1,5-*a*]pyridine-2,3,5,6-tetracarboxylate 8, and Tetramethyl 6,7-Dihydro-pyrazolo[1,5-*a*]-pyridine-2,3,5,6-tetracarboxylate 9. The reaction of **3** with DMAD gave a mixture, which was purified by flash chromatography [hexane, ethyl acetate−hexane (1:2), then ethyl acetate−hexane (1:1)] to give in order of elution **7** as a yellow solid (10%) and a mixture of **8** and **9** as a white solid (ratio 28:72) (45%). **Data for 7**: mp 94.7−96.8 °C (from diethyl ether-hexane). IR (KBr) 1730, 1578, 1428, 1328, 1245 cm^{-1}; ^{1}H NMR 3.96 (3H, s), 3.97 (3H, s), 3.98 (3H, s), 4.05 (3H, s), 8.40 (1H, s), 9.01 (1H, s); ^{13}C NMR 52.1, 53.2, 53.3, 105.4, 118.5, 120.2, 131.7, 132.0, 140.7, 149.6, 161.6, 162.3, 163.9, 166.1; MS (EI) *m/z* 350 (M^+, 63%), 319 (100), 229 (7), 201 (7); HRMS (EI) *m/z* 350.0757 ($C_{15}H_{14}N_2O_8$ [M^+], 350.0750). **Data for 8 and 9**: mp 71.9−73.3 °C (from diethyl ether). IR (KBr) 1738, 1721, 1486, 1433, 1256, 1215 cm^{-1}; ^{1}H NMR (minor isomer **8**) 3.88 (3H, s), 3.90 (3H, s), 3.91 (3H, s), 3.99 (3H, s), 4.71 (2H, s), 5.26 (2H, s); (major isomer **9**) 3.69 (3H, s), 3.90 (3H, s), 3.91 (3H, s), 3.96 (3H, s), 4.19 (1H, dd, J = 1.3 and 6.7 Hz), 4.30 (1H, dd, J = 6.7 and 13.8 Hz), 5.04 (1H, dd, J = 1.3 and 13.8 Hz), 7.93 (1H, s); MS (EI) *m/z* 352 (M^+, 11%), 321 (15), 307 (12), 293 (30), 261 (100), 203 (8). Anal. Calcd for $C_{15}H_{16}N_2O_8$: C, 51.14; H, 4.58; N, 7.95. Found: C, 51.12; H, 4.99; N, 7.63.

Trimethyl 4,7-Dihydropyrazolo[1,5-*a*]pyridine-2,3,6-tricarboxylate 10 and Trimethyl 4,7-Dihydropyrazolo[1,5-*a*]pyridine-2,3,5-tricarboxylate 11. The reaction of **3** with methyl propiolate gave a mixture, which was purified by flash chromatography [hexane, then ethyl acetate−hexane (1:2)] to give **10** (28%) and **11** (33%) as white solids. **Data for10**: mp 119.5−121.0 °C (from ethyl acetate−hexane). IR (KBr) 1744, 1697, 1431, 1293, 1251, 1220, 1087 cm^{-1}; ^{1}H NMR 3.86 (3H, s), 3.86 (3H, s), 3.90 (1H, dd, J = 5.5 and 3.9 Hz), 3.92 (1H, dd, J = 5.5 and 3.8 Hz), 3.97 (3H, s), 4.95 (1H, dd, J = 5.6 and 2.1 Hz), 4.97 (1H, dd, J = 5.6 and 2.0 Hz), 7.22−7.24 (1H, m); ^{13}C NMR 25.6, 46.8, 51.7, 52.4, 52.6, 110.1, 124.5, 132.5, 140.2, 144.2, 162.3, 162.5, 164.3. HRMS (CI) *m/z* 295.0930 ($C_{13}H_{15}N_2O_6$ [M − H^+], 295.0930). **Data for 11**: mp 141.1−142.5 °C (from ethyl acetate−hexane). ^{1}H NMR 3.86 (3H, s), 3.88 (3H, s), 3.94 (1H, dd, J = 5.6 and 1.8 Hz), 3.96 (1H, m), 3.96 (3H, s), 4.95 (1H, dd, J = 5.6 and 3.4 Hz), 4.97 (1H, dd, J = 5.6 and 3.4 Hz), 7.13−7.16 (1H, m); ^{13}C NMR 24.5, 47.8, 51.8, 52.4, 52.6, 110.6, 125.5, 129.9, 141.3, 144.3, 162.3, 162.5, 165.2. HRMS (CI) *m/z* 295.0929 ($C_{13}H_{15}N_2O_6$ [M − H^+], 295.0930).

Dimethyl 6-Phenyl-5,7-dioxo-4a,5,6,7,7a,8-hexahydro-5*H*-pyrrolo[3′,4′:5,6]pyrazolo[1,5-*a*]pyridine-2,3-dicarboxylate 12. The reaction of **3** with *N*-phenylmaleimide required longer reaction time (11 h), giving a product that was purified by flash chromatography [hexane, ethyl acetate−hexane (2:1), then ethyl acetate−hexane (4:1)] to give **12** as a white solid (98%): mp 144.8−146.7 °C (from diethyl ether). IR (KBr) 1715, 1497, 1385, 1221, 1150 cm^{-1}; ^{1}H NMR 3.20 (1H, dd, J = 7.2 and 16.4 Hz), 3.58−3.70 (2H, m), 3.85 (3H, s), 3.93 (3H, s), 3.93−4.00 (1H, m), 4.31 (1H, dd, J = 5.7 and 13.9 Hz), 4.90 (1H, dd, J = 2.5 and 13.9 Hz), 7.07−7.10 (2H, m), 7.37−7.44 (3H, m); ^{13}C NMR 22.5, 37.1, 40.4, 46.1, 51.9, 52.6, 112.0, 126.1, 129.0, 129.2, 131.0, 141.5, 143.3, 162.0, 174.9, 176.0; MS (EI) *m/z* 383 (M^+, 28%), 351 (100), 204 (61), 176 (12), 147 (7), 119 (8), 77 (7). Anal. Calcd for $C_{19}H_{17}N_3O_6$: C, 59.53; H, 4.47; N, 10.96. Found: C, 59.49; H, 4.64; N, 10.84.

Dimethyl 5-Phenyl-6-(phenylsulfonyl)-4,5,6,7-tetrahydropyrazolo[1,5-*c*]pyrimidine-2,3-dicarboxylate 13. The reaction of **3** with *N*-benzylidenebenzenesulfonamide[7] gave a product, which was purified by flash chromatography [hexane, ethyl acetate−hexane (1:4), then ethyl acetate−hexane (1:2)] to give **13** as a solid (45%). mp 165−170 °C (from diethyl ether); ^{1}H NMR 3.02 (1H, dd, J = 7.3 and 18.6 Hz), 3.6 (1H, d, J = 18.6 Hz), 3.81 (3H, s), 3.95 (3H, s), 4.74 (1H, d, J = 14.3 Hz) 5.54 (1H, d, J = 7.3 Hz), 5.96 (1H, d, J = 14.3 Hz), 7.16−7.96 (10H, m); MS (EI) *m/z* 455 (M^+, 8%), 424 (13), 286 (100), 253 (30), 223 (15), 210 (94), 151 (90), 77 (17). HRMS (EI) *m/z* 445.1159 ($C_{22}H_{21}N_3O_6S$ [M^+], 445.1151).

5,6-Diethyl 2,3-Dimethyl 4,5,6,7-Tetrahydropyrazolo[1,5-*d*]-[1,2,4]triazine-2,3,5,6-tetracarboxylate 14. The reaction of **3** with diethyl diazene-1,2-dicarboxylate gave a product, which was purified by flash chromatography [hexane, ethyl acetate−hexane (1:4), then ethyl acetate−hexane (1:2)] to give a colorless oil (65%): IR (KBr) 1733, 1402, 1211, 1090; ^{1}H NMR 1.30−1.34 (6H, m), 3.87 (3H, s), 3.97 (3H, s) 4.27−4.29 (4H, m), 4.7 (1H, bs), 5.40 (2H, bs), 6.2 (1H, bs); ^{13}C NMR 14.3, 14.5, 42.5 (bs), 52.0, 52.7, 61.4 (bs), 63.4, 64.2, 110.8, 139.3, 143.9, 154.0, 161.8; MS (EI) *m/z* 384 (M^+, 11%), 352 (83), 284 (45), 235 (46), 207 (83), 179 (100), 151 (44). HRMS (EI) *m/z* 384.1274 ($C_{15}H_{20}N_4O_8$ [M^+], 384.1281).

Tetramethyl 7-Methyl-4,7-dihydro-pyrazolo[1,5-*a*]pyridine-2,3,5,6-tetracarboxylate 21 and Tetramethyl 7-Methyl-6,7-dihydro-pyrazolo[1,5-*a*]pyridine-2,3,5,6-tetracarboxylate 22. The reaction of **19a** with DMAD (reaction time 3 h) gave a mixture, which was purified by flash chromatography [hexane, ethyl acetate−hexane (1:2), then ethyl acetate−hexane (1:1)] to give a mixture of **21** and **22** (ratio 40:60) as a yellowish oil (85%). IR (KBr) 1730, 1433, 1217, 1090 cm^{-1}; ^{1}H NMR (minor isomer **21**) 1.40 (3H, d, J = 6.9 Hz), 3.68 (3H, s), 3.86 (3H, s), 3.90 (3H, s), 3.96 (3H, s), 4.05−4.07 (1H, m), 4.52−4.56 (1H, m), 5.22−5.32 (1H, m); (major isomer **22**) 1.78 (3H, d, J = 6.8 Hz), 3.66 (3H, s), 3.86−3.98 (2H, m), 3.88 (3H, s), 3.91 (3H, s), 3.96 (3H, s), 7.96 (1H, s); MS (EI) *m/z* 366 (M^+, 9%), 335 (14), 307 (48), 275 (100), 261 (19), 59 (9). HRMS (EI) *m/z* 366.1062 ($C_{16}H_{18}N_2O_8$ [M^+], 366.1064).

Trimethyl 7-Methyl-4,7-dihydropyrazolo[1,5-*a*]pyridine-2,3,6-tricarboxylate 24 and Trimethyl 7-Methyl-4,7-dihydropyrazolo-[1,5-*a*]pyridine-2,3,5-tricarboxylate 25. The reaction of **19a** with methyl propiolate gave a mixture, which was purified by flash chromatography [hexane, then ethyl acetate−hexane (1:2)] to give **24** (30%) and **25** (38%). **Data for 24**: obtained as a colorless oil; ^{1}H NMR 1.63 (3H, d, J = 6.5 Hz), 3.78−4.04 (2H, m), 3.86 (3H, s), 3.87 (3H, s), 3.97 (3H, s), 5.31−5.38 (1H, m), 7.18−7.21 (1H, m); ^{13}C NMR 22.7, 25.2, 51.7, 52.3, 52.6, 53.6, 109.9, 130.6, 132.4, 139.8, 144.1, 162.6, 162.7, 164.4; MS (EI) *m/z* 308 (M^+, 2%), 277 (14), 261 (100), 217 (11). HRMS (CI+) *m/z* 309.1087 ($C_{12}H_{16}N_2O_4$ [MH^+], 309.1087). **Data for 25**: obtained as a white solid; mp 99−100 °C (from ethyl acetate−hexane). IR (KBr) 1745, 1721, 1710, 1313, 1270, 1091, 1064 cm^{-1}; ^{1}H NMR 1.69 (3H, d, J = 6.9 Hz), 3.84 (3H, s), 3.87 (3H, s), 3.91 (1H, dd, J = 5.0 and 2.1 Hz), 3.94 (1H, dd, J = 5.0 and 1.6 Hz), 3.97 (3H, s), 5.07−5.08 (1H, m), 7.05 (1H, approximately dt, $J \approx$ 2.1, 1.6 and 3.6 Hz); ^{13}C NMR 21.6, 24.4, 51.7, 52.4, 52.6, 53.8, 110.2, 124.3, 135.6, 140.8, 144.3, 162.6, 162.7, 165.4; MS (EI) *m/z* 308 (M^+, 4%),277 (20), 261 (100), 217 (15). HRMS (CI+) *m/z* 309.1083 ($C_{12}H_{16}N_2O_4$ [MH^+], 309.1087).

(4a*S*,7a*S*,8*S*)-Dimethyl 8-Methyl-5,7-dioxo-6-phenyl-4a,5,6,7,-7a,8-hexahydro-1*H*,3*H*-pyrazolo[1,5-*a*]pyrrolo[3,4-*d*]pyridine-2,3-dicarboxylate 26 and (4a*S*,7a*S*,8*R*)-8-Methyl-5,7-dioxo-6-phenyl-4a,5,6,7,7a,8-hexahydro-1*H*,3*H*-pyrazolo[1,5-*a*]pyrrolo[3,4-*d*]pyridine-2,3-dicarboxylate 27. The reaction of **19a** with *N*-phenylmaleimide (reaction time 3 h) gave a mixture, which was purified by flash chromatography [hexane, ethyl acetate−hexane (2:1), then ethyl acetate] to give in order of elution **27** as an oil (13%) and **26** as a white solid (81%). **Data for 26**: mp 155.6−157.7 °C (from ethyl acetate−hexane); IR (KBr) 1735, 1716, 1562, 1473, 1447, 1383, 1222 cm^{-1}; ^{1}H NMR 1.69 (3H, d, J = 7.0 Hz), 3.53−3.72 (4H, m), 3.87 (3H, s), 3.95 (3H, s), 4.85−4.94 (1H, m), 7.15−7.18 (2H, m), 7.41−7.47 (3H, m); ^{13}C NMR 15.4, 21.2, 37.3, 44.7, 51.9, 52.7, 53.3, 111.9, 126.2, 129.1, 129.3, 131.0, 141.0,

143.4, 162.3, 162.4, 173.3, 176.2; MS (EI) *m*/*z* 397 (M^+, 15%), 365 (100), 218 (13), 203 (54), 77 (8). Anal. Calcd for $C_{20}H_{19}N_3O_6$: C, 60.45; H, 4.82; N, 10.57. Found: C, 60.63; H, 4.99; N, 10.43. **Data for 27**: IR (KBr) 1740, 1715, 1670, 1541, 1491, 1393, 1229 cm^{-1}; ^1H NMR 1.69 (3H, d, J = 7.0 Hz), 3.37 (1H, dd, J = 8.2 and 16.8 Hz), 3.42 (1H, dd, J = 2.9 and 9.6 Hz), 3.61 (1H, ddd, J = 3.1, 8.2 and 9.6 Hz), 3.86 (3H, s), 3.92 (1H, dd, J = 3.1 and 16.8 Hz), 3.94 (3H, s), 5.12 (1H, dq, J = 2.9 and 7.0 Hz), 7.12−7.27 (2H, m), 7.38−7.46 (3H, m); ^{13}C NMR 20.5, 22.0, 36.4, 46.2, 52.0, 52.6, 53.9, 112.2, 126.1, 129.0, 129.2, 131.0, 140.2, 143.4, 162.1, 162.2, 174.8, 176.2; MS (EI) *m*/*z* 397 (M^+, 24%), 365 (100), 217 (10), 203 (59), 183 (8). HRMS (EI) *m*/*z* 397.1279 ($C_{20}H_{19}N_3O_6$ [M^+], 397.1274).

Dimethyl 7-Methyl-5-phenyl-6-(phenylsulfonyl)-4,5,6,7-tetrahydropyrazolo[1,5-*c*]pyrimidine-2,3-dicarboxylate 28. The reaction of **19a** with *N*-benzylidenebenzenesulfonamide[7] (reaction time 3 h) gave a product, which was purified by flash chromatography [hexane, then ethyl acetate−hexane (2:1)] to give **28** as a white foam (81%): IR (KBr) 1745, 1736, 1336, 1216, 1173, 1082 cm^{-1}; ^1H NMR 1.18 (3H, d, J = 6.6 Hz), 2.91 (1H, dd, J = 17.8 and J = 7.4 Hz), 3.75 (1H, dd, J = 17.8 and J = 2.4 Hz), 3.86 (3H, s), 3.94 (3H, s) 5.57 (1H, dd, J = 7.4 and J = 2.4 Hz), 6.31 (1H, q, J = 6.6 Hz), 7.27−7.33 (4H, m), 7.49−7.52 (4H, m), 7.80−7.83 (2H, m); ^{13}C NMR 23.1, 24.1, 51.2, 51.8, 52.7, 68.1, 110.2, 126.8, 127.4, 128.4, 128.9, 129.7, 133.6, 138.3, 139.0, 140.4, 143.8, 162.5. HRMS (EI) *m*/*z* 469.1297 ($C_{23}H_{23}N_3O_6S$ [M^+], 469.1308).

5,6-Diethyl 2,3-Dimethyl 7-methyl-4,5,6,7-tetrahydropyrazolo[1,5-*d*][1,2,4]triazine-2,3,5,6-tetracarboxylate 29. The reaction of **19a** with diethyl diazene-1,2-dicarboxylate gave **29** as a white solid (79%): mp 119−119.5 °C (from diethyl ether); IR (KBr) 1753, 1741, 1721 1376, 1338, 1314, 1289, 1210; ^1H NMR (DMSO-d_6) (the ^1H NMR spectrum showed the existence of two rotamers) (major rotamer) 1.16−1.21 (6H, m), 1.60 (3H, d, J = 6.4 Hz), 3.77 (3H, s), 3.84 (3H, s), 4.10−4.21 (4H, m), 4.58 (1H, d, J = 17.2 Hz), 5.27 (1H, d, J = 17.2 Hz), 6.39 (1H, q, J = 6.4 Hz); ^{13}C NMR (DMSO-d_6) 14.1, 14.3, 19.6, 41.8, 51.8, 52.5, 60.6, 62.7, 63.5, 108.8, 138.6, 143.6, 154.3, 161.3, 162.3; MS (EI) *m*/*z* 398 (M^+, 4%), 367 (16), 284 (100), 253 (19), 221 (19), 193 (50), 180 (144), 116 (42). HRMS (EI) *m*/*z* 398.1426 ($C_{16}H_{22}N_4O_8$ [M^+], 398.1438).

General Procedure for Flash Vacuum Pyrolysis. Pyrolysis of the appropriate 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole-6,7-dicarboxylate (1.0 mmol) at 500−800 °C and 2 × 10^{-2} to 4 × 10^{-2} mbar onto a surface cooled at −196 °C over a period of 1.5−2 h gave a colorless pyrolysate. [The rate of volatilization of the starting material was controlled by the use of a Kugelrohr oven, which heated the sample at 80−180 °C]. After cooling to room temperature the pyrolysate was removed from the cold finger with dichloromethane, and the solvent was removed in vacuo.

Dimethyl 5-Methyl-1-vinyl-1*H*-pyrazole-3,4-dicarboxylate 30 and Dimethyl 5-Methyl-2-vinyl-2*H*-pyrazole-3,4-dicarboxylate 31. Pyrolysis of **19a** at 700 °C/4 × 10^{-2} mbar gave a mixture, which was purified by flash chromatography [ethyl acetate−hexane (1:2), then ethyl acetate−hexane (1:1)] to give in order of elution **31** as a colorless oil (4%) and **30** as a white solid (59%). **Data for 30**: mp 46.3−48.0 °C (from diethyl ether−hexane); IR (KBr) 1740, 1719, 1648, 1320, 1269, 1088 cm^{-1}; ^1H NMR 2.56 (3H, s), 3.85 (3H, s), 3.95 (3H, s), 5.14 (1H, dd, J = 0.9 and 8.8 Hz), 5.95 (1H, dd, J = 0.9 and 15.2 Hz), 6.99 (1H, dd, J = 8.8 and 15.2 Hz); ^{13}C NMR 10.3, 51.7, 52.5, 106.4, 112.6, 128.2, 142.9, 144.4, 162.8, 163.0; MS (EI) *m*/*z* 224 (M^+, 28%), 193 (100), 163 (27), 133 (12), 68 (9). Anal. Calcd for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.39; N, 12.49. Found: C, 53.75; H, 5.28; N, 12.39. **Data for 31**: IR (KBr) 1719, 1646, 1545, 1442, 1260, 1109 cm^{-1}; ^1H NMR 2.46 (3H, s), 3.84 (3H, s), 3.96 (3H, s), 5.03 (1H, dd, J = 0.7 and 8.8 Hz), 5.87 (1H, dd, J = 0.7 and 15.2 Hz), 7.19 (1H, dd, J = 8.8 and 15.2 Hz); ^{13}C NMR 13.4, 51.8, 53.2, 105.0, 114.1, 129.7, 145.0, 151.0, 160.7, 163.1; MS (EI) *m*/*z* 224 (M^+, 40%), 192 (100), 167 (7), 135 (11), 79 (6).

Dimethyl 5-Methyl-1-vinyl-1*H*-pyrazole-3,4-dicarboxylate 30. Pyrolysis of **19a** at 500 °C/2 × 10^{-2} mbar gave a product, which was purified by flash chromatography [ethyl acetate−hexane (1:2), then ethyl acetate−hexane (1:1)] to give **30** as a white solid (51%). Compound **30** was identified by comparison with the specimen previously prepared (see above).

Dimethyl 1-Methyl-5-(prop-1-en-2-yl)-1*H*-pyrazole-3,4-dicarboxylate 33. Pyrolysis of **19b** at 600 °C/2 × 10^{-2} gave a product, which was purified by flash chromatography [ethyl acetate−hexane (1:1)] to give **33** as a white foam (90%): IR (KBr) 1745, 1736, 1475, 1317, 1221, 1074 cm^{-1}; ^1H NMR 2.07 (3H, bs), 3.83 (3H, s), 3.85 (3H, s), 3.91 (3H, s), 5.13 (1H, bs), 5.54 (1H, m); ^{13}C NMR 22.6, 37.3, 51.9, 52.5, 112.8, 121.2, 133.6, 142.1, 147.4, 162.2, 163.0; MS (EI) *m*/*z* 238 (M^+, 17%), 206 (100), 195 (25), 248 (24), 120 (12). HRMS (EI) *m*/*z* 238.0963 ($C_{11}H_{14}N_2O_4$ [M^+], 238.0954).

Dimethyl 1-Ethyl-5-(prop-1-en-2-yl)-1*H*-pyrazole-3,4-dicarboxylate 35. Pyrolysis of **19c** at 650 °C/2 × 10^{-2} gave a product, which was purified by flash chromatography [ethyl acetate−hexane (1:1)] to give as a colorless oil (92%): IR (film) 1746, 1730, 1480, 1320, 1216, 1083 cm^{-1}; ^1H NMR 1.44 (3H, t, J = 7.2 Hz), 2.08 (3H, m), 3.83 (3H, s), 3.94 (3H, s), 4.16 (2H, q, J = 7.2 Hz), 5.13 (1H, m), 5.53 (1H, m); ^{13}C NMR 15.8, 23.0, 45.1, 51.8, 52.4, 112.5, 120.9, 133.7, 142.4, 146.9, 162.5, 163.0; MS (EI) *m*/*z* 252 (M^+, 21%), 220 (100), 205 (73), 193 (12), 161 (12). HRMS (EI+) *m*/*z* 252.1111 ($C_{12}H_{16}N_2O_4$ [M^+], 252.1110).

General Procedure for Solution Thermolysis. A solution of the appropriate 1,1-dimethyl-2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]-thiazole-6,7-dicarboxylate (0.30 mmol) in 1,2,4-trichlorobenzene (1.8 mL) was heated at reflux under dry nitrogen for 13−14 h. After cooling to room temperature, the mixture was purified by flash chromatography [hexane] to remove 1,2,4-trichlorobenzene followed by elution with ethyl acetate−hexane to give the products.

Dimethyl 1-Methyl-5-(prop-1-en-2-yl)-1*H*-pyrazole-3,4-dicarboxylate 33. Compound **33** was obtained from **19b** in 65% yield. Pyrazole **33** was purified by flash chromatography [hexane, then ethyl acetate−hexane (1:1)] and was identified by comparison with the specimen previously prepared (see above).

Dimethyl 1-Ethyl-5-(prop-1-en-2-yl)-1*H*-pyrazole-3,4-dicarboxylate 35. Compound **35** was obtained from **19c** in 86% yield. Pyrazole **35** was purified by flash chromatography [hexane, then ethyl acetate−hexane (1:3)] and was identified by comparison with the specimen previously prepared (see above).

Tetramethyl Pyrazolo[1,5-*a*]pyridine-2,3,5,6-tetracarboxylate 7 from 8 and 9. A suspension of the mixture of 4,7-dihydropyrazolo[1,5-*a*]pyridine-2,3,5,6-tetracarboxylate **8** and 6,7-dihydropyrazolo[1,5-*a*]pyridine-2,3,5,6-tetracarboxylate **9** (0.09 g, 0.26 mmol) and DDQ (0.07 g, 1.2 equiv, 0.31 mmol) in 1,2,4-trichlorobenzene (5.0 mL) was heated in sealed tube at 260 °C for 3 h. After cooling to room temperature, the tube was opened, and the mixture filtered through celite. The crude product was purified by flash chromatography [hexane] to remove 1,2,4-trichlorobenzene followed by elution with ethyl acetate−hexane (1:1), then ethyl acetate−hexane (2:1) to give **7** as a yellow solid (44%). Compound **7** was identified by comparison with the specimen previously prepared.

Tetramethyl 7-Methylpyrazolo[1,5-*a*]pyridine-2,3,5,6-tetracarboxylate 23. A suspension of the mixture 7-methyl-4,7-dihydropyrazolo[1,5-*a*]pyridine-2,3,5,6-tetracarboxylate **21** and 7-methyl-6,7-dihydro-pyrazolo[1,5-*a*]pyridine-2,3,5,6-tetracarboxylate **22** (0.04 g, 0.12 mmol) and DDQ (0.03 g, 1.2 equiv., 0.14 mmol) in 1,2,4-trichlorobenzene (2.0 mL) was heated in sealed tube at 260 °C for 3 h. After cooling to room temperature, the tube was

opened and the mixture was filtered through celite. The crude product was purified by flash chromatography [hexane] to remove 1,2,4-trichlorobenzene followed by elution with ethyl acetate−hexane (1:2), then ethyl acetate−hexane (1:1) to give **23** (40%) as a yellow solid: mp 110.5−111.3 °C (from ethyl ether−hexane); IR (KBr) 1744, 1714, 1304, 1272, 1210, 1120 cm^{-1}; ^1H NMR 2.85 (3H, s), 3.97 (6H, s), 3.99 (3H, s), 4.05 (3H, s), 8.68 (1H, s); ^{13}C NMR 15.3, 52.1, 53.1, 53.2, 53.3, 105.5, 119.7, 120.1, 130.0, 138.9, 139.8, 148.5, 162.0, 163.1, 164.6, 166.6; MS (EI) *m*/*z* 364 (M^+, 70%), 333 (100), 301 (14), 274 (29), 246 (16), 59 (11). Anal. Calcd for $C_{16}H_{16}N_2O_8$: C, 52.75; H, 4.43; N, 7.69. Found: C, 52.79; H, 4.66; N, 7.68.

Acknowledgment. We thank Chymiotechnon, *Fundação para a Ciência e a Tecnologia* (POCI/QUI/55584/2004 and SFRH/BD/9123/2002) and FEDER for financial support.

Supporting Information Available: Experimental procedures and characterization data for compounds **16a**−**16c**, **17a**−**17c**, **18a**−**18c**, and **19a**−**19c**. NMR spectra for all new compounds. Crystallographic data for dimethyl 8-methyl-5,7-dioxo-6-phenyl-4a,5,6,7,-7a,8-hexahydro-1*H*,3*H*-pyrazolo[1,5-*a*]pyrrolo[3,4-*d*]pyridine-2,3-dicarboxylate **26** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

JO070265X