Addition of Twisted 1,1-Bis(thioacyl)-2,2-diaminoethylenes to Dimethyl Acetylenedicarboxylate. Part I. Formation of New Thiopyrone Derivatives on Reaction in Acetonitrile Containing Traces of Water

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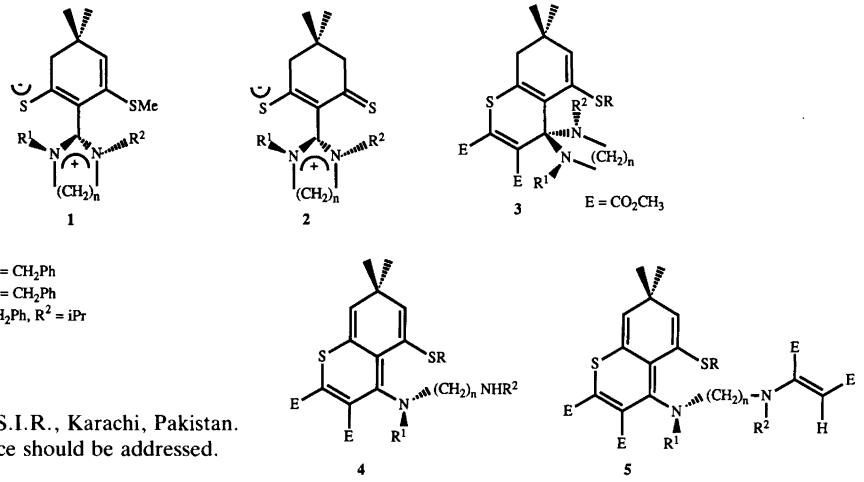
When 1,3-dialkyl-2-(4,4-dimethyl-2,6-dithioxocyclohexylidene)-1,3-diazacyclanes (**2**), which can be described as twisted push–pull ethylenes with thiocarbonyl groups as acceptors, react with dimethyl acetylenedicarboxylate (DMAD) in a 1:2 ratio in acetonitrile containing ca. 1 % of water, two types of product are isolated, which are completely different from those formed on reaction in carefully dried acetonitrile.

The major products, 1,3-dialkyl-2-(2-methoxycarbonyl-5,5-dimethyl-4,7-dioxo-5,6,7,8-tetrahydro-4*H*-benzo[*b*]thiopyran-8-ylidene)-1,3-diazacyclanes (**6**) are formed by addition of one molecule of DMAD to the 2-thione group followed by elimination of methanol to give a thiopyrone ring annellated in positions 2 and 3. The 6-C=S is changed to a C=O group. The minor products, 1,3-dialkyl-2-{2-methoxycarbonyl-5,5-dimethyl-7-[(*E*)- or (*Z*)-1,2-bis(methoxycarbonyl)vinylthio]-4-oxo-5,8-dihydro-4*H*-benzo[*b*]thiopyran-8-ylidene}-1,3-diazacyclanes (**7**) are formally 1:2 adducts of **2** and DMAD, which have eliminated methanol to give the same type of thiopyrone ring as in the major products, and have *E*- or *Z*-1,2-bis(methoxycarbonyl)vinylthio substituents in position 7. A sequence of reactions is proposed to account for the role of water in the formation of compounds **6** and **7**.

In other studies we have examined the reactions of sterically congested 1-thioacyl-2,2-diaminoethylenes (**1**)[1] and 1,1-bis(thioacyl)-2,2-diaminoethylenes (**2**)[2] with dimethyl acetylenedicarboxylate (DMAD). Compounds **1** and **2** are strongly twisted about the formal double bond and are therefore best described as betaines. When carefully dried toluene, dichloromethane or acetonitrile was used as the solvent, the products were thiopyran-4-spiro-2′-1′,3′-diazacyclanes (**3**) and compounds formed by opening of the diazacyclane ring (**4**) and further reaction with DMAD (**5**, Scheme 1).

When on one occasion a dilute solution of DMAD in undried acetonitrile (analytical grade, distilled, containing ca. 1 % water) was added in a molar ratio of 2:1 to a solution of **2a** in the same solvent, and the reaction mixture was worked up by column chromatography, a 77 % yield of a crystalline product was obtained with the molecular formula $C_{30}H_{30}N_2O_4S$ (**6a**, Scheme 2). This compound could have been formed by reaction between **2a** and DMAD in the molar ratio 1:1 with elimination of one molecule of methanol and replacement of one sulfur atom by an oxygen



a, n = 2, $R^1 = R^2 = CH_2Ph$
b, n = 3, $R^1 = R^2 = CH_2Ph$
c, n = 3, $R^1 = CH_2Ph$, R^2 = iPr

Scheme 1.

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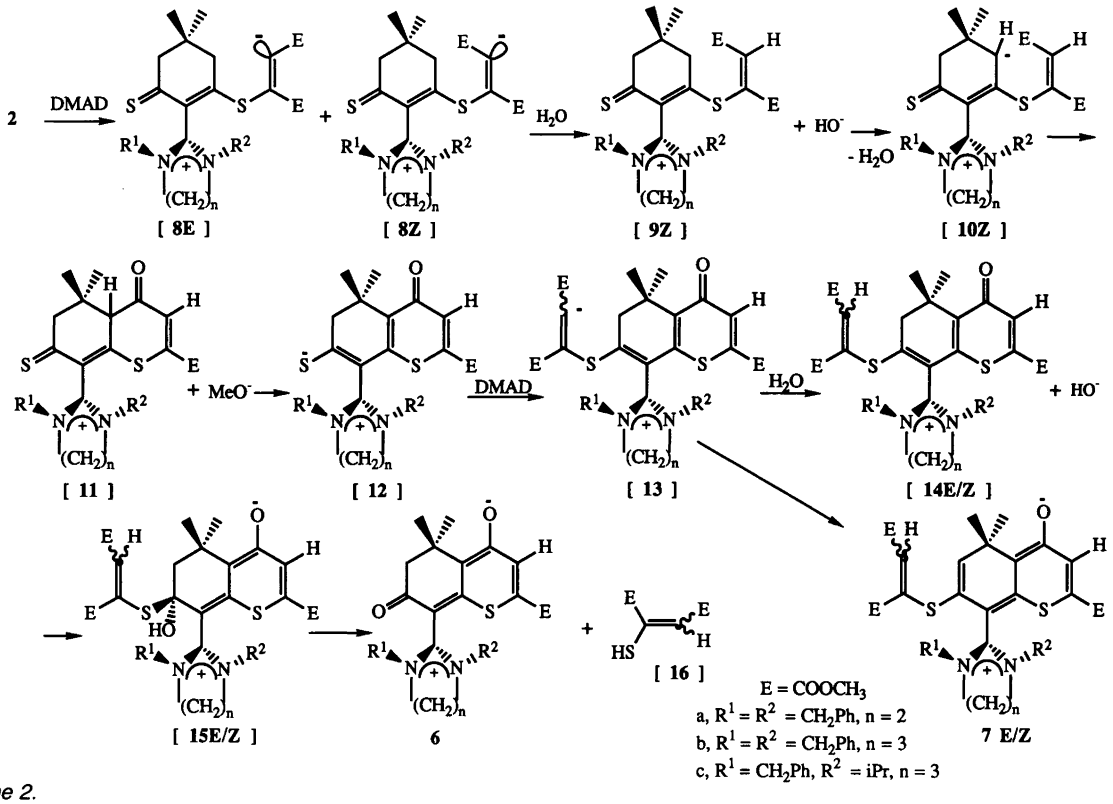


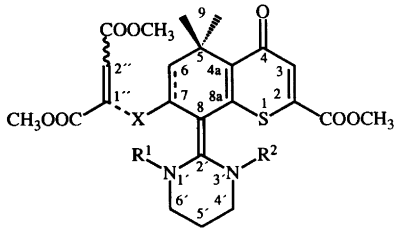
Scheme 2.

Table 1. ^{1}H and ^{13}C NMR chemical shifts for **6a**, **6b** and **6c** in $CDCl_3$. Singlets unless otherwise noted. For the numbering, see Scheme 3.

	6a	**6b**	**6c**
H-3	6.83	6.73	6.82
H-6	2.46	2.38	2,36, 2.40 (15.9)[a]
H-9	1.36	1.29	1.30, 1.38
H-4′, H-6′	3.57–3.62[b]	3.32 (m)	3.27 (m), 3.38 (m)
H-5′		1.85 (m)	2.05 (quint.)
$PhCH_2$	4.39, 4.56 (15.0)[a]	4.56, 4.76 (14.9)[a]	4.33, 4.85 (14.7)[a]
$(CH_3)_2CH$			1.23, 1.25 (6.6)[c]
$(CH_3)_2CH$			4.36 (6.6)[c]
CO_2CH_3	3.84	3.81	3.81
C-2	151.5	160.3	152.2
C-3	112.6	108.2	111.6
C-4	180.4	175.5	178.6
C-4a	116.5	111.7	114.9
C-5	34.1	30.4	34.1
C-6	52.4	48.3	52.7
C-7	189.6	185.4	188.8
C-8	89.8	93.5	97.7
C-8a	165.9	158.6	161.2
C-9	26.4	22.9	26.6
C-2′	164.0	170.7	163.2
C-4′, C-6′	45.5	41.5	39.0, 45.1
C-5′		16.8	19.8
$PhCH_2$	53.1	54.6	58.0
$(CH_3)_2CH$			20.16, 20.22
$(CH_3)_2CH$			54.6
CO_2CH_3	52.0	49.2	51.9
CO_2CH_3	168.1	164.2	168.1

[a] J_{AB}/Hz. [b] AA′BB′ system. [c] J_{A6X}/Hz.

atom. The product is quite different from those (**3–5**) formed from the same reagents in carefully dried solvents.[2] While compounds **1** reacted smoothly with one equivalent of DMAD to give the spiro compounds **3**, it was necessary to add three equivalents of DMAD to compounds **2** to achieve complete consumption of the starting material in dry solvents, and a 1:2 ratio of **2a** to DMAD was necessary for complete reaction in undried acetonitrile. This last observation indicates that **6a** may be preceded by an intermediate, which is a 1:2 adduct. In the chromatographic work-up, small amounts of two isomers, $\mathbf{7a}_1$ and $\mathbf{7a}_2$, were also isolated. These compounds have the molecular formula $C_{36}H_{36}N_2O_6S_2$, indicating that they are formed by elimination of methanol from a 1:2 adduct of **2a** to DMAD. They are labile and decompose in solution at room temperature. Analogous compounds, **6b**, **6c** and **7c**, were isolated from the reactions of **2b** and **2c** with DMAD in undried acetonitrile.



6 (X = O)
7 (X = S, ----)

Scheme 3.

The structures of compounds **6** and **7** follow from their ^1H and ^{13}C NMR spectra. In particular, **6c** has been studied by means of coupled ^{13}C spectra, selective decoupling, and the DEPT pulse sequence[3] to permit a complete assignment of all ^{13}C resonances (Table 1). It is evident that **2** adds to a DMAD molecule with one of its sulfur atoms and that the DMAD part gives rise to a 2-methoxycarbonyl-4-thiopyrone ring annellated to the cyclohexene ring with preservation of the 1,3-diazacyclan-2-yl substituent. The other sulfur atom is, during the course of the reaction, exchanged for oxygen. Compounds **7** contain the same diazacyclanyl-substituted cyclohexeno-thiopyrone skeleton as **6**, but also a 1,2-bis(methoxycarbonyl)vinylthio substituent and one more double bond in the C_6 ring. The isomerism observed in compounds **7a** is the *E*/*Z* isomerism in the substituent (Table 2).

Compounds **6** and **7** belong to the group of twisted push–pull ethylenes with high barrier to passage through the planar state.[4] In the time average the diazacyclane ring is

Table 2. ^1H and ^{13}C NMR chemical shifts for $\mathbf{7a}_1$, $\mathbf{7a}_2$ and **7c** in $CDCl_3$. Singlets unless otherwise noted.

	$\mathbf{7a}_1$ (*E*)	$\mathbf{7a}_2$ (*Z*)	**7c** (*Z*)
H-3	6.71	6.70	6.78
H-6	5.72/5.93	5.28	– [a]
H-9	1.59	1.48	1.77, 1.82
H-4′, H-6′	3.52–3.64 [b]	3.55 [c]	3.38 (m), 3.44 (m)
H-5′			2.10 (m)
H-2″	5.93/5.72	6.50	– [a]
Ph*CH*$_2$	4.49, 4.64 (14.9) [d]	4.66, 4.70 (14.8) [d]	4.63, 4.73 (14.5) [d]
(*CH*$_3$)$_2$CH			1.28, 1.30 (6.7) [e]
(CH$_3$)$_2$*CH*			4.49 (6.7) [e]
CO_2CH_3	3.44, 3.82, 3.92	3.64, 3.82, 3.84	3.78, 3.92, 3.95
C-2	155.1	153.1	152.5
C-3	108.7	108.3	108.8
C-4	168.6	168.8	168.4
C-4a			128.6
C-5	39.4	39.0	39.5
C-6	114.1	121.0	125.2
C-7	– [f]	– [f]	140.1
C-8	– [f]	– [f]	– [f]
C-8a	– [f]	– [f]	– [f]
C-9	28.1	27.9	26.8, 26.9
C-2′	– [f]	– [f]	– [f]
C-4′, C-6′	45.3	45.1	39.5, 45.8
C-5′			20.5
C-1″	– [f]	– [f]	– [f]
C-2″	145.3	137.9	– [g]
Ph*CH*$_2$	53.3	53.1	58.6
(*CH*$_3$)$_2$CH			20.5, 21.1
(CH$_3$)$_2$*CH*			55.5
CO_2CH_3	51.7, 51.7, 52.9	51.7, 52.1, 52.8	51.6, 52.2, 52.9
*C*O$_2$CH$_3$	163.7, 164.0, 166.0	164.5, 165.1, 165.7	160.1, 161.4, 167.6

[a] In region of aromatic CH. [b] AA′BB′ system. [c] Accidental equivalence. [d] J_{AB}/Hz. [e] J_{A_6X}/Hz. [f] Not identified. [g] One of four CH resonances in the range 128.1–129.3 ppm.

Table 3. UV spectra of compounds **6** and **7** in ethanol.

Compound	λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})
6a	492 (10000), 363 (21000), 293 (6000), 241 (17500), 205 (25000)
6b	498 (6500), 364 (13100), 300 (5200), 233 (18500)
6c	496 (10200), 364 (19200), 302 (4900), 265 S[a] (5600), 231 (19500), 208 S (21000)
7a$_2$	528 (14200), 360 (13500), 298 (12200), 239 (25000), 203 (42000)
7c	555 (12100), 395 (5600), 364 (10250), 314 S (4800), 284 (6800), 224 (19600)

[a]S = shoulder.

perpendicular to the cyclohexene/cyclohexadiene ring. This follows from the benzylic methylene ^{1}H resonances, which appear as *one* AB system for all compounds, and from the *C*-methyl ^{1}H resonances, which give singlets in the spectra of **6a**, **6b** and **7a** and symmetrical doublets in the spectra of **6c** and **7c**. *N*-Isopropyl methyl resonances of **6c** and **7c** are doublets of doublets.

A reaction pathway, which explains the formation of compounds **6** and **7** and which accounts for the effect of traces of water in the solvent is proposed in Scheme 2. The first step is the addition of a sulfur atom in **2** to a DMAD molecule to give a vinyl carbanion (**8**), which probably exists as a mixture of rapidly equilibrating stereoisomers (**8***E* and **8***Z*).[5,6] The same carbanion has been suggested as an intermediate in the reaction of **2** with DMAD in dry solvents,[2] but there it preferentially abstracts a proton from the neighbouring cyclohexene methylene group. Since both *E* and *Z* products are formed, inter- and intra-molecular proton abstraction may occur. In undried acetonitrile, however, protonation of **8***Z* by water leading to **9***Z* seems more feasible. The structure of the amidinium hydroxide **9** has some similarity to that of the salt formed by reaction of **2** with methyl iodide.[1] This methiodide is deprotonated already in aqueous sodium hydrogencarbonate solution, and deprotonation of **9***Z* by OH^- followed by Claisen condensation to give **11** therefore seems feasible. A new deprotonation gives the betaine **12**, in which the thiolate sulfur atom can be expected to be strongly nucleophilic and to add rapidly to a second molecule of DMAD. The new vinyl anion **13** may undergo inter- or intra-molecular proton transfer to give **7***E* and **7***Z* or, more importantly, be protonated by water to give the amidinium hydroxide **14**. This can be seen as a vinylogous thiocarboxylate and should be hydrolysable to give **6**, the major product of the reaction.

Compounds **6** and **7** contain extended conjugated systems, and as a consequence they display absorption bands well within the visible range (Table 3). The difference between the spectra of **6a** and **6b/6c** shows that the size of the diazacyclane ring has an effect on the spectrum, possibly by influencing the torsion angles about the formal double bond. A similar difference is observed between the spectra of **7a** and **7c**. Compounds **6** (but not **7**) show strong red fluorescence.

Experimental

The preparation of the dithioxo compounds **2** used as starting materials has been described (**2a**, **2c**)[7,8] or will be published elsewhere (**2b**).[1]

Two molar equivalents of newly distilled DMAD as a 0.012 M solution in distilled but undried acetonitrile (Merck, *p.a.*) was added dropwise with stirring at ambient temperature to a 0.006 M solution of one molar equivalent of the appropriate dithioxo compound **2** in the same solvent. After 16 to 24 h TLC indicated that all starting material had been consumed, and the mixture was concentrated and subjected to flash chromatography[9] on silica (Merck 60).

*1,3-Dibenzyl-2-(2-methoxycarbonyl-5,5-dimethyl-4,7-dioxo-5,6,7,8-tetrahydro-4H-benzo[*b*]thiopyran-8-ylidene)imidazolidine* (**6a**) was obtained in 77 % yield as red prisms, m.p. 123–125 °C after recrystallization from toluene. For ^{1}H and ^{13}C NMR spectra, see Table 1. MS [CI-NH_3, *m/z* (%)]: 515 (M^+ +1, 100), 483 (9), 427 (20). Elemental analysis: $C_{30}H_{30}N_2O_4S + H_2O$.

The hexahydropyrimidine analogue **6b** was obtained in 65 % yield as red prisms, m.p. 110–112 °C after recrystallization from toluene. MS [70 eV]: 528 (M^+, 11), 513 (35), 91 (100). The 1-isopropyl-3-benzylhexahydropyrimidine analogue **6c** was obtained in 37 % yield as red plates, m.p. 103.5–105 °C after recrystallization from toluene. MS [16 eV]: 480 (M^+, 100), 465 (10), 91 (8), 58 (11).

On continued chromatography, *1,3-dibenzyl-2-{2-methoxycarbonyl-5,5-dimethyl-7-[(Z)-1,2-bis(methoxycarbonyl)vinylthio]-4-oxo-5,8-dihydro-4H-benzo[*b*]thiopyran-8-ylidene}imidazolidine,* **7a**$_2$ was obtained in 3 % yield as a dark mauve, semi-solid material. For ^{1}H and ^{13}C NMR spectra, see Table 2. MS [CI-NH_3]: 673 (M^+ +1, 10), 657 (20), 545 (12), 531 (42), 515 (70), 241 (40), 191 (46), 174 (100), 134 (30). The *E* isomer, **7a**$_1$, was obtained in 0.35 % yield. MS [CI-CH_4]: 673 (M^+ +1, 1.3), 577 (3), 547 (22), 533 (63), 518 (33), 517 (100), 516 (43), 515 (47), 427 (32).

The corresponding compounds from **2b** were formed in very low yields and could not be obtained pure, and from the reaction with **2c** only the *Z* isomer **7c**$_2$ was isolated in 5 % yield as a dark mauve solid, m.p. 110–113 °C. MS [CI-NH_3]: 639 (M^+ +1, 100), 595 (32), 581 (40), 549 (35), 449 (28), 207 (85), 164 (34), 158 (25).

^{1}H and ^{13}C NMR spectra were recorded with a Varian Model XL-300 NMR spectrometer, UV spectra with a Cary Model 2290 spectrophotometer, and mass spectra with Finnigan Model 4021 and JEOL Model SX-102 mass spectrometers.

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