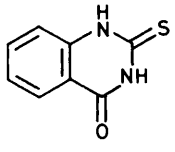
Synthesis and Structure Determination of Products from Addition of Dimethyl Acetylenedicarboxylate to 2,3-Dihydro-2-thioxoquinazolin-4(1*H*)-one. *X*-Ray Molecular Structure of the Dimethyl esters of 1,2-Dihydro-5-oxo-5*H*-thiazolo[3,2-*a*]quinazoline-1,2-dicarboxylic, 2,3-Dihydro-5-oxo-5*H*-thiazolo-[2,3-*b*]quinazoline-2,3-dicarboxylic, and 5-Oxo-5*H*-thiazolo[2,3-*b*]quinazoline-2,3-dicarboxylic Acids

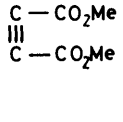
Libero Italo Giannola and Salvatore Palazzo
Istituto di Tecnologie Farmaceutiche dell'Università, via Archirafi 32, 90123 Palermo, Italy
Liliana Lamartina
Istituto di Chimica Farmaceutica e Tossicologica dell'Università, via Archirafi 32, 90123 Palermo, Italy
Ludovico Riva di Sanseverino and Piera Sabatino
Istituto di Mineralogia e Petrografia dell'Università, piazza Porta S. Donato 1, 40127 Bologna, Italy

The addition of dimethyl acetylenedicarboxylate to 2,3-dihydro-2-thioxoquinazolin-4(1*H*)-one afforded four main cycloadducts, the structures of which were unequivocally solved by ^{13}C n.m.r. spectroscopy and confirmed by *X*-ray crystallographic analysis. The products were identified as dimethyl 1,2-dihydro-5-oxo-5*H*-thiazolo[3,2-*a*]quinazoline-1,2-dicarboxylate, dimethyl 2,3-dihydro-5-oxo-5*H*-thiazolo[2,3-*b*]quinazoline-2,3-dicarboxylate, dimethyl 5-oxo-5*H*-thiazolo[2,3-*b*]quinazoline-2,3-dicarboxylate, and tetramethyl 2,2'-(1",2",3",4"-tetrahydro-4-oxo-2-thioxoquinazoline-1",3"-diyl)difumarate.

Recently we reported [1] that the addition of dimethyl acetylenedicarboxylate (DMAD) (**1**) to 3-thioxo-1,2,4-triazin-5-ones affords 2,6-disubstituted thiazolo[3,2-*b*][1,2,4]triazine-3,7-diones. The reaction offers a versatile approach to the synthesis of a variety of condensed heterocyclic systems containing a thiazole ring. The addition of DMAD (**1**) to 2,3-dihydro-2-thioxoquinazoline-4(1*H*)-one (**2**) was examined in order to study the pharmacological properties of the resulting compounds; it is reported [2] that 5*H*-thiazolo[2,3-*b*]quinazoline derivatives show good antihypertensive activities. Some derivatives also exhibit selective herbicidal activity.[3,4]

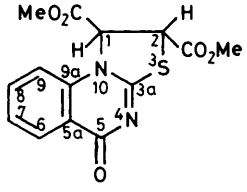


(**2**)

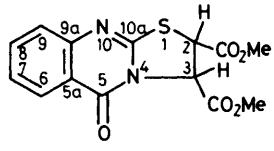


(**1**)

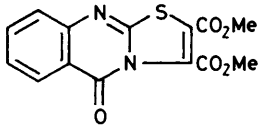
When compound (**2**) was allowed to react with DMAD in boiling methanol, it afforded five products, (**3**)—(**7**), the reaction being complete within a few hours. The analytical and molecular-weight data showed that both compounds (**3**) and (**4**) corresponded to 1 : 1 molar adducts (M^+, 320). The i.r. spectra of both compounds showed two carbonyl bands and the absorption of a strongly polar C=N double bond. The absence of NH bands both in the i.r. and in the ^1H n.m.r. spectra suggested that a cyclization had occurred to give products (**3**) and (**4**). In particular, the ^1H n.m.r. spectrum ($CDCl_3$) of product (**3**) exhibited two singlets for two OMe groups, two CH doublets (both with *J ca.* 1 Hz) at δ 4.73 and 6.10 respectively, besides a multiplet centered at δ 7.45 for three aromatic protons, and a double doublet at δ 8.47 (*J* 7.5 and 1.8 Hz) for the aromatic proton '*peri*' to the carbonyl group. A similar trend was observed in the ^1H n.m.r. spectrum of product (**4**) for both chemical shifts and coupling constants. The two compounds



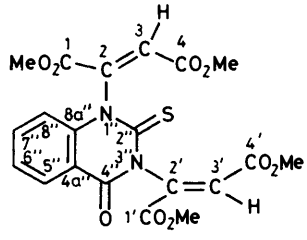
(**3**)



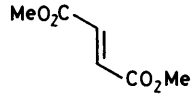
(**4**)



(**5**)

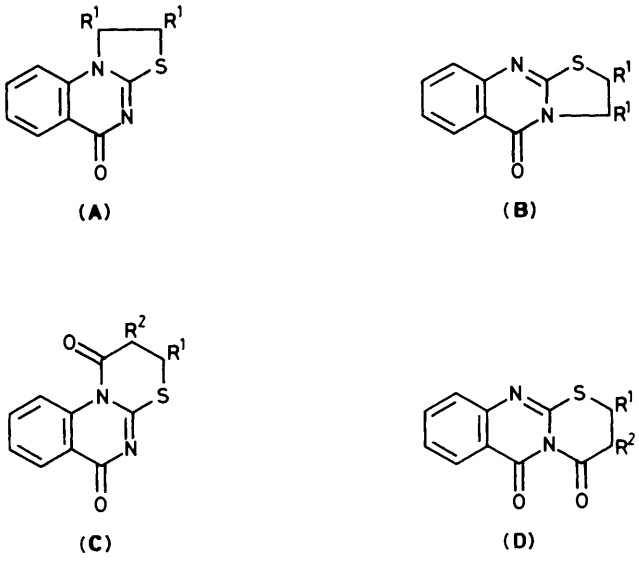


(**6**)



(**7**)

were similarly conjugated as indicated by their u.v. spectra which were of similar form, but which had different $\lambda_{max.}$ values. Thus, compounds (**3**) and (**4**) were isomers and the collected data were consistent with the possible structures (**A**) and (**B**) or (**C**) and (**D**). Structures C and D were ruled out by analysis of mass spectral data. The mass spectra of compounds (**3**) and (**4**), together with the typical fragmentations of compounds bearing



a quinazolinone nucleus[5] (peaks at *m/z* 145, 116, 102, and 90), showed the metastable peaks which supported consecutive loss of two methoxycarbonyl radicals:

$$M^+ \xrightarrow{-CO_2Me} m/z\ 261 \xrightarrow{-CO_2Me} m/z\ 202$$

The assignment of structure to the two isomers was made by ^{13}C n.m.r. spectral data from both proton-decoupled and off-resonance experiments. The ^{13}C n.m.r. spectrum of compound (**3**) [$(CD_3)_2SO$] showed six resonances without one-bond interactions; of these, the four at lower field near δ_C 167 p.p.m. were assigned to the two ester CO groups, C-5, and C-3a, and the other two resonances, at δ_C 139.03, and 116.96 p.p.m., to the sp^2 carbons C-9a and C-5a, respectively. Furthermore the spectrum exhibited signals for the C–H aromatic carbons at δ_C 134.25, 127.71, 125.83, and 116.09 p.p.m., together with two resonances for C–H alicyclic carbon atoms and only one signal for the methoxy groups. The ^{13}C n.m.r. spectrum of compound (**4**) [$(CD_3)_2SO$], when compared with that of (**3**), showed very similar resonance values for the alicyclic moiety, but marked differences in the resonances of the quinazolinone ring-carbon atoms. The C–H aromatic carbons were found at δ_C 135.36, 126.61, 126.29, and 126.16 p.p.m.; the C-5 and C-10a [C-3a of (**3**)] signals were shifted upfield by *ca.* 7 p.p.m. and that of C-9a downfield by *ca.* 9 p.p.m. The chemical-shift values of the C-5 carbonyl and C-9 carbon atoms appeared to be very significant and allowed us to assign structure (**A**) to the compound (**3**) and structure (**B**) to (**4**). Because the resonance for the carbonyl carbon is affected by the nature of the adjacent nitrogen,[1,6] the CO chemical shift at higher field is attributed to structure (**B**) having an adjacent sp^3 nitrogen, whereas the CO chemical shift at lower field is for structure (**A**) with an adjacent sp^2 nitrogen. On the other hand, the C-9 chemical-shift value of compound (**3**) (116.09 p.p.m.) is diagnostic in the assignment of structure (**A**). The presence of the sp^3 N-10 nitrogen atom shifts upfield the '*peri*' C-9 signal; this is in accord with the literature.[7] Therefore compounds (**3**) and (**4**) were identified as dimethyl 1,2-dihydro-5-oxo-5*H*-thiazolo[3,2-*a*]quinazoline-1,2-dicarboxylate and dimethyl 2,3-dihydro-5-oxo-5*H*-thiazolo[2,3-*b*]quinazoline-2,3-dicarboxylate, respectively. The geometry of the thiazolidine ring was fixed by the small value (*ca.* 1 Hz) of the vicinal coupling constant between the alicyclic C–H protons observed in the ^1H n.m.r. spectra of both compounds. It agrees with a *trans* diequatorial configuration of the aforementioned protons and was confirmed by *X*-ray analysis (see below).

Analytical data and the molecular weight (M^+, 318) of compound (**5**) suggested that it was a dehydrogenated derivative of the adducts (**3**) or (**4**). Other evidence supported this conclusion. As did those of adducts (**3**) and (**4**), the mass spectrum of compound (**5**) showed the typical quinazolinone system fragmentations, together with metastable peaks, which indicated consecutive loss of two methoxycarbonyl radicals, of markedly lower intensity. Both ^1H and ^{13}C n.m.r. spectra of compound (**5**) showed absence of the aliphatic CH signals. As above, the structure of dimethyl 5-oxo-5*H*-thiazolo[2,3-*b*]-quinazoline-2,3-dicarboxylate was assigned on the basis of the C-5 and C-9 chemical-shift values, similar to those of adduct (**4**).

Compound (**6**) was a 1:2 molar adduct of 2,3-dihydro-2-thio-oxoquinazolin-4(1*H*)-one and DMAD, as indicated by analytical and molecular-weight data. The ^1H n.m.r. spectrum ($CDCl_3$) showed singlets for four OMe groups and two vinyl protons, besides a multiplet for three aromatic protons and a double doublet for the aromatic proton '*peri*' to the carbonyl group. No signals exchangeable with D_2O were observed. Its ^{13}C n.m.r. spectrum [$(CD_3)_2SO$] exhibited a signal at δ_C 173.93 p.p.m. for a thiocarbonyl carbon, which compares well with that found for the thiocarbonyl carbon atom of compound (**2**).* The chemical shift of the C-4 carbonyl carbon at 157.76 p.p.m. indicated an adjacent sp^3 nitrogen atom. Furthermore, the chemical shifts of C-8″ and C-8a″, at δ_C *ca.* 116 and 140 p.p.m., respectively, indicated that N-1″ was an sp^3 nitrogen atom also. The compound was thus identified as tetramethyl 2,2′-(1″,2″,-3″,4″tetrahydro-4-oxo-2-thioxoquinazoline-1″,3″-diyl)difu-marate. The *trans* configuration of the methoxycarbonyl groups of the two side-chains was assigned by chemical-shift values of the CH system: δ_C *ca.* 127 p.p.m., δ_H *ca.* 7.15 and 7.30.[8]

Compound (**6**) was obtained as a mixture of rotational isomers about the RN bond as evidenced by multiple signals of methoxy groups in the ^1H n.m.r. spectrum, and by those of C-4a″, C-8″, C-2, C-2′, C-3, and C-3′ in the ^{13}C n.m.r. spectrum.

Finally, dimethyl fumarate (**7**) was isolated in small amounts. It was identified by comparison of physical and spectral data with those of an authentic pure sample.

The structure of compounds (**3**), (**4**), and (**5**) were confirmed unambiguously by *X*-ray crystallographic analysis.

Experimental

M.p.s were determined on a Büchi-Tottoli capillary apparatus and are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 983 G spectrophotometer for Nujol mulls, and u.v. spectra for methanolic solutions with a Perkin-Elmer model 200 spectrophotometer (methanol was dried with magnesium and distilled). ^1H N.m.r. spectra were recorded for $CDCl_3$ solutions (unless otherwise specified) at 60 MHz on a Varian EM-360 instrument, with $SiMe_4$ as internal standard. ^{13}C N.m.r. spectra at natural abundance were recorded in $(CD_3)_2SO$ solutions at 20 MHz on a Varian FT-80A pulsed Fourier transform spectrometer. The chemical shifts were measured from the central solvent peak and converted into the $SiMe_4$ scale by using the difference $\Delta\delta_C$ 39.60 p.p.m. between $(CD_3)_2SO$ and $SiMe_4$. All assignments were confirmed by off-resonance experiments. Mass spectra were run on a JEOL-JMS-01SG-2 double-focusing mass spectrometer operating with an electron-beam energy of 75 eV and an accelerating voltage of 10 kV. T.l.c.

* ^{13}C N.m.r. chemical shifts of (**2**) [$(CD_3)_2SO$]: δ_C 115.82 (d, C-8), 116.19 (s, C-4a), 124.31, 126.70, and 135.31 (each d, C-5, -6, and -7), 140.39 (s, C-8a), 159.57 (s, CO), and 174.31 p.p.m. (s, CS).

Table 1. Atomic co-ordinates ($\times 10^4$) for compound (**3**) with e.s.d.s in parentheses

Atom	*x*	*y*	*z*
S(1)	6 950(0.3)	2 944(0.4)	1 466(0.3)
N(2)	9 042(1)	2 079(1)	1 293(1)
C(3)	11 121(1)	1 547(2)	1 367(1)
C(4)	11 995(2)	482(2)	1 382(1)
C(5)	11 729(2)	−1 059(2)	1 324(1)
C(6)	10 594(2)	−1 528(2)	1 247(1)
C(7)	8 468(2)	−972(2)	1 142(1)
C(8)	9 187(1)	3 703(2)	1 476(1)
C(9)	7 968(1)	4 394(2)	1 189(1)
C(10)	7 955(1)	1 518(2)	1 320(1)
N(11)	7 624(1)	118(2)	1 253(1)
C(12)	9 968(1)	1 062(2)	1 300(1)
C(13)	9 687(1)	−479(2)	1 234(1)
C(14)	7 713(1)	4 837(2)	103(1)
O(15)	8 422(1)	4 831(2)	−453(1)
O(16)	6 597(1)	5 218(1)	−145(1)
C(17)	6 224(2)	5 704(3)	−1 154(1)
C(18)	9 668(1)	4 082(2)	2 554(1)
O(19)	10 019(1)	5 321(1)	2 803(1)
O(20)	9 617(1)	2 917(1)	3 154(1)
C(21)	9 949(2)	3 205(2)	4 205(1)
O(22)	8 167(1)	−2 285(1)	969(1)

for confirming compound purity utilized 0.25 mm silica gel plates (Merck) with fluorescent indicator and ethyl acetate–benzene (7:3) or ethyl acetate–methanol (8:2) solvent systems.

Addition of DMAD (**1**) *to* 2,3-*Dihydro*-2-*thio*-*oxoquinazolin*-4(1H)-*one* (**2**).—A solution of DMAD (**1**) (4.26 g, 0.03 mol) in warm methanol (20 ml) was gently added to a stirred suspension of the thione (**2**) (3.56 g, 0.02 mol) in methanol (200 ml). The mixture was refluxed and stirred for 3 h and then set aside overnight during which time crystals separated. The resulting crude mass was collected, washed with cold methanol, and recrystallized from methanol. Two recrystallizations were sufficient to produce an analytically pure sample of *dimethyl* 1,2-*dihydro*-5-*oxo*-5*H*-*thiazolo*[3,2-a]*quinazoline*-1,2-*dicarboxy*-ylate (**3**) (1.56 g, 20%) as crystals, m.p. 182—183 °C (Found: C, 52.6; H, 3.75; N, 8.7; S, 9.95. $C_{14}H_{12}N_2O_5S$ requires C, 52.5; H, 3.8; N, 8.75; S, 10.0%); $\nu_{max.}$ 1 740 (ester CO) and 1 665 cm^{-1} (amide CO); $\lambda_{max.}$ 316sh, 307, 248sh, and 238 nm; δ_H 3.90 (3 H, s, OMe), 3.93 (3 H, s, OMe), 4.73 (1 H, d, *J ca.* 1 Hz, 2-H), 6.10 (1 H, d, *J ca.* 1 Hz, 1-H), 7.00—7.90 (3 H, m, ArH), and 8.47 (1 H, dd, J_o 7.5, J_m 1.8 Hz, 6-H); δ_C 45.34 (d, C-2), 53.67 (q, OMe), 64.09 (d, C-1), 116.09 (d, C-9), 116.96 (s, C-5a), 125.83, 127.71, and 134.25 (d, C-6, -7, and -8), 139.03 (s, C-9a), and 166.36, 166.86, 167.11, and 168.95 (s, C-3a, -5, and ester CO); *m*/*z* 320 (M^+, 71%), 261 (100), 217 (97), 202 (15), 174 (27), 145 (27), 116 (12), 102 (7), and 90 (12).

From the methanolic mother liquors of reaction, after removal of compound (**3**) and a little evaporation, a product separated. It was collected, washed with a small amount of iced methanol, dried, and recrystallized twice from ethyl acetate and to afford *dimethyl* 2,3-*dihydro*-5-*oxo*-5H-*thiazolo*[2,3-b]*quinazoline*-2,3-*dicarboxylate* (**4**) (1.72 g, 22%) as crystals, m.p. 178—179 °C (Found: C, 52.65; H, 3.7; N, 8.75; S, 9.9%); $\nu_{max.}$ 1 730 (ester CO) and 1 690 cm^{-1} (amide CO); $\lambda_{max.}$ 324sh, 310, 284sh, 273, and 232 nm; δ_H 3.90 (6 H, s, 2 × OMe), 4.57 (1 H, d, *J* 1.4 Hz, 2-H), 6.05 (1 H, d, *J* 1.4 Hz, 3-H), 7.40—8.00 (3 H, m, ArH), and 8.35 (1 H, dd, J_o 7.5, J_m 1.8 Hz, 6-H); δ_C 44.75 (d, C-2), 53.55 (q, OMe), 62.02 (d, C-3), 118.51 (s, C-5a), 126.16, 126.29, 126.61, and 135.36 (d, C-6, -7, -8, and -9), 148.35 (s, C-9a), 157.41 and 159.09 (s, C-5 and -10a), and 167.11 and 169.03 (s, ester CO); *m*/*z* 320 (M^+, 57%), 261 (100), 217 (25), 202 (76), 174 (15), 145 (6), 116 (5), 102 (15), and 90 (21).

Table 2. Atomic co-ordinates for compound (**4**) ($\times 10^4$) with e.s.d.s in parentheses

Atom	*x*	*y*	*z*
S(1)A	1 619(2)	4 063(2)	1 106(2)
N(2)A	2 098(5)	3 556(6)	2 807(5)
C(3)A	2 551(6)	3 043(8)	4 301(6)
C(4)A	3 096(6)	3 177(9)	5 082(7)
C(5)A	3 735(6)	4 033(9)	5 180(6)
C(6)A	3 804(6)	4 705(9)	4 472(6)
C(7)A	3 371(5)	5 306(8)	2 935(6)
C(8)A	2 842(6)	5 616(7)	1 341(6)
C(9)A	1 964(5)	5 491(7)	798(6)
C(10)A	2 217(5)	4 186(8)	2 153(6)
N(11)A	2 808(4)	5 059(6)	2 180(4)
C(12)A	2 645(5)	3 719(7)	3 583(6)
C(13)A	3 280(5)	4 574(8)	3 666(6)
C(14)A	1 342(6)	6 372(8)	1 022(7)
O(15)A	1 426(5)	6 924(7)	1 687(5)
O(16)A	690(4)	6 473(6)	379(5)
C(17)A	52(7)	7 296(10)	522(8)
C(18)A	3 506(6)	5 142(7)	823(6)
O(19)A	3 574(4)	5 465(6)	101(4)
O(20)A	3 997(4)	4 350(5)	1 283(4)
C(21A)	4 633(6)	3 834(9)	832(6)
O(22)A	3 890(4)	6 090(6)	2 922(4)
S(1)B	3 444(2)	5 901(2)	7 719(2)
N(2)B	2 933(4)	6 481(6)	6 053(5)
C(3)B	2 430(6)	7 043(9)	4 549(7)
C(4)B	1 867(7)	6 945(9)	3 788(7)
C(5)B	1 231(7)	6 175(9)	3 714(7)
C(6)B	1 122(7)	5 438(10)	4 412(7)
C(7)B	1 608(6)	4 757(8)	5 926(6)
C(8)B	2 180(5)	4 361(7)	7 490(5)
C(9)B	3 052(5)	4 513(8)	8 050(6)
C(10)B	2 823(5)	5 809(7)	6 672(5)
N(11)B	2 206(4)	4 963(6)	6 675(4)
C(12)B	2 349(6)	6 348(8)	5 277(6)
C(13)B	1 701(6)	5 506(8)	5 192(6)
C(14)B	3 667(6)	3 569(8)	7 850(7)
O(15)B	3 602(4)	3 030(6)	7 185(5)
O(16)B	4 306(4)	3 450(6)	8 519(4)
C(17)B	4 955(6)	2 596(8)	8 395(7)
C(18)B	1 502(6)	4 832(8)	8 012(6)
O(19)B	1 481(5)	4 538(7)	8 738(5)
O(20)B	969(4)	5 533(6)	7 537(4)
C(21)B	272(7)	5 930(12)	7 944(8)
O(22)B	1 085(4)	3 984(6)	5 938(4)

Further evaporation of the mother liquors gave *dimethyl* 5-*oxo*-5H-*thiazolo*[2,3-b]*quinazoline*-2,3-*dicarboxylate* (**5**) (1.95 g, 25%), as crystals from methanol, m.p. 199—200 °C (Found: C, 52.9; H, 3.1; N, 8.75; S, 10.0. $C_{14}H_{10}N_2O_5S$ requires C, 52.85; H, 3.15; N, 8.8; S, 10.05%); $\nu_{max.}$ 1 740 (ester CO) and 1 695 cm^{-1} (amide CO); $\lambda_{max.}$ 384, 360, 305, 292, 282, and 250 nm; δ_H[$(CD_3)_2SO$] 3.90 (3 H, s, OMe), 3.96 (3 H, s, OMe), 6.90—8.00 (3 H, m, ArH), and 8.25 (1 H, dd, J_o 7.5, J_m 2.0 Hz, 6-H); δ_C 53.67 (q, OMe), 114.14 (s, C-2), 116.70 (s, C-5a), 126.09, 126.28, 126.78, and 135.94 (d, C-6, -7, -8, and -9), 132.20 (s, C-3), 147.40 (s, C-9a), 155.38 and 158.08 (s, C-5 and -10a), and 159.35 (s, ester CO); *m*/*z* 318 (M^+, 100%), 287 (27), 260 (6), 259 (3), 202 (3), 201 (2), 200 (1), 162 (6), 145 (1), 116 (2), 102 (13), and 90 (6).

The residual mother liquors were evaporated to dryness under reduced pressure. The resulting mixture was treated with boiling cyclohexane to remove soluble material. The solution was evaporated to give a crude solid material which was collected, washed with cyclohexane, dried, and recrystallized from benzene–cyclohexane (1:1). Two recrystallizations were

Table 3. Atomic co-ordinates for compound (**5**) ($\times 10^4$) with e.s.d.s in parentheses

Atom	*x*	*y*	*z*
S(1)	4 974(2)	3 718(2)	2 915(2)
N(2)	6 523(6)	3 794(7)	1 228(7)
C(3)	7 969(7)	3 751(9)	−278(9)
C(4)	8 282(8)	3 190(10)	−1 760(10)
C(5)	7 530(7)	2 170(10)	−3 185(10)
C(6)	6 379(7)	1 641(8)	−3 247(9)
C(7)	4 853(6)	1 652(8)	−1 788(9)
C(8)	3 450(6)	2 072(8)	22(8)
C(9)	3 569(7)	2 686(8)	1 683(9)
C(10)	5 466(6)	3 289(8)	1 142(9)
N(11)	4 549(5)	2 340(6)	−239(6)
C(12)	6 795(6)	3 249(7)	−276(9)
C(13)	6 005(6)	2 201(8)	−1 751(9)
C(14)	2 435(8)	2 732(9)	2 294(10)
O(15)	1 375(6)	2 222(7)	1 417(6)
O(16)	2 855(5)	3 390(7)	3 930(8)
C(17)	1 883(8)	3 549(12)	4 766(10)
C(18)	2 206(7)	1 391(9)	−1 456(9)
O(19)	1 377(5)	2 227(6)	−2 371(5)
O(20)	2 197(4)	−159(5)	−1 456(5)
C(21)	923(7)	−855(10)	−2 678(10)
O(22)	4 098(5)	718(6)	−2 945(7)

sufficient to give pure *tetramethyl* 2,2′-(1″,2″,3″,4″-*tetrahydro*-4-*oxo*-2-*thioxoquinazoline*-1″,3″-*diyl*)*difumarate* (**6**) (1.4 g, 18%) as pale yellow crystals, m.p. 134—135 °C (Found: C, 52.05; H, 3.8; N, 6.0; S, 6.85. $C_{20}H_{18}N_2O_9S$ requires C, 51.95; H, 3.9; N, 6.1; S, 6.95%); $\nu_{max.}$ 3 100infl (NH), 1 740 (ester CO), and 1 700 cm^{-1} (amide CO); $\lambda_{max.}$ 314, 278, and 234 nm; δ_H 3.62—3.84 (12 H, singlets, 4 × OMe), 7.15 (1 H, s, vinyl H), 7.30 (1 H, s, vinyl H), 6.91—7.67 (3 H, m, ArH), and 8.28 (1 H, dd, J_o 7.5, J_m 2.0 Hz, 5″-H); δ_C 52.39, 53.40, and 53.56 (q, OMe), 115.34 and 115.53 (s, C-4a″), 116.10 and 116.18 (d, C-8″), 125.84, 128.33, and 136.76 (d, C-5″, -6″, and -7″), 126.87, 127.10, 128.69, and 129.01 (d, C-3 and 3′), 135.91, 136.09, 136.59, and 137.01 (s, C-2 and -2′), 140.07 (s, C-8a″) 157.76 (s, C-4″), 161.30, 161.43, 162.18, and 162.54 (s, ester CO), and 173.93 (s, C-2″); *m/z* 462 (M^+, 25%), 431 (15), 403 (100), 285 (16), 202 (8), 170 (31), 145 (2), 116 (4), 115 (10), 102 (8), and 90 (11).

Finally, the cyclohexane solution from which compound (**6**) separated was evaporated to dryness under reduced pressure and the residue was treated with boiling n-pentane. After having cooled, the n-pentane solution gave a small amount of dimethyl fumarate (**7**); its purity was checked by t.l.c. The m.p. and spectral data of the compound were found to be identical with those of an authentic pure sample. The m.p. was undepressed when mixed.

*Crystallography.**—Tables 1, 2, and 3 contain atomic co-ordinates for compounds (**3**), (**4**), and (**5**), respectively. Figures 1—4 show *X*-ray molecular structures of compounds (**3**), (**4**), and (**5**). Bond lengths, bond angles, torsion angles, and thermal parameters are deposited as Supplementary Publication No. SUP 56628 (15 pp.).†

Crystal data of Compound (**3**). $C_{14}H_{12}N_2O_5S$, monoclinic, a = 11.578(1), b = 8.834(2), c = 13.660(2) Å, β = 99.06(1)°, V = 1 377.95 Å^3, Z = 4, D_c = 1.54 g cm^{-3}. Space group $P2_1/n$, μ(Mo-K_α) = 2.5 cm^{-1}.

Structure determination of compound (**3**). Intensities were collected on an Enraf-Nonius CAD-4 diffractometer using a

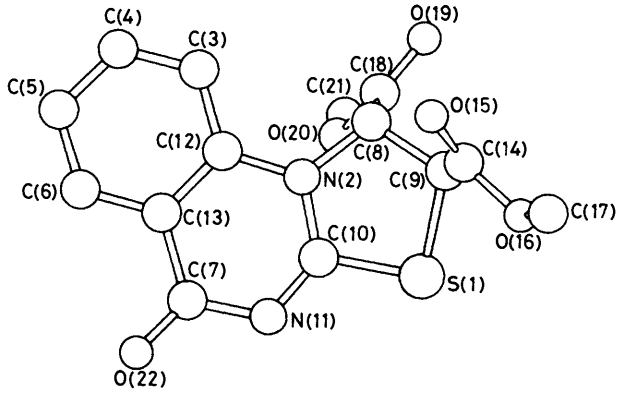


Figure 1. *X*-Ray molecular structure of dimethyl 1,2-dihydro-5-oxo-5*H*-thiazolo[3,2-*a*]quinazoline-1,2-dicarboxylate (**3**). View perpendicular to the plane defined by C(13), N(11), and N(2)

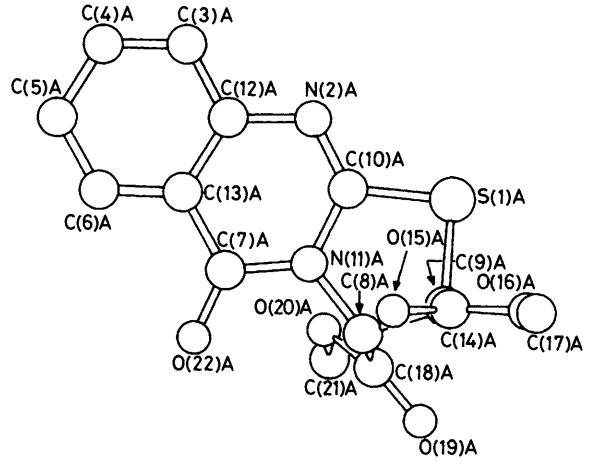


Figure 2. *X*-Ray molecular structure of dimethyl 2,3-dihydro-5-oxo-5*H*-thiazolo[2,3-*b*]quinazoline-2,3-dicarboxylate (**4**) (molecule A). View perpendicular to the plane defined by C(13)A, N(11)A, and N(2)A

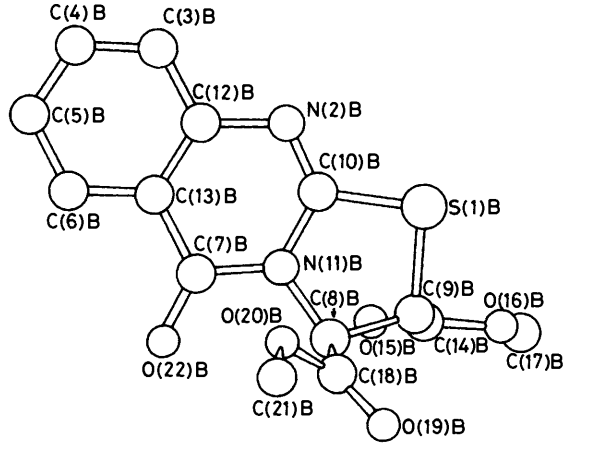


Figure 3. *X*-Ray molecular structure of dimethyl 2,3-dihydro-5-oxo-5*H*-thiazolo[2,3-*b*]quinazoline-2,3-dicarboxylate (**4**) (molecule B). View perpendicular to the plane defined by C(13)B, N(11)B, and N(2)B

* Crystallographic numbering used in this section and in Figures and Tables.

† For details of the Supplementary Publications Scheme, see Instructions for Authors (1986), *J. Chem. Soc., Perkin Trans. 1*, 1986, issue 1.

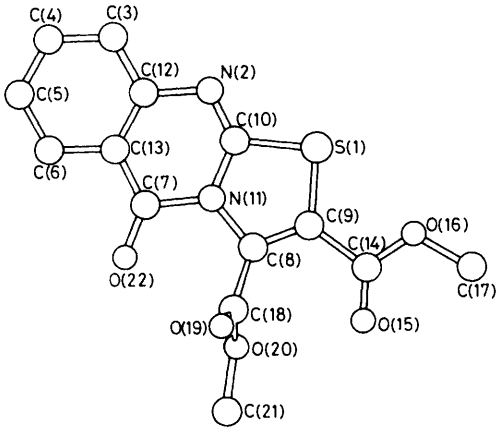


Figure 4. *X*-Ray molecular structure of dimethyl 5-oxo-5*H*-thiazolo-[2,3-*b*]quinazoline-2,3-dicarboxylate (**5**). View perpendicular to the plane defined by C(13), N(11), and N(2)

crystal of dimensions *ca.* 0.19 × 0.26 × 0.55 mm, and Mo-K_α radiation (λ = 0.7107 Å). 3 004 Unique reflections ($2° < \theta < 27°$) were measured, 2 414 of which, having $I > 3\sigma(I)$, were considered observed. Intensities were corrected for Lorentz and polarization effects, not for absorption. The structure was solved by direct methods (Multan 81).[9] Refinement by full-matrix least-squares, carried out using standard scattering factors,[10] yielded an *R* factor of 0.036 (R_w = 0.05). All calculations were done with the CAD-4-SDP suite of programs.[11] All non-hydrogen atoms were refined with anisotropic thermal parameters. The weighting scheme was $w^2 = 1/[\sigma^2(I) + (0.08\ F^2)^2]$.

The two observed short intermolecular contacts, C(9)···O(22) = 2.96 Å and C(14)···O(22) = 2.82 Å, fall into the donor–acceptor interactions described by Bent.[12]

Crystal data of compound (**4**). $C_{14}H_{12}N_2O_5S$, monoclinic, a = 16.019(3), b = 11.583(2), c = 15.420(5) Å, β = 98.33(2)°, V = 2 828.45 Å^3, Z = 8, D_c = 1.50 g cm^{-3}. Space group $P2_1/c$, μ(Mo-K_α) = 2.06 cm^{-1}.

Structure determination of compound (**4**). Intensities were collected on a Philips PW 1 100 four-circle diffractometer using the $\omega/2\theta$ scan technique with θ range $1° < \theta < 25°$ and graphite-monochromatized Mo-K_α radiation. The approximate sample dimensions were 0.15 × 0.30 × 0.7 mm. A total of 2 307 independent reflections was measured with intensities greater than 2.5-times their standard deviation. No absorption correction was applied. The structure was solved by direct methods with the SHELX 76 suite of programs.[13] A block-diagonal least-squares refinement was used for the two independent molecules until a final residual R = 0.089 (R_w = 0.094). Anisotropic temperature factors were applied to the S atoms and the methoxycarbonyl groups only. The weighting scheme was $w = 1.6767/(\sigma^2F_o + 0.006\,456F_o^2)$.

The two crystallographically independent molecules have inverted conformations of the two methoxycarbonyl groups.

Crystal data of compound (**5**). $C_{14}H_{10}N_2O_5S$, triclinic, a = 10.700(9), b = 8.483(7), c = 8.810(6) Å, α = 107.57(8)°, β = 114.12(9)°, γ = 75.58(8)°, V = 664.16 Å^3, Z = 2, D_c = 1.59 g cm^{-3}. Space group $P\bar{1}$, μ(Cu-K_α) = 22.17 cm^{-1}.

Structure determination of compound (**5**). Intensities were collected on a Philips PW 1 100 diffractometer using a crystal of *ca.* 0.22 × 0.35 × 0.75 mm. A total of 1 151 independent reflections (θ range $1° < \theta < 25°$) was measured. Intensities were corrected for Lorentz and polarization effects and for absorption. The structure was solved by direct methods using SHELX 76.[13] All non-hydrogen atoms were refined isotropically, except for S and the atoms of the two methoxycarbonyl groups, by block-diagonal least-squares. The weighting scheme used was $w = 1/(\sigma^2F_o + 0.048\,997F_o^2)$. The final residual R is 0.105, the high value having been attributed to the bad quality of the crystal used.

All crystallographic drawings were realized by using the program SCHAKAL.[14]

Acknowledgements

We thank Dr. Bianca Carlisi for the support given in the synthesis of compounds. Financial support by Ministero della Pubblica Istruzione (Rome) is gratefully acknowledged.

References

1 L. I. Giannola, G. Giammona, S. Palazzo, and L. Lamartina, *J. Chem. Soc., Perkin Trans. 1*, 1984, 2707.
2 K. C. Liu, J. W. Chern, M. H. Yen, and Y. O. Lin, *Arch. Pharm.*, 1983, **316**, 569 (*Chem. Abstr.*, 1983, **99**, 88155*g*).
3 G. Seybold and B. Wuerzer, Ger. Offen. DE 3 142 728 (*Chem. Abstr.*, 1983, **99**, P18106*t*).
4 G. Seybold and B. Wuerzer, Ger. Offen, DE 3 142 727 (*Chem. Abstr.*, 1983, **99**, P53778*k*).
5 L. I. Giannola, G. Giammona, B. Carlisi, and S. Palazzo, *J. Heterocycl. Chem.*, 1981, **18**, 1557.
6 J. Daunis, M. Follet, and C. Marzin, *Org. Magn. Reson.*, 1980, **13**, 330.
7 A. R. Katritzky, J. Ellison, J. Frank, P. Råkòczy, L. Radics, and E. Gàes-Baitz, *Org. Magn. Reson.*, 1981, **16**, 280.
8 R. M. Letcher and R. M. Acheson, *Org. Magn. Reson.*, 1981, **16**, 316.
9 P. Main, S. E. Hull, G. Germain, J. P. Declercq, and M. M. Woolfson, 'A System of Computer Programs for the Automatic Solution of Crystal Structures from *X*-ray Diffraction Data,' University of York, England and Louvain, Belgium, 1981.
10 International Tables for *X*-ray Crystallography, Kynoch Press, Birmingham, 1974, vol. IV.
11 D. A. Frenz, 'Computing in Crystallography,' eds. H. Schenk, R. Olthof-Hazekamp, H. van Koningsveld, and G. C. Bassi, University Press, Delft, 1978, p. 47.
12 H. A. Bent, *Chem. Rev.*, 1968, **68**, 587.
13 G. M. Sheldrick, SHELX 76. Program for Crystal Structure Determination, University of Cambridge, 1976.
14 E. Keller, SCHAKAL. A Fortran Program for the Graphical Representation of Molecular Models, University of Freiburg, 1982.

Received 21*st November* 1985; *Paper* 5/2051