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AN UNUSUAL REACTION BETWEEN THE ESTERS OF N-HYDROXY-2-THIOPYRIDONE AND ACTIVATED AZO COMPOUNDS†

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Abstract - The esters 1 of N-hydroxy-2-thiopyridone react smoothly at room temperature in a thermal reaction with diethyl azodicarboxylic ester to furnish adducts 2 of a novel structure. Photolysis of these adducts affords a convenient route to the little known tetrazanes 8. Azo compounds without electron withdrawing groups do not react. The Cookson reagent, however, is so reactive that it gives diacyl derivatives of type 14.

The esters of N-hydroxy-2-thiopyridone of general formula 1 are a useful source of carbon[1,2] and nitrogen radicals.[3] Carbon radicals produced in this way are "disciplined" by the thiocarbonyl group and thus can be used efficiently in synthesis.[1]. We have recently developed a method based on the radical chemistry of 1 which involves the removal of the carboxyl group and its replacement by another carboxyl group suitably labelled for biological studies.[4] It would also be convenient for the partial synthesis of potentially biologically active compounds to have a method to replace a carboxyl group by a nitrogen function under mild radical conditions. Such a method would be well adapted for the manipulation of the carboxyl of side chains of peptides.[5]

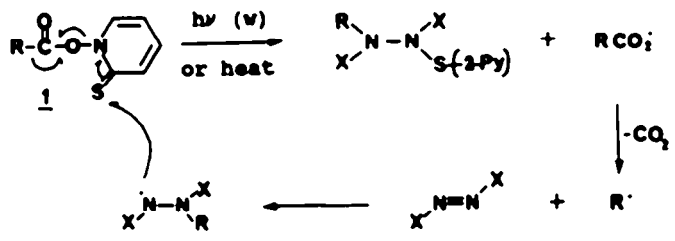
We planned, therefore, to examine the reactions of radicals generated from esters of formula 1 on the azo linkage. We could foresee the radical chain sequence outlined in Scheme 1.

In fact, we could not realize this Scheme because esters of type 1 react rapidly (in less than 1 hr.) with activated (electron deficient) azo groups at room temperature to furnish a new class of compounds of general formula 2. The reaction proceeded in the dark, hence it was not photolytic.

The reaction was discovered using diethyl azodicarboxylate 3 (X=CO_2Et). Reaction of an excess of this ester with a series of derivatives of 1 afforded the novel compounds 2. A second derivative of 3 (X=CO_2Et) was also formed and is the known[6] compound 4. The isolated yields of 2 were as follows: 2a (72%), 2b (78%), 2c (51%), 2d (70%), 2e (63%) and 2f (81%).

The chemical evidence for the general formula 2 was as follows. Hydrolysis of 2a with 1N sodium hydroxide afforded the parent hydrocinnamic acid (66%). Reduction with sodium in ammonia gave dihydrocinnamic acid amide.[7] There is precedent for this reaction.[8] Then, on the analogous palmitoyl compound 2b, the thiopyridine-N-oxide residue was removed with Raney Nickel in ethanol to furnish the amide 5 (70%) (See Experimental).

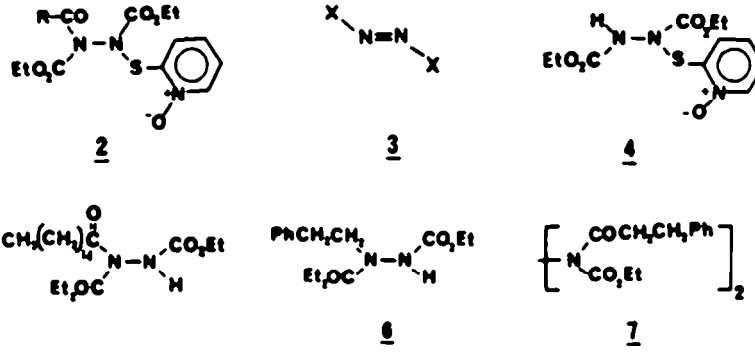
† Dedicated with appreciation to Professor M. J. S. Dewar on the occasion of his seventieth birthday.



Scheme 1

1, 2, 8, 14

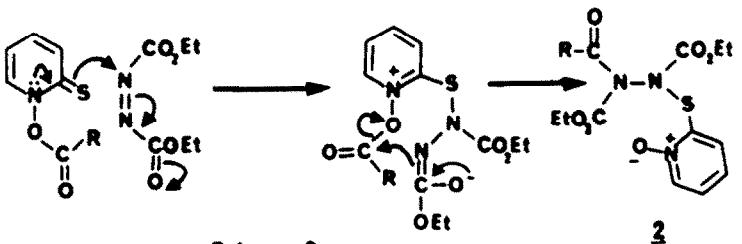
a. R = $PhCH_2CH_2$-
b. R = $CH_3(CH_2)_{14}$-
c. R = CH_2=CH-
d. R = CH_2=CH-CH_2-
e, R = Cyclohexyl-
f, R = 1-Adamantyl-



In the course of this work we synthesized the derivative of 1a that could have resulted from addition of the 2-phenylethyl radical to the azo-linkage. Thus the appropriate Grignard reagent was added to 3 (X=CO_2Et) using cuprous iodide as catalyst to afford the desired compound 6 in reasonable (60%) yield. There is good precedent for this addition.[9] With this compound in hand we could, of course, check that it did not afford any dihydrocinnamic acid on hydrolysis.

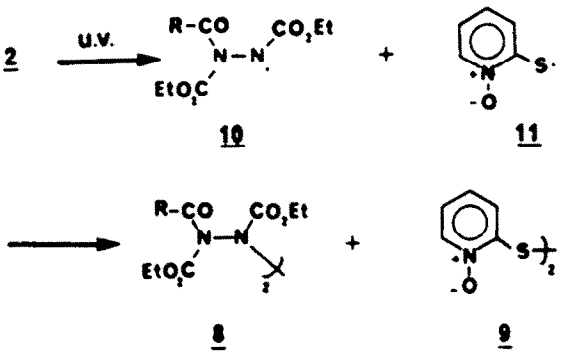
Treatment of 1,2-dicarbethoxyhydrazine with base and palmitoyl chloride afforded the same compound 5 (71%) as was formed by the Raney Nickel reduction of 2b (see above). Similarly, reaction with base and an excess of dihydrocinnamoyl chloride gave the bis-derivative 7.

N-Hydroxy-2-thiopyridone itself did not react with 3 (X=CO_2Et) and azobenzene 3, (X=Ph) was also unreactive towards several compounds of type 1. The reaction to give 2 is not effected by tungsten light and so it clearly is not a radical reaction. It can be represented by the ionic type process shown in Scheme 2. Electron donation from the thiocarbonyl group is the key factor which initiates the process.



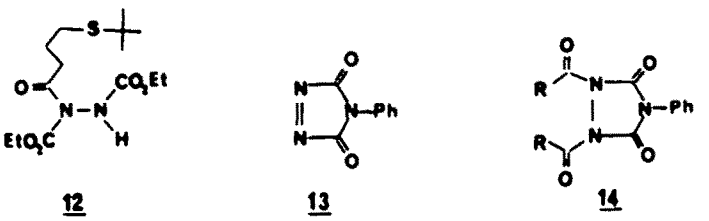
Scheme 2

Further evidence for the presence of a sulfur-nitrogen bond in compounds 2 came from photolysis experiments. Irradiation of compounds 2b, 2c, 2d, 2e and 2f in acetonitrile with a medium pressure mercury lamp at room temperature furnished in isolated yields of 72, 64, 78, 70, and 67% the corresponding dimers 8b, 8c, 8d, 8e and 8f respectively as well as the expected disulfide[10] 9. Clearly the weak sulfur-nitrogen bond has photolyzed (Scheme 3) to give N(10) and S(11) radicals, each of which has dimerized. The dimers of type 8 are astonishingly stable to heat. Indeed, this type of compound has already been described in the literature in the seminal work of Cadogan[11].



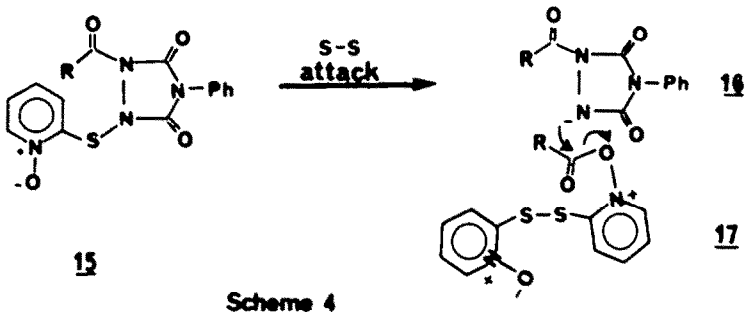
Scheme 3

Photolysis of ester 2d in the presence of *t*-butylthiol afforded the reduced adduct 12 (67%). There was no sign of ring closure. A ring closure reaction was not expected since it would have been the transformation of a stabilized radical to a less stabilized radical.



Finally, the reaction of esters of type 1 with the Cookson reagent[12] 13 was studied. Again we were surprised to obtain diacyl derivatives 14a, 14e and 14f in yields of 58, 50 and 80% (n.m.r.) respectively from 1a, 1e and 1f. In addition, the disulfide 9 was produced quantitatively.

The previously proposed mechanism (Scheme 2) can readily be adapted to explain the observed products. Thus (Scheme 4), the first step is the formation of the adduct 15 which then reacts with a second molecule of the ester 1 as indicated in Scheme 4. Thus the thione function of 1 attacks the sulfur of 15 to give the anion 16 and the cation 17. Mutual interaction affords the observed products 14 and the disulfide 9.



Scheme 4

Experimental

Proton and ^{13}C-n.m.r. spectra were recorded with a Varian XL-200E spectrometer for $CDCl_3$ solutions (δ scale, TMS as internal standard.) Mass spectra (70 ev.; electron impact) were obtained using a Hewlett-Packard 5995C quadrupole gc-ms instrument. Positive ion FAB spectra were recorded with a VG Analytical 70S high resolution double focusing magnetic sector mass spectrometer with attached VG Analytical 11/250J data system. FAB measurements were performed in a m-nitrobenzyl alcohol (Aldrich, 95%) matrix using argon as a bombarding gas at 6-8 Kev energy. The ir spectra were measured with a Perkin-Elmer 881 spectrometer; only the most significant absorptions are listed. The UV spectra were recorded on a Beckmann DU-7 spectrometer. Microanalyses were performed at the Center of Trace Characterization, Texas A&M University. Melting points are determined on a Kofler hot stage and are uncorrected. N-Hydroxy-pyridine-2-thione was prepared from the 40% aqueous solution of its sodium salt (trade name: sodium omadine from the Olin Corp.)

General Procedures for the Preparation of Thiohydroxamic Esters 1:

All these experiments were performed under an inert atmosphere in dry solvents and the reaction vessel was wrapped with aluminum foil.

a) A solution of the carboxylic acid (0.82 mmol) in C_6H_6 (2 ml) and 1 drop of DMF was treated with oxalyl chloride (0.18 ml, 2.1 mmols). One hour after the evolution of gas ceased, the solvent and excess of oxalyl chloride were evaporated at reduced pressure. N-Hydroxy-2-thiopyridone (0.11 gr, 0.86 mmols) in C_6H_6 (2 ml) was added dropwise followed by a solution of pyridine (70 µl, 0.86 mmol) in C_6H_6 (0.2 ml). The cooling bath was removed and stirring continued for 2 hrs. The reaction mixture was diluted with C_6H_6, filtered and concentrated at reduced pressure. The residue was purified by chromatography on silica and then recrystallized from hexane/CH_2Cl_2 where appropriate.

b) N-Hydroxy-2-thiopyridone (10.5 mmols) was dissolved in CH_2Cl_2 (15 ml) and the solution was cooled to 0-5°C. The carboxylic acid (10.5 mmols) was then added followed by dicyclohexylcarbodiimide (DCC) (2.3 g, 11 mmols). After 10 mins., the cooling bath was removed and the stirring was continued for an additional hour at room temperature. The reaction mixture was then filtered and the precipitate was washed with CH_2Cl_2 (15 ml). This solution of thiohydroxamic acid ester in CH_2Cl_2 (30 ml) was used in the next step. The data are summarised in the Table.

Table

Ester	Yield (%)	Procedure	M.p.(°C)	Lit.(Ref.)
1a	90	a	134-135	134-135 (4)
1b	87	a	74- 76	74- 76 (4)
1c	70	b	--	
1d	80	b	--	
1e	91	a	110	110 (13)
1f	85	a	165-166	165 (13)

Reaction Between Thiohydroxamic Esters 1 and Diethyl Azodicarboxylic Ester (DEAD):

Typical procedure: The thiohydroxamic ester 1 (2 mmols) was dissolved in CH_2Cl_2 (5-8 ml), DAD (8.7 g, 50 mmol) was added and the reaction mixture was stirred at room temperature (15-20°C) until completion (t.l.c.) (less than 1 hr.). The solvent was evaporated off and the reaction mixture was filtered over silica (C_6H_6 then EtOAc). Most of the DAD was recovered at this stage whereas the pure derivative 2 was isolated by chromatography over silica gel (EtOAc).

2a: mp. 115-117°C; ν (CH_2Cl_2): 1750 (broad), 1280 cm^{-1}; δ ^1H: 8.10 (1H,d), 7.65 (1H,s), 7.31 (1H,t), 7.23-7.05 (6H,m), 4.25 (2H,q), 4.22 (2H,q), 3.19 (2H,t), 2.94 (2H,t), 1.31 (3H,t), 1.20 (3H,t); δ ^{13}C: 172.0, 155.9, 152.1, 140.2, 137.2, 128.4, 128.3, 126.4, 126.2, 122.4, 121.5, 64.9, 64.6, 39.0, 30.6, 14.3, 14.1; m/z (%): 433 (8.8) M+, 133 (16.6), 127 (30.1), 105 (75.5), 91 (100); FAB m/z (%): 434 (33.3) M+1, 302 (27.7), 128 (79), 105 (100), 91 (71).

2b: mp. 64-65°C, ν (CH_3CN): 1745, 1258 cm^{-1}; δ ^1H: 8.11 (1H,d), 7.90 (1H,s), 7.34 (1H,t), 7.12 (1H,t), 4.24 (2H,q), 4.22 (2H,q), 2.88 (2H, oct.), 1.61 (2H,m), 1.30 (3H,t) 1.29-1.15 (27H,m), 0.83 (3H,t); δ ^{13}C: 172.8, 155.7, 152.2, 137.2, 126.6, 122.5, 121.5, 64.8, 64.6, 37.3, 31.9, 29.6-29.0, 24.6, 22.7, 14.3, 14.2, 14.1; m/z (%): 539 (0.5) M+, 414 (1.1) 239 (24.5), 176 (100), 128 (41.2).

2c: pale yellow oil, ν ($CHCl_3$): 1739, 1290 cm^{-1}; δ ^1H: 8.10 (1H,d), 7.80 (1H,s), 7.29 (1H,t), 7.05 (1H,t), 6.97 (1H,dd), 6.32 (1H,d), 5.71 (1H,d), 4.21 (2H,q), 4.12 (2H,q),1.21 (3H,t), 1.10 (3H,t); δ ^{13}C: 165.2, 155.3, 152.0, 137.2, 131.5, 129.9, 126.9, 122.1, 121.7, 64.8, 64.7, 14.2, 14.0; FAB m/z (%): 356 (91.8) M+1, 355 (3.7), 302 (6.7), 182 (100), 128 (71.7).

2d: yellow oil, ν ($CHCl_3$): 1745, 1276 cm^{-1}; δ ^1H: 8.05 (1H,d), 7.80 (1H,s), 7.27 (1H,t), 7.04 (1H,t), 5.83 (1H,m), 5.12 (1H,s), 5.04 (1H,d), 4.22 (2H,q), 4.15 (2H,q), 3.59 (2H,m), 1.22 (3H,t), 1.10 (3H,t); δ ^{13}C: 171.3, 155.5, 152.6, 137.7, 130.2, 127.2, 122.9, 122.1, 119.5, 65.1, 64.9, 42.0, 14.4, 14.3; FAB m/z (%): 370 (95) M+1, 369 (16.6), 302 (75.4), 128 (100).

2e: colorless oil, ν (CH_2Cl_2): 1750, 1280 cm^{-1}; δ ^1H: 8.10 (1H,d), 7.85 (1H,s), 7.32 (1H,t), 7.09 (1H,t), 4.28 (2H,q), 4.20 (2H,q), 3.33 (1H,tt), 1.97-1.65 (5H,m), 1.45-1.23 (5H,m), 1.31 (3H,t), 1.19 (3H,t); δ ^{13}C: 175.8, 155.5, 152.1, 137.2, 126.7, 122.4, 121.4, 64.7, 64.4, 44.2, 29.2, 25.7, 25.4, 14.2, 14.1; m/z (%): 127 (14.8), 111 (61.7), 83 (100). Because of the instability of this compound, a good microanalysis could not be obtained.

2f: mp. 60-62 °C, ν (CH_2Cl_2): 1750, 1278 cm^{-1}; δ ^1H: 8.10 (1H,d), 7.62 (1H,d), 7.31 (1H,t), 7.09 (1H,t), 4.27 (2H,q), 4.22 (2H,q), 1.99 (6H,s), 1.96 (3H,s), 1.64 (6H,s), 1.30 (3H,t), 1.21 (3H,t); δ ^{13}C: 182.1, 155.9, 153.0, 137.4, 126.7, 121.9, 121.4, 64.8, 64.2, 45.6, 38.1, 36.2, 28.1, 14.3, 14.2; m/z (%): 463 (0.3) M+, 163 (55.7) 136 (100) 127 (19.5). (Calc. for $C_{22}H_{29}N_3O_6S$: C: 57.00, H: 6.30, N:9.06 Found: C: 56.56, H:5.87, N:9.16%).

Alkaline Hydrolysis of Amide 2a:

To a solution of the hydrazide 2a (0.295 g; 0.68 mmol) in ethanol (20 ml) was added a 3N aqueous solution of NaOH (5 ml). The reaction mixture was stirred overnight at R.T. and then neutralized (H_2SO_4). The precipitate of Na_2SO_4 was filtered off, washed with ethanol, then the solvents were removed under vacuum. The white residue obtained was taken up in C_6H_6, filtered and the solvent was evaporated to furnish dihydrocinnamic acid, 66 mg (66%).

Reduction of the Derivative 2a with Sodium in Liquid Ammonia:

The hydrazine 2a (0.28 g; 0.64 mmol) was dissolved in dry Et_2O (3 ml) and dry ammonia (40 ml)at -80°. Small lumps of Na metal were added (under reflux) until a permanent blue color persisted. The blue color was maintained during 1 hr. additional reflux. Then the reaction mixture was treated with an excess of NH_4Cl (added in portions) and the solvent was allowed to evaporate. The residue was taken up in ethyl acetate, filtered and the ethyl acetate was removed under vacuum. The amide was isolated by prep. t.l.c. on silica (EtOAc): 48 mg (50%). This compound had identical spectral data to those reported in the literature.[7]

Cleavage of the N-S Bond by Reduction of 2b with Raney Nickel:

The hydrazine derivative 2b (0.62 g, 1.15 mmol) was dissolved in EtOH (5 ml). This well-stirred solution was treated with an excess of Raney Nickel and the stirring was continued overnight at R.T. The reaction mixture was then filtered and the solvents were removed under vacuum. The residue was dissolved in Et_2O, washed with water and dried over $MgSO_4$. Evaporation of the solvent furnished the compound 5 as a white solid, 0.33 g (70%). This compound was identical in all respects with an authentic sample.

Preparation of the Hydrazine Derivative 5:

To a solution of hexamethyldisilazane (HMDS) (0.26 ml; 1.23 mmol) in THF (2 ml) cooled at -20°C, n-BuLi (sol. 1.6 M in hexane; 1.23 mmol) was added dropwise and the solution stirred at -20°C for 30 min. 1,2-Dicarbethoxyhydrazine (0.35 g; 1.98 mmol) dissolved in THF (3 ml) was then added and the cooling bath was removed. To this solution, palmitoyl chloride (1.50 ml; 5.20 mmol) was quickly added. A precipitate formed. When this precipitate had disappeared, the reaction mixture was treated with an excess of aqueous NH_4Cl (saturated sol.) and extracted with ether. The combined extracts were dried over $MgSO_4$. Evaporation of the solvent furnished a white precipitate which was dissolved in ether (3 ml) and triethylamine (0.7 ml, 5.2 mmol) and then chromatographed on silica (Et_2O). Evaporation of the solvent gave the compound 5 as a white solid; 0.36 g (71%); mp: 50-53°C, ν ($CHCl_3$): 3405, 1740 cm^{-1}; δ ^1H: 6.47 (1H,s), 4.23 (2H,q), 4.19 (2H,q), 2.92 (2H,t), 1.63 (2H,m), 1.45-1.25 (30H,m), 0.84 (3H,t); δ ^{13}C: 171.8, 151.9, 63.7, 36.8, 31.9, 29.6, 29.5, 29.4, 29.3, 29.0, 24.5, 22.6, 14.4, 14.1; m/z (%): 415 (35.6) M+1, 414 (4.3), 239 (43.7) 176 (100); HR-MS m/z=415.31656 [Calc. for $C_{22}H_{43}N_2O_5$ (M^++1): 415.31720].

Preparation of the Hydrazine Derivative 6:

The Grignard reagent, prepared from $PhCH_2CH_2Br$ (2.71 g, 14.6 mmol) and Mg turnings (0.45 g) in Et_2O (10 ml), was added to a solution of Cu_2I_2 (0.27 g; 1.4 mmol) in dimethyldisulfide (2 ml) and ether (7 ml) cooled at -68°C. The reaction mixture was stirred for 5 min., then DAD (2.5 ml; 15 mmols) in Et_2O (5 ml) was added dropwise. At the end of the addition, the reaction mixture was diluted with ether (50 ml) and the temperature was allowed to rise to room temperature. Then the reaction was quenched with aqueous NH_4Cl (10%). The ether layer was washed with NH_4Cl, then with water and dried ($MgSO_4$). After concentration, the residual yellow oil was taken up in hexane and extracted with CH_3CN. The solvent was removed under vacuum and the product was isolated by chromatography on silica (hexane/CH_2Cl_2/Et_2O 50:40:1 to give 2.4 g (60%) of a colorless oil 6: ν ($CHCl_3$): 3402, 1752, 1708 cm^{-1}; δ ^1H: 7.35-7.20 (5H,m), 6.46 (1H,s), 4.21 (2H,q), 4.15 (2H,q), 3.76 (2H,t), 2.90 (2H,t), 1.26 (3H,t), 1.22 (3H,t); δ ^{13}C: 156.3, 138.6, 128.7, 128.5, 126.4, 62.4, 62.1, 51.6, 33.9, 14.4; m/z (%): 281 (10.4) M+1, 280 (12.4), 235 (62.9), 207 (57.5), 105 (30), 89 (100), (Calc. for $C_{14}H_{20}N_2O_4$: C: 59.98; H:7.19; N:9.99; Found: C: 60.15; H:7.36; N:9.53%).

Preparation of the Hydrazine Derivative 7:

To a suspension of NaH (2.98 mmol) in THF (2 ml) at room temperature, a solution of 1,2-dicarbethoxyhydrazine (0.50 g; 2.84 mmol) in THF (4 ml) was added. When H_2 evolution ceased, the dihydrocinnamoyl chloride (3.1 mmol) in THF (3 ml) was added. The reaction mixture was stirred at room temperature for 15 min., then treated with an aqueous solution of NH_4Cl (20%), extracted with ether and the combined extracts were dried over $MgSO_4$. The solvent was removed under vacuum, and the residual solid was taken up in C_6H_6, filtered and the filtrate washed with an aqueous solution of NaOH (7%). Evaporation of the solvent furnished 7 as a white solid, 0.36 g (54%): mp: 70-72°C, ν ($CHCl_3$): 1749 cm^{-1}; δ ^1H: 7.35-7.25 (10H,m), 4.21 (4H,q), 3.33 (4H,t), 3.00 (4H,t), 1.21 (6H,t); δ ^{13}C: 171.0, 151.8, 140.5, 128.5, 128.4, 126.2, 64.0, 38.5, 30.5, 14.0; m/z (%): 440 (0.5) M+, 176 (22.1), 133 (11.7), 105 (48), 104 (49.3), 91 (51), 29 (100) (Calc. for $C_{24}H_{28}N_2O_6$: C:65.44; H:6.41; N:6.36. Found: C:65.08; H:6.42; N:6.20%)

Photolysis of Compounds 2 to Furnish Tetrazanes 8:

The hydrazine derivative 2 (0.115 mmol) was dissolved in dry and well-degassed CH_3CN (2 ml). This stirred solution was irradiated by a medium pressure mercury lamp at a constant temperature of 26°C. After completion, this solution was filtered and concentrated under vacuum. Chromatography on silica (EtOAc) afforded the pure tetrazanes 8 as yellow oils:

8b: ν (CH_2Cl_2): 1745 cm^{-1}; δ ^1H: 4.29 (4H,q), 4.20 (4H,q), 2.88 (4H,t), 1.64 (4H,m), 1.35-1.25 (36H,m), 0.85 (6H,t); δ ^{13}C: 173.8, 155.5, 153.1, 63.8, 62.5, 37.0, 31.9, 29.7-29.1, 24.6, 22.7, 14.3, 14.1;FAB, m/z (%): 828 (0.6) M+1, 827 (1.4), 589 (3.7), 415 (6.3), 177 (100).

8c: ν ($CHCl_3$): 1748 cm^{-1}; δ ^1H: 7.13 (2H,dd), 6.47 (2H,d), 5.83 (2H,d), 4.29 (4H,q), 4.20 (4H,q), 1.32 (6H,t), 1.27 (6H,t); δ ^{13}C: 170.6, 155.4, 153.1, 131.3, 128.8, 64.2, 62.7, 14.3, 14.1; FAB, m/z (%): 459 (22.4) M+1, 458 (0.5), 405 (8), 303 (5.7), 231 (100).

8d: ν (neat): 1745 cm^{-1}; δ ^1H: 5.96 (2H,m), 5.20 (2H,s), 5.13 (2H,d), 4.29 (4H,q), 4.20 (4H,q), 3.68 (4H,d), 1.31 (6H,t), 1.25 (6H,t); δ ^{13}C: 171.2, 155.4, 153.0, 130.0, 118.9, 64.0, 62.6, 41.5, 14.3, 14.1; FAB, m/z (%): 487 (11) M + 1, 485 (0.3), 429 (7.5), 245 (35), 177 (100).

8e: ν (neat): 1750 cm^{-1}; δ ^1H: 4.28 (4H,q), 4.19 (4H,q), 3.36 (2H,tt), 1.95-1.66 (10H,m), 1.45-1.20 (22H,m); δ ^{13}C: 177.0, 155.6, 153.1, 63.8, 62.5, 44.0, 29.3 (t), 25.8 (t), 25.6 (t), 14.4 (q), 14.1 (q); FAB, m/z (%): 569 (1.9) M+1 568 (2.5), 287 (7), 111 (69), 95 (100).

8f: ν (neat): 1745 cm^{-1}; δ ^1H: 4.28 (4H,q), 4.20 (4H,q), 2.03 (18H,s), 1.69 (12H,s), 1.31 (6H,t), 1.25 (6H,t), δ ^{13}C: 175.7, 156.1, 154.2, 63.9, 62.7 45.0, 38.2, 35.4, 28.1, 14.4, 14.2; FAB, m/z (%): 675 (6.9) M+1, 674 (10.1), 538 (3.0), 337 (5), 161 (43), 135 (100).

Irradiation of 2d in the Presence of t-BuSH to Furnish Derivative 12:

The hydrazine derivative 2d (0.150g; 0.41 mmol) was dissolved in CH_3CN (13 ml) and then t-BuSH (0.5 ml, 4.3 mmol) was added. This stirred solution was irradiated (Hg lamp) at 26°C for 75 min. The solvent and the excess of t-BuSH were removed under vacuum and the residue was purified by chromatography on silica (CH_2Cl_2 then EtOAc) (67%) (n.m.r.). Compound 12 was a yellow oil; ν neat: 3331, 1746, 1243 cm^{-1}; δ ^1H: 6.69 (1H,s), 4.28 (2H,q), 4.18 (2H,q), 3.03 (2H,t), 2.56 (2H,t), 1.91 (2H, quint.), 1.32 (3H,t), 1.29 (12H,m); δ ^{13}C: 173.2, 160.4, 155.5, 63.9, 62.2, 62.2, 42.1 36.2, 30.9, 27.5, 14.4, 14.1; m/z (%): 334 (2) M+, 176 (74), 159 (12.6), 131 (15.6), 103 (90), 57 (100).

C) Reaction of the Esters 1 with Cookson's Reagent:

The ester 1 (1.05 mmol) was dissolved in C_6H_6 or CH_2Cl_2 (4 ml) and then the triazolinedione (185 mg, 1.05 mmol) was added and the solution stirred at room temperature for 1-4 hrs. The precipitate of pyridine-2,2'-dithiobis-1,1'-dioxide was filtered off and the solvent removed under reduced pressure. Purification by chromatography on silica (CH_2Cl_2) afforded the adduct 14 as a white crystalline solid. The compound 14f decomposed on purification; it had ν (CH_2Cl_2): 1750 cm^{-1}; δ ^1H: 7.56-7.45 (5H,m), 2.19 (12H,s), 2.03 (6H,s), 1.76 (12H,s).

14a: mp. 129-130°C, ν (CH_2Cl_2): 1747 cm^{-1}; δ ^1H: 7.50-7.40 (5H,m), 7.17-7.35 (10H,m), 3.32 (4H,t), 3.07 (4H,t); δ ^{13}C: 167.3, 147.6, 139.8, 130.0, 129.3, 129.1, 128.5, 128.4, 126.4, 126.1, 38.0, 30.1; m/z (%): 441 (0.5) M+, 322 (9.2), 133 (39.6), 119 (34.5), 105 (69.2), 91 (100).

14e mp. 160-163°C, ν ($CHCl_3$): 1753 cm^{-1}; δ ^1H: 7.56-7.43 (5H,m), 3.39 (2H,tt), 2.02 (4H,d), 1.81-1.23 (16H,m); δ ^{13}C: 171.4, 147.5, 129.6, 129.5, 129.4, 126.1, 44.5, 29.0, 25.6, 25.4; m/z (%): 397 (1.1) M+, 288 (3.9), 178 (20.5), 119 (10.5), 111 (60), 83 (100); HR-MS m/z=397.20033 [Calc: for $C_{22}H_{27}N_3O_4$ (M^+):397.20016].

Pyridine-2,2'-dithiobis-1,1'-dioxyde 9:

The disulfide 9 was obtained as a white crystalline solid. The I.R. and U.V. sprectra were identical to those reported in the literature.[10]
mp. 235-237°C; δ ^1H: 8.28 (2H,d), 7.58 (2H,d), 7.22 (4H,m); δ ^{13}C: 148.5, 138.7 126.6 (d), 122.5 (d), 121.9 (d); m/z (%): 254 (0.3) M+2, 253 (0.3), 252 (0.5), 236 (1.4), 220 (49), 127 (12.4), 126 (14.4), 78 (100).

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