CARBENE VERSUS DIMER FORMATION FROM DIAZO DERIVATIVES: THE ANOMALOUS BEHAVIOUR OF 2-DIAZOTHIAZOLINES

Josep Castells*, Francisco López Calahorra, and Fernando Geijo
Departamento de Química Orgánica, División de Ciencias Experi-
mentales y Matemáticas, Facultad de Química, Universidad de
Barcelona, Martí i Franqués, 1, 08028 Barcelona, Spain

Abstract- Different oxidation procedures of 2-thiazolinone
hydrazones, the anomalous behaviour of the resulting 2-diazo-
thiazolines and a quantum-theoretical interpretation based in
MNDO calculations are reported.

INTRODUCTION

Thermolysis of diazoalkanes is a well known procedure for the generation of carbene intermediates. However, the procedure has not been succesfully applied to the generation of N-substituted thiazolin-2-ylidenes. These species are interesting: a), from a structural view-point, because in resonance parlance they are hybrids between a carbene form and a conjugate base form[1] ; b), from a synthetic view-point because they are cyanide-like catalysts in many mechanistically related reactions[2] the common step of which is inversion of reactivity at a carbonyl grouping.

According to reported results[3], oxidation of 3-methyl-2-hydrazinobenzothiazolium tetrafluoroborate affords neither the diazo derivative nor the related carbene intermediate; instead, other nitrogen-containing substances are isolated.

In the present paper, new experimental results which confirm the differential behaviour of diazothiazolines are reported and a quantum-theoretical interpretation of it is given. Attention is focused on the oxidation of 2-thiazolone hydrazones.

PREPARATION OF 2-THIAZOLONE HYDRAZONES

3-Benzyl-4,5-dimethyl-2-thiazolone hydrazone 1a and 3-ethyl-4,5-dimethyl-2-thiazo-lone hydrazone 1b were used as starting materials. They were prepared as indicated[4] in Scheme 1 and spectroscopically characterized.
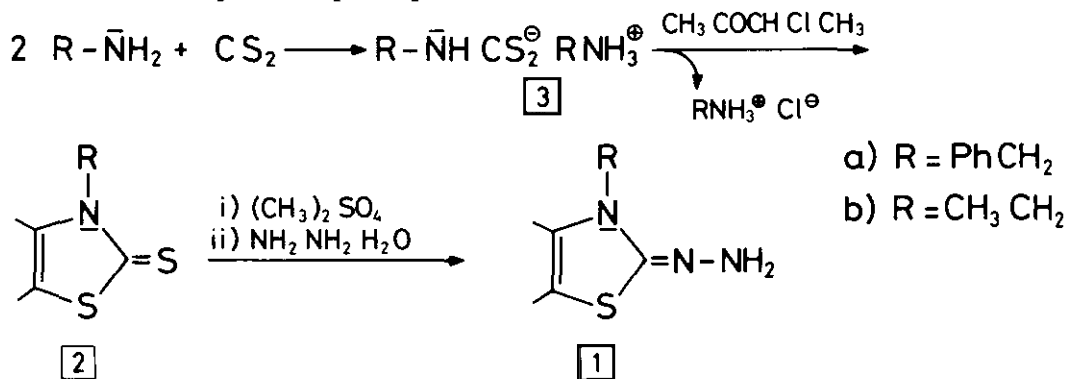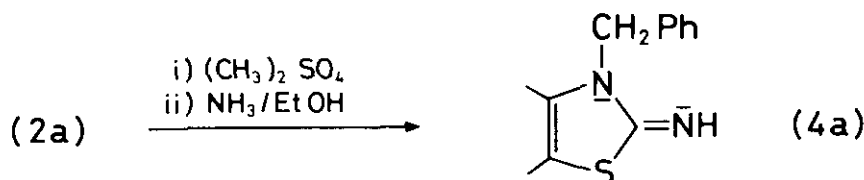

SCHEME 1

CHEMICAL OXIDATIONS WITH MERCURY(II) OXIDE

Hydrazones 1a and 1b were chemically oxidized by means of mercury(II) oxide[5] and it was found that the composition of the resulting reaction mixtures was highly dependent on the presence or absence of a dehydrating agent but in any cases neither the diazothiazoline nor products derived from the corresponding carbene were observed.

Hydrazone 1a in ether was oxidized with an excess of mercury(II) oxide in the presence of anhydrous sodium sulphate to give ether soluble and ether insoluble products which were studied independently.

Removal of the solvent from the ether solution led to an oily material (10-15% of the starting hydrazone) from which two substances were isolated. They were identified as 3-benzyl-4,5-dimethylthiazolin-2-imine 4a and 2-|5-(3-benzyl-4,5-dimethyl-thiazolin-2-yliden)pentaza|thiazolium 5a hydroxide. Structural assignments were guided and supported by the reported results[3] of the oxidation of 3-methyl-2-hydrazinobenzothiazolium tetrafluoroborate with lead tetraacetate. Imine 4a was identified by comparison with an authentic specimen prepared according to Scheme 2.

$$(2a) \xrightarrow{\begin{array}{c} i) (CH_3)_2 SO_4 \\ ii) NH_3/EtOH \end{array}} \quad (4a)$$
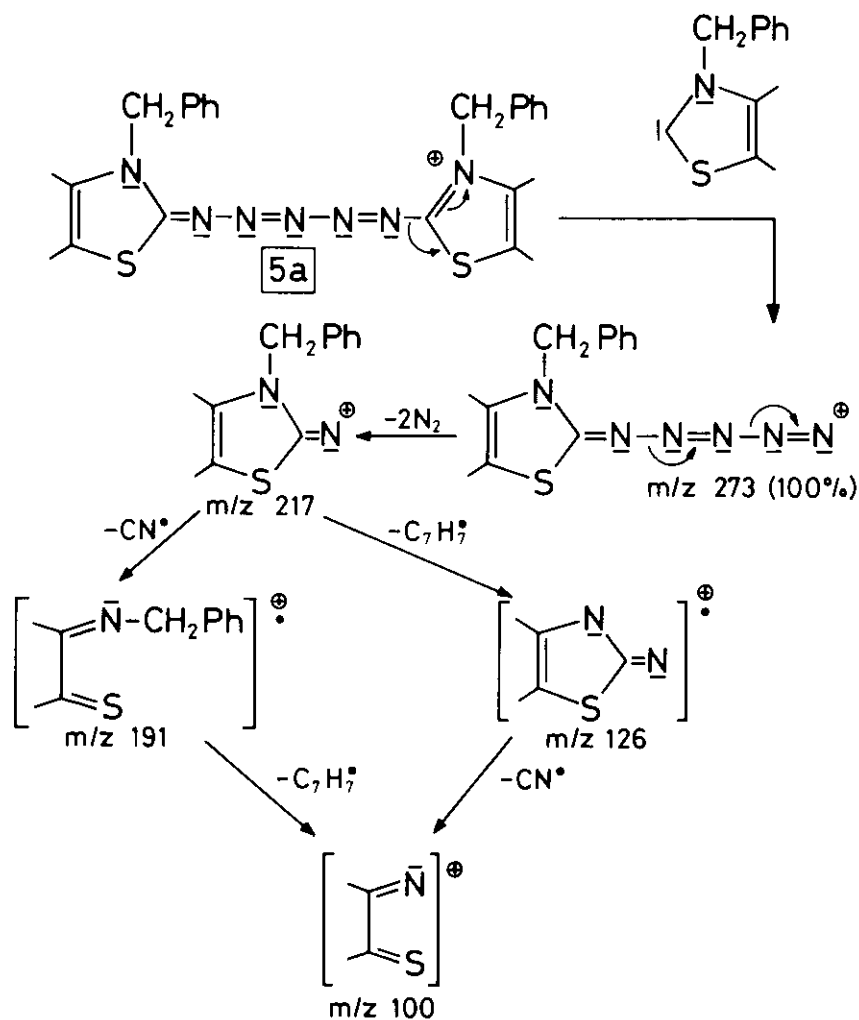
SCHEME 2

Benzothiazolin-2-imines have been identified in the thermolysis of pentaza-pentame-thinecyanine derivatives in solution[6].

The structure of the thiazolium hydroxide 5a was confirmed by its mass spectrum (Scheme 3).

Chloroform extraction in a soxhlet apparatus of the ether insoluble part (made up of excess mercury(II) oxide, metallic mercury, sodium sulphate and organic mate-rial) led to a yellow solid which accounted for 80-85% of the starting hydrazone. On the basis of its spectral data and complementary work on oxidation of hydrazone 1b (see below), the structure of the main product was assigned to be 1,4-bis(3-benzyl-4,5-dimethylthiazolin-2-yliden)tetrazene (6a; undefined stereochemistry), (Figure 1). Uv : λ_{max} = 408 nm (ϵ = 1100, in chloroform); Ir : 1510 and 1495 cm^{-1}; ^{1}H-nmr (δ in DMSO-d$_6$): 7.1 (5 H), 4.4 (2 H) and 2.0 (6 H); ms : m/z 462 (M$^+$).

Oxidation of hydrazone 1b led to parallel results but with higher experimental difficulties in the working up of the resulting reaction mixtures. In this series, the tetrazene derivative was identified by comparison with an authentic specimen of 1,4-bis(3-ethyl-4,5-dimethylthiazolin-2-ylidene)tetrazene 6b. Balli et al. have reported[7] that thermolysis at 0ºC of 2-diazoazo-3-ethylbenzothiazoline 7 (Scheme 4) leads to 1,4-bis(3-ethylbenzothiazolin-2-ylidene)tetrazene 8. Following Balli's procedure, we have prepared the 2-diazoazo-4,5-dimethyl-3-ethylthiazoline 9 and established that its thermolysis (at 0ºC) leads (Scheme 5) to a substance identi-cal to the main oxidation product from hydrazone 1b to which structure 6b can be assigned by analogous reasoning. Furthermore, we have found that thermolysis at -20ºC leads to a mixture which shows activity as benzoin condensation catalyst; this

means that 3-ethylthiazolin-2-ylidene is present in the mixture. Depending on the
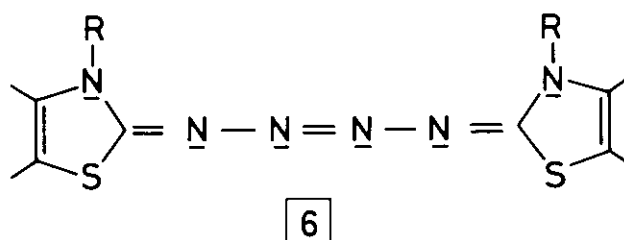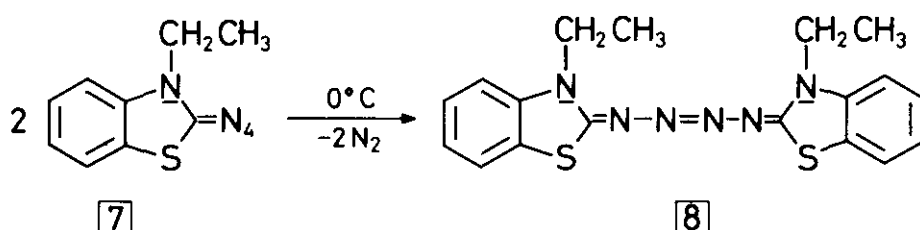working conditions, benzoin yields of 20-60% were achieved.
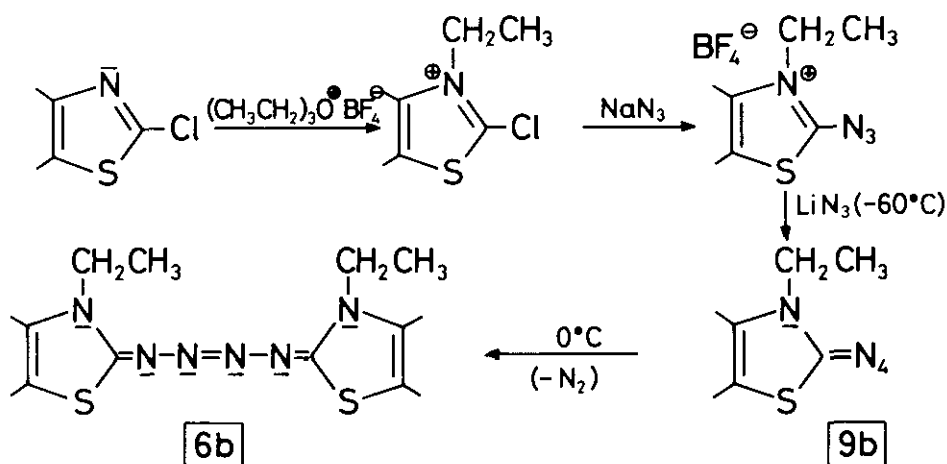
SCHEME 3

FIGURE 1

When hydrazones 1a and 1b were oxidized in the absence of a dessicating agent the composition of the products was strongly altered: the amount of the compounds 4 and 5 accounted for up to 85-90% of the starting hydrazone and that of the compound 6 for only 5-10%.

SCHEME 4

SCHEME 5

CHEMICAL OXIDATION WITH O-NITROBENZENESULPHENYL CHLORIDE

Oxidation of hydrazone 1b with o-nitrobenzenesulphenyl chloride[8] led to a complex mixture from which tetrazene 6b was obtained as a sole identifiable compound. Its formation is discussed later.

ELECTROCHEMICAL OXIDATION

A cyclic voltammetry of hydrazone 1a in an anhydrous acetonitrile saturated so-lution using 0.1M sodium perchlorate as supporting electrolyte (Figure 1) exhibits a semiwave potential of 60 mV; no maximum in the polarographic wave is observed when a humid acetonitrile solution is used. Electrolysis at 60 mV of the anhydrous solution , afforded tetrazene 6a in a quantitative electrochemical yield (12% chemical yield, after 6 h); on the contrary, when humid acetonitrile was used, a

mixture of compounds **4a** and **5a** was obtained in 90% yield, compound **6a** being formed in only 8% yield (practically quantitative chemical yield). These results are clo-
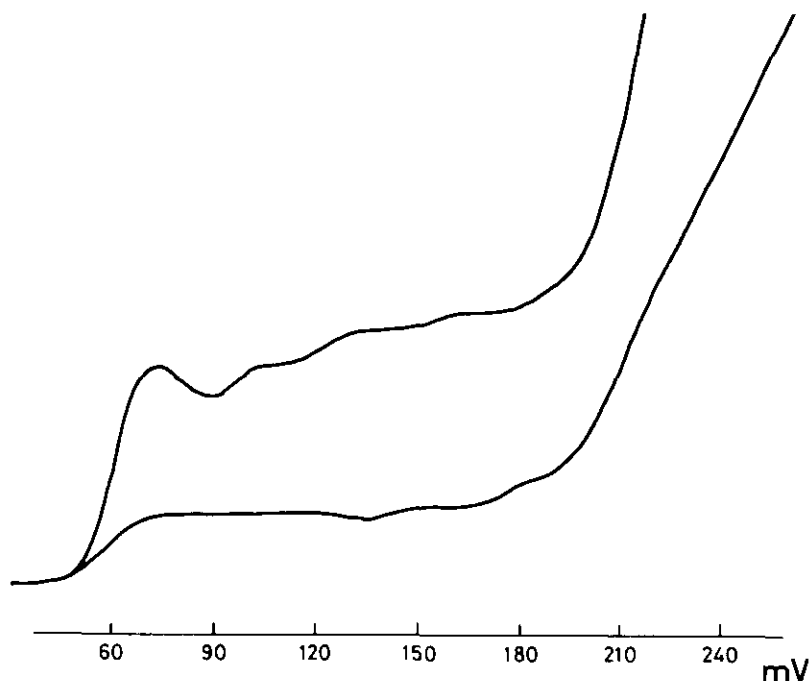

FIGURE 2

sely similar to the results of chemical oxidations described above.

The chemical yield difference between the two electrolyses can be imputed to inac-tivation of the working electrode by tetrazene when an anhydrous acetonitrile solution is used; this explanation is in line with the shapes of the corresponding polarographic waves.

MECHANISTIC AND QUANTUM-THEORETICAL CONSIDERATIONS

Formation of compounds of types **4** and **5** when 2-hydrazinobenzothiazolium salts
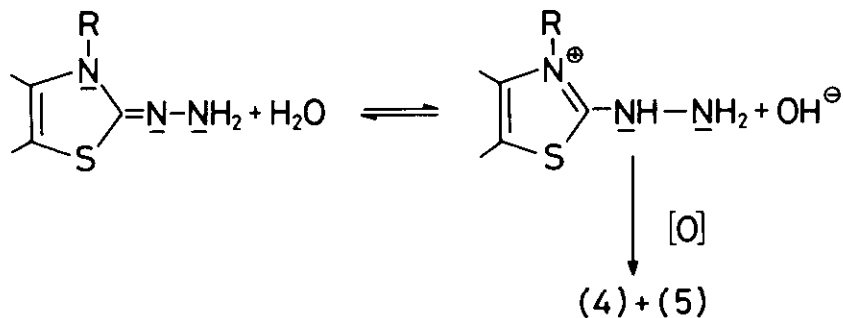
SCHEME 6

are oxidized has already been rationalized[3]; consequently, the same reasoning can account for the formation of compounds of these types in the mercury(II) oxidation of wet hydrazone (I) solutions, in which 2-hydrazinothiazolium hydroxides will be present (Scheme 6).

The really intriguing question is the appearance of tetrazene 6 when anhydrous solutions are employed. Tetrazene 6 is, formally, a dimer of diazothiazoline 10 (the initially expected product), (Figure 3), but, up to now, dimerization of diazo derivatives to tetrazene derivatives has not been reported. Quantum-mechanical calculations on 2-diazo-3-methylthiazoline (10c = 10, R=CH$_3$), taken as a model, afford an explanation of the easy dimerization of diazo derivatives 10a and 10b.

The geometry and electronic structure of 10c are far different of those which would be expected of a conventional diazo derivative. The CNN angle is of about 140° (the calculated value depends on the method of calculus employed) and these three atoms define a plane which is perpendicular to the ring plane. Bond orders are those given in Figure 4.
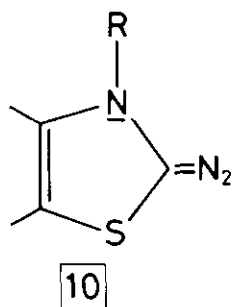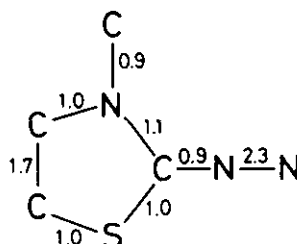

FIGURE 3   FIGURE 4

On the other hand, the expected value of the S^2 operator in the UHF (Unrestricted Hartree-Fock) solution is 0.860 with the spin density distribution given in Figure 5, which clearly shows up the strong bi-radical character of 2-diazothiazolines. Figure 6 gives a pictorial view of the above information.

The strong radical character of the terminal diazo nitrogen explains quite satisfactorily the ease of dimerization of 2-diazothiazolines to tetrazene derivatives and, as a consequence, the failure in their isolation or conversion to carbene derivatives.
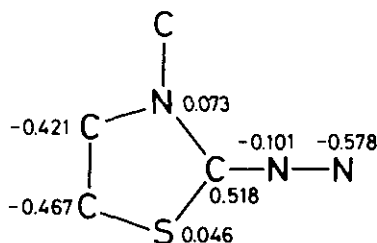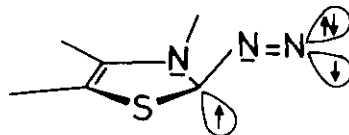

FIGURE 5   FIGURE 6

EXPERIMENTAL

General aspects
Melting points were determined in a Büchi "Schmeltzpunktbestimungs apparat nach Dr. Tottoli" and are uncorrected. The ms spectra were recorded in a Hewlett-Packard 5930A Mass spectrometer. Ir spectra were recorded in a Perkin-Elmer 681 spectrophotometer, and only noteworthy absortions (cm^{-1}) are listed. Nmr spectra are expresed in δ units with TMS as internal standard and were recorded in a Perkin-Elmer R-24B ([1]H-nmr). Uv spectrum was recorded in a Perkin-Elmer Lambda 5 spectrophotometer.

Computational procedure
The reported calculations were obtained using a locally modified version of the MNDO program[9], reprogrammed for an IBM 4341/2 computer, with standard parameters[10]. The equilibrium geometry was determined by minimizing the total energy with respect to all geometrical variables using the standard DFP algoritm[11].

Alkylammonium alkyldithiocarbamates (3). Carbon disulfide and ethanol are placed in a three necked flask provided with a mechanic stirrer, an addition funnel and a low temperature thermometer. The mixture is cooled below 0°C in an ice-salt bath and the suitable amine is slowly added maintaining the temperature of the reaction mixture under 10°C. After the addition is finished, the stirring is stopped, the mixture is allowed to settle out and the resulting crystalline precipitate is filtered, washed with ethanol and dried in vacuo.

Benzylammonium benzyldithiocarbamate (3a). Carbon disulfide (282 g, 3.7 mmols), ethanol (250 ml) and benzylamine (640 g, 6 mmols) are used and 873 g of 3a are obtained (96 %):mp 143-145°C; nmr (DMSO-d_6): 4.0 (s,2H,CH$_2$), 4.6 (d,2H, CH$_2$), 7.3-6.8 (br,10H,2 Ph), 8.0 (br,3H, NH$_3$), 8.5 (t,1H,NH).
Ethylammonium ethyldithiocarbamate (3b). Carbon disulfide (76 g, 1 mol) and 84.2 g of 3b are obtained (63.5 %): mp 101-102°C; nmr (DMSO-d_6): 0.85 (t,3H,CH$_3$), 1.0 (t,3H,CH$_3$), 2.75 (q,2H,CH$_2$), 3.2 (dq,2H,CH$_2$), 7.4 (br,3H,NH$_3$), 8.2 (br,1H,NH).

3-Alkylthiazolin-2-thiones (2). A solution of the suitable alkylammonium alkyldithiocarbamate (69.6 mmols) and 3-chlorobutanone (7.9 g, 74.2 mmols) in ethanol (75 ml) is refluxed for 5.5 h. The solvent is removed in vacuo, and the residue is shaken with water (25 ml) and chloroform (25 ml). The organic layer is washed with water (2 x 25 ml), dried over anhydrous sodium sulfate, filtered and evaporated to dryness. The residue is recrystallized from ethanol, yielding the corresponding 3-alkylthiazolin-2-thione 2.
3-Benzylthiazolin-2-thione (2a). From 20 g of 3a, 12.5 g of 2a are obtained (77 %); mp 113-114°C; nmr (CDCl$_3$): 2.0 (s,3H,CH$_3$), 2.1 (s,3H,CH$_3$), 5.4 (s,2H, CH$_2$), 7.1 (br,5H,Ph); ir (KBr): 1205 (C=S). Anal. Calcd for C$_{12}$H$_{13}$NS$_2$: C, 61.28; H, 5.53; N, 5.96. Found: C, 61.22; H, 5.53; N, 5.97.
3-Ethylthiazolin-2-thione (2b). From 8.5 g of 3b, 7.2 g of 2b are obtained (59.5 %); mp 59-61°C; nmr (CDCl$_3$): 1.3 (t,3H,CH$_3$-CH$_2$), 2.2 (s,6H,2 CH$_3$), 4.2 (q,2H, CH$_2$).

3-Alkylthiazolin-2-one hydrazones (1). A mixture of the suitable 3-alkyl-4,5-dimethylthiazolin-2-thione (5 g) and the stoichiometric amount of dimethyl sulfate is smoothly heated to fusion ia a beaker. The melt is cooled and dissolved in ethanol (80 ml) and 95 % hydrazine hydrate (20 ml) is added. The resulting solution is heated for 30 min at 70°C and diluted with water (750 ml) is added until permanent turbidity and cooled in a refrigerator overnight. The hydrazone crystallizes out and is separated by filtration.
3-Benzyl-4,5-dimethylthiazolin-2-one hydrazone (1a). From 2a (5 g, 21.3 mmols) and dimethyl sulfate (2.7 g, 21.3 mmols) are obtained 4.0 g of 1a (81 %);mp 92-94°C; nmr (CDCl$_3$): 1.8 (s,3H,CH$_3$), 2.0 (s,3H,CH$_3$), 4.0 (s,2H,NH$_2$), 4.8 (s,2H,CH$_2$), 7.1 (br,5H, Ph); ir (KBr): 3310 (N-H), 1620 (C=C), 1610 (C=N). Anal. Calcd for C$_{12}$H$_{15}$N$_3$S: C,61.80; H, 6.44; N,18.03. Found: C, 62.07; H, 6.42; N,18.02.
3-Ethyl-4,5-dimethylthiazolin-2-one hydrazone (1b). From 2b (5 g, 28.9 mmols) and dimethyl sulfate (3.6 g, 28.9 mmols) are obtained 3.5 g of 1b in the form of a yellow orange oil (70 %); nmr (CDCl$_3$): 1.3 (t,3H,CH$_3$-CH$_2$), 1.9 (s,3H, CH$_3$), 2.0 (s,3H.CH$_3$), 4.1 (q,2H,CH$_2$); ir (film): 3300 (N-H), 1650 (C=C), 1630 (C=N).

Oxidation of 1a with mercury (II) oxide. In a flask provided with a calcium chloride tube and a magnetic stirrer are placed 1a (0.5 g, 2.1 mmols), mercury (II) oxide (0.98 g, 4.5 mmols), anhydrous sodium sulfate (0.25 g) and anhydrous ethyl ether (4 ml). A saturated methanolic solution of potassium hydroxide is slowly added until the solution darkens; afterwards, the mixture is maintained at room temperature for 1 h. The crude mixture is filtered and the solid residue is extracted in a soxhlet with ether. The above filtrate and the extract are combined. The solid is again extracted with chloroform. The ether solution is dried, yielding 60 mg of an oil, that after cristallization affords 40 mg of 5a (8 %); mp 140-145°C (dec.); nmr (DMSO-d_6): 1.9 (s,6H,2 CH$_3$), 2.0 (s,6H,2 CH$_3$), 5.0 (s,4H,2 CH$_2$), 7.2 (br,10H,2 Ph); ir (KBr): 3700-3150 (O-H), 1570, 1560 (C=N-N=N-N=N-C). Ms: 476 (M$^+$), 273 ((M-C$_{12}$H$_{13}$NS)$^+$), 217 ((273-2N$_2$)$^+$).
From the mother liquors, 15 mg of 4a (3 %) as a coloured oil are obtained; nmr (DMSO-d_6): 1.8 (s,3H,CH$_3$), 2.0 (s,3H,CH$_3$), 4.9 (s,2H,CH$_2$), 5.5-4.0 (br,1H,N-H), 7.2 (br,5H,Ph); ir (film): 3330, 3290 (N-H), 1575 (C=NH). Ms: 218 (M$^+$), 141 ((M-Ph)$^+$), 127 ((M-C$_7$H$_7$)$^+$), 100 ((127-CNH)$^+$), 91 ((C$_7$H$_7$)$^+$, 100 %).

The chloroform extract affords, after removing the solvent, 396 mg of 6a (82 %); mp 255-257°C; nmr (DMSO-d_6): 2.0 (br,12H,4 CH$_3$); 4.4 (s,4H, 2 CH$_2$); 7.1 (br,10H, 2 Ph); ir (KBr): 1495 (C=N-N=N-N=C). Ms: 462 (M$^+$), 434 ((M-N$_2$)$^+$), 343 ((434-C$_7$H$_7$)$^+$), 91 (C$_7$H$_7^+$, 100 %).

Oxidation of 1b with mercury (II) oxide. A suspension of 1b (1.0 g, 5.8 mmols), mercury (II) oxide (2.8 g, 12.9 mmols), anhydrous sodium sulfate (0.5 g) and anhydrous ethyl ether (5 ml) is stirred at room temperature for 1h and filtered out. The solid residue is carefully washed with ether and extracted with chloroform in a soxhlet apparatus. The resulting chloroform solution is evaporated and 0.42 g of tetrazene 6b are obtained (51 %); mp 219-222°C; uv (CHCl$_3$): $_{max}$ 405.9 nm, =1.1 x 10^4; nmr (DMSO-d_6): 1.2 (t,6H,2 CH$_3$-CH$_2$), 2.0 (s,12H,4 CH$_3$), 3.9 (q,4H,2 CH$_2$); ir (KBr): 1495 (C=N-N=N-N=C). Ms: 338 (M$^+$).

Preparation of 4a. This substance was prepared in the same way as hydrazones 1a, by changing hydrazine hydrate by a saturated ethanolic ammonia solution; yield, 91 %. The analytical data are identical to the described above.

Oxidation of 1a via decomposition of its o-nitrobenzenesulfenyl derivative. Triethylamine (434 mg, 4.3 mmol) dissolved in chloroform (25 ml) is added to 1a (1 g, 4.3 mmol) placed in a flask provided with magnetic stirrer. After complete addition, the reaction mixture was washed with water (3 x 25 ml), dried over anhydrous sodium sulfate, the solvent removed and the residue chromatographed on silica gel. Elution with benzene afforded 1.1 g of o-nitrobenzene disulfide (83 %) and elution with chloroform 0.47 g of 6a (47 %).

Electrochemical oxidation of 1a. In a 250 ml electrolytic cell provided with platinum electrodes and a calomel reference electrode, 1a (439 mg, 1.9 mmol) and a solution of sodium perclorate 0.1 M in acetonitrile (200 ml) were placed and a potential of 60 mV was established. After consuming 42.8 C (6 h) the current intensity was nule. The anode was coated by a precipitate identical to the one in the bottom of the cell; such precipitate was identified as 6a (51 mg). Chemical yield: 12 %; electrochemical yield: 100 %.

Preparation of 2-diazo-4,5-dimethyl-3-ethylthiazoline (9b) and its use in the benzoin condensation. The preparation and thermolysis at 0°C of 9b was carried out essentially by the procedure described by Balli[6] for the related benzo derivative. The thermolysis at -20 °C was carried in the presence of benzaldehyde. Benzoin was obtained in variable yields (20-60%), depending on the reaction time and the heating speed of the solution.

REFERENCES

1. F. Geijo, F. López Calahorra and S. Olivella, J. Heterocyclic Chem., 1984, 21, 1785.

2. (a) T. Ugai, S. Tanaka and S. Dakowa, J. Pharm. Soc. Japan, 1963, 63, 269; (b) H. Stetter and G. Lorenz, Chem. Ber., 1985, 118, 1115; (c) J. Castells, F. Pujol, H. Llitjós and M. Moreno Mañas, Tetrahedron, 1982, 38, 337; (d) J. Castells, F. López Calahorra and F. Geijo, Carbohydrate Res., 1983, 116, 197.

3. S. Hünig, H. Balli and H. Quast, Angew. Chem., 1962, 74, 28.

4. (a) S. Hünig, H. Balli, K. H. Fristsch, H. Herrmann, G. Köbrich, W. Werner, E. Grigat, F. Müller, H. Nother and K. H. Oete, Angew. Chem., 1958, 70, 215; (b) H. Bulka, H. G. Rohde and M. Beyer, Chem. Ber., 1965, 98, 259.

5. C. f., L. I. Smith and K. L. Howard, Org. Synth., Col. Vol. III, 315 (1955).

6. H. Quast and S. Hünig, Ann., 1968, 711, 157.

7. (a) H. Balli, Angew. Chem., 1964, 76, 995; (b) H. Balli, Angew. Chem., 1966, 78, 146.

8. D. E. Dana and J. P. Anselme, Tetrahedron Lett., 1975, 19, 1565.

9. W. Thiel, QCPE, 1978, 10, 353.

10. M. J. Dewar and W. Thiel, J. Am. Chem. Soc., 1977, 99, 4899; (b) M. J. S. Dewar, M. L. McKee and H. S. Rzepa, J. Am. Chem. Soc., 1978, 100, 3607.

11. (a) R. Fletcher and M. J. D. Powell, Compt. J., 1963, 6, 163; (b) W. C. Davidon, Compt. J., 1968, 10, 406.