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REDUCTION OF SOME SUBSTITUTED 1,2,4-TRIAZINES WITH SODIUM BOROHYDRIDE

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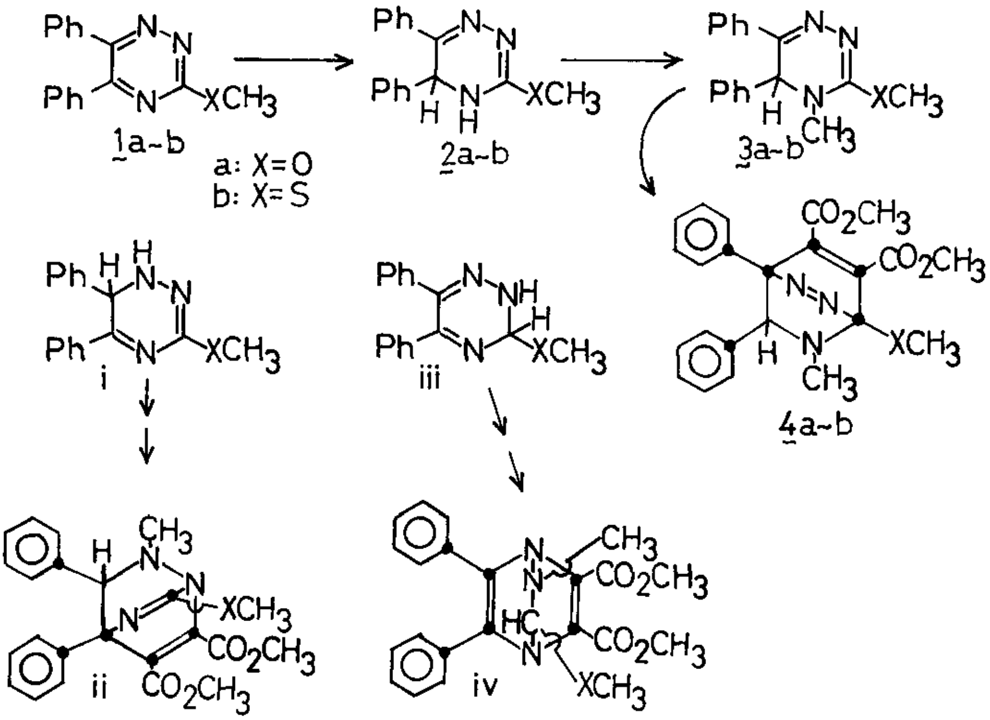
The structures of dihydro-1,2,4-triazines (2a-b) derived from 3-methoxy- (1a) and 3-methylthio-5,6-diphenyl-1,2,4-triazine (1b) were determined on the basis of the ^{13}CNMR-spectra of the cyclo-adducts of the mono-methylated derivatives (3a-b) of 2a-b.

Efforts have been devoted to disclosing the chemical behaviors of 1,2,4-triazine and its substituted derivatives on oxidation with organic peracids in relation to the synthesis of their N-oxides[1], whereas the documented data for their reductive transformations are amazingly limited.[2] In recent years, Neunhoeffer[3] and Sauer[4] have noted that 1,2,4-triazines are usually reactive electron-deficient dienes which can cycloadd to electron-rich mono-olefins in the sence of a Diels-Alder reaction with inverse electron demand. We report here that some dihydro-1,2,4-triazines behave as normal dienes that can cycloadd to electron-deficient

Scheme 1



dimethyl acetylenedicarboxylate (DMAD) and that the structural determination of the adducts can serve to deducing the structures of the original reduction products.

Reduction of 3-methoxy-5,6-diphenyl-1,2,4-triazine (1a) and its 3-methylthio analog (1b)[5] with a slight excess of sodium borohydride in a mixture of THF and methanol at room temperature gave 3-methoxy-5,6-diphenyl-4,5-dihydro-1,2,4-triazine (2a) and its 3-methylthio analog (2b) in 71 and 92% yield, respectively :2a, mp 160-163°; λ max (MeOH) 291 (ε 7300) and 220 nm (ε 13600, sh); ^{1}HNMR (DMSO-d_6)δ 3.66 (3H, s, OMe), 5.81 (1H, s, C_5-H), 7.2-7.9

(10H, m, phenyl), 10.42 (1H, br s, N^4-H, D_2O-exchangeable); 2b, mp 227-230°; λ max (MeOH) 300 (ε 8500) and 230 nm (ε 13800, sh); ^{1}HNMR (DMSO-d_6)δ 2.35 (3H, s, SMe), 5.91 (1H, s, C_5-H), 7.2-7.9 (10H, m, phenyl), 10.90 (1H, br s, N^4-H).

Methylation of 2a-b with methyl iodide/NaH in DMF gave 3-methoxy-5,6-diphenyl-4-methyl-4,5-dihydro-1,2,4-triazine (3a) and its 3-methylthio analog (3b) in 89 and 72% yield, respectively: 3a, mp 77-78°; λmax (MeOH) 305 (ε 7800) and 228 nm (ε 13400, sh); ^{1}HNMR ($CDCl_3$)δ 3.36 (3H, s, NMe), 3.76 (3H, s, OMe), 5.75 (1H, s, C_5-H), 7.1-7.8 (10H, m, phenyl); 3b, mp 78-81°; λmax (MeOH) 310 (ε 7900) and 235 nm (ε 14900, sh); ^{1}HNMR ($CDCl_3$)δ 2.40 (3H, s, SMe), 3.45 (3H, s, NMe), 5.88 (1H, s, C_5-H), 7.1-7.9 (10H, m, phenyl).

Heating 3b with 5-fold excess sodium methoxide in methanol to reflux for 90 hr afforded 3a in 58% yield, thus proving the skeletal identity of both compounds.

A mixture of 3a and two fold excess DMAD in toluene was heated in a pressure tube under argon at 110° for 12 hr to give 2-methoxy-2,5-azo-3,4-bis-methoxycarbonyl-5,6-diphenyl-1-methyl-1,2,5,6-tetrahydropyridine (4a) as a single product in 65% yield: mp 174-176°; λmax (MeOH) 296 nm (ε 10400); ^{1}HNMR ($CDCl_3$)δ 3.17 (3H, s, NMe), 3.22 (3H, s, OMe), 3.67 (3H, s, methoxycarbonyl), 3.73 (3H, s, methoxycarbonyl), 5.49 (1H, s, C_5-H), 7.1-7.8 (10H, m, phenyl). Analogous treatment of 3b gave the 2-methylthio analog (4b) in 66% yield: mp 155-156°; λmax (MeOH) 303 (ε 11900) and 225 nm (ε 12100, sh); ^{1}HNMR ($CDCl_3$)δ 1.87 (3H, s, SMe), 3.34 (3H,

Table I. ^{13}C Chemical Shifts^{a,b} of 2-methoxy-2,5-azo-3,4-bis-methoxycarbonyl-5,6-diphenyl-1-methyl-1,2,5,6-tetrahydropyridine (4a) and its 2-methylthio analog (4b) in $CDCl_3$.

4a		4b	
33.98 (q)	NCH_3	14.16 (q)	SCH_3
52.89 (q)	ester-CH_3 x 2	33.46 (q)	NCH_3
54.06 (q)	OCH_3	52.76 (q)	ester-CH_3
76.08 (s)	C_5	52.95 (q)	
81.61 (d)	C_6	82.97 (s)	C_5
113.83 (s)	C_2	84.79 (d)	C_6
125.79 $\sim$ 130.27 (m)	$C_{2'}\sim C_{6'}$, $C_{2''}\sim C_{6''}$	96.74 (s)	C_2
131.70 (s)	C_3, C_4 $C_{1'}$, $C_{1''}$ C=O x 2	125.66 $\sim$ 130.73 (m)	$C_{2'}\sim C_{6'}$, $C_{2''}\sim C_{6''}$
134.82 (s)		131.51 (s)	C_3, C_4 $C_{1'}$, $C_{1''}$ C=O x 2
137.87 (s)		133.85 (s)	
161.07 (s)		136.71 (s)	
161.40 (s)		161.07 (s)	
166.66 (s)		161.59 (s)	
		167.05 (s)	

a: in ppm from internal tetramethylsilane. b: Multiplicities of ^{13}C signals in the partially decoupled spectra are given in the parentheses. q=quartet, d=doublet, s=singlet.

s, NMe), 3.67 (3H, s, methoxycarbonyl), 3.78 (3H, s, methoxycarbonyl), 5.68 (1H, s, C_5-H), 7.2-7.9 (10H, m, phenyl).

The ^{13}CNMR signals of 4a and 4b are given in Table I. Two other possible structures (ii and iv) for the cycloadducts derivable from the corresponding geometric isomers (i and iii) are depicted in Scheme 1 for comparison (the black points denote quaternary carbon atoms). The total number of the quaternary olefinic and aromatic carbons for ii, iv and 4 is 5, 6 and 4, respectively.

Although the strict assignments of the signals for these carbon atoms are excluded at present, the observed six quaternary carbon signals at lower fields should be ascribed to the two carbonyl groups and four olefinic and/or aromatic carbons. Thus, the other signals at higher fields are compatible only with the structure 4 and can be reasonably assigned as shown. The notable downfield shift of the signal of quaternary carbon (C_2) α to the methoxyl in the spectrum of 4a, relative to the corresponding chemical shift of 4b, also indicates that a new carbon-carbon bond formation occured at the 3,6-positions of 1a-b.

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