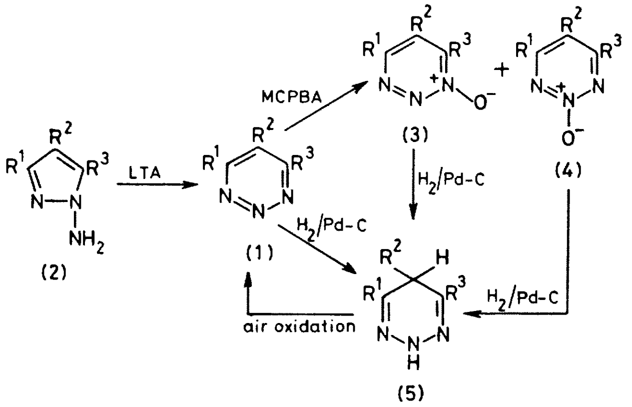
Synthesis, Oxidation, and Reduction of Monocyclic 1,2,3-Triazines

By AKIO OHSAWA, HEIHACHIRO ARAI, HIDEFUMI OHNISHI, and HIROSHI IGETA*
(*School of Pharmaceutical Sciences, Showa University, Tokyo* 142, *Japan*)

Summary Alkyl substituted monocyclic 1,2,3-triazines and their 1- and 2-oxides have been synthesized; catalytic reduction (on Pd–C) of the triazines afforded their 2,5-dihydro compounds.

ALTHOUGH the chemical and physical properties of 1,2,3-triazines have been of interest and condensed 1,2,3-triazines have been widely investigated, little is known concerning the monocyclic 1,2,3-triazines (**1**).[1] The preparation of compounds (**1**) has been limited to cases in which $R^1 = R^2 = R^3 =$ alkyl, aryl, or halogen, or a group (alkylamino, alkoxy, *etc.*) introduced by nucleophilic substitution of halogen.[1,2]†



a; $R^1 = R^2 = H, R^3 = Me$
a′; $R^1 = Me, R^2 = R^3 = H$
b; $R^1 = R^3 = Me, R^2 = H$
c; $R^1 = Ph, R^2 = H, R^3 = Me$
d; $R^1 = R^2 = R^3 = Me$

We have found that alkyl or aryl substituted 1,2,3-triazines (**1**) can be obtained by lead tetra-acetate (LTA) oxidation of *N*-aminopyrazoles (**2**) according to the procedures developed by Rees and Storr *et al.*[3] for the synthesis of 1,2,3-benzotriazines.

Careful oxidation of (**2**) with 1·1 mol. equiv. of LTA in CH_2Cl_2 at 0 °C, and cautious separation of the products using alumina column chromatography afforded (**1**) in moderate yields as shown in Table 1. The ^1H n.m.r. spectrum of (**1a**) showed signals at δ 2·70 (3H, s, 4-Me), 7·33 (1H, d, J 6·0 Hz, 5-H), and 8·94 (1H, d, 6-H); (**1b**), δ 2·68 (6H, s, 4- and 6-Me) and 7·11 (1H, s, 5-H): (**1c**), δ 2·76 (3H, s, 4-Me), 7·46—7·67 (4H, m, 5-H and 3 ArH), and 8·10—8·30 (2H, m, 2 ArH); (**1d**), δ 2·28 (3H, s, 5-Me) and 2·62 (6H, s, 4- and 6-Me).

TABLE 1. 1,2,3-Triazines (**1**).

Starting material	% Yield	M.p./°C
(**2a**) + (**2a′**) (mixture[a])	30	31
(**2c**)	70	88
(**2b**)	58	159
(**2d**)	68	145

[a] The separation and estimation of the amounts of (**2a**) and (**2a′**) in the mixture were unsuccessful.

Compound (**1d**) has been synthesised previously from 1,2,3-trimethylcyclopropenyl azide, and the physical data for the compound we obtained were identical with those reported by Closs *et al.*[4]

Oxidation of compounds (**1**) with *m*-chloroperbenzoic acid (MCPBA) in CH_2Cl_2 at room temperature and careful column chromatography (alumina) afforded their 1-oxides (**3**)‡ and 2-oxides (**4**) as shown in Table 2. The sites of the *N*-oxidations were determined by ^1H n.m.r. and (high-

TABLE 2. 1,2,3-Triazine *N*-oxides (**3**) and (**4**).

			Mass spectral peaks (*m/e*)		^1H n.m.r. (δ, J in Hz) spectra Positions		
N-Oxide	% Yield	M.p./°C	$M^+ - N_2$	$MeCNO^+$	4	5	6
(**3a**)	11	162	83[a]	57[b]	2·52 (3H, s)	7·44 (1H, br.d, 5·0)	8·43 (1H, d, 5·0)
(**3b**)	20	182	97[c]	57[d]	2·46 (3H, s) or 2·60 (3H, s)	7·68 (1H, s)	2·46 or 2·60
(**3c**)	29	197	159[e]	57[f]	2·57 (3H, s)	7·81 (1H, s)	7·47—7·66 (3H, m), 8·01—8·16 (2H, m)
(**3d**)	10	140	111	57(w[g])	Three singlets: 2·32 (3H), 2·46 (3H), 2·56 (3H)		
(**4a**)	30	95	abs.[h]	vw[i]	2·53 (3H, s)	6·79 (1H, d, 6·0)	8·50 (1H, br.d, 6·0)
(**4b**)	48	88	abs.	vw	2·46 (6H, s)	6·70 (1H, s)	2·46
(**4c**)	60	178	abs.	vw	2·58 (3H, s)	7·21 (1H, s)	7·48—7·67 (3H, m), 8·00—8·16 (2H, m)
(**4d**)	31	112	abs.	vw	2·44 (6H, s)	2·23 (3H, s)	2·44

[a] Obs. 83·037; calc. 83·037. [b] Obs. 57·022; calc. 57·021. [c] Obs. 97·054; calc. 97·053. [d] Obs. 57·022. [e] Obs. 159·069; calc. 159·068. [f] Obs. 57·022. [g] Weak. [h] Absent. [i] Very weak.

---

† This synthetic limitation has arisen chiefly from the lack of stability and availability of appropriate cyclopropenes or cyclopropenyl cations; compounds (**1**) have generally been synthesized *via* cyclopropenyl azides obtained from these compounds.

‡ Several attempts to detect and isolate 4-Me-1,2,3-triazine 1-oxide and 4-Me-6-Ph-1,2,3-triazine 1-oxide have been unsuccessful. These compounds are most likely absent in the reaction mixture (^1H-n.m.r. and t.l.c.).

Table 3. 2,5-Dihydro-1,2,3-triazines (**5**).

		¹H n.m.r. (δ, J in Hz) Positions			
Compound	M.p./°C	2-(NH)	4	5	6
(**5b**)	65	8·35 (1H, br.s)	2·00 (6H, s)	2·45 (2H, s)	2·00
(**5c**)	60	9·02 (1H, br.s)	2·05 (3H, s)	2·80 (2H, s)	7·20—7·50 (3H, m), 7.60—7.80 (2H, m)
(**5d**)	54	8·45 (1H, br.s)	2·00 (6H, s)	1·02 (3H, d, 6·6), 2·67 (1H, q, 6·6)	2·00

resolution) mass spectroscopy.§ In the latter, (**3a**—**d**) all showed both peaks due to ($M^+ - N_2$) and ($MeCNO^+$),§ while these ions are absent or very weak in the spectra of (**4a**—**d**). The reason why 4-methyl-1,2,3-triazine 1-oxide and 4-methyl-6-phenyl-1,2,3-triazine 1-oxide were not obtained is unclear at present.‡

Catalytic hydrogenation of (**1b**—**d**) on Pd–C (1 atm; room temp.) afforded the dihydro-compounds (**5b**—**d**) in almost quantitative yields; this presents a striking contrast to the similar reduction of 4,5,6-triphenyl-1,2,3-triazine (**1**, $R^1 = R^2 = R^3 =$ Ph) from which 3,4,5-triphenylpyrazole was obtained.[5]¶ The structures of the 2,5-dihydro-1,2,3-triazines were supported by ¹H n.m.r. spectroscopy as shown in Table 3: *e.g.*, (**5d**) showed a quartet at δ 2·67 (J 6·6 Hz) due to the 5-methine proton and a doublet at δ 1·02 (J 6·6 Hz) due to the 5-methyl group, besides the signals of two methyl and NH groups. There was no n.m.r. evidence for the participation of other (*e.g.*, 1,4-) dihydro-structures for (**5b**, **c** and **d**). 5-H in (**5b**) was not exchangeable with CD_3OD (n.m.r.). These data show that there is no tautomerization of these dihydro-compounds and the protons are fixed in the 2,5-dihydro-form.

Catalytic reduction of (**3b**) and (**4b**), and reduction of (**1b**) with $NaBH_4$ (in MeOH) also gave (**5b**) in reasonable yields.

Additionally, (**5b**—**d**) were oxidised to give (**1b**—**d**) when solutions in $CDCl_3$, CCl_4, CH_2Cl_2, *etc.*, were exposed to air; the mechanism of this is under investigation.

Finally, all attempts to synthesize the unsubstituted 1,2,3-triazine ($R^1 = R^2 = R^3 = H$) by the oxidation of *N*-aminopyrazole with LTA under various conditions have so far failed.

We thank the Central Research Laboratories of Sankyo Co., Ltd. for the high-resolution mass spectra of the samples in Table 2.

(*Received*, 29*th July* 1980; *Com.* 833.)

---

§ See the footnotes in Table 2.

¶ Pyrazoles were not found in the present study.

[1] R. J. Kobylecki and A. McKillop, *Adv. Heterocyclic Chem.*, 1976, **19**, 215, and refs. cited therein.

[2] G. Seybold, U. Jersak, and R. Gompper, *Angew. Chem., Int. Ed. Engl.*, 1973, **12**, 847; R. Gompper and K. Schönafinger, *Chem. Ber.*, 1979, **112**, 1514, 1529, 1535.

[3] B. M. Adger, S. Bradbury, M. Keating, C. W. Rees, R. C. Storr, and M. T. Williams, *J. Chem. Soc., Perkin Trans.* 1, 1975, 31.

[4] G. L. Closs and A. M. Harrison, *J. Org. Chem.*, 1972, **37**, 1051.

[5] E. A. Chandross and G. Smolinsky, *Tetrahedron Lett.*, 1960, 19.