Revised Structure of *N*-Oxidation Products of 4,5,6-Triaryltriazines: 1,2,3-Triazine 2-Oxides

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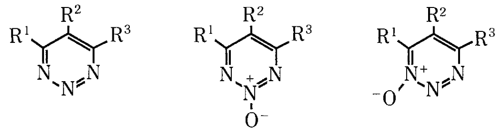
The *N*-oxidation products of 4,5,6-triaryl-1,2,3-triazines were decided to be the 2-oxides on the basis of spectral data and X-ray crystallography; the structures are different from those reported previously.

Keywords 1,2,3-triazine; oxidation; triaryl-1,2,3-triazine; triaryl-1,2,3-triazine *N*-oxide; *m*-chloroperbenzoic acid; peracetic acid; X-ray crystallography

In the field of heteroaromatic chemistry, there is considerable interest in the selectivity on *N*-oxidation of polyazaheteroaromatic compounds,1) and several studies have appeared on the position of *N*-oxidation of 1,2,3-triazines **2**.2−5) However, there have been conflicting results. The present authors have reported2) that some phenyl-substituted triazines (**1a** and **1b**) underwent the oxidation with *m*-chloroperbenzoic acid (*m*CPBA) at N-2 exclusively, whereas there are reviews4) and articles5) in which predominant formation of the 1-oxides **3** upon oxidation of 4,5,6-triaryl-1,2,3-triazines with peracetic acid (PAA) is claimed. These reports prompted us to reinvestigate the structure of 1,2,3-triazine *N*-oxide, and whether or not changes in the oxidation conditions would alter the reaction sites.

As model reactions, we employed the oxidation of 4,5,6-triphenyl-1,2,3-triazine **1b** with PAA and of 4,5,6-tris(*p*-tolyl)-1,2,3-triazine **1c** with *m*CPBA and PAA, and the structure of a major product (the sole *N*-oxide) from **1c** was definitively determined by X-ray crystallography.



1 **2** **3**

- **a** : R^1=R^3=Ph, R^2=H
- **b** : R^1=R^2=R^3=Ph
- **c** : R^1=R^2=R^3=*p*-MeC$_6$H$_4$
- **d** : R^1=R^3=Ph, R^2=*p*-MeC$_6$H$_4$
- **e** : R^1=R^2=Ph, R^3=*p*-MeC$_6$H$_4$

Chart 1

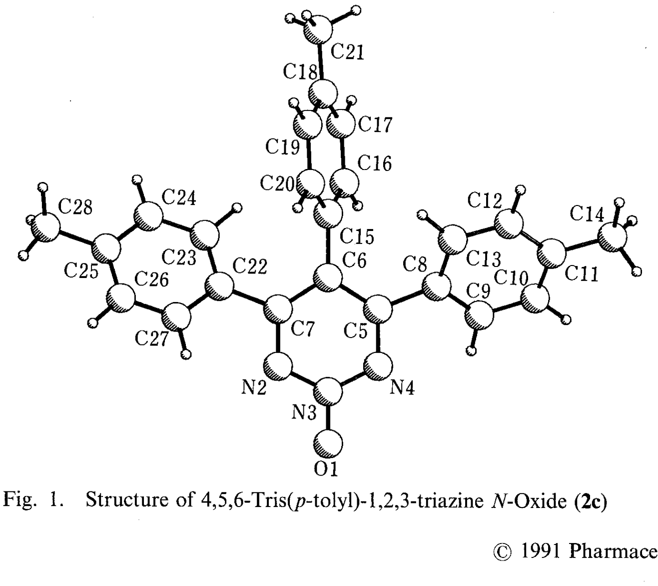


Fig. 1. Structure of 4,5,6-Tris(*p*-tolyl)-1,2,3-triazine *N*-Oxide (**2c**)

First, **1b** was oxidized with PAA according to Neunhoeffer's method (with 40% AcOOH–AcOH/CHCl$_3$, under reflux for 4 h).5) The major product (77% from consumed **1b**) of the reaction was identical with the one that had been obtained as the major product of the reaction of **1b** with *m*CPBA, and whose structure had been determined as the 2-oxide **2b**.2) Other compounds isolated were the starting material **1b** and 3,4,5-triphenylisoxazole (**4**, trace), and the 1-oxide was not found despite careful examination of the reaction mixture.

Secondly, the oxidation of **1c** with *m*CPBA in methylene chloride at room temperature gave a single product (95%). The proton and carbon-13 nuclear magnetic resonance (^{1}H- and ^{13}C-NMR) spectra revealed a highly symmetrical character, indicating it to be the 2-oxide **2c**. An X-ray crystallographic analysis was carried out to elucidate the structure unequivocally, and the result are shown in Fig. 1 and Table I.

The oxidation of **1c** with PAA under Neunhoeffer's

TABLE I. Fractional Atomic Coordinates and Isotropic Thermal Parameters of **2c**

	x	y	z	B_{eq} a)
O(1)	0.0951 (0)	0.1084 (0)	0.7742 (0)	5.97 (10)
N(2)	0.2536 (5)	0.3151 (5)	0.9957 (8)	4.16 (9)
N(3)	0.2309 (4)	0.2077 (4)	0.8305 (8)	4.01 (9)
N(4)	0.3406 (5)	0.1968 (5)	0.7204 (8)	3.89 (9)
C(5)	0.4870 (5)	0.3041 (5)	0.7797 (8)	3.51 (10)
C(6)	0.5258 (5)	0.4232 (5)	0.9510 (8)	3.47 (10)
C(7)	0.4014 (5)	0.4226 (5)	1.0557 (8)	3.82 (11)
C(8)	0.5972 (5)	0.2766 (5)	0.6443 (8)	3.75 (10)
C(9)	0.5380 (5)	0.2070 (5)	0.4150 (9)	3.90 (11)
C(10)	0.6325 (6)	0.1687 (5)	0.2895 (9)	4.51 (12)
C(11)	0.7872 (6)	0.1936 (6)	0.3846 (9)	5.00 (13)
C(12)	0.8459 (6)	0.2646 (6)	0.6139 (10)	5.35 (14)
C(13)	0.7543 (5)	0.3055 (6)	0.7418 (9)	4.51 (12)
C(14)	0.8863 (8)	0.1446 (9)	0.2530 (12)	7.49 (22)
C(15)	0.6873 (5)	0.5430 (5)	1.0122 (8)	3.66 (10)
C(16)	0.7431 (5)	0.6406 (5)	0.8594 (9)	4.15 (11)
C(17)	0.8895 (5)	0.7579 (5)	0.9226 (9)	4.53 (12)
C(18)	0.9858 (5)	0.7785 (5)	1.1371 (9)	4.44 (12)
C(19)	0.9299 (6)	0.6787 (5)	1.2880 (9)	4.52 (12)
C(20)	0.7836 (6)	0.5627 (5)	1.2276 (9)	4.27 (11)
C(21)	1.1423 (6)	0.0060 (7)	1.2079 (11)	5.84 (16)
C(22)	0.4097 (5)	0.5358 (5)	1.2418 (9)	4.23 (12)
C(23)	0.5056 (7)	0.6830 (5)	1.2540 (10)	5.31 (15)
C(24)	0.5041 (8)	0.7848 (6)	1.4256 (10)	6.03 (16)
C(25)	0.4054 (7)	0.7438 (6)	1.5832 (10)	6.17 (17)
C(26)	0.3125 (7)	0.5977 (7)	1.5727 (10)	6.09 (16)
C(27)	0.3134 (6)	0.4949 (6)	1.4053 (10)	4.98 (13)
C(28)	0.4044 (13)	0.8574 (9)	1.7634 (12)	9.29 (32)

a) $B_{eq}=(1/3)\Sigma_i\Sigma_j B_{ij}a_i^*a_j^*\mathbf{a}_i\mathbf{a}_j$.

Table II. *N*-Oxidation of Aryl-1,2,3-triazines **1**

Triazine (**1**)	Reagent	Product(s)	Yield (%)	Recovery of **1** (%)	By-product
1a	*m*CPBA[a]	**2a**	81	Trace	—
1b	*m*CPBA[a]	**2b**	53 (72)[b]	26	—
1b	PAA[c]	**2b**	54[d] (77)[b]	30	Isoxazole (**4**) (Trace)[e]
1c	*m*CPBA	**2c**	95	Trace	—
1c	PAA[c]	**2c**	51[f]	Trace	mp 208 °C (16%)[g]
1c	PAA[h]	**2c**	55 (74)[b]	25	mp 208 °C (Trace)[g]
1d+**e**[i]	*m*CPBA	**2d**+**2e**	90	Trace	—
1d+**e**[i]	PAA[c]	**2d**+**2e**	34 (50)[h]	22	mp 209 °C (5%)[j]

a) See ref.[2] *b*) Percent from consumed **1**. *c*) At 80 °C (bath temp.). *d*) Neunhoeffer *et al.* reported a yield of 65% for **3b**[5]; yield 35% by reaction with H_2O_2–AcOH, reflux.[2] *e*) Yield 4% by reaction with H_2O_2–AcOH, reflux.[2] *f*) Ref. 5 reports a yield of 70% for **3c**. *g*) See note.[6] *h*) At 65 °C (bath temp.). *i*) See note.[7] *j*) See note.[10]

conditions gave **2c** as a major product (51%), accompanied with a minor product(s) described in the experimental section.[6] Thorough inspection of the reaction mixture proved that the corresponding 1-oxide (**3c**) was not formed. The oxidation of **1c** under milder condition (heated at 65 °C) afforded a 74% yield (base on the consumed **1c**) of **2c**.

Finally, the oxidation of a mixture[7] of 4,6-diphenyl-5-tolyl **2d** and 4,5-diphenyl-6-tolyltriazines **2e** with *m*CPBA and with PAA also gave their 2-oxides (mixture) as major products (see Experimental and Notes). The data are summarized in Table II. In conclusion, we have proved that *N*-oxidation of the triaryltriazines gives exclusively the corresponding 2-oxides, irrespective of the reaction conditions.[8]

Experimental

All melting points were taken on a Yanaco micro melting point apparatus and are uncorrected. The mass spectra (MS) were measured with a JEOL JMS-D300 instrument. The NMR spectra were taken on a JEOL GX400 spectrometer using tetramethylsilane as an internal standard.

Oxidation of 1b with *m*CPBA The procedure and results are described in our previous paper,[2] yield of **2b** 53%, recovery of **1b** 26%, and no by-products were detected.

Oxidation of 1b with PAA A 1 ml aliquot of 90% H_2O_2 was added to 5 ml of Ac_2O under cooling on an ice bath, and the mixture was allowed to stand at room temperature for 24 h (aging), then used as the reagent; the calculated content of PAA is *ca.* 42%. PAA solution (PAA, 200 mg, *ca.* 1.11 mmol) was added to a solution of **1b** (100 mg, 0.32 mmol) in $CHCl_3$ (10 ml), and the mixture was refluxed for 4 h at 80 °C. The CH_2Cl_2 (90 ml) was added, and the solution was washed with 10% aqueous $KHCO_3$, dried over $MgSO_4$, and evaporated. Thin layer chromatography (TLC, Merck Aluminiumoxid 5713/Et_2O–hexane–trace acetone) of the reaction mixture showed two major (**1b** and **2b**) and one minor (**4**)[2] spots. Recrystallization of the mixture gave 22 mg of prisms (**2b**). The residual solvent was evaporated off and the residue was subjected to preparative TLC (Merck Aluminiumoxid 5726/Et_2O–hexane–trace acetone) to give a trace of **4**,[9] 30 mg (30%) of **1b**, and an additional 35 mg of **2b** (total 54%).[5] No other products were obtained.

Oxidation of 1c with *m*CPBA A solution of **1c** (110 mg, 0.31 mmol) and *m*CPBA (100 mg, 0.58 mmol) in CH_2Cl_2 (25 ml) was allowed to stand at room temperature for 24 h. The reaction mixture was washed with aqueous $KHCO_3$, dried over $MgSO_4$, and evaporated. TLC of the residue showed only two spots. The residue (130 mg) was recrystallized from MeOH–Et_2O–hexane to give 85 mg of colorless thick needles (**2c**). The mother liquor was evaporated and the residue, which contained *m*-chlorobenzoic acid, was submitted to alumina column chromatography (Et_2O–hexane–trace acetone) to give a trace of **1c** and additional **2c** (25 mg). The total yield of **2c** was 95%. No other products were detected. **2c**: mp 219 °C (ref.[5] gives mp 223 °C for **3c**). *Anal.* Calcd for $C_{24}H_{21}N_3O$: C, 78.45; H, 5.76; N, 11.44. Found: C, 78.21; H, 5.67; N, 11.38. IR (KBr): 1600 (strong), 1523, 1431 (strongest), 1345, 1275, 1170, 1018, 815, 780, 733 cm^{-1}. MS (MS, EI/70 eV); *m*/*z*: 367 (40%, M^+), 337 (20%, $M^+ - NO$), 309 (13%, $M^+ - N_3O$), 220 (35%, Tol_2C_2N), 206 (100%, Tol_2C_2), 205 (28%), 202 (9%), 191 (22%), 189 (20%), 119 (7%), 117 (8%), 103 (25%). (Ref.[5] gives values for **3c**, 367 (6%), 206 (100%), 205, 202, 191, 189, 119, 117). ^1H-NMR ($CDCl_3$) δ: 2.32 (9H, s), 6.84 (2H, d, J=8 Hz), 7.02 (2H, d, J=8 Hz), 7.05 (4H, d, J=8 Hz), 7.21 (4H, d, J=8 Hz). ^{13}C-NMR ($CDCl_3$) δ: 21.19, 21.25, 119.81, 128.76, 129.47, 129.66, 129.76, 130.26, 130.40, 138.32, 140.59, 166.21.

Oxidation of 1c with PAA under Reflux A mixture of **1c** (160 mg, 0.456 mmol), PAA solution (260 mg, *ca.* 1.44 mmol), and $CHCl_3$ (10 ml) was refluxed for 4 h at 80 °C. The reaction mixture was treated as described for **1b**. The residue showed one major (**2c**) and one minor TLC spots. Repeated cautious separation by preparative TLC (Et_2O–hexane–trace acetone) gave 85 mg (51%) of **2c**, a minor product (30 mg, 16%, mp 208 °C, colorless prisms from MeOH–Et_2O–hexane), and a trace of **1c**. Spectral data of the minor product excluded the structure of **3c**[6]: ^1H-NMR; three methyl signals, two benzylic signals at δ 4.54 and 4.55, intensity ratio *ca.* 8:5 together with rather complex signals in the aromatic region: The ^{13}C-NMR spectrum showed five signals in the aliphatic region and twenty signals in the aromatic region, some signals appearing as shoulders. MS *m*/*z*: 403 (35%, exact mass; 403.129. This value is consistent with $C_{24}H_{20}N_3{}^{37}ClO = 403.127$), 401 (100%, exact mass; 401.130. This value is consistent with $C_{24}H_{20}N_3{}^{35}ClO = 401.130$, M^+), 373 (22%, $M^+ + 2 - NO$), 371 (65%, $M^+ - NO$), 366 (18%, $M^+ - Cl$), 256 (22%, $C_{16}H_{13}N^{37}Cl$), 254 (66%, $C_{16}H_{13}N^{35}Cl$), 242 (20%, $C_{16}H_{13}{}^{37}Cl$), 240 (60%, $C_{16}H_{13}{}^{35}Cl$), 220 (60%, Tol_2C_2N), 219 (22%), 206 (78%), 195 (95%), 103 (54%): The IR spectrum was analogous to that of **2c**.

Oxidation of 1c with PAA at 65 °C A mixture of **1c**, PAA, and $CHCl_3$ was heated at 65 °C for 4 h. Then the reaction mixture was washed with $KHCO_3$, dried over $MgSO_4$, and evaporated. The residue was chromatographed on alumina to give **1c**, **2c**, and a trace amount of by-product.

Oxidation of 1d+1e with *m*CPBA A mixture of **1d** and **1e**[7] (260 mg, 0.80 mmol) in CH_2Cl_2, was treated with 280 mg (1.6 mmol) of *m*CPBA, and the solution was allowed to stand at room temperature for 24 h. Then the reaction mixture was treated as mentioned above. The residue showed two spots on TLC, one of which was due to *m*-chlorobenzoic acid. The residue was recrystallized from $CHCl_3$–CH_3OH(trace)–hexane to give 155 mg of colorless needles. The mother liquor, which contained mainly *m*-chlorobenzoic acid, was evaporated and the residue was subjected to alumina preparative TLC to give a trace amount of starting material and an additional 90 mg of the same product (the total yield 90% (145 mg); mp 196—210 °C (br); ref. 5 gives mp 198 °C for **3d**). The constitution of the product was suggested to be a mixture of the *N*-oxides **2d** and **2e** from the data shown below. *Anal.* Calcd for $C_{22}H_{17}N_3O$: C, 77.85; H, 5.05; N, 12.38. Found: C, 78.15; H, 5.28; N, 12.11. MS *m*/*z*: 339 (78%, M^+), 309 (20%, $M^+ - NO$), 281 (5%, $M^+ - N_3O$), 206 (30%, Tol(Ph)C_2N), 192 (100%, Tol(Ph)C_2), 191, 189, 178 (22%, Ph_2C_2. This peak suggests the presence of two phenyl groups on adjacent carbons). Reference 5 reports a similar *m*/*z* for **3d**. ^1H-NMR ($CDCl_3$) δ: 2.31 (3H, br s), 6.72—7.43 (10H, m). The ^{13}C-NMR spectrum showed two signals due to the C-5 in triazine rings at δ 119.2 and 120.1. These data are inconsistent with the structure of **3d** in the literature.[5]

Oxidation of 1d+1e with PAA A mixture of **1d**+**1e**[7] (260 mg, 0.80 mmol), PAA solution (650 mg, *ca.* 3.60 mmol), and $CHCl_3$ (10 ml) was refluxed at 80 °C for 4 h, and treated as described before. The residue thus obtained consisted of the starting material, major products (**2d**+**2e**), and a minor product, as detected by TLC. The residue was chromatographed on alumina, and overlapping fractions were submitted repeatedly to preparative TLC to give the starting material (58 mg), a major product (colorless needles, 107 mg), and a by-product (mp 190—209 °C (br)). The major product was identical with that from the *m*CPBA oxidation. The minor one showed spectral data which were inconsistent with the structure **3d**, and contained a chlorine atom.[10]

Structural Analysis of 2c by X-Ray Crystallography The observed cell parameters for **2c** (0.30 × 0.20 × 0.50 mm, from MeOH–Et_2O–hexane) were as follows: M.W. 367.45 ($C_{24}H_{21}N_3O$), space group $P1$ (monoclinic), $Z=1$, $a=9.333(1)$, $b=10.073(1)$, $c=5.903(1)$ Å, $\alpha=94.23(1)$, $\beta=98.62(1)$, $\gamma=113.01(1)°$, $V=116.9(2)$ Å^3, $D_C=1.222$ $g\,cm^{-3}$. Data were collected on a Rigaku AFC-5 diffractometer using graphite monochromated Cu$K\alpha_1$ radiation by the θ–2θ scan method. The scan speed was 16° min^{-1}. The data were corrected for Lorentz and polarization factors, but no absorption correction was applied. A total of 1697 reflections were measured within the 2θ angle of 120°. The crystal structure was determined by the direct method and refined by the full-matrix least-squares method. The final R value was 0.042 for 1459 reflections above $3\sigma(F)$ including anisotropic thermal factors for nonhydrogen atoms and isotropic ones for hydrogen atoms. The final atomic coordinates are listed in Table I.

References and Notes

1) A. R. Katritzky and J. M. Lagowski, "Chemistry of the Heterocyclic *N*-Oxides," Academic Press, London, 1971, p. 70, and references cited therein.

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4) H. Neunhoeffer: Chemistry of 1,2,3-Triazine," The Chemistry of Heterocyclic Compounds," ed. by A. Weissberger and E. C. Taylor, Wiley, New York, 1978, p. 6, and references cited therein.

5) H. Neunhoeffer, M. Clausen, H.-D. Vötter, H. Ohl, C. Krüger, and K. Angermund, *Justus Liebigs Ann. Chem.*, **1985**, 1732.

6) This product is assumed to be mixed crystals of 4-(*p*-chloromethylphenyl)-5,6-bis(*p*-tolyl)-1,2,3-triazine 2-oxide and 5-(*p*-chloromethylphenyl)-4,6-bis(*p*-tolyl)-1,2,3-triazine 2-oxide, although the formation mechanism is unclear (they were probably derived from **2c** *via* radical abstraction of a chlorine atom from the solvent molecule). TLC of the compound(s) using alumina or silica gel showed one clear spot with all solvents examined, and the separation was unsuccessful.

7) The report by Neunhoeffer *et al.*[11] claimed that the reaction of 1,2-diphenyl-3-(*p*-tolyl)cyclopropenyl salt with sodium azide (a modification of the method of Chandross *et al.*, *Tetrahedron Lett.*, **1960**, 19) gave 4,6-diphenyl-5-(*p*-tolyl)-1,2,3-triazine (**1d**) predominantly (isomer 0—15%) because of the electron-donating effect of the methyl group. However, we obtained different results: the procedure according to Neunhoeffer *et al.* afforded a major product in 24% yield, whose melting point was 218 °C (lit. 222 °C as **1d**). Its ^{13}C-NMR spectrum showed signals at δ 21.25 and 21.28 due to methyl groups. The ^{1}H-NMR spectrum showed methyl signals at δ 2.34 and 2.36 (shoulder), and they were split into two signals at δ 2.48 and 2.60 in the ratio of *ca.* 63 : 37 upon addition of Eu(FOD)$_3$, which also suggested the presence of two kinds of methyl groups. The MS showed intense peaks at *m/z* 178 (30%, Ph_2C_2) and 192 (100%, Tol(Ph)C_2). The former fragment implied the presence of two phenyl groups on adjacent carbons. Thus the product is thought to be a mixture of **1d** and its isomer, 4,5-diphenyl-6-(*p*-tolyl)-1,2,3-triazine **1e**. All attempts to separate them were unsuccessful.

8) We think that the misassignment in the previous report[4,5] is due to misreading of the mass fragmentation and the lack of high resolution NMR spectra.

9) Compound **4** was obtained in 4% yield on oxidation with H_2O_2–AcOH under reflux.

10) This compound is probably a mixture of 5-(*p*-chloromethylphenyl)-4,6-diphenyl-1,2,3-triazine 2-oxide and 4-(*p*-chloromethylphenyl)-5,6-diphenyl-1,2,3-triazine 2-oxide. The MS showed peaks at *m/z* 375 (33%, $C_{22}H_{16}N_3{}^{37}ClO$) and 373 (100%, $C_{22}H_{16}N_3{}^{35}ClO$). The ^{1}H-NMR spectrum showed two chloromethyl signals at δ 4.52 and 4.53.

11) H. Neunhoeffer, H-D. Vötter, and H. Ohl, *Chem. Ber.*, **103**, 3695 (1972).