1,2,4-Triazine Chemistry. 10.[1] Dihydro-1,2,4-triazines: Structural Studies of 5,6-Diaryldihydro-1,2,4-triazines through the Reactions with Dimethyl Acetylenedicarboxylate

Tadashi Sasaki,* Katsumaro Minamoto, and Katsuhiko Harada

Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya, Japan

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Sodium borohydride reduction of 3-(methylthio)-5,6-diphenyl- (**1a**), 3-(methylthio)-5,6-ditolyl- (**1c**), 3-(methylthio)-5,6-dianisyl- (**1e**), and 3-(methylthio)-5,6-bis(*p*-chlorophenyl)-1,2,4-triazine (**1g**) afforded the corresponding 2,5-dihydro-1,2,4-triazines (**2a,c,e,g**). 3-Methoxy-5,6-diphenyl- (**1b**), 3-methyoxy-5,6-ditolyl- (**1d**), 3-methoxy-5,6-dianisyl- (**1f**), and 3-methoxy-5,6-bis(*p*-chlorophenyl)-1,2,4-triazine (**1h**) also gave the corresponding 2,5-dihydro-1,2,4-triazines (**2b,d,f,h**) on similar reduction. Reaction of **2a–h** with MeI/NaH generally gave the corresponding N_2-methylated analogues **3a–h** as major products. The structures of **3a** and **3b** were established by their chemical conversions to known 2-methyl-5,6-diphenyl-1,2,4-triazin-3(2*H*)-one (**6**) and its 4,5-dihydro derivative (**5**), respectively. Treatment of **3a–h** with dimethyl acetylenedicarboxylate (DMAD) gave the corresponding 2,6-diaryl-4-methyl-5-(methylthio)- (or -5-methoxy-) 1,8-bis(methoxycarbonyl)-3,4,7-triazabicyclo-[3.3.0]octa-2,7-dienes (**9a–f**) and the similar analogue **9g** from **3h**. Acidic hydrolysis of **9a** (or **9b**), **9d**, and **9e** gave another new ring system of 2-methyl-3-oxo-4,8-diaryl-6,7-bis(methoxycarbonyl)-1,2,5-triazabicyclo[4.2.0]-octa-7-enes (**10a–c**). On the other hand, DMAD with 2,3-dimethyl-5,6-diphenyl-2,5-dihydro-1,2,4-triazine (**14**) afforded two 1:2 adducts (**15** and **16**) of unknown structure, while DMAD with 3-(methylthio)-2,5,6-trimethyl-1,2,4-triazine (**17**) gave a small amount of 2,3-bis(methoxycarbonyl)-4,5-dimethylpyrrole (**20**). Some mechanistic comments are given for the formation of **9** and **20**.

Since the first results of structural studies on 1,2,4-triazine *N*-oxides were disclosed in 1964 by Atkinson[2] and by us,[3] numerous publications on similar subjects have appeared,[4] and these studies have been reviewed recently.[5] No systematic structural studies of the reduction products of substituted 1,2,4-triazines have been attempted; as Neunhoeffer[6] states "...we usually use the 4,5-dihydro-1,2,4-triazine structure, but this does not imply that this structure is well established". In view of the natural occurrence of the 1,2,4-triazine ring system in antibiotics such as fervenulin, 2-methylfervenulone, and toxoflavin[7] and the broad spectrum of biological activity claimed for the derivatives of 1,2,4-triazine,[8] the reduced forms of the 1,2,4-triazine ring system would involve new aspects of biochemical and chemical interest.

This paper describes reduction of 5,6-diaryl-1,2,4-triazines to the corresponding 2,5-dihydro-1,2,4-triazines with sodium borohydride and some interesting chemistry of their 2-methylated analogues discovered in connection with their structure determination. The accompanying paper treats similar reduction of other 3-methoxy- and 3-(methylthio)-1,2,4-triazines which are differently substituted at the 5- and/or 6-positions.

Scheme I

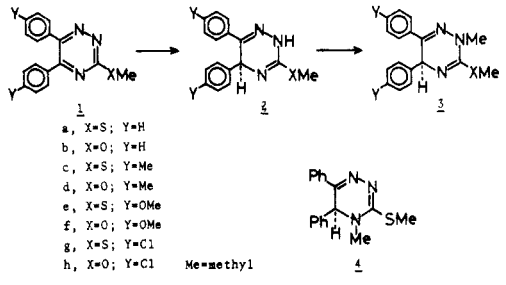
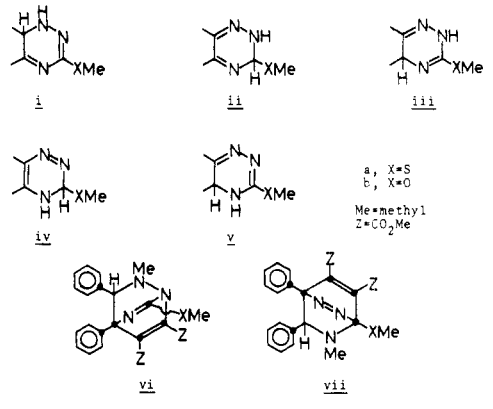


Chart I



At the outset, the easily available 3-(methylthio)- (**1a**)[9] as well as the 3-methoxy-5,6-diphenyl-1,2,4-triazine (**1b**)[9] was reduced with an equimolar amount of sodium borohydride to give the corresponding 3-(methylthio)- and 3-methoxy-5,6-diphenyl-2,5-dihydro-1,2,4-triazines (**2a,b**) in good yields (Scheme I, Table I). The structures of these products were established as shown below. The similar ^1H NMR resonance patterns of **2a,b** showing singlets for

(1) *as*-Triazinechemie. 9: Sasaki, T.; Minamoto, K.; Murata, M. *Chem. Ber.* **1968**, *101*, 3696.
(2) Atkinson, C. M.; Ibbitson, D.-A.; Rice, F. J.; Sandall, J. P. B. *J. Chem. Soc.* **1964**, 4209.
(3) Sasaki, T.; Minamoto, K. *Chem. Pharm. Bull.* **1964**, *12*, 1327.
(4) (a) Sasaki, T.; Minamoto, K. *J. Org. Chem.* **1966**, *31*, 3914, 3917; (b) *J. Heterocycl. Chem.* **1967**, *4*, 571; (c) *Tetrahedron* **1969**, *25*, 1021. (d) Paudler, W. W.; Chen, Teh-Kuei *J. Org. Chem.* **1971**, *36*, 787. (e) Radel, R. J.; Keen, B. T.; Wong, C.; Paudler, W. W. *Ibid.* **1977**, *42*, 546. (f) Keen, B. T.; Radel, R. J.; Paudler, W. W. *Ibid.* **1977**, *42*, 3498. (g) Radel, R. J.; Atwood, J. L.; Paudler, W. W. *Ibid.* **1978**, *43*, 2514. (h) Neunhoeffer, H.; Weischedel, F.; Böhnish, V. *Justus Liebigs Ann. Chem.* **1971**, 750, 12. (i) Neunhoeffer, H.; Frühauf, H.-W. *Ibid.* **1972**, 758, 111. (j) Neunhoeffer, H.; Böhnish, V. *Ibid.* **1976**, 153.
(5) Neunhoeffer, H.; Wiley, P. F., Eds. "Chemistry of 1,2,3-Triazines and 1,2,4-Triazines, Tetrazines, and Pentazines"; Wiley-Interscience: New York, 1978; p 554.
(6) Reference 5, p 575.
(7) Pfleiderer, W., Ed. "Chemistry and Biology of Pteridines"; Walter de Gruyter: New York, 1975; pp 575–601.
(8) Reference 5, p 1001.
(9) Paudler, W. W.; Chen, Teh-Kuei *J. Heterocycl. Chem.* **1970**, *7*, 767.

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Table I. Yields, Melting Points, Reaction Times, and Spectroscopic Data for 5,6-Diaryl-2,5-dihydro-1,2,4-triazines 2a-h and 13

compd	yield, %	t, h	mp, °C	λ_{max},[d] nm (ϵ)	^{1}H NMR,[a] δ		
					C_5 H	NH	other
2a	92	24	227-230	234* (13 800), 300 (8800)	5.91	10.90	2.35[e]
2c	93	24	168-169	218* (21 400), 240* (13 500), 301 (9500)	5.82	8.18	2.42[e]
2e	91	23	163-165	223* (19 200), 250* (10 800), 283 (10 600), 303 (12 300)	5.76	8.15	2.44[e]
2g	93	12	185-187	218* (22 500), 238* (15 500), 304 (9900)	5.81	8.29	2.43[e]
2b	71	24	160-163	224* (16 500), 292 (9200)	5.81	10.42	3.66[f]
2d	88	24	141.5-143	218* (18 000), 292 (9100)	5.71	7.83	3.76[f]
2f	64	23	142-145	220* (16 900), 283* (12 000), 294 (12 100)	5.68	7.80	3.78[f]
2h	82	14	230-232	221 (19 700), 298 (9500)	5.81	10.54	3.65[f]
13	59[b]	24	167-168[c]	230* (11 900), 303 (6500)	5.72	8.76	1.98[g]

[a] The spectra of 2a,b,h were measured in Me_2SO-d_6 and the others in $CDCl_3$. The imino protons are D_2O exchangeable. The signals of the C_5 H and CH_3 are all sharp singlets, while the NH signals are broad singlets. [b] Recovery of the starting triazine was 22%. [c] This sample contained 1/2 equiv of MeOH. [d] An asterisk indicates inflection; solvent was 95% EtOH. [e] SCH_3. [f] OCH_3. [g] C_3 CH_3.

Table II. Yields, Melting Points, and Spectroscopic Data for 3a-h, 4, and 14

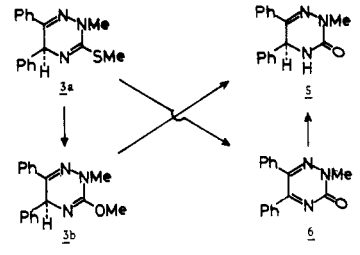
compd	yield, %	mp, °C	λ_{max},[b] nm (ϵ)	^{1}H NMR ($CDCl_3$),[a] δ		
				C_5 H	NCH_3	other
3a	77	78-81	235* (10 400), 309 (5400)	5.88	3.45	2.40[c]
3c	57	125-126	220* (18 100), 235* (14 100), 310 (8000)	5.72	3.44	2.42[c]
3e	83	90-91.5	225* (21 600), 245* (13 800), 282 (8300), 312 (11 900)	5.78	3.44	2.39[c]
3g	77	127.5-128.5	220 (23 300), 240* (17 700), 314 (9900)	5.80	3.43	2.42[c]
4	7.9	140-141	247 (6600), 339 (5700)	5.17	3.08	2.59[c]
3b	89	77-78	228* (16 500), 303 (8000)	5.76	3.36	3.76[d]
3d	70	73.5-75.5	220* (17 100), 234* (13 800), 304 (9100)	5.72	3.36	3.72[d]
3f	44	79-81	223* (17 700), 252* (9900), 284* (8900), 305 (11 600)	5.66	3.35	3.78[d]
3h	45	71-73	222 (18 800), 240* (15 500), 310 (9700)	5.71	3.39	3.80[d]
14	47	119-120	230* (13 900), 314 (7100)	5.67	3.43	2.11[e]

[a] All signals are singlets. [b] Solvent 95% EtOH; asterisk indicates inflection. [c] SCH_3. [d] OCH_3. [e] C_3 CH_3.

one NH and one methine proton (Table I) suggested the skeletal identity of both compounds, which might be 1,6-, 2,3-, 2,5-, 3,4-, or 4,5-dihydro-1,2,4-triazines (Chart I, i–v). Structures of the type ii or iv are improbable in view of the stability of these compounds when treated with aqueous acetic acid or silicic acid. Models of the *vic*-dihydro structures i and v show that the hydrogen atoms can have a dihedral angle of ca. 90°, and therefore the multiplicity of the ^{1}H NMR resonances allows no credible judgement in the present case.

As one of the chemical approaches to the structural elucidations, the Diels–Alder reaction with dimethyl acetylenedicarboxylate (DMAD) was considered in order to distinguish between i, iii, and v. Since the N-methylated analogues of the dienes of type i or v were expected to give the 1:1 cycloadducts vi or vii with DMAD with different numbers of quaternary olefinic and aromatic carbon atoms, it was expected that the structure could be established by ^{13}C NMR spectroscopy. In fact, it is known that substituted 1,2,4-triazines can cycloadd to electron-rich monoolefins with inverse electron demand,[10] while electron-rich 1,2,4-triazines cycloadd to electron-deficient DMAD with normal electron demand.[11]

Scheme II



With a view to excluding possible side reactions in the cycloaddition reactions, **2a,b** were methylated with CH_3I/NaH to give 2-methyl-3-(methylthio)-5,6-diphenyl-2,5-dihydro-1,2,4-triazine (**3a**) and its 3-methoxy analogue **3b** (Table II). The skeletal identities of **3a** and **3b** with their respective precursors (**2a** and **2b**) were confirmed by the similarities of their UV and ^{1}H NMR spectra (see Tables I and II). Methylation of **2a** on a larger scale permitted the isolation in 8% yield of a byproduct believed to be 4-methyl-3-(methylthio)-5,6-diphenyl-4,5-dihydro-1,2,4-triazine (**4**) on the grounds of the extensive bathochromic shifts of its UV absorptions as compared to those of **3a** (Table II). The upfield shift of ca. 0.7 ppm of the

(10) (a) Burg, B.; Dittmar, W.; Reim, H.; Steigel, A.; Sauer, J. *Tetrahedron Lett.* **1975**, 2897. (b) Reim, H.; Steigel, A.; Sauer, J. *Ibid.* **1975**, 2901. (c) Neunhoeffer, H.; Frühauf, H.-W. *Justus Liebigs Ann. Chem.* **1972**, *758*, 120; (d) *Ibid.* **1972**, *758*, 125. (e) Alder, J.; Böhnish, V. Neunhoeffer, H. *Chem. Ber.* **1978**, *11*, 240.

(11) (a) Neunhoeffer, H.; Lehmann, B. *Justus Liebigs Ann. Chem.* **1977**, 1413. (b) Neunhoeffer, H.; Lehmann, B.; Ewald, H. *Ibid.* **1977**, 1421. (c) Ewald, H.; Lehmann, B.; Neunhoeffer, H. *Ibid.* **1977**, 1718.

Table III. Ultraviolet Absorptions and ^{1}H NMR Resonances of Compounds 9a-h and 10a-c

compd	λ_{max}, nm (ϵ)	^{1}H NMR ($CDCl_3$), δ SMe	NMe	OMe	CO_2Me	C_6 H	C_4 H	N_5 H
9a	225 (12 100, infl), 303 (11 900)[a]	1.87 (s)	3.34 (s)		3.67 (s), 3.78 (s)	5.68 (s)		
9b	215 (14 800, infl), 296 (10 400)[a]		3.17 (s), 3.22 (s)[c]		3.67 (s), 3.73 (s)	5.49 (s)		
9c	220 (19 200, infl), 304 (13 700)[b]	1.87 (s)	3.32 (s)		3.70 (s), 3.87 (s)	5.66 (s)		
9d	217 (20 700, infl), 296 (17 900)[b]		3.18 (s), 3.21 (s)[c]		3.71 (s), 3.75 (s)	5.46 (s)		
9e	226 (20 200), 303 (14 600)[b]	1.87 (s)	3.30 (s)		3.70 (s)[e]	5.63 (s)		
9f	225 (20 200), 296 (14 100)[b]		3.20 (s)[d]		3.73 (s), 3.77 (s)	5.44 (s)		
9g	221 (24 100), 300 (15 100)[b]		3.17 (s), 3.22 (s)[c]		3.73 (s)[d]	5.47 (s)		
10a[f]	219 (24 300)[a]		3.55 (s)		3.93 (s), 4.06 (s)		6.7 (d)	9.2 (d)
10b[f]	222 (31 400)[b]		3.58 (s)		3.92 (s), 4.03 (s)		6.7 (d)	9.6 (d)
10c[f]	228 (33 400),[b] 270 (15 600, infl)		3.62 (s)		3.92 (s), 4.03 (s)		6.67 (d)	9.8 (d)

[a] In MeOH. [b] In 95% EtOH. [c] These signals are not assignable. [d] Overlapped signal. [e] Merged with the signal of the anisoyl methyl protons. [f] J_{H_4,N_5H} = 10 Hz.

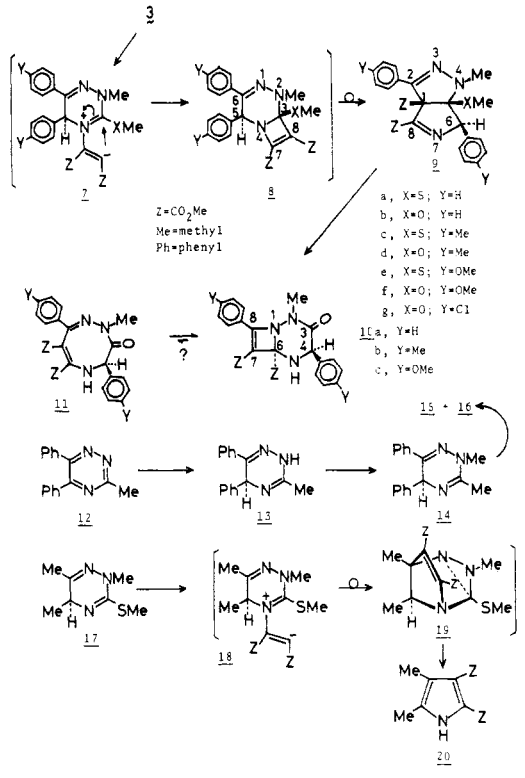
methine proton signal in the ^{1}H NMR spectrum of **4** is in accord with shielding by a neighboring methyl group. Chemical interconversions of **3a**, **3b**, 2-methyl-5,6-diphenyl-4,5-dihydro-1,2,4-triazin-3(2*H*)-one (**5**),[12] and 2-methyl-5,6-diphenyl-1,2,4-triazin-3(2*H*)-one (**6**)[13] are shown in Scheme II: **3a** with sodium methoxide gave **3b** which was hydrolyzed to **5**, while the oxidative hydrolysis of **3a** with NBS/90% dioxane afforded **6** which was reduced to **5** with sodium borohydride in high yield.

Reactions of **3a** and **3b** with 2 equiv of DMAD in toluene at 110 °C invariably gave 1:1 adducts to which the 2-(methylthio)- and 2-methoxy-2,5-azo-3,4-bis(methoxycarbonyl)-5,6-diphenyl-1-methyl-1,2,5,6-tetrahydropyridine structures (Chart I, viia,b) had been assigned, mainly on the basis of their ^{13}C NMR spectra.[14] Since, more recently, these compounds proved to resist thermal decomposition with nitrogen release even at 250 °C, compound **3a** and its DMAD adduct were submitted to X-ray analysis in the laboratory of Ashida's group.[15] The structure of **3a** was confirmed, but its adduct was shown to be 2,6-diphenyl-4-methyl-5-(methylthio)-1,8-bis(methoxycarbonyl)-3,4,7-triazabicyclo[3.3.0]octa-2,7-diene (**9a**, Scheme III, Table III).

The novel heterocycles **9** are of interest since they are potential precursors for the as yet unknown substituted 1,2,5-triazocines and other related compounds. Intense efforts have persisted to the present day for the synthesis, as well as physical and chemical studies of azocine,[16] diazocine,[17] and their derivatives as π-equivalent heterocyclic congeners of cyclooctatetraene and pentalene.

Establishment of the structure of **9a** should now permit the use of spectroscopic methods for facile elucidation of the structures of other DMAD adducts. 5,6-Diaryl-1,2,4-triazines (**1c–h**),[18] having para substituents of different

Scheme III



electronegativity, were synthesized and subjected to the same sequence of reactions. Major chemical and physical data of **2c–h** and **3c–h** are included in Tables I and II. As is seen, the major UV absorptions of **2c–h** are similar to

(12) Pinson, J.; M'Packo, J.-P.; Vinot, N.; Armand, J.; Bassinei, P. *Can. J. Chem.* **1972**, *50*, 1581.
(13) Paulder, W. W.; Lee, J. *J. Org. Chem.* **1971**, *36*, 3921.
(14) Sasaki, T.; Minamoto, K.; Harada, K. *Heterocycles* **1978**, *10*, 93.
(15) Paudler, W. W.; Lee, J. *J. Org. Chem.* **1971**, *36*, 3921.
(16) (a) Snyder, J. P.; Lee, L.; Farnum, D. G. *J. Am. Chem. Soc.* **1971**, *93*, 3816. (b) McNeil, D. W.; Kent, M. E.; Hedaya, E.; D'Angelo, P. F.; Schissel, P. O. *Ibid.* **1971**, *93*, 3817. (c) Paquette, L. A.; Kakihana, T.; Hansen, J. F.; Philips, J. C. *Ibid.* **1971**, *93*, 152. (d) Paquette, L. A. *Tetrahedron* **1975**, *31*, 2855.
(17) (a) Trost, B. M.; Corey, R. M. *J. Am. Chem. Soc.* **1971**, *93*, 5573. (b) Turro, N. J.; Scudder, P. H.; Corey, R. M. *J. Org. Chem.* **1979**, *44*, 1264.
(18) Although the literature[19,20] described the condensation of 4,4'-dimethylbenzil or 4,4'-dimethoxybenzil with thiosemicarbazide to give the corresponding 3-mercapto-5,6-disubstituted-1,2,4-triazines and their successive conversion to **1c,d** or **1e,f** by conventional methods, we used the direct condensation of these 4,4'-disubstituted benzils with 3-methylthiosemicarbazide to obtain **1c** and **1e** as in the case of **1a**.[9]
(19) For compounds **1c,d**, see: (a) Lacefield, W. B. *Berg.* 839469; *Chem. Abstr.* **1977**, *87*, 68431. (b) U.S. Patent 4013654; *Chem. Abstr.* **1977**, *87*, 39541.
(20) For compounds **1e,f**, see: (a) Polonovski, M.; Pesson, M. *C. R. Hebd. Seances Acad. Sci.* **1951**, *232*, 1260. (b) Gianturco, M. *Gazz. Chim. Ital.* **1952**, *82*, 595. (c) Lacefield, W. B. U. S. Patent 3948894; *Chem. Abstr.* **1978**, *85*, 33089.

Table IV. Ions from the Major Mass Fragmentations of 9a,b,d,f,g and 10a-c [*m/e* (Relative Intensity)]

compd	M^+	a	b	c	d	e	f	g
9a	437 (16.1)	390 (6.9)	215 (2.6)	175 (100)	200 (<1)	143 (98.8)	378 (5.8)	275 (2.2)
9b	421 (15)	390 (<1)	215 (2.0)	175 (70.7)	200 (2.6)	143 (100)	362 (17.1)	259 (10.1)
9d	449 (41.7)	418 (2.8)	229 (5.6)	189 (36.2)	214 (4.1)	157 (20.6)	390 (21.3)	273 (100)
9f	481 (22.2)	450 (4.3)	245 (4.4)	205 (96.8)	230 (4.3)	173 (51)	422 (12.7)	289 (100)
9g	489 (26.7)	458 (1.7)	249 (9.2)	209 (100)	234 (7.6)	177 (35.1)	430 (22.6)	293 (>100)

compd	M^+	h	i	j	k	l
10a	407 (7.1)	375 (97.2)	316 (11.1)	287 (4.0)	288 (100)	315 (28.6)
10b	435 (3.4)	403 (83.2)	344 (9.8)	315 (3.4)	316 (100)	343 (27.5)
10c	467 (5.2)	435 (99.3)	376 (14.1)	347 (2.7)	348 (100)	375 (45.3)

Table V. ^{13}C NMR Chemical Shifts[a,b] of 2,6-Diphenyl-4-methyl-5-(methylthio)-1,8-bis(methoxycarbonyl)-3,4,7-triazabicyclo[3.3.0]octa-2,7-diene (9a), Its 5-Methoxy Analogue (9b), and 2-Methyl-3-oxo-4,8-diphenyl-6,7-bis(methoxycarbonyl)-1,2,5-triazabicyclo[4.2.0]octa-7-ene (10a) in Chloroform at 25 °C

9a	9b	10a
14.16 (q) SCH_3	33.98 (q) NCH_3	37.66 (q) N-CH_3
33.46 (q) NCH_3	52.89 (q) 2 ester CH_3's	48.11 (d) C_4
52.76 (q), 52.95 (q) } ester CH_3	54.06 (q) OCH_3	51.49 (q), 53.63 (q) } ester CH_3
82.97 (s) C_1	76.08 (s) C_1	109.54 (s) C_6
84.79 (d) C_6	81.61 (d) C_6	125.96, 129.14 } (m) $C_{2'}$-$C_{6'}$, $C_{2''}$-$C_{6''}$
96.74 (s) C_5	113.83 (s) C_5	132.78 (s)
125.66, 130.73 } (m) $C_{2'}$-$C_{6'}$, $C_{2''}$-$C_{6''}$	125.79, 130.27 } (m) $C_{2'}$-$C_{6'}$, $C_{2''}$-$C_{6''}$	137.00 (s)
131.51 (s)	131.70 (s)	145.45 (s)
133.85 (s)	134.82 (s)	153.04 (s)
136.71 (s)	137.87 (s)	156.22 (s)
161.07 (s)	161.07 (s)	160.57 (s)
161.59 (s)	161.40 (s)	164.79 (s)
167.05 (s)	166.66 (s)	
C_2, C_8, $C_{1'}$, $C_{1''}$, 2 C=O	C_2, C_8, $C_{1'}$, $C_{1''}$, 2 C=O	C_3, C_7, C_8, $C_{1'}$, $C_{1''}$, 2 ester C=O's

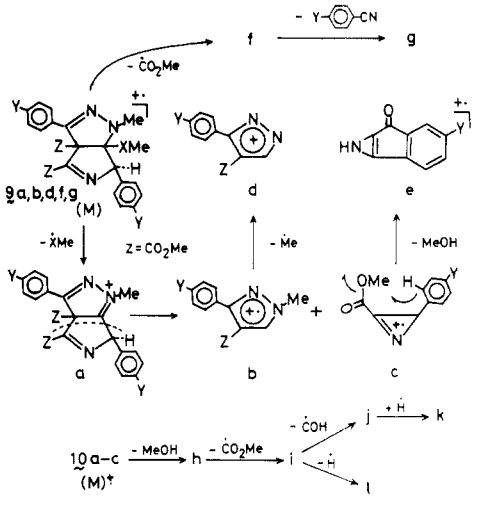
[a] In parts per million from internal tetramethylsilane. [b] Multiplicities of the signals in the partially decoupled spectra are given in the parentheses: q = quartet, d = doublet, s = singlet.

those of the corresponding 3-methylthio or 3-methoxy compounds **2a,b**, almost independent of the para substituents. The absorption patterns of compounds **3** parallel those of the corresponding precursors **2** and show the bathochromic shifts of 9–12 nm of the longer wavelength absorptions associated with methyl hyperconjugation. The general agreement of ^1H NMR resonances confirms the skeletal identity of **2** and **3**.

The reactions of **3c–f** with DMAD proceeded similarly to give **9**, but the reaction of **3h** was very sluggish and gave considerable side products. **3g** gave a complex mixture, which was abandoned. Not surprisingly, the electron-withdrawing chlorine atoms appreciably reduced the reactivity of the dihydrotriazine system toward DMAD as judged by the contrasting high-yield reactions of **3e,f** (see Experimental Section). The yields of **9** and the reaction times permit no reasoning of the reaction mechanism. The skeletal identity of these compounds is established by UV and ^1H NMR spectral comparisons within the methylthio or 5-methoxy series (see Table III). The mass spectra of the available samples of this system (Scheme IV, Table IV) confirm the structural similarity; differences in intensities are in part due to the use of different instruments.[21]

Although the configuration at C_6 cannot be rigorously specified, the same sterochemistry in **9a,c,e** is indicated

Scheme IV. Major Mass Fragmentation Paths of Compounds 9a,b,d,f,g and 10a-c



by the similarity of the chemical shifts of the methylthio and C_6 protons. The relatively high-field resonance of the methylthio group is in better accord with a *cis*-aryl group as shown, when the anisotropic influence by the 6-aryl ring is taken into account. The same is true for the 6-hydrogen signals of 5-methoxy analogues (the signals of NMe and OMe cannot be specifically assigned).

The formation of **9** from **3** and DMAD (see Scheme III) can be explained as follows: the initially formed dipoles (**7**)[22] lead to transient intermediates (**8**),[23] which rearrange

(21) The mass spectra were measured in the laboratory of the Daiichi Pharmaceutical Co., Ltd., to which we are grateful. The spectra of **9a,b** were recorded on a JES-OISG mass spectrometer at the ionization voltage (IV) of 75 eV and the ionizing current (IC) of 200 μA with sample temperatures between 130 and 175 °C, while those of **9d,f,g** were recorded on a JMS-D300 mass spectrometer at an IV of 70 eV and an IC of 300 μA (temperature 150–250 °C). The spectra of **10a–c** were measured with the latter spectrometer at an IV of 70 eV, an IC of 300 μA, and sample temperatures of 100–220 °C.

(22) Formation of such dipolar intermediates are well documented. See for example: Acheson, R. M. *Adv. Heterocycl. Chem.* **1963**, *1*, 125.

to 9; new bonds are formed between C_6 and C_8, and the bonds between C_3–N_4 and C_5–C_6 are broken in 8. No deep-seated mechanism for this extensive rearrangement is known at present.[24] Anyway, the rather selective formation of such a sterically crowded molecule is interesting and suggests that quite a little magic chemistry remains to be scooped out of the sink of polyaza heterocycles containing relatively localized electron density.

Controlled acidic hydrolysis of either **9a** or **9b** gave the same product in 58 and 64% yield, respectively. The absence of the chromophore absorbing near 300 nm indicates that a skeletal rearrangement has occurred. The ^{1}H NMR spectrum of this compound, which displayed a benzylic methine proton signal at 6.7 ppm coupling with an NH signal with J = 10 Hz (Table III), is in accord with either structure **10a** or 11. The ^{13}C NMR spectrum (Table V) of this compound showed the presence of eight quaternary carbon atoms, three of which could be ascribed to carbonyl groups and only four to olefinic and/or aromatic carbons. This product was therefore assigned structure **10a**, 2-methyl-3-oxo-4,8-diphenyl-6,7-bis(methoxycarbonyl)-1,2,5-triazabicyclo[4.2.0]octa-7-ene, rather than structure 11 (Y = H) which contains five quaternary olefinic and/or aromatic carbon atoms. Analogously, **9d** and **9e** were converted to the 4,8-ditolyl (**10b**) and 4,8-dianisyl (**10c**) analogues, respectively. Their ultraviolet, ^{1}H NMR, and mass spectra (Tables III and IV, Scheme IV) displayed excellent correspondence with those of **10a**. The possibility of the conversion of 10 to 11 or of 11 to an 8-π triazocine system and the evidence of a dynamic equilibrium between 10 and 11 will be fascinating subjects for future studies.

In order to determine the scope of the formation of the bicyclo[3.3.0] compounds **9** from 2,5-dihydro-1,2,4-triazines and DMAD, we carried out several other reactions. 2,3-Dimethyl-5,6-diphenyl-2,5-dihydro-1,2,4-triazine (**14**) was synthesized from 3-methyl-5,6-diphenyl-1,2,4-triazine (**12**)[25] through the corresponding 2,5-dihydrotriazine (**13**). The structures of **13** and **14** are assigned on the basis of their spectral properties (Tables I and II). The reaction of **14** with either 1 or 2 equiv of DMAD proceeded unusually rapidly to give 1:2 adducts of **14** and DMAD (see Experimental Section), the structures of which will be uncovered in the future. On the other hand, 2-acetyl-3-(methylthio)-5,6-diphenyl-2,5-dihydro-1,2,4-triazine synthesized from **2a** failed to give the desired product.[26] Finally, 2,5,6-trimethyl-3-(methylthio)-2,5-dihydro-1,2,4-triazine (**17**)[27] reacted with neat DMAD almost explosively at room temperature to give an intractable tar. Treatment of **17** with diluted DMAD at room temperature gave a tarry mixture from which a small amount of 2,3-bis(methoxycarbonyl)-4,5-dimethylpyrrole (**20**) could be isolated. Structure **20** followed from its elemental analysis and the resemblance of its ^{1}H NMR spectrum to that of the known[28] 2,3-bis(methoxycarbonyl)-1,4,5-trimethylpyrrole (see Experimental Section). Optimization of the yield of **20** and the detailed investigation of other products from **17** were abandoned, but as far as **20** is concerned, its formation seems to be rationalized by the formation of intermediate **18** (see Scheme III), followed by rearrangement to **19** and subsequent fragmentation to the pyrrole **20**.

It thus appears that the extensive skeletal rearrangement occurs only with specific 2,5-dihydro-1,2,4-triazines, and this discrepancy of reactivity will be discussed in the future on the basis of more detailed experiments and/or calculations.

Experimental Section

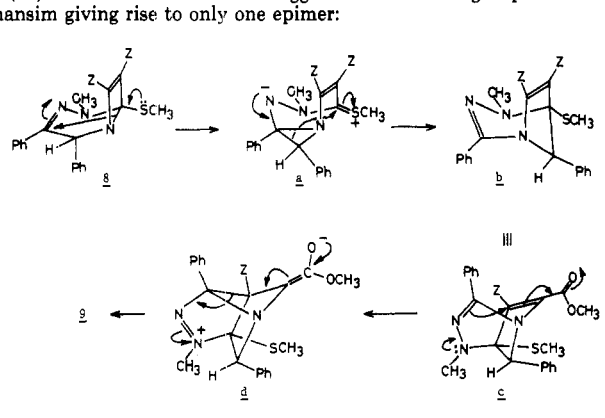
All melting points are uncorrected. The ultraviolet spectra were measured on a Hitachi Model 200-10 spectrophotometer. The ^{1}H NMR spectra were determined by using a JNM C-60 HL spectrometer and Me_4Si as internal standard, while ^{13}C NMR spectra were recorded on a JNM-FX60 FT NMR spectrometer using Me_4Si as internal standard. Elemental analyses were conducted by Miss Kawai using a Perkin-Elmer 240 elemental analyzer in this laboratory. For preparative TLC, glass plates coated with a 2-mm thickness of Wakogel B-5 silica gel or Alumi-Layer G (Nakarai Chemicals Ltd.) were used after activation at 110 °C for 7–10 h, while for column chromatography Mallinkrodt silicic acid (100 mesh) or neutral alumina (300 mesh) was used. All evaporations were carried out in vacuo at or below 40 °C. Satisfactory analytical values (±0.4% for C, H, N) were reported for compounds **1c–h**, **2a–h**, **3a–h**, **4**, **9a–g**, **10a–c**, **13**, **14**, and **20**.

3-(Methylthio)-5,6-ditolyl-1,2,4-triazine (1c). To a solution of 4,4′-dimethylbenzil (1.0 g, 4.2 mmol) in methanol (30 mL) were added *S*-methylthiosemicarbazide (1.3 g, 5.58 mmol) and sodium bicarbonate (352 mg, 4.2 mmol), and the mixture was left at room temperature for 12 h. After evaporation, the residue was partitioned between chloroform (30 mL) and water (10 mL). The residue from the $CHCl_3$ extract was recrystallized from a mixture of methanol and chloroform to give 1.08 g (84%) of **1c** as yellow crystals: mp 172–174 °C; λ_{max} (95% EtOH) 230 nm (ϵ 16 900, sh), 282 (24 200), 353 (5400); ^{1}H NMR ($CDCl_3$) δ 2.36 (6 H, s, 2 tolyl methyls), 2.73 (3 H, s, SMe), 7.0–7.6 (8 H, m, aryl protons).

3-Methoxy-5,6-ditolyl-1,2,4-triazine (1d). A mixture of **1c** (1.09 g, 3.53 mmol) and sodium methoxide (230 mg, 4.24 mmol) in anhydrous methanol (20 mL) was stirred at room temperature for 24 h and then at 60 °C for 8 h. After neutralization with excess dry ice, the mixture was evaporated, the residue was digested with ether, and the inorganic materials were filtered off. The filtrate was evaporated and the residue subjected to column chromatography using alumina and chloroform. Recrystallization of the major fraction from a mixture of ether and *n*-hexane gave 705

(23) (a) For examples of stepwise additions of acetylenic compounds to form cyclobutenes, see: Bastide, J.; Henri-Rousseau, O. "The Chemistry of the Carbon-carbon Triple Bond"; Patai, S., Ed.; Wiley-Interscience: New York, 1978; Part 1, p 447. (b) The reality of such intermediates with a fused azetidinene ring seems to be strengthened by a recent publication of the synthesis of azabicycloheptadienes with a similar four-membered ring: Göckel, York, Hartmannsgruber, U.; Steigel, A.; Sauer, J. *Tetrahedron Lett.* **1980**, 595.

(24) One of the referees has suggested the following sequential mechansim giving rise to only one epimer:



This mechanism seems to be realistic in view of the different reactivities of **12** and **17** as well as the 2-acetyl derivative of **2a** (see the text); the phenyl-promoted, specific C–C bond fission of the aziridine ring in a, the sterically favorable equatorial (cis to SCH_3) phenyl in b, and the participation of the lone pair on the 3-SCH_3 in 8 and on the 2-N in c are in accord with the experimental results.

(25) Neunhoeffer, H.; Frühauf, H.-W.; Henning, H.; Mutterer, M. *Tetrahedron Lett.* **1969**, 3147.

(26) The reaction with DMAD is so sluggish and nonselective that no product was isolated. Starting material was recovered in 30% yield after heating of the mixture in toluene at 110 °C for 12 days.

(27) The synthesis and characterization of this compound are described in: Sasaki, T.; Minamoto, K.; Harada, K. *J. Org. Chem.*, following paper in this issue.

(28) Baumes, R.; Jacquier, R.; Tarrago, G. *Bull. Soc. Chim. Fr.* **1974**, 1174. This literature does not contain UV data.

mg (69%) of yellow crystals: mp 129.5–131 °C; λ_{max} (95% EtOH) 220 nm (ε 22 800, sh), 262 (13 100), 334 (8700); ^{1}H NMR ($CDCl_3$) δ 2.36 (6 H, s 2 tolyl methyls), 4.23 (3 H, s, OMe), 7.0–7.6 (8 H, m, aryl protons).

3-(Methylthio)-5,6-dianisyl-1,2,4-triazine (1e). A mixture of 4,4′-dimethoxybenzil (1.72 g, 6.37 mmol), *S*-methylthiosemicarbazide (1.96 g, 8.41 mmol), and sodium bicarbonate (544 mg, 6.48 mmol) in methanol (35 mL) was stirred at 60 °C for 8 h. After the solvent was evaporated, the residue was partitioned between chloroform and water and the $CHCl_3$ extract applied on an alumina column (3 × 17 cm). Elution with chloroform gave 2.1 g (97%) of TLC-homogeneous yellow solid, a part of which was recrystallized from methanol for analysis: mp 139–140 °C (lit.[20a] mp 154 °C); λ_{max} (95% EtOH) 220 nm (ε 16 500, sh), 268 (17 500, sh), 291 (22 000), 363 (8000); ^{1}H NMR ($CDCl_3$) δ 2.73 (3 H, s, SMe), 3.84 (6 H, s, 2 OMe), 6.7–7.7 (8 H, m, aryl protons).

3-Methoxy-5,6-dianisyl-1,2,4-triazine (1f). A mixture of **1e** (3.55 g, 10.5 mmol) and sodium methoxide (570 mg, 12.5 mmol) in methanol (50 mL) was stirred at room temperature for 24 h. Workup as with **1d** gave 3.23 g (95%) of yellow crystals: mp 137.5–139 °C (MeOH); λ_{max} (95% EtOH) 240 nm (ε 16 200), 281 (13 900), 351 (10 700); ^{1}H NMR ($CDCl_3$) δ 3.82 (6 H, s, 2 OCH_3), 4.23 (3 H, s, OCH_3), 6.7–7.7 (8 H, m, aryl protons).

3-(Methylthio)-5,6-bis(*p*-chlorophenyl)-1,2,4-triazine (1g). A mixture of 4,4′-dichlorobenzil (5.12 g, 18.3 mmol), *S*-methylthiosemicarbazide (5.67 g, 24.3 mmol), and sodium bicarbonate (1.54 g, 18.3 mmol) in methanol (100 mL) was left at room temperature for 13 h. Workup as in the case of **1c** gave 6.17 g (97%) of yellow crystals: mp 142–143 °C (MeOH); λ_{max} (95% EtOH) 220 nm (ε 8600, sh), 282 (13 200), 350 (2100); ^{1}H NMR ($CDCl_3$) δ 2.75 (3 H, s, SCH_3), 7.2–7.6 (8 H, m, aryl protons).

3-Methoxy-5,6-bis(*p*-chlorophenyl)-1,2,4-triazine (1h). A mixture of **1g** (3.0 g, 8.61 mmol) and sodium methoxide (558 mg, 10.4 mmol) in methanol (60 mL) was stirred at room temperature for 24 h and worked up similarly to the procedure for **1d** and **1f** to give 2.63 g (92%) of yellow crystals: mp 154–156 °C (MeOH); λ_{max} (95% EtOH) 218 nm (ε 23 300, sh), 259 (15 800), 326 (9000); ^{1}H NMR ($CDCl_3$) δ 4.28 (3 H, s, OCH_3), 7.2–7.7 (8 H, m, aryl protons).

3-(Methylthio)- or 3-Methoxy-5,6-diaryl-2,5-dihydro-1,2,4-triazines (2a–h) and 3-Methoxy-5,6-diphenyl-2,5-dihydro-1,2,4-triazine (13). General Procedure. To an ice-cooled, deoxygenated solution of **1a-h** or **12** (1 mmol) in a mixture of THF and MeOH (4:1 v/v; 6–12 mL, depending upon the solubilities of **1a–h**) was added sodium borohydride (1 mmol; less than 1 mmol for **13**, see below), and the mixture was stirred under argon at room temperature for the period specified in Table I. Generally, the stirring was continued until the starting materials disappeared. The mixture was then carefully neutralized with AcOH/MeOH (1:5 v/v) and evaporated. The organic materials were isolated by digesting the residue with ice-water or by extraction with chloroform. In most cases, direct recrystallization gave good yields. Further crops were obtained by column or thick-layer chromatography using silica gel or alumina. Recrystallization solvents were as follows: methanol for **2b,c,e,h**, ethyl acetate for **2a**, ether/*n*-hexane for **2d**.

Example 1. A solution of **1a** (2.2 g, 7.88 mmol) and sodium borohydride (275 mg, 7.88 mmol) in THF/MeOH (4:1, 48 mL) was stirred under argon for 24 h at room temperature. After the mixture was neutralized with AcOH/MeOH (1:5), the solvent was evaporated and the residue digested with ice-water. The solid precipitate was collected, dried, and recrystallized from EtOAc to give a 92% yield of **2a**.

Example 2. To an ice-cooled, stirred solution of **12** (2.4 g, 9.7 mmol) in THF/MeOH (4:1, 20 mL) was added sodium borohydride (184 mg, 4.85 mmol). After the mixture was stirred at room temperature under argon for 20 h, further sodium borohydride (92 mg, total 7.28 mmol) was added. After a total of 24 h, the mixture was neutralized with AcOH/MeOH (1:5), evaporated, and partitioned between EtOAc (50 mL) water (10 mL). Recrystallization of the EtOAc-extracted material from a small volume of methanol gave 1.31 g of **13**. The filtrate was evaporated and the residue subjected to column chromatography using alumina and chloroform to give an additional crop (0.29 g) of **13** (total 59%) and 0.53 g (22%) of starting material. **13** was recrystallized from methanol.

2-Methyl-3-(methylthio)- (or -3-methoxy-) 5,6-diaryl-2,5-dihydro-1,2,4-triazines (3a–h), 4-Methyl-3-(methylthio)-5,6-diphenyl-4,5-dihydro-1,2,4,-triazine (4), and 2,3-Dimethyl-5,6-diphenyl-2,5-dihydro-1,2,4-triazine (14). General Procedure. To a solution of **2a–h** or **13** (1 mmol) in DMF (6–7 mL for **2a–h**, 3.8 mL for **13**) was added 50% oil-immersed sodium hydride (1.1 mmol). After 10–20 min, methyl iodide (1.1 mmol) was added, and the mixture was stirred at room temperature for 3–4 h and then thoroughly evaporated. The residue was partitioned between ethyl acetate or chloroform and water. The material in the organic layer was subjected to column chromatography (silica gel/$CHCl_3$ for **3a,b** and **4**, activated alumina/*n*-hexane for **3c-h** and **14**). Recrystallization solvents were as follows: methanol for **3a,b**, ether/*n*-hexane for **3c–h** and **14**.

Example 1. To a stirred solution of **2a** (3.5 g, 12.4 mmol) in DMF (80 mL) was added 50% oil-immersed sodium hydride (658 mg, 13.7 mmol). After 15 min, methyl iodide (0.85 mL, 13.7 mmol) was added and the mixture stirred at room temperature for 3 h. The solvent was removed and the residue partitioned between chloroform (80 mL) and water (30 mL). The $CHCl_3$-soluble material was applied on a silica gel column (2.5 × 18 cm). Elution with chloroform gave from the first fraction 2.82 g (77%) of **3a** and from the second 290 mg (8%) of **4** after recrystallization from ether.

Example 2. The mixture obtained from **13** (1.31 g, 5.25 mmol), DMF (20 mL), 50% oil-immersed sodium hydride (265 mg, 5.52 mmol), and methyl iodide (0.35 mL, 5.52 mmol) after being processed as above was evaporated and partitioned between ethyl acetate (40 mL) and water (10 mL). The EtOAc-soluble material was applied on a column (3 × 10 cm) of alumina and eluted with *n*-hexane to give from the major band 47% of **14** after recrystallization.

Conversion of 3a to 3b. A mixture of **3a** (100 mg, 0.34 mmol) and sodium methoxide (30 mg, 0.56 mmol) in methanol (4 mL) was heated to reflux. After 35 and 60 h, further sodium methoxide (30 mg) was added (total 90 mg, 1.68 mmol) and heating continued for 90 h overall. The mixture was neutralized with excess dry ice and evaporated, and the residue was digested with acetone. The insoluble inorganic material was filtered off, the filtrate evaporated, and the residue purified by preparative TLC (silica gel, 10 × 20 cm; $CHCl_3$/EtOAc, 5:1) to give 55 mg (58%) of **3b**, identical with an authentic sample according to IR, UV, and ^{1}H NMR spectra.

Acidic Hydrolysis of 3b to 2-Methyl-5,6-diphenyl-4,5-dihydro-1,2,4-triazin-3(2*H*)-one (5). Compound **3b** (79 mg, 0.28 mmol) in a mixture of methanol and concentrated hydrochloric acid (3:1 v/v, 3 mL) was warmed at 50 °C for 1 h. After neutralization with triethylamine, the solvent was thoroughly evaporated and the residue partitioned between ethyl acetate (30 mL) and water (7 mL). The solid obtained from the organic layer was recrystallized from methanol to give 77% of **5** [mp 201–202 °C (lit.[12] mp 195 °C] identical with an authentic specimen in terms of IR and UV spectra.

Oxidative Hydrolysis of 3a to 2-Methyl-5,6-diphenyl-1,2,4-triazin-3(2*H*)-one (6). To a solution of **3a** (100 mg, 0.34 mmol) in 90% dioxane (2 mL) was added NBS (91 mg, 0.51 mmol), and the mixture was stirred at room temperature for 17 h. The solvent was evaporated, and the residue was repeatedly coevaporated with methanol and then partitioned between chloroform (20 mL) and 5% sodium bicarbonate (10 mL). The separated $CHCl_3$ layer was dried over sodium sulfate and evaporated, and the residue was recrystallized from methanol to give 80 mg (90%) of **6** [mp 155–157 °C (lit.[13] mp 152 °C)] identical with an authentic sample[13] according to IR and ^{1}H NMR spectra and a mixture melting point determination.

Sodium Borohydride Reduction of 6 to 5. To a stirred solution of **6** (100 mg, 0.38 mmol) in THF/MeOH (4:1, 2.5 mL) was added sodium borohydride (16 mg, 0.42 mmol), and the mixture was stirred at room temperature for 1 h. After being neutralized with AcOH/MeOH (1:5), the mixture was evaporated, treated with water (5 mL), and extracted with ethyl acetate (30 mL). Recrystallization of the EtOAc extract from a small volume of methanol gave 66 mg (66%) of colorless crystals, identical with **5** obtained above.

2,6-Diaryl-4-methyl-5-(methylthio)- (or -5-methoxy-) 1,8-bis(methoxycarbonyl)-3,4,7-triazabicyclo[3.3.0]octa-2,7-di-

Table VI

compd	t, h	vol of toluene, mL/ mmol of 3	yield, %	mp, °C
9a	6.5	5.2	55	155-156
9b	12	4.0	65	174-176
9c	9	7.3	36	192-194
9d	16	3.2	59	185.5-187.5
9e	12	4.5	60	200-202
9f	6	4.4	80	219-221
9g	60	5.1	22	152-154

enes (9a–g). General Procedure. A mixture of **3a–f** or **3h** and 2 equiv of DMAD in toluene was heated at 110 °C under argon for the period specified in Table VI. After evaporation of the solvent, the residue was brought to crystallization by rubbing with a small volume of methanol. All compounds were recrystallized from methanol. Reaction times, volumes of toluene (mL/1 mmol of **3**), yields, and melting points are given in Table VI. All are yellow compounds.

2-Methyl-3-oxo-4,8-diphenyl-6,7-bis(methoxycarbonyl)-1,2,5-triazabicyclo[4.2.0]octa-7-ene (10a). Compound **9b** (200 mg, 0.48 mmol) in a mixture of methanol and concentrated hydrochloric acid (10:1 v/v, 22 mL) was warmed at 55 °C for 50 min. The mixture was rapidly cooled to room temperature, evaporated, and repeatedly coevaporated with methanol to remove the residual acid (use of EtOH instead of MeOH caused partial ester exchange). The residue was again dissolved in methanol and neutralized with concentrated ammonia/methanol (1:3 v/v), and the mixture was evaporated. The residue was partitioned between chloroform (30 mL) and water (5 mL). The material obtained from the organic layer was applied on a silica gel column (2 × 20 cm) and eluted with $CHCl_3$/EtOAc (7:1). Recrystallization of the main fraction from methanol gave 123 mg (64%) of colorless fine needles, mp 108–110 °C.

This compound was also obtained from **9a** in 58% yield after similar processing.

2-Methyl-3-oxo-4,8-ditolyl-6,7-bis(methoxycarbonyl)-1,2,5-triazabicyclo[4.2.0]octa-7-ene (10b). Compound **9d** (300 mg, 0.67 mmol) in MeOH/concentrated HCl (10:1, 33 mL) was warmed at 50 °C for 30 min and the mixture rapidly cooled to room temperature. The workup followed was the same as that for **10a**. During coevaporation with methanol, considerable decomposition of the major product was observed. Column chromatography using silica gel (2.5 × 20 cm) and chloroform gave 45 mg (15%) of **10b** as colorless crystals, mp 89–91 °C (after recrystallization from ether/*n*-hexane).

2-Methyl-3-oxo-4,8-dianisyl-6,7-bis(methoxycarbonyl)-1,2,5-triazabicyclo[4.2.0]octa-7-ene (10c). Compound **9e** (100 mg, 0.19 mmol) in MeOH/concentrated HCl (10:1, 9 mL) was heated at 55–60 °C. After 10 min, acetone (2 mL, to help solubilize **9e**) and concentrated HCl (0.2 mL) were added, and warming was continued for an additional 1 h. After evaporation and coevaporation with methanol, the residue was taken up in methanol, neutralized with triethylamine, and again evaporated. The residue was partitioned between ethyl acetate (25 mL) and water (5 mL), and the EtOAc extract was subjected to preparative TLC (silica gel, 5 × 20 cm; $CHCl_3$/EtOAc, 5:1) to give 40 mg (43%) of a paste, which was dried at 45–50 °C under high vacuum.

Reaction of 2,3-Dimethyl-5,6-diphenyl-2,5-dihydro-1,2,4-triazine (14) with DMAD. A solution of **14** (400 mg, 1.58 mmol) and DMAD (450 mg, 3.16 mmol) in toluene (5 mL) was left at room temperature for 3 h under argon. TLC (alumina, $CHCl_3$) of the dark reaction mixture showed no starting material and two major and two minor products. After the solvent was evaporated, the residue was subjected to column chromography using alumina (2.5 × 13 cm) and $CHCl_3$/benzene (1:1) to give from the earlier fractions 100 mg (12%) of yellowish green crystals (**15**): mp 190–193 °C (MeOH); IR (KBr) 1740, 1670 cm^{-1} ($\nu_{C=O}$); λ_{max} (95% EtOH) 220 nm (ϵ 13 400, sh), 234 (4600), 357 (15 200).

Anal. Calcd for $C_{29}H_{29}N_3O_8$·MeOH: C, 62.17; H, 5.74; N, 7.25. Found: C, 62.49; H, 5.56; N, 7.00.

Later fractions gave 226 mg (26%) of another 1:2 adduct (**16**) as yellow crystals: mp 218 °C dec (MeOH); IR (KBr) 1750, 1720, 1680 cm^{-1} ($\nu_{C=O}$); λ_{max} (95% EtOH) 283 nm (ϵ 6700), 305 (6600, sh), 418 (3400).

Anal. Calcd for $C_{29}H_{29}N_3O_8$·MeOH: C, 62.17; H, 5.74; N, 7.25. Found: C, 61.99; H, 5.55; N, 7.48.

Reaction of 2,5,6-Trimethyl-3-(methylthio)-2,5-dihydro-1,2,4-triazine (17) with DMAD. A solution of **17** (400 mg, 2.34 mmol) in toluene (2 mL) was deoxygenated by argon bubbling. DMAD (665 mg, 4.68 mmol) was added in portions, and the mixture was left at room temperature. After a few hours, the mixture began to be crimson colored. After the mixture was allowed to stand overnight, TLC indicated the persistence of the starting material and a complex distribution of products. After being allowed to stand for 6 days under argon, the tarry mixture was evaporated, applied on a silica gel column (2.5 × 18 cm), and eluted with $CHCl_3$/EtOAc (3:1) to give 20 mg (4%) of **20** as the only crystalline product: mp 148–150 °C (MeOH); λ_{max} (95% EtOH) 220 nm (ϵ 17 000), 258 (9200), 304 (21 100); ^1H NMR ($CDCl_3$) δ 2.06 (3 H, s, C_4Me), 2.21 (3 H, s, C_5Me), 3.83 (3 H, s, C_2CO_2Me), 3.87 (3 H, s, C_3CO_2Me), 9.3 (1 H, br s, NH, D_2O exchangeable). For 2,3-bis(methoxycarbonyl)-1,4,5-trimethylpyrrole:[28] ^1H NMR ($CDCl_3$) δ 2.05 (3 H, s, C_4Me), 2.15 (3 H, s, C_5Me), 3.82 (3 H, s, C_2CO_2Me), 3.85 (3 H, s, C_3CO_2Me), 3.75 (3 H, s, NMe). UV absorptions are not described for this compound.

Registry No. 1a, 28735-33-3; **1b**, 2478-16-2; **1c**, 63031-38-9; **1d**, 63074-37-3; **1e**, 58848-77-4; **1f**, 63119-34-6; **1g**, 69466-88-2; **1h**, 69467-22-7; **2a**, 70299-26-2; **2b**, 70299-25-1; **2c**, 74930-09-9; **2d**, 74930-10-2; **2e**, 54866-80-7; **2f**, 74930-11-3; **2g**, 74930-12-4; **2h**, 74930-13-5; **3a**, 74930-14-6; **3b**, 74930-15-7; **3c**, 74930-16-8; **3d**, 74930-17-9; **3e**, 74930-18-0; **3f**, 74930-19-1; **3g**, 74930-20-4; **3h**, 74930-21-5; **4**, 70299-28-4; **5**, 37469-25-3; **6**, 18510-97-9; **9a**, 74930-22-6; **9b**, 74930-23-7; **9c**, 74930-24-8; **9d**, 74930-25-9; **9e**, 74930-26-0; **9f**, 74930-27-1; **9g**, 74930-28-2; **10a**, 74930-29-3; **10b**, 74930-30-6; **10c**, 74930-31-7; **12**, 24108-37-0; **13**, 74930-32-8; **14**, 74930-33-9; **17**, 74930-34-0; **20**, 947-51-3; 4,4'-dimethylbenzil, 3457-48-5; *S*-methylthiosemicarbazide, 44387-06-6; 4,4'-dimethoxybenzil, 1226-42-2; 4,4'-dichlorobenzil, 3457-46-3; DMAD, 762-42-5.