153. Azomalonate Syntheses

Part II

Synthesis and Reactivity of Novel 1,2,4-Triazin-5-one Derivatives[1])

by **Roland Heckendorn**

Research Department, Pharmaceuticals Division, *Ciba-Geigy Ltd.*, CH-4002 Basel

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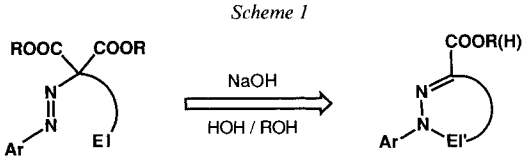
Base treatment of azomalonates derived from *N*-substituted dialkyl (2-chloroacetamido)malonates results in the formation of 4-substituted alkyl 5-oxo-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylates. The same malonates coupled with diazotized 2-amino-5-chlorobenzophenone or methyl anthranilate afford triazinones which can be cyclized into novel triazino[1,6-*a*]indoles. Two representative heterocycles are further characterized by typical reactions. Whereas oxidation gives the corresponding triazine-5,6-diones, the outcome of the reduction is strongly dependent on the nature of the substituent at C(4). Bromination followed by aqueous workup leads to the 6-hydroxy derivatives. Some mechanistic aspects of this novel triazinone synthesis are discussed.

1. Introduction. – In [2], we have presented a general synthetic principle which consists in the one-step conversion of azomalonates **A**, carrying electrophilic side-chain centers (El), into heterocycles of type **B** (*Scheme 1*). Using diethyl (2-chloroacetamido)-malonates as coupling components, we, thus, prepared 1-aryl-5-(chloromethyl)-1*H*-1,2,4-triazole-3-carboxylic acids – valuable precursors for novel fused heterocycles. The present work describes experimental results obtained with azo compounds derived from *N*-substituted dialkyl (2-chloroacetamido)malonates and aromatic amines.

Scheme 1



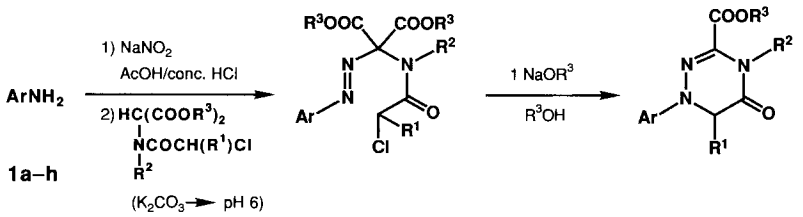
A **B**

2. Results. – 2.1. *Coupling and Ring Closure of* N-*Phenyl-Substituted (2-Chloroacetamido)malonates.* In initial experiments, diazotized 4-chloroaniline (**1b**) was coupled with readily available diethyl (2-chloro-*N*-phenylacetamido)malonate **2** [3] at pH 6. Upon dilution of the reaction mixture with H_2O, the pure azo compound **3b** (*Scheme 2*) was isolated in high yield by simple filtration. When an ethanolic solution of **3b** was treated with 3 or 4 equiv. of 1N NaOH, only impure and ill-defined acidic products were formed. However, treatment of **3b** with only 1 equiv. of aqueous base resulted in the rapid

[1]) Presented in part at the 'XII European Colloquium on Heterocyclic Chemistry', Reims, France, September 1986 [1].

formation of a crystalline neutral product, showing the characteristic properties of the expected triazinone **4b**. Since the yield (57%) was moderate, we turned our attention to the use of non-aqueous bases and found that treatment of an ethanolic solution of **3b** at room temperature with 1 equiv. of 1N NaOEt/EtOH for 15 min furnished pure **4b** (Ar = 4-chlorophenyl) in 87% yield by simple filtration. Examination of the mother liquor revealed the presence of 1 equiv. of diethyl carbonate. Thus, the following stoichiometric course of the reaction is evident: **3b** + NaOEt → **4b** + $CO(OEt)_2$ + NaCl. (For mechanistic aspects, see *Discussion*.)

Scheme 2



R^1 = H, R^2 = Ph, R^3 = Et	**2**	**3a–h**	**4a–h**
R^1 = Me, R^2 = Ph, R^3 = Et	**5a**	**6a**	**7a**
R^1 = Ph, R^2 = Ph, R^3 = Et	**5b**	**6b**	**7b**
R^1 = H, R^2 = Me, R^3 = Me	**10x**		
R^1 = Me, R^2 = Me, R^3 = Me	**10y**	**11a–i**	**12a–i**
R^1 = Ph, R^2 = Me, R^3 = Me	**10z**		

Table 1. *Selected Data of the Azo Compounds* **3** *and the Triazinones* **4**[a])

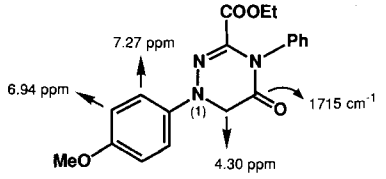
Compound	Ar	Yield [%][b])	M.p. [°]	^{1}H-NMR δ [ppm][c])	
				$ClCH_2$	Ring CH_2
3a	Ph	[d])	oil	3.87	
3b	4-Cl–C_6H_4	88	102–104	3.90	
3c	4-Me–C_6H_4	[d])	oil	3.85	
3d	4-MeO–C_6H_4	[d])	oil	3.86	
3e	4-NO_2–C_6H_4	[d])	oil	3.85	
3f	4-NH_2SO_2–C_6H_4	61	153–155 (dec.)	3.88	
3g	5-Chloro-2-(2′,4′-dichlorophenoxy)phenyl	91	107–109	3.53	
3h	2-Chloro-3-pyridyl	87	104–106	3.83	
4a	Ph	80[e])	163–165		4.38
4b	4-Cl–C_6H_4	87	156–158		4.32
4c	4-Me–C_6H_4	72[e])	135–137		4.35
4d	4-MeO–C_6H_4	70[e])	125–127		4.30
4e	4-NO_2–C_6H_4	86[e])	175–177		4.48
4f	4-NH_2SO_2–C_6H_4	67	218–220		4.62
4g	5-Chloro-2-(2′,4′-dichlorophenoxy)phenyl	91	151–153		4.31
4h	2-Chloro-3-pyridyl	75	132–134		4.20

[a]) See *Exper. Part* for complete data.
[b]) Yield of analytically pure products.
[c]) Solvent: $CDCl_3$ except for **4f**: (D_6)DMSO.
[d]) The crude azo compound was cyclized.
[e]) Overall yield based upon malonate **2**.

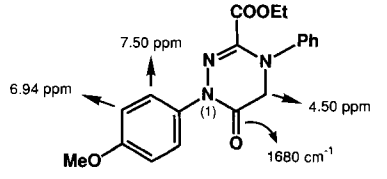
Various other aromatic amines were then used for the azo coupling with **2** (*Scheme 2*); the results are summarized in *Table 1*. Similar to **1b**, the arylamines **1a–g** gave the corresponding triazinones **4a–g** *via* the yellow coupling products **3a–g**. In some cases (**3b**, **f**, and **g**), these were pure, crystalline, and stable solids. In other cases, the crude, oily azo compounds were characterized by IR and ^{1}H-NMR spectroscopy and then directly used for the slightly exothermic cyclization step. Good yields of **4** (generally isolated by filtration) were obtained from electron-rich (**1d**, **1g** [4]) as well as electron-poor (**1e**, **1f**) anilines. Also, 3-amino-2-chloropyridine (**1h**) afforded the triazinone **4h**, but the coupling procedure had to be modified (see *Exper. Part*). The novel triazinones **4a–h** are all crystalline, colorless solids except for the yellow 4-nitrophenyl derivative **4e**.

They show the following typical spectral characteristics: the IR stretching vibrations of the EtOCO and the lactam C=O group appear as overlapping bands between 1745 and 1710 cm^{-1}. The high frequency (1710–1720 cm^{-1}) is unusual for a lactam C=O group. It can be attributed to the conjugation of the lactam N-atom with the hydrazone C=N bond, which, due to its π-acceptor effect, imparts some 'imide character' on the C=O group. This is also reflected by the reactivity towards $NaBH_4$ (see *Sect. 2.4*). In the ^{1}H-NMR spectra, the ring CH_2 groups appear as *s* at 4.20–4.38 ppm (**4a**, **b**, **c**, **d**, **g**, and **h**) and at 4.48–4.62 ppm for the 4-nitrophenyl (**4e**) and the 4-sulfamoyl (**4f**) derivatives, respectively.

Purification of compound **4d** by crystallization left a mother liquor from which a small amount (12%) of the isomeric triazinone **4*d** was isolated.



4d



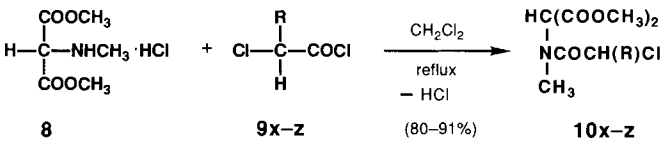
4*d

The structure was assigned of the basis of the IR spectrum which showed absorption bands for the ester C=O at 1735 and the lactam C=O at 1680 cm^{-1}, now in the normal position, since the lactam N-atom is connected to the N-terminal of the C=N bond. In the ^{1}H-NMR spectrum, the *s* for the ring CH_2 appears at 4.50 and the *d* for the *ortho*-H-atoms of the 4-methoxyphenyl ring is shifted downfield to 7.50 ppm. This is in accordance with the decreased electron-donating effect of N(1), which also explains the shift of the UV maximum from 350 nm (ε = 11200) in **4d** to 321 nm (ε = 7600) in isomer **4*d**. A pathway for the rearrangement leading to this compound is proposed in the discussion.

To check the validity of our reaction scheme for the synthesis of 6-substituted triazinones, we prepared the new malonates **5a** and **5b** from diethyl anilinomalonate available in high yield from diethyl 2-bromomalonate by the method of *Blank* [5a]. Coupling of diazotized 4-chloroaniline with **5a** and **5b** gave the crude, oily azo compounds **6** (*cf. Scheme 2*) which, upon base treatment, afforded the 6-substituted triazinones **7** in good yield.

2.2. *Coupling and Ring Closure of* N*-Methyl-Substituted (2-Chloroacetamido)malonates.* Anticipating better crystalline character of the products, we chose dimethylmalonate derivatives **10** as coupling components for this series. The starting material **8** was prepared in large amounts from dimethyl 2-bromomalonate according to the two-step procedure of *Uhle* and *Harris* [6] with minor modifications. Direct acylation of the hydrochloride **8** under non-basic conditions with the acid chlorides **9x–z** gave the oily malonates **10x**, **10y**, and the crystalline **10z** (*Scheme 3*).

Scheme 3



8 **9x–z** (80–91%) **10x–z**

x R = H **y** R = Me **z** R = Ph

The results of the azo coupling and the subsequent cyclization are summarized in *Table 2* (*cf. Scheme 2*). Again, pure azo compounds were fully characterized, while others were cyclized without further purification.

Good yields of the crystalline and generally colorless (only the 4-nitrophenyl derivatives **12h** and **12i** are yellow) triazinones **12** were obtained.

Table 2. *Selected Data of the Azo Compounds* **11** *and the Triazinones* **12**[a])

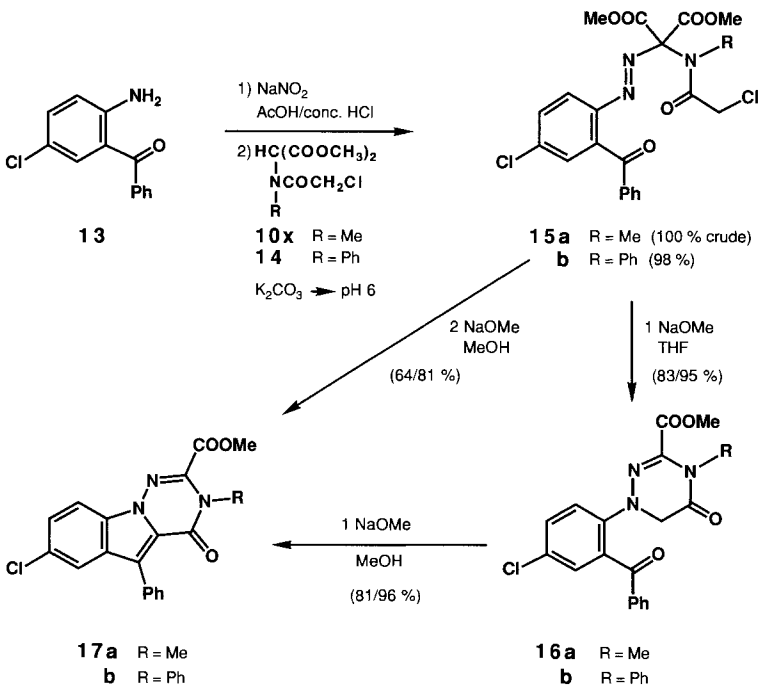
Compound	Ar	R^1	Yield [%][b])	M.p. [°]	^{1}H-NMR ($CDCl_3$) δ [ppm]
11a	Ph	H	[c])	oil	4.22 (*s*, $ClCH_2$)
11b	4-Cl–C_6H_4	H	88	111–112	4.22 (*s*, $ClCH_2$)
11c	4-Cl–C_6H_4	Me	[c])	oil	4.81 (*q*, MeCHCl)
11d	4-Cl–C_6H_4	Ph	[c])	oil	5.80 (*s*, PhCHCl)
11e	4-Me–C_6H_4	H	[c])	oil	4.23 (*s*, $ClCH_2$)
11f	4-MeO–C_6H_4	H	75	116–119	4.21 (*s*, $ClCH_2$)
11g	4-MeO–C_6H_4	Me	[c])	oil	4.71 (*q*, MeCHCl)
11h	4-NO_2–C_6H_4	H	87	95–97	4.24 (*s*, $ClCH_2$)
11i	4-NO_2–C_6H_4	Me	[c])	oil	4.70 (*q*, MeCHCl)
12a	Ph	H	64[d])	98–100	4.20 (*s*, ring CH_2)
12b	4-Cl–C_6H_4	H	88	130–131	4.16 (*s*, ring CH_2)
12c	4-Cl–C_6H_4	Me	77[d])	104–106	4.82 (*q*, ring CH)
12d	4-Cl–C_6H_4	Ph	73[d])	123–125	5.84 (*s*, ring CH)
12e	4-Me–C_6H_4	H	68[d])	94–95	4.27 (*s*, ring CH_2)
12f	4-MeO–C_6H_4	H	74	103–104	4.13 (*s*, ring CH_2)
12g	4-MeO–C_6H_4	Me	71[d])	73–74	4.84 (*q*, ring CH)
12h	4-NO_2–C_6H_4	H	82	185–187	4.36 (*s*, ring CH_2)
12i	4-NO_2–C_6H_4	Me	81[d])	148–151	4.93 (*q*, ring CH)

[a]) See *Exper. Part* for complete data.
[b]) Yield of analytically pure products.
[c]) The crude azo compound was cyclized.
[d]) Overall yield based upon $ArNH_2$.

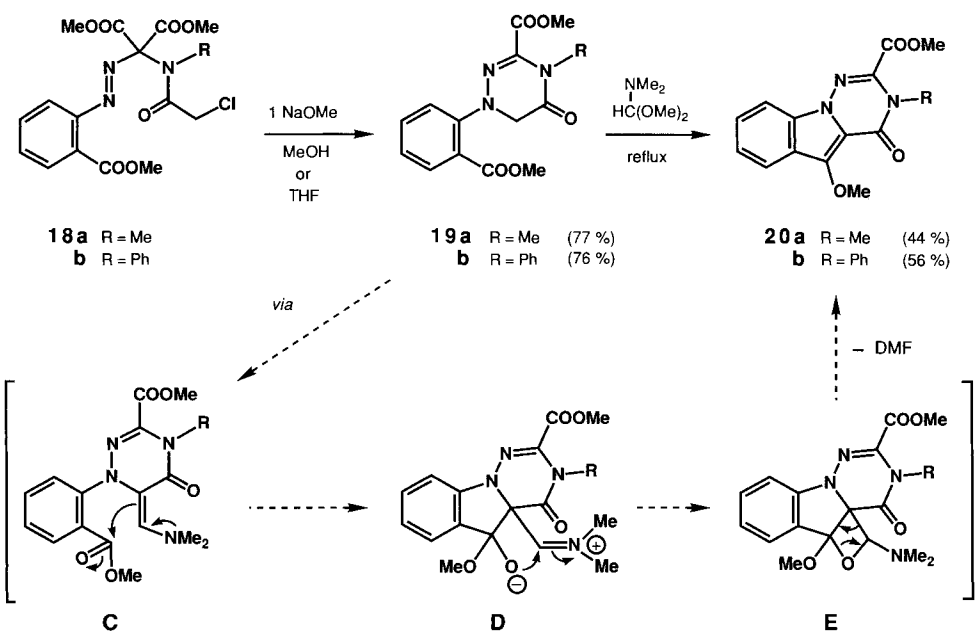
The spectral data of the compounds **12**, unsubstituted at C(6), are very similar to those of the corresponding *N*-phenyl derivatives **4**. In the ^{1}H-NMR spectra, the 6-methyl compounds **12c**, **g**, and **i** show the *q* for the ring CH at 4.82–4.93 ppm, and the *s* for the same proton in **12d** appears at 5.84 ppm. It is interesting to note that in the 4-methoxyphenyl case (**12f**) there was no evidence for the formation of an isomeric triazinone corresponding to **4*d**.

2.3. *2-Amino-5-chlorobenzophenone* (**13**) *and Methyl Anthranilate as Aromatic Amines.* Aiming at the synthesis of novel heterotricycles, we coupled two aniline derivatives carrying electrophilic *ortho*-substituents with malonates **10x** and **14** (*Scheme 4*). The

Scheme 4



Scheme 5



latter was conveniently prepared *via* dimethyl anilinomalonate [7]. The azomalonates **15** obtained from **13** indeed reacted with 2 equiv. of base directly to the triazino[1,6-*a*]-indoles **17**.

Alternatively, the intermediate triazinones **16** were isolated in good yield, when only 1 equiv. of NaOMe in THF at −5° was used. Further aldol-type condensation took place with another equiv. of base in MeOH.

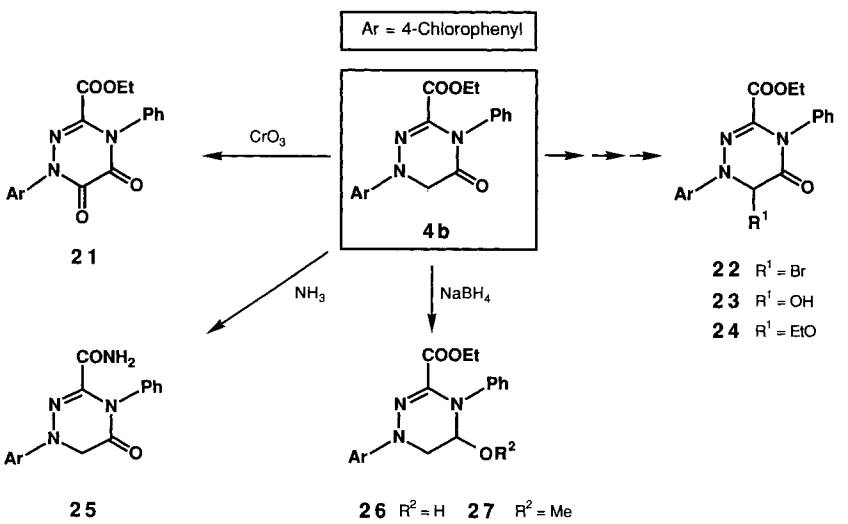
Although the azomalonates **18** (*Scheme 5*), derived from methyl anthranilate, gave the expected triazinones **19**, we were unable to prepare the envisaged tricycles **20** in acceptable yield by the action of base. Eventually – in an attempt to functionalize the ring CH_2 group – ring closure to **20** was achieved in moderate yield by refluxing **19** in DMF dimethyl acetal.

A possible pathway for this condensation may involve the enamine **C** created by the reaction of the acetal with the CH_2 group. Closure of the five-membered ring (→ **D**) might then be followed by the formation of a tetracyclic intermediate **E** which is split into DMF and the observed product **20**.

2.4. *Reactivity of the Triazinones.* The triazinones **4b** and **12b** were selected for further transformations (*Scheme 6* and *7*). Oxidation afforded the triazinediones **21** and **28**, while reaction with NH_3/MeOH led to the carboxamides **25** and **33**. Whereas we were unable to hydrolize the ester function of **4b** without concomitant cleavage of the lactam bond, compound **12b** gave a high yield of the acid **29** which underwent decarboxylation at 180° to furnish triazinone **30**[2]).

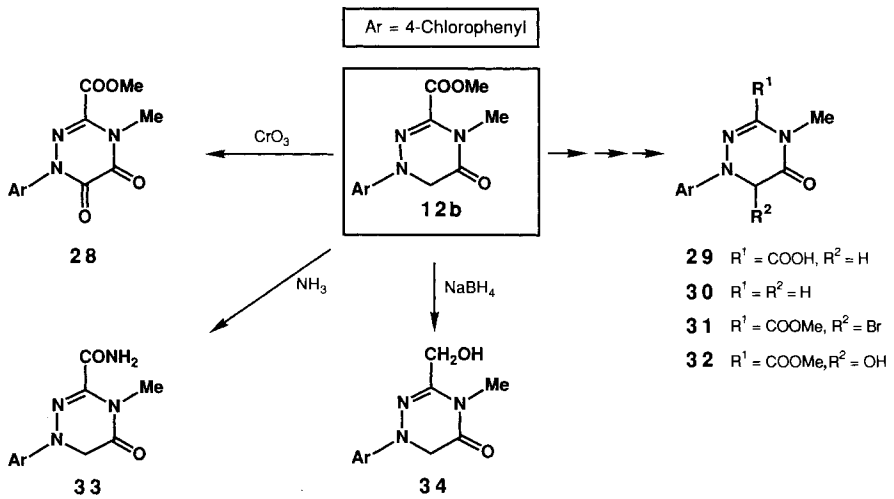
Reduction of **4b** with $NaBH_4$ occurred almost exclusively at the lactam C=O function to provide the hydroxy compound **26**, which, upon acid-catalyzed methanolysis, gave the methoxy derivative **27**. $NaBH_4$ treatment of **12b**, on the other hand, mainly resulted in the

Scheme 6



[2]) By condensing ethyl (1-phenylhydrazino)acetate with *N*-methylformamide, *Harries* [8] has prepared the *N*(1)-phenyl analogue of **30** in 1895.

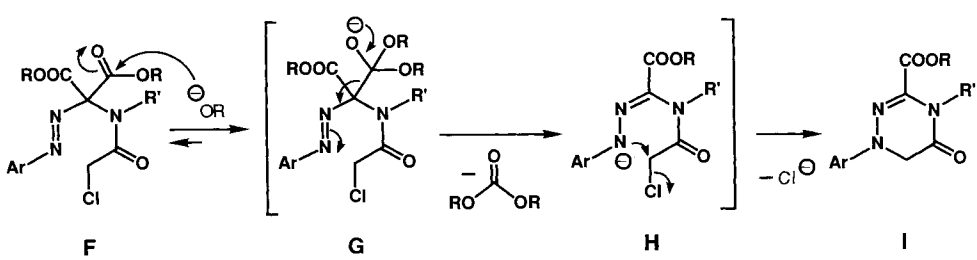
Scheme 7



reduction of the MeOCO group to furnish alcohol **34** besides overreduced unstable side products. Bromination of **4b** as well as **12b** under anhydrous conditions afforded the reactive, crystalline bromides **22** and **31**, whereas aqueous workup led directly to the 6-hydroxy derivatives **23** and **32**. In contrast to compound **32**, which reacts only very sluggishly with alcohols, the *N*-Ph-substituted derivative **23** is highly reactive. It suffices to heat an ethanolic solution for 1 h to induce the conversion – most probably *via* the iminium ion formed by loss of OH^- ion – to the ethoxy derivative **24**. Based on this reactivity, compounds of type **23** can be expected to exhibit α-amido-alkylating [9] properties. With the exception of **32** and **34**, the other derivatives, **21**–**33**, were obtained in high yield (see *Exper. Part*).

3. Discussion. – To detect any intermediates during the conversion of the azomalonates into the triazinones, the representative azo compound **3b** (*Scheme 2*) was reacted under very mild conditions with base. However, even at low reaction temperatures and by applying less than 1 equiv. of NaOEt in dilute solution, we were only able to observe (TLC) the ring-closed product **4b** besides starting material. Thus, one might postulate the general reaction mechanism in *Scheme 8*.

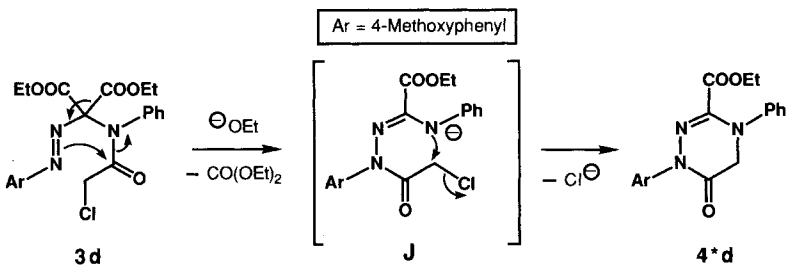
Scheme 8



Azomalonates **F**, presented here in a favored conformation[3]), contain – besides the relatively unreactive amide C=O group – two other electrophilic centers, *i.e.* the ester C=O and the $ClCH_2$ group. According to the principle of hard and soft acids and bases [10], the hard alkoxide nucleophile attacks preferably one of the hard alkoxycarbonyl groups instead of the relatively soft alkyl halide. The resulting intermediate **G** suffers malonate cleavage due to the frangomeric effect [11] of the arylazo function. Dialkyl carbonate is split off, and the strongly nucleophilic aryl N-anion in **H** interacts immediately with the internal halide to give **I**. The existence of the short-lived intermediate **H** is manifested by the deep magenta color [12] of the reaction solution which disappears upon ring closure.

The formation of the isomeric triazinone **4*d** can be explained by the pathway shown in *Scheme 9*.

Scheme 9



Azo compound **3d** – after malonate fragmentation – leads to an aryl N-anion with increased nucleophilicity imparted by the *p*-MeO substituent. In a side reaction, the nucleophile reacts with the amide C=O group *via* a five-membered transition state to give the transacylated anion **J** which cyclizes to generate **4*d**. In the *N*-Me analogue **11f** (*Scheme 2*), transacylation after fragmentation is less favored, since it would lead to a N-anion with decreased mesomeric stabilization. Thus, only one triazinone **12f** is formed.

In conclusion, our experiments have provided a rather general and convenient access to novel, functionalized 1,2,4-triazin-5-ones.

I thank *W. Gunzenhauser* and *J. Hunkeler* for skillful experimental assistance. Further thanks are due to *K. Friedrich* for the GLC analysis, *J. Meier* for the IR, *M. Knothe* and *D. Moss* for the UV, *W. Schmidlin* for the NMR spectra, and to Dr. *W. Padowetz* for the elemental analyses. I also acknowledge helpful discussions with Dres. *H. Allgeier*, *D. Bellus*, *A. Gagneux*, *A. Storni*, and *T. Winkler*.

Experimental Part

General. See [2]. Evaporation means removal of solvent by use of a *Büchi* rotary evaporator at 40–60° (20–200 Torr) followed by evaporation at 0.01 Torr. Drying agent for org. extracts: Na_2SO_4. GLC: *Varian 6000* GC with FID (270°); 2 m (int. diam. 2 mm) dimethylsilicon-fused silica column (10% *OV-101*); temp. program 50° (5 min), with 10°/min up to 250°: N_2 (20 ml/min). Unless noted otherwise, UV spectra were recorded in EtOH, IR spectra in CH_2Cl_2, and ^{1}H-NMR spectra in $CDCl_3$.

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[3]) For comments regarding conformational aspects of the azomalonate synthesis, see [2].

Diethyl (2-Chloro-N-phenylacetamido)malonate (**2**). This compound was prepared by a new variant of the published methods [3a,b]. A mixture of 47.75 g (0.19 mol) of diethyl anilinomalonate [3b] [5b] and 16.65 ml (23.6 g, 0.209 mol) of chloroacetyl chloride in 670 ml of toluene was stirred at 80° (bath temp. 90°) for 17 h. The HCl formed was eliminated by a water trap at the top of the condenser. The clear soln. was evaporated at 60°, the residue dissolved in 50 ml of toluene, and evaporated again. The solid product was recrystallized from CH_2Cl_2/hexane: 59.5 g (95%) of **2**. M.p. 93–94° ([3b]: 93–94°).

General Procedure for the Preparation of the Azo Compounds **3a–g**. To a suspension or soln. of the aromatic amine **1** in AcOH/conc. HCl 4:1 was slowly added 1 equiv. of aq. 5M $NaNO_2$ at the indicated temp. After the addition, stirring was continued for 15 min. Then, crushed ice was added, and a soln. of **2** (1 equiv.) in acetone was dropped in rapidly. To the resulting well stirred mixture, sat. aq. K_2CO_3 was added dropwise at 5–10°, until the pH finally reached 6–6.5. Stirring was continued at 10° for 1 h followed by addition of H_2O. Oily azomalonates were extracted twice with AcOEt. The org. extracts were washed copiously with H_2O and finally with brine, dried, and evaporated to give the crude products. Solid azomalonates were filtered off and purified (if necessary) by recrystallization.

Diethyl 2-(2-Chloro-N-phenylacetamido)-2-(phenylazo)malonate (**3a**). A soln. of 2.28 ml (2.33 g, 25 mmol) of aniline in 26 ml of AcOH and 6.4 ml of conc. HCl was diazotized with 5.0 ml (25 mmol) of aq. 5M $NaNO_2$ at 2–5°. Crushed ice (25 g) and a soln. of 8.0 g (24.5 mmol) of **2** in 50 ml of acetone were added, followed by sat. aq. K_2CO_3 (44 ml). Workup with AcOEt gave 10.73 g of crude **3a** as an oil. IR: 1770–1750*s*, 1700–1690*s*, 1605*m*, 1500*m*, 1380*m*, 1235*s*. ^{1}H-NMR (60 MHz): 1.19 (*t*, $J = 7$, 2 CH_3CH_2O); 3.87 (*s* CH_2Cl); 4.21 (*q*, $J = 7$, 2 CH_3CH_2O); 7.20–7.55 (*m*, 2 Ph).

Diethyl 2-(2-Chloro-N-phenylacetamido)-2-[(4-chlorophenyl)azo]malonate (**3b**). A soln. of 7.65 g (60 mmol) of *p*-chloroaniline in 60 ml of AcOH and 15 ml of conc. HCl was diazotized with 12.0 ml (60 mmol) of aq. 5M $NaNO_2$ at 0–2°. Crushed ice (40 g) and a soln of 19.5 g (59.5 mmol) of **2** in 97 ml of acetone were added, followed by sat. aq. K_2CO_3 (108 ml). After addition of 120 ml of H_2O and stirring for 1 h at 0°, the crystalline solid was filtered, washed copiously with H_2O, then with hexane (removes colored impurities), and once more with H_2O and hexane, and dried for 2 days at r.t over $CaCl_2$ *in vacuo*: 24.5 g (88%) of **3b**. M.p. 102–104°. UV: 285 (12900). IR: 1770–1750*s*, 1690*s*, 1600*m*, 1495*m*, 1360*m*, 1235*s*, 1020*m*, 845*m*. ^{1}H-NMR (60 MHz): 1.18 (*t*, $J = 7$, 6 H); 3.90 (*s*, 2 H); 4.20 (*q*, $J = 7$, 4 H); 7.32–7.70 (*m*, 9 arom. H). Anal. calc. for $C_{21}H_{21}Cl_2N_3O_5$ (466.32): C 54.09, H 4.54, Cl 15.21, N 9.01; found: C 53.8, H 4.6, Cl 15.1, N 9.0.

Diethyl 2-(2-Chloro-N-phenylacetamido)-2-[(4-methylphenyl)azo]malonate (**3c**). A suspension of 1.32 g (12.3 mmol) of *p*-toluidine in 13 ml of AcOH and 3 ml of conc. HCl was diazotized with 2.46 ml (12.3 mmol) of aq. 5M $NaNO_2$ at 4–6°. Crushed ice (12 g) and a soln. of 4.0 g (12.2 mmol) of **2** in 25 ml of acetone were added, followed by sat. aq. K_2CO_3 (20 ml). Workup with AcOEt gave 5.63 g of crude **3c** as an oil. IR: 1770–1750*s*, 1700*s*, 1605*m*, 1500*m*, 1385*m*, 1235*s*. ^{1}H-NMR (60 MHz): 1.20 (*t*, $J = 7$, 6 H); 2.40 (*s*, 3 H); 3.85 (*s*, 2 H); 4.21 (*q*, $J = 7$, 4 H); 7.15–7.65 (*m*, 9 arom. H).

Diethyl 2-(2-Chloro-N-phenylacetamido)-2-[(4-methoxyphenyl)azo]malonate (**3d**). A soln. of 3.08 g (25 mmol) of *p*-anisidine in 26 ml of AcOH and 6 ml of conc. HCl was diazotized with 5.0 ml (25 mmol) of aq. 5M $NaNO_2$ at 0–2°. Crushed ice (24 g) and a soln. of 8.0 g (24.5 mmol) of **2** in 50 ml of acetone were added, followed by sat. aq. K_2CO_3 (48 ml). Workup with AcOEt gave 11.75 g of crude **3d** as an oil. IR: 1770–1750*s*, 1700–1690*s*, 1610*s*, 1520*s*, 1500*m*, 1380*m*, 1235*s*, 1160*s*, 1040*m*, 850*m*. ^{1}H-NMR (60 MHz): 1.20 (*t*, $J = 7$, 6 H); 3.86 (*s*, 2 H); 3.91 (*s*, MeO); 4.20 (*q*, $J = 7$, 4 H); 6.90–7.65 (*m*, 9 arom. H).

Diethyl 2-(2-Chloro-N-phenylacetamido)-2-[(4-nitrophenyl)azo]malonate (**3e**). A suspension of 3.38 g (24.5 mmol) of *p*-nitroaniline in 25 ml of AcOH and 6 ml of conc. HCl was diazotized with 4.90 ml (24.5 mmol) of aq. 5M $NaNO_2$ at 5–8°. Crushed ice (24 g) and a soln. of 8.0 g (24.5 mmol) of **2** in 50 ml of acetone were added, followed by sat. aq. K_2CO_3 (40 ml). Workup with AcOEt gave 12.15 g of crude **3e** as an oil. IR: 1770–1750*s*, 1695*s*, 1605*m*, 1540*s* (NO_2, asymm. str.), 1500*m*, 1345*s* (NO_2, symm. str.), 1330*s*, 865*m*. ^{1}H-NMR (100 MHz): 1.18 (*t*, $J = 7$, 6 H); 3.85 (*s*, 2 H); 4.17 (*q*, $J = 7$, 4 H); 7.35–7.65 (*m*, Ph); 7.85 (*d*, $J = 9$, 2 H *ortho* to N=N); 8.34 (*d*, $J = 9$, 2 H *ortho* to NO_2).

Diethyl 2-(2-Chloro-N-phenylacetamido)-2-[(4-sulfamoylphenyl)azo]malonate (**3f**). A suspension of 1.76 g (10.2 mmol) of sulfanilamide in 9.5 ml of AcOH and 2.5 ml of conc. HCl was diazotized with 2.04 ml (10.2 mmol) of aq. 5M $NaNO_2$ at 15–17°. Crushed ice (10 g) and a soln. of 3.28 g (10 mmol) of **2** in 33 ml of acetone were added, followed by sat. aq. K_2CO_3 (23 ml). Workup with AcOEt gave an oily residue (5.2 g) which was crystallized from i-PrOH at 2° to afford 3.14 g (61%) of **3f**. M.p. 153–155° (dec.). UV: 276 (13760). IR: 3450 and 3320*w* (NH_2), 1770–1750*s*, 1695*s*, 1605*w*, 1495*m*, 1350*s* (SO_2), 1230*s*, 1175*s* (SO_2). ^{1}H-NMR (100 MHz): 1.17 (*t*, $J = 7$, 6 H); 3.88 (*s*, 2 H); 4.17 (*q*, $J = 7$, 4 H); 5.45 (*s*, SO_2NH_2); 7.30–7.62 (*m*, Ph); 7.74 (*d*, $J = 9$, 2 H *ortho* to N=N); 7.95 (*d*, $J = 9$,

2 H *ortho* to NH_2SO_2). Anal. calc. for $C_{21}H_{23}ClN_4O_7S$ (510.95): C 49.36, H 4.54, Cl 6.94, N 10.97, S 6.27; found: C 49.64, H 4.84, Cl 7.11, N 10.84, S 5.94.

*Diethyl 2-{[5-Chloro-2-(2',4'-dichlorophenoxy)phenyl]azo}-2-(2-chloro-*N*-phenylacetamido)malonate* (**3g**). A soln. of 2.88 g (10 mmol) of 5-chloro-2-(2',4'-dichlorophenoxy)aniline [4] in 9.5 ml of AcOH and 2.5 ml of conc. HCl was diazotized with 2.0 ml (10 mmol) of aq. 5M $NaNO_2$ at 2–5°. Crushed ice (10 g) and a soln. of 3.28 g (10 mmol) of **2** in 30 ml of acetone were added, followed by sat. aq. K_2CO_3 (23 ml). Workup with AcOEt gave an oily residue (6.5 g). Crystallization from i-PrOH afforded 5.7 g (91%) of **3g**. M.p. 107–109°. UV: 269 (9900), 325 (2920). IR: 1770–1750*s*, 1700*s*, 1470*s*, 1360*m*, 1235*s*. ^{1}H-NMR (100 MHz): 1.13 (*t*, *J* = 7, 6 H); 3.53 (*s*, 2 H); 4.14 (*q*, *J* = 7, 4 H); 6.75–7.70 (*m*, 11 arom. H). Anal. calc. for $C_{27}H_{23}Cl_4N_3O_6$ (627.31): C 51.70, H 3.70, Cl 22.61, N 6.70; found: C 51.86, H 3.78, Cl 22.61, N 6.93.

*Diethyl 2-[2'-Chloro-3'-pyridyl)azo]-2-(2-chloro-*N*-phenylacetamido)malonate* (**3h**). To a soln. of 6.0 g (46.5 mmol) of 3-amino-2-chloropyridine (*Fluka*) in 46 ml of AcOH and 11.5 ml of conc. HCl, 9.3 ml (46.5 mmol) of aq. 5M $NaNO_2$ was added dropwise at 2–5°. The resulting cold (*ca.* 5°) diazonium-salt soln. was transferred into a dropping funnel (small pieces of ice being added occasionally to keep the soln. cool) and added slowly to a soln. of 15.2 g (46.5 mmol) of **2** in 300 ml of MeOH at 15°. Simultaneously, sat. aq. $KHCO_3$ was dropped in at such a rate that the pH of the mixture was maintained at *ca.* 5. Towards the end of the addition of **2**, a yellow precipitate appeared. More sat. aq. $KHCO_3$ (total 230 ml) was added, until the pH was 6. After stirring for 2 h at 2°, the crystals were filtered, washed copiously with H_2O, and dried over $CaCl_2$ at r.t. in *vacuo*. The product (20.2 g) was recrystallized from 80 ml of i-PrOH to give 19.0 g (87%) of **3h**. M.p. 104–106°. UV: 260 (sh), 298 (5860). IR: 1770–1750*s*, 1690*s*, 1590*w*, 1480*m*, 1400‹*s*, 1360*m*, 1225*s*, 1075*m*. ^{1}H-NMR (60 MHz): 1.12 (*t*, *J* = 7, 6 H); 3.83 (*s*, 2 H); 4.13 (*q*, *J* = 7, 4 H); 7.20–7.65 (*m*, Ph, H–C(5')); 7.85 (*dd*, *J* = 1.5, 8, H–C(4')); 8.52 (*dd*, *J* = 1.5, 8, H–C(6')). Anal. calc. for $C_{20}H_{20}Cl_2N_4O_5$ (467.31): C 51.40, H 4.31, Cl 15.17, N 11.99; found: C 51.50, H 4.39, Cl 15.34, N 12.02.

General Procedure for the Conversion of the Azomalonates **3a–g** *into the 1,2,4-Triazinones* **4a–g**. To a well stirred soln. or suspension of **3** in EtOH, 1 equiv. of 1N NaOEt/EtOH was added at the indicated temp. After the exothermic reaction had subsided, the suspension (pH *ca.* 7) was stirred for 1 h at 0°. The products **4** were filtered, washed with a little of cold EtOH, plenty of H_2O (removes NaCl), and hexane, and further purified (if necessary) by recrystallization.

Ethyl 1,4,5,6-Tetrahydro-1,4-diphenyl-5-oxo-1,2,4-triazine-3-carboxylate (**4a**). From 10.7 g (max. 24.5 mmol) of crude **3a** in 100 ml of EtOH, treated at 15° with 25 ml (25 mmol) of 1N NaOEt/EtOH, 6.75 g of crude product was obtained. Recrystallization from i-PrOH gave 6.34 g (80% from **2**) of **4a**. M.p. 163–165°. UV: 230 (14000), 260 (sh), 340 (12000). IR: 1745–1720*s* (C=O, ester and lactam), 1605*m*, 1500*m*, 1330*m*, 1300–1250*m*, 1210*m*, 1200*m*, 1180*m*, 1160*m*. ^{1}H-NMR (60 MHz): 1.02 (*t*, *J* = 7, CH_3CH_2O); 4.10 (*q*, *J* = 7, CH_3CH_2O); 4.38 (*s*, CH_2(6)); 7.05–7.60 (*m*, 2 Ph). Anal. calc. for $C_{18}H_{17}N_3O_3$ (323.35): C 66.86, H 5.30, N 13.00; found: C 66.6, H 5.5, N 13.1.

Ethyl 1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-5-oxo-4-phenyl-1,2,4-triazine-3-carboxylate (**4b**). From 16.5 g (35.4 mmol) of **3b** in 300 ml of EtOH, treated with 36 ml (36 mmol) of 1N NaOEt/EtOH at 15°, 11.05 g (87%) of pure **4b** were obtained. M.p. 156–158°. UV: 241 (14100), 342 (13400). IR: 1745–1710*s*, 1600*m*, 1490*s*, 1350*m*, 1325*s*, 1290*s*, 1205*s*, 1170*s*, 1150*s*, 1095*m*, 1055*m*, 990*m*, 825*m*. ^{1}H-NMR (60 MHz): 1.01 (*t*, *J* = 7, 3 H); 4.08 (*q*, *J* = 7, 2 H); 4.32 (*s*, 2 H); 7.10–7.60 (*m*, 9 arom. H). Anal. calc. for $C_{18}H_{16}ClN_3O_3$ (357.80): C 60.42, H 4.51, Cl 9.91, N 11.74; found: C 60.54, H 4.53, Cl 9.80, N 11.58.

Separate Experiment for the Determination of Diethyl Carbonate. To a well stirred suspension of 1.65 g (3.54 mmol) of **3b** in 30.2 ml of EtOH, 3.6 ml (3.6 mmol) of 1N NaOEt/EtOH were added at 15°. After the exothermic reaction, the mixture was stirred for 30 min at 0°. The crystalline product (**4b**) was filtered off without washing. The ethanolic mother liquor (total 33.7 ml, *d* = 0.784) was submitted to GLC (0.1 µl injected). A standard soln. of diethyl carbonate in EtOH was used for the calculation of the percentage which amounted to 1.49%. Thus, a total of 394 mg (3.34 mmol, 94% of the theoretical amount) of diethyl carbonate was present.

Ethyl 1,4,5,6-Tetrahydro-1-(4-methylphenyl)-5-oxo-4-phenyl-1,2,4-triazine-3-carboxylate (**4c**). From 5.6 g (12.3 mmol) of crude **3c** in 90 ml of EtOH, treated with 12.8 ml (12.8 mmol) of 1N NaOEt/EtOH at 10°, 2.99 g (72% from **2**) of pure **4c** were obtained. M.p. 135–137°. UV: 235 (14600), 344 (12200). IR: 1745–1710*s*, 1605*m*, 1520*s*, 1500*m*, 1365*m*, 1335*s*, 1300–1250*m*, 1210*m*, 1160*m*, 1065*m*, 1000*m*. ^{1}H-NMR (60 MHz): 1.07 (*t*, *J* = 7, 3 H); 2.37 (*s*, arom. CH_3); 4.10 (*q*, *J* = 7, 2 H); 4.35 (*s*, 2 H); 7.15–7.60 (*m*, 9 arom. H). Anal. calc. for $C_{19}H_{19}N_3O_3$ (337.38): C 67.64, H 5.68, N 12.46; found: C 67.5, H 5.7, N 12.5.

Ethyl 1,4,5,6-Tetrahydro-1-(4-methoxyphenyl)-5-oxo-4-phenyl-1,2,4-triazine-3-carboxylate (**4d**) *and Ethyl 1,4,5,6-Tetrahydro-1-(4-methoxyphenyl)-4-phenyl-6-oxo-1,2,4-triazine-3-carboxylate* (**4*d**). From 11.7 g (max. 24.5 mmol) of crude **3d** in 140 ml of EtOH, treated with 25 ml (25 mmol) of 1N NaOEt/EtOH at 10°, 8.25 g of crude product were obtained. Two recrystallizations from i-PrOH gave 6.04 g (70%) of **4d**. M.p. 125–127°. *TLC*: R_f

(toluene/AcOEt 4:1) 0.43. UV: 235 (14700), 350 (11200). IR: 1735–1715*s*, 1595*m*, 1510*s*, 1490*m*, 1355*m*, 1325*s*, 1240*s*, 1205–1150*s*, 1060*m*, 1030*m*, 990*m*, 940*m*, 835*m*. ^{1}H-NMR (100 MHz): 1.03 (*t*, *J* = 7, 3 H); 3.82 (*s*, MeO); 4.07 (*q*, *J* = 7, 2 H); 4.30 (*s*, 2 H); 6.94 (*d*, *J* = 9, 2 H *ortho* to MeO); 7.27 (*d*, *J* = 9, 2 H *ortho* to triazinone); 7.30–7.45 (*m*, Ph). Anal. calc. for $C_{19}H_{19}N_3O_4$ (353.38): C 64.58, H 5.42, N 11.89; found: C 64.8, H 5.4, N 11.9.

CC of the mother liquor (2.52 g after evaporation) of the above crystallization on 250 g of silica gel with toluene/AcOEt 4:1 followed by crystallization from i-PrOH gave 1.03 g (12%) of **4*d**. M.p. 143–145°. TLC: R_f (toluene/AcOEt 4:1) 0.31. UV: 242 (17299), 321 (7600). IR: 1735*s*, 1680*s*, 1590*s*, 1510*s*, 1495*s*, 1460*m*, 1400*m*, 1380*m*, 1360*m*, 1300*s*, 1225*s*, 1195*m*, 1120*m*, 1030*w*, 830*w*. ^{1}H-NMR (100 MHz): 1.06 (*t*, *J* = 7, 3 H); 3.82 (*s*, MeO); 4.14 (*q*, *J* = 7, 2 H); 4.50 (*s*, 2 H); 6.94 (*d*, *J* = 9, 2 H *ortho* to MeO); 7.00–7.45 (*m*, Ph); 7.50 (*d*, *J* = 9, 2 H *ortho* to triazinone). Anal. calc. for $C_{19}H_{19}N_3O_4$ (353.38): C 64.58, H 5.42, N 11.89; found: C 64.82, H 5.62, N 12.01.

Ethyl 1,4,5,6-Tetrahydro-1-(4-nitrophenyl)-5-oxo-4-phenyl-1,2,4-triazine-3-carboxylate (**4e**). From 12.1 g (max. 24.5 mmol) of crude **3e** in 150 ml of EtOH, treated with 25 ml (25 mmol) of 1N NaOEt/EtOH at 6°, 7.75 g (86% from **2**) of pure **4e** were obtained. M.p. 175–177°. UV: 250 (sh), 373 (24800). IR: 1750–1710*s*, 1600*s*, 1520–1510*s* (NO_2), 1340*s* (NO_2), 1320*s*, 1290–1250*s*, 1210*m*, 1170*s*, 1115*s*, 843*m*. ^{1}H-NMR (100 MHz): 1.08 (*t*, *J* = 7, 3 H); 4.09 (*q*, *J* = 7, 2 H); 4.48 (*s*, 2 H); 7.20–7.50 (*m*, Ph, 2 H *ortho* to triazinone); 8.25 (*d*, *J* = 9, 2 H *ortho* to NO_2). Anal. calc. for $C_{18}H_{16}N_4O_5$ (368.35): C 58.69, H 4.38, N 15.21; found: C 58.63, H 4.35, N 15.08.

Ethyl 1,4,5,6-Tetrahydro-5-oxo-4-phenyl-1-(4-sulfamoylphenyl)-1,2,4-triazine-3-carboxylate (**4f**). From 3.0 g (5.87 mmol) of **3f** in 100 ml of EtOH, treated with 6.0 ml (6 mmol) of 1N NaOEt/EtOH at 40° for 20 h, 1.70 g of crude product were obtained. Recrystallization from CH_2Cl_2/EtOH gave 1.63 g (67%) of **4f**, containing 0.74 mol-equiv. of H_2O. M.p. 218–220°. UV: 255 (14580), 343 (18040). IR (nujol): 3360 and 3250*m* (NH_2), 1735–1710*s*, 1640*m*, 1600*m*, 1375*s*, 1320*s* (SO_2), 1245*m*, 1215*s*, 1155*s* (SO_2), 1105*m*, 1055*m*, 840*m*, 815*s*, 758*m*, 693*m*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 0.90 (*t*, *J* = 7, 3 H); 3.32 (*s*, H_2O); 3.98 (*q*, *J* = 7, 2 H); 4.62 (*s*, 2 H); 7.20–7.31 (*m*, NH_2SO_2, 2 arom. H); 7.35–7.52 (*m*, 2 H *ortho* to triazinone, 3 arom. H); 7.80 (*d*, *J* = 9, 2 H *ortho* to NH_2SO_2). Anal. calc. for $C_{18}H_{18}N_4O_5 \cdot 0.74\ H_2O$ (415.76): C 52.01, H 4.75, N 13.48, S 7.71, H_2O 3.20; found: C 51.95, H 4.77, N 13.49, S 7.63, H_2O 3.20.

Ethyl 1-[5-Chloro-2-(2',4'-dichlorophenoxy)phenyl]-1,4,5,6-tetrahydro-5-oxo-4-phenyl-1,2,4-triazine-3-carboxylate (**4g**). From 5.34 g (8.5 mmol) of **3g** in 70 ml of EtOH, treated with 8.5 ml (8.5 mmol) of 1N NaOEt/EtOH at 25°, 4.02 g (91%) of pure **4g** were obtained. M.p. 151–153°. UV: 284 (sh), 294 (sh), 322 (8580). IR: 1745–1715*s*, 1600*m*, 1495*s*, 1480*s*, 1330*s*, 1235*m*, 1190*s*, 1140*m*, 1100*m*, 990*m*. ^{1}H-NMR (100 MHz): 1.02 (*t*, *J* = 7, 3 H); 4.08 (*q*, *J* = 7, 2 H); 4.31 (*s*, 2 H); 6.77 (*d*, *J* = 6, H–C(6')); 6.85 (*d*, *J* = 6, H–C(3)); 7.10–7.50 (*m*, 8 arom. H); 7.75 (*d*, *J* = 2.4 H–C(6)). Anal. calc. for $C_{24}H_{18}Cl_3N_3O_4$ (518.78): C 55.57, H 3.50, Cl 20.50, N 8.10; found: C 55.35, H 3.59, Cl 21.01, N 8.10.

Ethyl 1-(2'-Chloro-3'-pyridyl)-1,4,5,6-tetrahydro-5-oxo-4-phenyl-1,2,4-triazine-3-carboxylate (**4h**). To a soln. of 19.0 g (40.7 mmol) of **3h** in 950 ml of EtOH, 41 ml (41 mmol) of 1N NaOEt/EtOH were added within 5 min at 20°. After stirring for 1 h at r.t., the pH of the mixture was adjusted to 5 by addition of AcOH. Evaporation left a residue which was partitioned between H_2O and CH_2Cl_2. The org. extracts were washed with cold 1N $KHCO_3$ and with brine, dried, and evaporated to give 14.0 g of crude product. Recrystallization from i-PrOH afforded 10.95 g (75%) of **4h**. M.p. 132–134°. UV: 228 (14000), 311 (9500). IR: 1745–1710*s*, 1600*m*, 1495*m*, 1405*m*, 1370*m*, 1345*m*, 1235*m*, 1195*s*, 1135*m*, 1095*m*. ^{1}H-NMR (60 MHz): 1.02 (*t*, *J* = 7, 3 H); 4.08 (*q*, *J* = 7, 2 H); 4.20 (*s*, 2 H); 7.10–7.55 (*m*, Ph, H–C(5')); 8.04 (*dd*, *J* = 1.5, 8, H–C(4')); 8.30 (*dd*, *J* = 1.5, 4.6, H–C(6')). Anal. calc. for $C_{17}H_{15}ClN_4O_3$ (358.78): C 56.91, H 4.21, Cl 9.88, N 15.62; found: C 56.83, H 4.30, Cl 9.92, N 15.55.

*Diethyl 2-(2-Chloro-*N*-phenylpropanamido)malonate* (**5a**). A mixture of 17.59 g (70 mmol) of diethyl anilinomalonate [3b] and 7.64 ml (9.78 g, 77 mmol) of 2-chloropropionyl chloride (*Fluka*) in 145 ml of CH_2Cl_2 (dried over $CaCl_2$) was stirred at reflux for 24 h. The HCl formed was eliminated by a water trap at the top of the condenser. After cooling, the soln. was washed with H_2O, cold 1N $KHCO_3$, and brine, dried, and evaporated to give 24.2 g of crude product. Crystallization from Et_2O hexane at 0° gave 17.5 g (73%) of **5a** M.p. 49–51°. IR: 1770–1750*s*, 1690*s*, 1605*m*, 1500*m*, 1400*m*, 1380*m*, 1310*m*, 1220*s*, 1200*s*, 1075*m*, 1040*m*. ^{1}H-NMR (100 MHz): 1.10–1.32 (2*t*, *J* = 7, 2 CH_3CH_2O); 1.57 (*d*, *J* = 7, CH_3CHCl); 4.04–4.40 (2 overlapping *q*, *J* = 7, CH_3CH_2O, CH_3CHCl); 5.36 (*s*, H–C(2)); 7.35–7.70 (*m*, Ph). Anal. calc. for $C_{16}H_{20}ClNO_5$ (341.79): C 56.23, H 5.90, Cl 10.37, N 4.10; found: C 56.1, H 6.0, Cl 10.4, N 4.0.

*Diethyl 2-(2-Chloro-2,*N*-diphenylacetamido)malonate* (**5b**). A mixture of 12.55 g (50 mmol) of diethyl anilinomalonate [3b] and 8.8 ml (11.44 g, 60.5 mmol) of 2-chloro-2-phenylacetyl chloride (*Fluka*) in 120 ml of CH_2Cl_2 (dried over $CaCl_2$) was stirred at reflux (HCl trapped) for 65 h. Workup as described for **5a** gave 21.1 g of the crude product as an oil that could not be purified by bulb-to-bulb destillation. FC on 250 g of silica gel (0.04–0.063 mm) with toluene/AcOEt 95:5 afforded 14.2 g (70%) of fairly pure **5b** as an oil. IR: 1760–1740*s*, 1685*s*, 1600*m*, 1490*m*,

1370*m*, 1215*s*, 1185*s*, 1035*m*. ^{1}H-NMR (100 MHz): 1.10–1.23 (2*t*, $J = 7$, 2 CH_3CH_2O); 4.05–4.20 (*m*, 2 CH_3CH_2O); 5.33 and 5.35 (2*s*, PhC*H*Cl, H–C(2)); 7.20–7.62 (*m*, 10 arom. H). Anal. calc. for $C_{21}H_{22}ClNO_5$ (403.86): C 62.46, H 5.49, Cl 8.78, N 3.47; found: C 62.9, H 5.6, Cl 8.3, N 3.8.

*Diethyl 2-(4-Chlorophenylazo)-2-(2-chloro-*N*-phenylpropanamido)malonate* (**6a**) *and Ethyl 1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-6-methyl-5-oxo-4-phenyl-1,2,4-triazine-3-carboxylate* (**7a**). According to the general coupling procedure given for **2**, a soln. of 955 mg (7.48 mmol) of *p*-chloroaniline in 9.3 ml of AcOH/conc. HCl 4:1 was diazotized at 0–2° with 1.49 ml (7.48 mmol) of aq. 5M $NaNO_2$. Crushed ice (11 g) and a soln. of 2.56 g (7.48 mmol) of **5a** in 25 ml of acetone were added, followed by sat. aq. K_2CO_3 (15 ml). Workup with AcOEt gave 3.65 g of crude **6a** as an oil. IR: 1760–1750*s*, 1685*s*, 1595*m*, 1490*m*, 1385*m*, 1235–1215*s*, 1090*m*, 1010*m*, 840*m*. ^{1}H-NMR (60 MHz): 1.17 (*t*, $J = 7$, 3 H); 1.54 (*d*, $J = 7$, CH_3CH); 4.23 (2 overlapping *q*, $J = 7$, CH_3CH, CH_3CH_2O); 7.25–7.65 (*m*, 9 arom. H).

To a soln. of the above azomalonate (3.63 g, max. 7.48 mmol) in 35 ml of EtOH, 7.48 ml (7.48 mmol) of 1N NaOEt/EtOH were added at r.t. After stirring for 30 min at r.t., the pH of the mixture was adjusted to 5 by addition of AcOH. Evaporation left a residue which was partitioned between AcOEt and H_2O. The org. extracts were washed with cold 1N $KHCO_3$ and brine, dried, and evaporated to give 3.10 g of an oil that was purified by FC on 100 g of silica gel (0.04–0.063 mm) with toluene. The clean fractions containing the product (TLC: R_f (toluene/AcOEt 9:1) 0.5) were combined (2.61 g) and crystallized from Et_2O/hexane to give 2.01 g (72% from *p*-chloroaniline) of **7a**. M.p. 102–103°. UV: 242 (14260), 345 (14220). IR: 1740–1710*s* (C=O, ester and lactam), 1600*m*, 1495*s*, 1330*s*, 1310*m*, 1235*m*, 1200*m*, 1160*m*, 1095*m*, 1010*m*, 995*m*, 830*m*. ^{1}H-NMR (250 MHz): 1.06 (*t*, $J = 7$, CH_3CH_2O); 1.37 (*d*, $J = 7.5$, CH_3–C(6)); 4.07 (*q*, $J = 7$, CH_3CH_2O); 4.92 (*q*, $J = 7.5$, H–C(6)); 7.20–7.50 (*m*, 9 arom. H). Anal. calc. for $C_{19}H_{18}ClN_3O_3$ (371.82): C 61.38, H 4.88, Cl 9.54, N 11.30; found: C 61.18, H 4.79, Cl 9.58, N 11.45.

*Diethyl 2-(2-Chloro-2,*N*-diphenylacetamido)-2-(4-chlorophenylazo)malonate* (**6b**) *and Ethyl 1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-5-oxo-4,6-diphenyl-1,2,4-triazine-3-carboxylate* (**7b**). A soln. of 1.28 g (10 mmol) of *p*-chloroaniline in 12 ml of AcOH/conc HCl (4:1) was diazotized with 2.0 ml (10 mmol) of aq. 5M $NaNO_2$. Crushed ice (14 g) and a soln. of 4.04 g (10 mmol) of **5b** in 40 ml of acetone were added, followed by sat. aq. K_2CO_3 (22 ml). Workup with AcOEt gave 5.85 g of crude **6b** as an oil. IR: 1760–1750*s*, 1690*s*, 1600*m*, 1505*m*, 1355*m*, 1235*s*, 1215*s*, 1080*m*, 1010*m*, 840*m*. ^{1}H-NMR (60 MHz): 0.95–1.12 (*sext.*, X_3 of ABX_3, 2 CH_3CH_2O); 3.92–4.36 (*m*, *AB* of ABX_3, 2 CH_3CH_2O); 5.30 (*s*, PhC*H*Cl); 7.05–7.65 (*m*, 14 arom. H).

To a soln. of 5.80 g (max. 10 mmol) of crude **6b** in 36 ml of EtOH, 10.2 ml (10.2 mmol) of 1N NaOEt/EtOH were added at 5°. After stirring for 15 min, the product crystallized and was collected by filtration after cooling for 1 h at 0°. The crystals were washed with Et_2O, H_2O and again Et_2O to give 3.60 g of crude product. Recrystallization from CH_2Cl_2/i-PrOH afforded 3.45 g (79% from *p*-chloroaniline) of **7b**. M.p. 165–167°. UV: 237 (14300), 267 (sh), 349 (14740). IR: 1740–1705*s*, 1600*m*, 1500*s*, 1335*s*, 1320*s*, 1235*s*, 1195*s*, 1150*s*, 1095*m*, 825*m*. ^{1}H-NMR (100 MHz, $CDCl_3$ + (D_6)DMSO): 0.98 (*t*, $J = 7$, 3 H); 4.02 (*q*, $J = 7$, 2 H); 6.15 (*s*, H–C(6)); 7.10–7.48 (*m*, 14 arom. H). Anal. calc. for $C_{24}H_{20}ClN_3O_3$ (433.90): C 66.44, H 4.65, Cl 8.17, N 9.69; found: C 66.17, H 4.63, Cl 8.55, N 9.86.

Large-Scale Preparation of Dimethyl 2-(Methylamino)malonate Hydrochloride (**8**). To a soln. of 97.5 ml (160 g, 0.76 mol) of dimethyl 2-bromomalonate in 310 ml of MeOH, 179 ml (170 g, 1.4 mol) of benzylamine were added dropwise within 30 min at 15°. After stirring at r.t. for 17 h, the clear soln. was evaporated, and 800 ml of Et_2O were added. The mixture was kept in freezer for 3 h, and the precipitated *N*-methylbenzylamine hydrochloride was filtered off and washed with Et_2O. The filtrate was washed with H_2O, cold 0.5 N HCl (the desired base remains in the org. phase at pH 2!), H_2O, and brine, dried, and evaporated to give 166.8 g (98%) of crude dimethyl *N*-benzyl-*N*-methylaminomalonate (purity ~ 90%). The base was dissolved in 1.7 l of MeOH and hydrogenated in the presence of 30 g of Pd/C (10%) at 20° (slight cooling was necessary) for 2.5 h. The catalyst was removed by filtration through a *Celite* pad and washed with MeOH. To the clear filtrate, 100 ml of ca. 6M HCl/MeOH were added with stirring (final pH 3). Evaporation followed by the addition of 100 ml of toluene and again evaporation left a residue which was triturated with 150 ml of CH_2Cl_2, 50 ml of AcOEt, and finally 100 of Et_2O. After standing at 0° for 16 h, the crystals were filtered, washed with cold AcOEt, and Et_2O, and dried at r.t. over $CaCl_2$ in *vacuo*, until the weight remained constant: 98.3 g (75%) of pure **8**. M.p. 122–124° (dec.) ([6]: 131–133° (dec.)). This synthon can be stored for years in a tightly closed bottle.

*Dimethyl 2-(2-Chloro-*N*-methylacetamido)malonate* (**10x**). A mixture of 52.0 g (263 mmol) of **8** and 23 ml (32.71 g, 289 mmol) of *chloroacetyl chloride* (**9x**) in 320 ml of CH_2Cl_2 (dried over $CaCl_2$) was stirred at reflux (HCl trapped) for 18 h. After cooling, the org. phase was washed with H_2O, cold 1N $KHCO_3$, and brine, dried, and evaporated to give 57.2 (91%) of fairly pure **10x** as an oil. IR: 1760/1750*s*, 1670*s*, 1440*m*, 1400*m*, 1335*m*, 1200*m*, 1170*m*, 1110*m*, 1040*m*, 1020*m*. ^{1}H-NMR (60 MHz): 3.25 (*s*, CH_3N); 3.90 (*s*, 2 CH_3OOC); 4.27 (*s*, CH_2Cl); 6.00 (*s*, H–C(2)). Anal. calc. for $C_8H_{12}ClNO_5$ (237.64): C 40.44, H 5.09, Cl 14.92, N 5.89; found: C 39.8, H 5.0, Cl 15.1, N 5.9.

*Dimethyl 2-(2-Chloro-*N*-methylpropanamido)malonate* (**10y**). A mixture of 19.41 g (98 mmol) of **8** and 10.7 ml (13.64 g, 107 mmol) of *2-chloropropionyl chloride* (**9y**) in 360 ml oif CH_2Cl_2 (dried over $CaCl_2$) was stirred at reflux (HCl trapped) for 20 h. Workup as described for **10x** gave 20.6 g (83%) of **10y** as a yellow oil. IR: 1760/1745*s*, 1665*s*, 1430*m*, 1400*m*, 1345*m*, 1285–1250*m*, 1200*m*, 1165*m*, 1125*m*, 1080*m*, 1065*m*, 1030*m*. ^{1}H-NMR (100 MHz): 1.68 (*d*, $J = 7$, CH_3CHCl); 3.24 (*s*, CH_3N); 3.80 (*s*, 2 CH_3OOC); 4.68 (*q*, $J = 7$, CH_3CHCl); 5.92 (*s*, H–C(2)). Anal. calc. for $C_9H_{14}ClNO_5$ (251.67): C 42.95, H 5.61, Cl 14.09, N 5.57; found: C 43.21, H 5.70, Cl 14.45, N 5.60.

*Dimethyl 2-(2-Chloro-*N*-methyl-2-phenylacetamido)malonate* (**10z**). A mixture of 19.41 g (98 mmol) of **8** and 15.7 ml (20.41 g, 108 mmol) of *2-chloro-2-phenylacetyl chloride* (**9z**) in 360 ml of CH_2Cl_2 (dried over $CaCl_2$) was stirred at reflux (HCl trapped) for 22 h. Workup as described for **10x** gave 32.37 g of crude product that crystallized upon standing in the freezer. Recrystallization from CH_2Cl_2/hexane gave 22.7 g (74%) of **10z**. M.p. 80–82°. IR: 1760/1745*s*, 1680*s*, 1435*m*, 1395*m*, 1325*m*, 1200*s*, 1170*s*, 1110*m*, 1035*m*. ^{1}H-NMR (60 MHz): 3.05 (*s*, CH_3N); 3.70 (*s*, 1 CH_3OOC); 3.77 (*s*, 1 CH_3OOC); 5.75 (*s*, H–C(2)); 5.92 (*s*, PhC*H*Cl); 7.20–7.52 (*m*, Ph). Anal. calc. for $C_{14}H_{16}ClNO_5$ (313.74); C 53.60, H 5.14, Cl 11.30, N 4.47; found: C 53.50, H 5.28, Cl 11.48, N 4.40.

General Procedure for the Preparation of the Azo Compounds **11a–i**. To a suspension or soln. of 20 mmol of the aromatic amine in 26 ml of AcOH/conc. HCl 4:1, 4.0 ml (20 mmol) of aq. 5M $NaNO_2$ was slowly added at 0–5°. After the addition, stirring was continued for 15 min at 5°. Then, 20 g of crushed ice were added, and a soln. of 20 mmol of **10** in 50 ml of acetone was dropped in rapidly. To the resulting, well stirred mixture, sat. aq. K_2CO_3 (38 ml) was added dropwise at 5–10°, until the pH finally reached 6–6.5. Stirring was continued at 10° for 1 h followed by addition of H_2O (200 ml). The azomalonates were extracted twice with AcOEt. The org. extracts were washed copiously with H_2O and finally brine, dried, and evaporated to give the crude products.

*Dimethyl 2-(2-Chloro-*N*-methylacetamido)-2-(phenylazo)malonate* (**11a**). Diazotization of 2.29 ml (2.33 g, 25 mmol) of aniline and coupling with 5.94 g (25 mmol) of **10x** gave 8.62 g of crude **11a** as an oil. IR: 1770–1750*s*, 1685*s*, 1445*m*, 1390*m*, 1290*m*, 1240*s*, 1190*m*. ^{1}H-NMR (100 MHz): 3.29 (*s*, CH_3N); 3.85 (*s*, 2 CH_3OOC); 4.22 (*s*, CH_2Cl); 7.35–7.58 (*m*, 3 arom. H); 7.70–7.85 (*m*, 2 arom. H).

*Dimethyl 2-(2-Chloro-*N*-methylacetamido)-2-(4-chlorophenylazo)malonate* (**11b**). Diazotization of 3.19 g (25 mmol) of *p*-chloroaniline and coupling with 5.94 g (25 mmol) of **10x** gave 9.8 g of crude product. Crystallization from i-PrOH afforded 8.3 g (88%) of **11b**. M.p. 111–112°. UV: 220 (12800), 290 (12100). IR: 1770–1750*s*, 1680*s*, 1480*m*, 1445*m*, 1385*m*, 1280*m*, 1230*s*, 1090*s*, 1010*m*, 840*m*. ^{1}H-NMR (250 MHz): 3.25 (*s*, 3 H); 3.85 (*s*, 6 H); 4.22 (*s*, 2 H); 7.47 (*d*, $J = 9$, 2 H); 7.73 (*d*, $J = 9$, 2 H). Anal. calc. for $C_{14}H_{15}Cl_2N_3O_5$ (376.20): C 44.70, H 4.02, Cl 18.85, N 11.17; found: C 44.48, H 4.10, Cl 18.81, N 11.10.

*Dimethyl 2-(2-Chloro-*N*-methylpropanamido)-2-(4-chlorophenylazo)malonate* (**11c**). Diazotization of 2.55 g (20 mmol) of *p*-chloroaniline and coupling with 5.03 g (20 mmol) of **10y** gave 8.15 g of crude **11c** as an oil. IR: 1770–1750*s*, 1680*s*, 1480*m*, 1430*m*, 1380*m*, 1230*s*, 1190*s*, 840*m*. ^{1}H-NMR (60 MHz): 1.78 (*d*, $J = 6.5$, CH_3CHCl); 3.22 (*s*, 3 H); 3.96 (*s*, 6 H); 4.81 (*q*, $J = 6.5$, CH_3CHCl); 7.52 (*d*, $J = 9$, 2 H); 7.83 (*d*, $J = 9$, 2 H).

*Dimethyl 2-(2-Chloro-*N*-methyl-2-phenylacetamido)-2-(4-chlorophenylazo)malonate* (**11d**). Diazotization of 2.55 g (20 mmol) of *p*-chloroaniline and coupling with 6.27 g (20 mmol) of **10z** gave 9.3 g of crude **11d** as an oil. IR: 1770–1750*s*, 1680*s*, 1375*m*, 1225*s*, 1090*m*, 840*m*. ^{1}H-NMR (200 MHz): 3.13 (*s*, 3 H); 3.82 (*s*, 3 H); 3.85 (*s*, 3 H); 5.80 (*s*, 1 H); 7.25–7.70 (*m*, 9 arom. H).

*Dimethyl 2-(2-Chloro-*N*-methylacetamido)-2-(4-methylphenylazo)malonate* (**11e**). Diazotization of 2.68 g (25 mmol) of *p*-toluidine and coupling with 5.94 g (25 mmol) of **10x** gave 9.15 g of crude **11e** as an oil. IR: 1770–1750*s*, 1685*s*, 1440*m*, 1390*m*, 1290*m*, 1235*s*, 1110*m*, 1090*m*, 1055*m*, 835*m*. ^{1}H-NMR (100 MHz): 2.42 (*s*, CH_3Ar); 3.28 (*s*, 3 H); 3.82 (*s*, 6 H); 4.23 (*s*, 2 H); 7.24 (*d*, $J = 9$, 2 H); 7.69 (*d*, $J = 9$, 2 H).

*Dimethyl 2-(2-Chloro-*N*-methylacetamido)-2-(4-methoxyphenylazo)malonate* (**11f**). Diazotization of 3.08 g (25 mmol) of *p*-anisidine and coupling with 5.94 g (25 mmol) of **10x** gave 9.51 g of crude product. Crystallization from i-PrOH afforded 7.02 g (75%) of **11f**. M.p. 116–119°. UV: 220 (9800), 235 (sh), 320 (12500). IR: 1770–1750*s*, 1685*s*, 1615*s*, 1595*m*, 1515*s*, 1440*m*, 1390*m*, 1290*m*, 1235*s*, 1156*s*, 1090*m*, 1040*m*, 845*m*. ^{1}H-NMR (100 MHz): 3.28 (*s*, 3 H); 3.83 (*s*, 6 H); 3.87 (*s*, CH_3OAr); 4.21 (*s*, 2 H); 6.95 (*d*, $J = 9$, 2 H); 7.77 (*d*, $J = 9$, 2 H). Anal. calc. for $C_{15}H_{18}ClN_3O_6$ (371.78): C 48.46, H 4.88, Cl 9.54, N 11.30; found: C 48.5, H 4.8, Cl 9.5, N 11.2.

*Dimethyl 2-(2-Chloro-*N*-methylpropanamido)-2-(4-methoxyphenylazo)malonate* (**11g**). Diazotization of 2.46 g (20 mmol) of *p*-anisidine and coupling with 5.03 g (20 mmol) of **10y** gave 7.95 g of crude **11g** as an oil. IR: 1770–1750*s* 1680*s*, 1600*m*, 1510*m*, 1230*s*, 1150*m*, 1030*m*, 840*m*. ^{1}H-NMR (100 MHz): 1.70 (*d*, $J = 6.5$, CH_3CHCl); 3.31 (*s*, 3 H); 3.74 (*s*, 3 H); 3.77 (*s*, 3 H); 3.81 (*s*, 3 H); 4.71 (*q*, $J = 6.5$, CH_3CHCl); 6.94 (*d*, $J = 9$, 2 H); 7.76 (*d*, $J = 9$, 2 H).

*Dimethyl 2-(2-Chloro-*N*-methylacetamido)-2-(4-nitrophenylazo)malonate* (**11h**). Upon diazotization of 3.46 g (25 mmol) of *p*-nitroaniline and coupling with 5.94 g (25 mmol) of **10x**, the azo compound crystallized directly from the mixture. After the addition of H_2O, the crystals were filtered, washed with H_2O and hexane to give 9.42 g

of crude product. Recrystallization from i-PrOH afforded 8.40 g (87%) of **11h**. M.p. 95–97°. UV: 280 (17600). IR: 1770–1750*s*, 1685*s*, 1540*s* (NO_2 asymm. str.), 1445*m*, 1385*m*, 1355*s* (NO_2, symm. str.), 1235*s*, 1090*m*, 865*m*. ^{1}H-NMR (60 MHz): 3.22 (*s*, 3 H); 3.95 (*s*, 6 H); 4.24 (*s*, 2 H); 7.90 (*d*, J = 9, 2 H); 8.43 (*d*, J = 9, 2 H). Anal. calc. for $C_{14}H_{15}ClN_4O_7$ (386.75): C 43.48, H 3.91, Cl 9.17, N 14.49; found: C 43.5, H 4.0, Cl 9.1, N 14.6.

*Dimethyl 2-(2-Chloro-*N*-methylpropanamido)-2-(4-nitrophenylazo)malonate* (**11i**). Diazotization of 2.76 g (20 mmol) of *p*-nitroaniline and coupling with 5.03 g (20 mmol) of **10y** gave 8.25 g of crude **11i** as an oil. IR: 1770–1750*s*, 1675*s*, 1525*s* (NO_2, asymm. str.), 1375*m*, 1345*s* (NO_2, symm. str.), 1220*s*, 1080*m*, 855*m*. ^{1}H-NMR (100 MHz): 1.68 (*d*, J = 7, CH_3CHCl), 3.27 (*s*, 3 H); 3.86 (*s*, 3 H); 3.88 (*s*, 3 H); 4.70 (*q*, J = 7, CH_3CHCl); 7.86 (*d*, J = 9, 2 H); 8.32 (*d*, J = 2 H).

General Procedure for the Conversion of the Azomalonates **11a–i** *to the 1,2,4-Triazine-5-ones* **12a–i**. To a well stirred soln. or suspension of 20 mmol of **11** in 40 ml of MeOH, 20 ml of 1N NaOMe/MeOH were added at r.t. After the exothermic reaction (controlled by cooling with ice/H_2O) had subsided, the suspension (pH *ca.* 7) was stirred for 1 h at 0°. The products **12** were filtered, washed with a little of cold MeOH, plenty of H_2O and Et_2O or hexane, and further purified (if necessary) by recrystallization. In the case of **12g**, an extractive workup was necessary.

Methyl 1,4,5,6-Tetrahydro-4-methyl-5-oxo-1-phenyl-1,2,4-triazine-3-carboxylate (**12a**). From 8.61 g (max. 25 mmol) of oily **11a**, 4.40 g of crude product were obtained. Recrystallization from CH_2Cl_2/hexane gave 3.96 g (64% from aniline) of **12a**. M.p. 98–100°. UV: 234 (12800), 346 (11900). IR: 1740*s* (C=O, ester), 1710*s*, (C=O, lactam), 1610*s*, 1590*m*, 1510*s*, 1450*s*, 1380*s*, 1340*s*, 1300–1255*s*, 1200*s*, 1180*s*, 1110*s*, 930*m*. ^{1}H-NMR (100 MHz): 3.39 (*s*, CH_3N); 3.89 (*s*, CH_3OOC); 4.20 (*s*, 2 H–C(6)); 7.05–7.45 (*m*, Ph). Anal. calc. for $C_{12}H_{13}N_3O_3$ (247.25): C 58.29, H 5.30, N 16.99; found: C 58.51, H 5.30, N 16.96.

Methyl 1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-4-methyl-5-oxo-1,2,4-triazine-3-carboxylate (**12b**). From 6.10 g (16.2 mmol) of **11b**, 4.02 g (88%) of pure **12b** were obtained. M.p. 130–131°. UV: 225 (sh), 242 (14000), 300 (sh), 347 (13600). IR: 1740*s*, 1710*s*, 1605*m*, 1500*s*, 1445*m*, 1370*m*, 1335*s*, 1295*s*, 1180*s*, 1110*s*, 1015*m*, 925*m*, 830*m*. ^{1}H-NMR (100 MHz): 3.40 (*s*, 3 H); 3.92 (*s*, 3 H); 4.16 (*s*, 2 H); 7.15 (*d*, J = 9, 2 H); 7.32 (*d*, J = 9, 2 H). Anal. calc. for $C_{12}H_{12}ClN_3O_3$ (281.70): C 51.17, H 4.30, Cl 12.59, N 14.92; found: C 50.98, H 4.28, Cl 12.64, N 15.05.

Methyl 1-(4-Chlorophenyl)-1,4,5,6-Tetrahydro-4,6-dimethyl-5-oxo-1,2,4-triazine-3-carboxylate (**12c**). From 8.10 g (max. 20 mmol) of oily **11c**, 5.10 g of crude product were obtained. Recrystallization from i-PrOH gave 4.55 g (77% from *p*-choroaniline) of **12c**. M.p. 104–106°. UV: 242 (13220), 351 (13500). IR: 1735*s*, 1700*s*, 1595*m*, 1490*s*, 1440*m*, 1370*m*, 1355*m*, 1330*s*, 1305*m*, 1240*m*, 1165*m*, 1105*s*, 1010*m*, 900*w*, 825*m*. ^{1}H-NMR (60 MHz): 1.20 (*d*, J = 7, CH_3(6)); 3.39 (*s*, 3 H); 3.96 (*s*, 3 H); 4.82 (*q*, J = 7, H–C(6)); 7.08–7.41 (*m*, 4 arom. H). Anal. calc. for $C_{13}H_{14}ClN_3O_3$ (295.73): C 52.80, H 4.77, Cl 11.99, N 14.21; found: C 52.47, H 4.77, Cl 12.18, N 14.16.

Methyl 1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-4-methyl-5-oxo-6-phenyl-1,2,4-triazine-3-carboxylate (**12d**). From 9.25 g (max. 20 mmol) of crude oily **11d**, 5.20 g (73% from *p*-chloroaniline) of pure **12** were obtained. M.p. 123–125°. UV: 241 (12940), 270 (sh), 305 (3600), 354 (14360). IR: 1725*s*, 1700*s*, 1595*m*, 1490*s*, 1440*m*, 1355*m*, 1330*s*, 1240*m*, 1200*m*, 1160*m*, 1100*s*, 825*m*. ^{1}H-NMR (100 MHz): 3.37 (*s*, 3 H); 3.90 (*s*, 3 H); 5.84 (*s*, H–C(6)); 7.05–7.35 (*m*, 9 arom. H). Anal. calc. for $C_{18}H_{16}ClN_3O_3$ (357.80): C 60.42, H 4.51, Cl 9.91, N 11.74; found: C 60.43, H 4.64, Cl 10.04, N 11.67.

Methyl 1,4,5,6-Tetrahydro-4-methyl-1-(4-methylphenyl)-5-oxo-1,2,4-triazine-3-carboxylate (**12e**). From 9.10 g (max. 25 mmol) of oily **11e**, 4.95 g of crude product were obtained. Recrystallization from CH_2Cl_2/hexane gave 4.41 g (68% from *p*-toluidine) of **12e**. M.p. 94–95°. UV: 239 (13100), 240 (sh), 300 (3200), 350 (12100). IR: 1735*s*, 1710*s*, 1620*w*, 1590*w*, 1520*s*, 1450*m*, 1380*m*, 1340*s*, 1300–1255*s*, 1200*m*, 1180*m*, 1110*s*, 925*w*, 815*w*. ^{1}H-NMR (60 MHz): 2.45 (*s*, arom. CH_3); 3.50 (*s*, 3 H); 4.01 (*s*, 3 H); 4.27 (*s*, 2 H–C(6)); 7.21 (*s*, 4 arom. H). Anal. calc. for $C_{13}H_{15}N_3O_3$ (261.28): C 59.76, H 5.79, N 16.08; found: C 59.6, H 6.0, N 16.0.

Methyl 1,4,5,6-Tetrahydro-1-(4-methoxyphenyl)-4-methyl-5-oxo-1,2,4-triazine-3-carboxylate (**12f**). From 6.65 g (17.9 mmol) of **11f**, 4.75 g of crude product were obtained. Recrystallization from CH_2Cl_2/hexane gave 3.72 g /75%) of **12f**. M.p. 103–104°. UV: 240 (12400), 309 (5000), 355 (11300). IR: 1735*s*, 1710*s*, 1610*w*, 1590*w*, 1520*s*, 1445*m*, 1380*m*, 1340*s*, 1250*s*, 1180*s*, 1110*s*, 1040*m*, 930*w*, 835*m*. ^{1}H-NMR (60 MHz): 3.40 (*s*, 3 H); 3.80 (*s*, arom. CH_3O); 3.93 (*s*, CH_3OOC); 4.13 (*s*, 2 H–C(6)); 6.92–7.28 (*m*, 4 arom. H). Anal. calc. for $C_{13}H_{15}N_3O_4$ (277.28). C 56.31, H 5.45, N 15.15; found: C 56.15, H 5.48, N 15.05.

Methyl 1,4,5,6-Tetrahydro-1-(4-methoxyphenyl)-4,6-dimethyl-5-oxo-1,2,4-triazine-3-carboxylate (**12g**). Crude oily **11g** (7.95 g, max. 20 mmol) was reacted with 20 ml (20 mmol) of 1N NaOMe/MeOH. The pH of the reaction soln. was adjusted to 5 by addition of AcOH. After evaporation, the residue was partitioned between H_2O and AcOEt. The org. extracts were washed with cold 1N $KHCO_3$, H_2O, and brine, dried, and evaporated to give 4.95 g of crude product as an oil. Crystallization from i-PrOH gave 4.16 g (71%) of **12g**. M.p. 73–74°. UV: 238 (12800), 305 (sh), 359 (11160). IR: 1730*s*, 1705*s*, 1515*s*, 1445*m*, 1380*m*, 1370*m*, 1335*s*, 1240*s*, 1175*s*, 1110*s*, 1040*m*, 830*m*.

^{1}H-NMR (100 MHz): 1.19 (*d*, *J* = 7, CH_3–C(6)); 3.38 (*s*, 3 H); 3.78 (*s*, 3 H); 3.90 (*s*, 3 H); 4.84 (*q*, *J* = 7, H–C(6)); 6.88 (*d*, *J* = 9, 2 H); 7.24 (*d*, *J* = 9, 2 H). Anal. calc. for $C_{14}H_{17}N_3O_4$ (291.31): C 57.72, H 5.88, N 14.42; found: C 57.86, H 5.91, N 14.62.

Methyl 1,4,5,6-Tetrahydro-4-methyl-1-(4-nitrophenyl)-5-oxo-1,2,4-triazine-3-carboxylate (**12h**). From 8.30 g (21.5 mmol) of **11h**, 5.83 g of crude product were obtained. Recrystallization from CH_2Cl_2/hexane gave 5.15 g (82%) of **12h**. M.p. 185–187°. UV: 218 (11550), 240 (10000), 300 (sh), 380 (24500). IR: 1735*s*, 1710*s*, 1590*s*, 1515–1500*s*, 1435*m*, 1360*m*, 1335*s*, 1320*s*, 1295*s*, 1175*s*, 1105*s*, 985*m*, 913*m*, 860*m*, 842*m*. ^{1}H-NMR (250 MHz): 3.41 (*s*, 3 H); 3.98 (*s*, 3 H); 4.36 (*s*, 2 H–C(6)); 7.33 (*d*, *J* = 9, 2 H); 8.25 (*d*, *J* = 9, 2 H). Anal. calc. for $C_{12}H_{12}N_4O_5$ (292.25): C 49.32, H 4.14, N 19.17; found: C 49.3, H 4.1, N 19.3.

Methyl 1,4,5,6-Tetrahydro-4,6-dimethyl-1-(4-nitrophenyl)-5-oxo-1,2,4-triazine-3-carboxylate (**12i**). From 8.20 g (max. 20 mmol) of oily **11i**, 4.97 g (81% from *p*-nitroaniline) of pure **12i** were obtained. M.p. 148–151°. UV: 220 (11980), 382 (24800). IR: 1735*s*, 1710*s*, 1595*s*, 1510–1500*s*, 1440*m*, 1380*m*, 1340–1330*s*, 1310*s*, 1285–1250*s*, 1195*w*, 1130*m*, 1105*s*, 860*m*, 845*m*. ^{1}H-NMR (100 MHz): 1.28 (*d*, *J* = 7, CH_3–C(6)); 3.37 (*s*, 3 H); 3.94 (*s*, 3 H); 4.93 (*q*, *J* = 7, H–C(6)); 7.31 (*d*, *J* = 9, 2 H); 8.20 (*d*, *J* = 9, 2 H). Anal. calc. for $C_{13}H_{14}N_4O_5$ (306.28): C 50.98, H 4.61, N 18.29; found: C 50.99, H 4.58, N 18.06.

*Dimethyl (2-Chloro-*N*-phenylacetamido)malonate* (**14**). A mixture of 44.64 g (0.20 mol) of dimethyl anilinomalonate (prepared in 77–83% yield from dimethyl 2-bromomalonate (1 equiv.) and aniline (2 equiv.) according to [7]) and 17.52 ml (24.84 g, 0.22 mol) of **9x** in 500 ml oif toluene was stirred at 80° (bath temp. *ca.* 90°) for 17 h (HCl trapped). The clear soln. was evaporated, until the volume was *ca.* 300 ml, cooled, washed with cold 1N HCl, cold 1 N $KHCO_3$ and brine, dried, and evaporated. Crystallization of the residue (59.95 g) from CH_2Cl_2/hexane gave 50.45 g (84%) of **14**. M.p. 74–75°. IR: 1765/1750*s*, 1690*m*, 1495*m*, 1440*m*, 1340*m*, 1240*m*, 1220*m*, 1170*m*, 1035*w*. ^{1}H-NMR (60 MHz): 34.85 (*s*, 6 H); 3.98 (*s*, CH_2Cl); 5.52 (*s*, H–C(2)); 7.59 (*s*, Ph). Anal. calc. for $C_{13}H_{14}ClNO_5$ (299.71): C 52.10, H. 4.71, Cl 11.83, N 4.67; found: C 52.1, H 4.7, Cl 11.9, N 4.7.

*Dimethyl 2-[(2-Benzoyl-4-chlorophenyl)azo]-2-(2-chloro-*N*-methylacetamido)malonate* (**15a**). To a soln. of 9.3 g (40.1 mmol) of *2-amino-5-chlorobenzophenone* (**13**, *Fluka*) in 40 ml of AcOH and 10 ml of conc. HCl, 8.0 ml (40 mmol) of aq. 5M $NaNO_2$ were added dropwise at 5–10°. After the addition, stirring was continued for 15 min at 10°. Then, 30 g of crushed ice were added, and a soln. of 9.6 g (40.5 mmol) of **10x** in 49 ml of acetone was dropped in rapidly. To the resulting, well stirred mixture, 70 ml of sat. aq. K_2CO_3 soln. were added dropwise at 5–10°, whereby the pH finally reached 6. After stirring for 1 h at r.t., the mixture was extracted with 2 × 100 ml of AcOEt. The org. extracts were washed with H_2O (3 ×) and brine, dried, and evaporated to give 19.7 g (> 100%) of crude **15a** as an oil. TLC: yellow spot, R_f(toluene/AcOEt 3:1) 0.4. IR: 1760*s* (C=O, ester), 1690–1675*s* (C=O, ketone and amide), 1600*w*, 1450*m*, 1440*μ*, 1380*m*, 1300–1250*m*, 1230*s*, 1180*m*, 1090*m*, 955*w*. ^{1}H-NMR (60 MHz): 2.77 (*s*, CH_3N); 3.80 (*s*, 2 CH_3OOC, CH_2Cl); 7.40–7.95 (*m*, 8 arom. H).

*Dimethyl 2-[(2-Benzoyl-4-chlorophenyl)azo]-2-(2-chloro-*N*-phenylacetamido)malonate* (**15b**). As described for **15a**, 9.27 g (40 mmol) of **13** were diazotized and coupled with 12.0 g (40 mmol) of **14**. After the addition of 70 ml of sat. aq. K_2CO_3, the mixture (pH 6) was diluted with 300 ml of H_2O whereupon the azo compound crystallized. The crystals were filtered after stirring for 1 h at r.t., washed copiously with H_2O, then with Et_2O, hexane 1:1 (removes colored impurities) and once more with H_2O and hexane, and dried for 2 days at r.t. over CaCl *in vacuo* to give 21.37 g (98%) of **15b**. M.p. 135–137°. UV: 253 (17960), 285 (sh). IR: 1770–1760*s* (C=O, ester), 1700*s*, (C=O, ketone), 1680*s* (C=O, amide), 1600*m*, 1500*m*, 1455*m*, 1440*m*, 1360*m*, 1300–1260*s*, 1235*s*, 1160*m*, 1135*m*, 1080*m*, 960*m*. ^{1}H-NMR (100 MHz): 3.24 (*s*, CH_2Cl); 3.52 (*s*, 2 CH_3OOC); 7.03–7.90 (*m*, 13 arom. H). Anal. calc. for $C_{26}H_{21}Cl_2N_3O_6$ (542.38): C 57.58, H 3.90, Cl 13.07, N 7.75; found: C 57.5, H 3.9, Cl 13.0, N 7.8.

Methyl 1-(2-Benzoyl-4-chlorophenyl)-1,4,5,6-tetrahydro-4-methyl-5-oxo-1,2,4-triazine-3-carboxylate (**16a**). To a soln. of 5.1 g (max. 10 mmol) of crude **15a** in 100 ml of THF, 9.9 ml (9.9 mmol) of 1N NaOMe/MeOH were added at 3° during 1 min. After stirring for 1 h at 5°, the mixture (pH 7) was diluted with 200 ml of AcOEt and 100 ml of H_2O. The aq. phase was discarded, and the org. extract was washed with H_2O (5 ×) and brine, dried, and evaporated. The solid residue (3.73 g) was recrystallized from CH_2Cl_2/i-PrOH (CH_2Cl_2 evaporated off at 80°) to give 3.21 (83%) of **16a**. M.p. 123–125°. UV: 234 (sh), 241 (21800), 295 (sh), 345 (12300). IR: 1730*s*, (C=O, ester), 1710*s* (C=O, lactam), 1670*s* (C=O, ketone), 1600*w*, 1490*m*, 1440*m*, 1330*s*, 1290*s*, 1270–1250*s*, 1180*m*, 1110*s*, 920*w*. ^{1}H-NMR (60 MHz): 3.20 (*s*, CH_3N); 3.59 (*s*, CH_3OOC); 4.23 (*s*, 2 H–C(6)); 6.98–7.95 (*m*, 8 arom. H).. Anal. calc. for $C_{19}H_{16}ClN_3O_4$ (385.81): C 59.15, H 4.18, Cl 9.19, N 10.89; found: C 58.94, H 4.28, Cl 8.98, N 10.93.

Methyl 1-(2-Benzoyl-4-chlorophenyl)-1,4,5,6-tetrahydro-5-oxo-4-phenyl-1,2,4-triazine-3-carboxylate (**16b**). To a soln. of 5.42 g (10 mmol) of **15b** in 100 ml of THF, 9.6 ml (9.6 mmol) of 1N NaOMe/MeOH were added at −5° during 1 min. After stirring for 1 h at −5°, the mixture was worked up as described for **16a** to give 4.45 g of crude product. Recrystallization from CH_2Cl_2/i-PrOH (CH_2Cl_2 evaporated off at 80°) gave 4.26 g (95%) of **16b**. M.p. 194–196°. UV: 238 (22500), 339 (13600). IR: 1750–1720*s* (C=O, ester and lactam), 1675*s* (C=O, ketone), 1600*m*,

1490*m*, 1445*m*, 1365*m*, 1330*s*, 1290*s*, 1250*s*, 1215*m*, 1195*m*, 1170*m*, 1130*m*, 955*m*. ^{1}H-NMR (100 MHz): 3.40 (*s*, 3 H); 4.28 (*s*, 2 H); 6.70–7.87 (*m*, 13 arom. H). Anal. calc. for $C_{24}H_{18}ClN_3O_4$ (447.88): C 64.36, H 4.05, Cl 7.91, N 9.38; found: C 64.4, H 4.4, Cl 8.0, N 9.6.

Methyl 7-Chloro-3,4-dihydro-3-methyl-4-oxo-5-phenyl-1,2,4-triazino[1,6-a]indole-2-carboxylate (**17a**). a) *From* **16a**. Compound **16a** (3.15 g, 8.2 mmol) were dissolved in 75 ml of MeOH at 45°. The soln. was cooled to 20°, and 8.2 ml (8.2 mmol) of 1N NaOMe/MeOH were added during 1 min. After 10 min, a crystalline precipitate appeared. Stirring was continued for 16 h at r.t. and 1 h at 0°. The crystals were filtered, washed with cold MeOH (until the filtrate reacted neutral) and hexane, and dried at 80°/0.05 Torr for 8 h to give 2.45 g (81%) of **17a**. M.p. 240° (sint.), 247° (dec.). UV: 245 (32000), 288 (28000), 345 (12000). IR: 1750*s* (C=O, ester), 1700*s* (C=O, lactam), 1425*m*, 1405*m*, 1365*s*, 1240*m*, 1120*m*, 1100*m*, 1065*m*, 960*m*. ^{1}H-NMR (250 MHz): 3.60 (*s*, CH_3N); 4.07 (*s*, CH_3OOC); 7.37–7.53 (*m*, 4 arom. H); 7.65 (*m*, 2 arom. H); 7.80 (*d*, $J = 1.2$, H–C(6)); 7.95 (*d*, $J = 9$, H–C(9)). Anal. calc. for $C_{19}H_{14}ClN_3O_3$ (367.79); C 62.05, H 3.84, Cl 9.64, N 11.43; found: C 62.0, H 3.9, Cl 9.5, N 11.5

b) *Directly from* **15a**. To a soln. of 9.8 g (max. 19 mmol) of crude **15a** in 150 ml of MeOH, 38 ml (38 mmol) of 1N NaOMe/MeOH were added at r.t. during 25 min. After stirring at r.t. for 7 h, the mixture was kept in the freezer (2°) for 16 h. The crystals were filtered, washed with cold MeOH (until neutral) and hexane to give 4.46 g (64%) of **17a**. M.p. 240° (sint.), 247° (dec.).

Methyl 7-Chloro-3,4-dihydro-4-oxo-3,5-diphenyl-1,2,4-triazino[1,6-a]indole-2-carboxylate (**17b**). a) *From* **16b**. To a suspension of 4.2 g (9.4 mmol) of **16b** in 300 ml of MeOH, 9.38 ml (9.38 mmol) of 1N NaOMe/MeOH were added at 45° during 1 min. A thick suspension resulted. After standing at r.t for 3 h and cooling for 1 h at 0°, the crystals were filtered, washed with cold MeOH (until neutral) and Et_2O to give 3.87 g (96%) of **17b**. M.p. 210–212°. UV: 242 (35600), 288 (32600), 349 (11300). IR: 1755*s* (C=O, ester), 1715*s* (C=O, lactam), 1600*m*, 1495*m*, 1410*m*, 1360*s*, 1330*m*, 1235*s*, 1210*m*, 1185*m*, 1070*m*, 965*m*. ^{1}H-NMR (100 MHz): 3.67 (*s*, CH_3OOC); 7.21–7.70 (*m*, 11 arom. H), 7.82 (*d*, $J = 1.5$, H–C(6)); 7.95 (*d*, $J = 9$, H–C(9)). Anal. calc. for $C_{24}H_{16}ClN_3O_3$ (429.86): C 67.06, H 3.75, Cl 8.25, N 9.78; found: C 66.8, H 3.8, Cl 8.2, N 9.7.

b) *Directly from* **15b**. To a soln. of 11.6 g (21.4 mmol) of **15b** in 500 ml of MeOH, 43 ml (43 mmol) of 1N NaOMe/MeOH were added at r.t. After stirring for 2 h at r.t., the crystalline product was filtered and washed with cold MeOH and Et_2O. Recrystallization of this crude product (8.35 g) from hot AcOEt gave 7.45 g (81%) of **17b**. M.p. 209–211°.

Dimethyl 2-(2-Chloro-N-methylacetamido)-2-[2-(methoxycarbonyl)phenylazo]malonate (**18a**) *and Methyl 1,4,5,6-Tetrahydro-1-[2-(methoxycarbonyl)phenyl]-4-methyl-5-oxo-1,2,4-triazine-3-carboxylate* (**19a**). The general protocol given for the preparation of the azo compounds **11** was followed. Diazotization of 5.2 ml (6.05 g, 40 mmol) of methyl anthranilate and coupling with 9.6 g (40.5 mmol) of **10x** gave 16.5 g (> 100%) of crude **18a** as an oil. TLC: yellow spot, R_f (toluene/AcOEt 3:1) 0.3. IR: 1765*s*, 1740*s*, 1680*s*, 1605*w*, 1440*m*, 1385*m*, 1310–1230*s*, 1135*m*, 1090*s*, 1050*m*. ^{1}H-NMR (60 MHz): 3.22 (*s*, CH_3N); 3.88 (*s*, CH_3OOC); 4.29 (*s*, CH_2Cl); 7.38–7.98 (*m*, 4 arom. H). To a soln. of 16.4 g (max. 40 mmol) of crude **18a** in 93 ml of MeOH, 39.5 ml (39.5 mmol) of 1N NaOMe/MeOH were added at 25° within 30 min. After stirring at r.t. for 1 h, the pH of the mixture was adjusted to 5 by addition of AcOH. Evaporation left a residue which was partitioned between H_2O and CH_2Cl_2. The org. extracts were washed with cold 1N $KHCO_3$, H_2O, and brine, dried, and evaporated to give 10.2 g of crude product. Crystallization from i-PrOH gave 9.4 g (77% from methyl anthranilate) of **19a**. M.p. 99–101°. UV: 208 (sh), 336 (10800). IR: 1755–1710*s* (C=O, ester and lactam), 1610*w*, 1505*w*, 1445*m*, 1375*m*, 1335*m*, 1310*m*, 1285–1250*m*, 1200*w*, 1185*w*, 1170*w*, 1135*w*, 1110*m*, 1095*m*, 930*w*. ^{1}H-NMR (60 MHz): 3.40 (*s*, CH_3N); 3.88 (*s*, 2 CH_3OOC); 4.18 (*s*, 2 H–C(6)); 7.12–7.82 (*m*, 4 arom. H). Anal. calc. for $C_{14}H_{15}N_3O_5$ (305.29): C 55.08, H 4.95, N 13.77; found: C 55.1, H 5.0, N 13.9.

Dimethyl 2-(2-Chloro-N-phenylacetamido)-2-[2-(methoxycarbonyl)phenylazo]malonate (**18b**) *and Methyl 1,4,5,6-Tetrahydro-1-[2-(methoxycarbonyl)phenyl]-5-oxo-4-phenyl-1,2,4-triazine-3-carboxylate* (**19b**). As described above for **18a**, 5.2 ml (6.05 g, 40 mmol) of methyl anthranilate were diazotized and coupled with 12.0 g (40 mmol) of **14** in 120 ml of acetone. After neutralization with sat. aq. K_2CO_3 and addition of 300 ml of H_2O, the azo compound crystallized out of the mixture. Stirring was continued for 1 h at r.t. The crystals were filtered, washed with H_2O and hexane to give 18.1 g (99%) of pure **18b**. M.p. 119–121°. UV: 274 (8160). IR: 1770*s*, 1720*s*, 1700*s*, 1605*w*, 1500*w*, 1440*m*, 1360*m*, 1300–1235*s*, 1125*m*, 1090*m*. ^{1}H-NMR (100 MHz): 3.70 (*s*, 2 CH_3OOC); 3.90 (*s*, arom. CH_3OOC and CH_2Cl): 7.18–7.90 (*m*, 9 arom. H). Anal. calc. for $C_{21}H_{20}ClN_3O_7$ (461.86): C 54.61, H 4.36, Cl 7.68, N 9.10; found: C 54.4, H 4.5, Cl 7.6, N 8.9.

To a soln. of 10.6 g (23 mmol) of **18b** in 230 ml of THF, 21 ml (21 mmol) of 1N NaOMe/MeOH were added at 0° within 1 h. After stirring for 30 min at 0°, the pH of the mixture was adjusted to 5 by addition of AcOH. Evaporation left a residue which was partitioned between H_2O and AcOEt. The org. extracts were washed with cold 1N $KHCO_3$, H_2O, and brine, dried, and evaporated to give 8.4 g of crude product. Crystallization from i-PrOH

gave 6.4 g (76%) of **19b**. M.p. 136–138°. UV: 250 (sh), 335 (11500). IR: 1755–1720*s*, 1605*m*, 1500*m*, 1440*m*, 1370*m*, 1330*s*, 1310*s*, 1250*m*, 1210*m*, 1170*m*, 1135*m*, 1090*w*, 1060*w*, 990*w*, 995*w*. ^{1}H-NMR (100 MHz): 3.64 (*s*, CH_3OOC); 3.93 (*s*, CH_3OOC); 4.32 (*s*, 2 H–C(6)); 7.15–7.80 (*m*, 9 arom. H). Anal. calc. for $C_{19}H_{17}N_3O_5$ (367.36): C 62.12, H 4.67, N 11.44; found: C 62.3, H 4.8, N 11.4.

Methyl 3,4-Dihydro-5-methoxy-3-methyl-4-oxo-1,2,4-triazino[1,6-a]indole-2-carboxylate (**20a**). A soln. of 6.71 g (22 mmol) of **19a** and 22 ml of DMF-dimethyl acetal was stirred at reflux (bath temp. 120°) for 26 h. The resulting suspension was cooled (r.t.), and 70 ml of Et_2O were added. After stirring for 1 h at r.t., the crystals were filtered, washed with H_2O and Et_2O, and dried at 100°/0.05 Torr for 16 h to give 2.76 g (44%) of **20a**. M.p. 170° (sint.), 175–177°. UV: 225 (21200), 280 (30800), 285 (sh), 340 (10800). IR: 1745*s* (C=O, ester), 1695*s* (C=O, lactam), 1610*w*, 1565*m*, 1450*m*, 1365*m*, 1325*s*, 1240*s*, 1150*m*, 1110*s*. ^{1}H-NMR (60 MHz): 3.54 (*s*, CH_3N); 4.00 (*s*, CH_3OOC); 4.25 (*s*, CH_3O); 7.10–7.95 (*m*, 4 arom. H). Anal. calc. for $C_{14}H_{13}N_3O_4$ (287.28): C 58.53, H 4.56, N 14.63; found: C 58.6, H 4.5, N 14.6.

Methyl 3,4-Dihydro-5-methoxy-4-oxo-3-phenyl-1,2,4-triazino[1,6-a]indole-2-carboxylate (**20b**). A soln. of 5.1 g (13.9 mmol) of **19b** in 25 ml of DMF-dimethyl acetal was stirred at 90° (bath temp.) for 18 h. After cooling, 20 ml of Et_2O were added, and stirring was continued at 5° for 1 h. The crystals were filtered, washed with H_2O and Et_2O, and dried at 100°/0.05 Torr for 6 h to give 2.73 g (56%) of **20b**. M.p. 179–181°. UV: 228 (23000), 281 (35600), 341 (11200). IR: 1750*s* (C=O, ester), 1705*s* (C=O, lactam), 1600*m*, 1560*m*, 1490*m*, 1450*m*, 1410*m*, 1390*m*, 1370*s*, 1325–1310*s*, 1230*m*, 1215*s*, 1190*m*, 1080*m*. ^{1}H-NMR (60 MHz): 3.68 (*s*, CH_3OOC); 4.30 (*s*, CH_3O); 7.20–8.02 (*m*, 9 arom. H). Anal. calc. for $C_{19}H_{15}N_3O_4$ (349.35): C 65.32, H 4.33, N 12.03; found: C 65.3, H 4.7, N 11.8.

Oxidation of **4b** *and* **12b**. *Ethyl 1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-5,6-dioxo-4-phenyl-1,2,4-triazine-3-carboxylate* (**21**). To a soln. of 1.25 g (3.5 mmol) of **4b** in 125 ml of acetone, 1.9 ml of *Jones* reagent (standard soln: 26.72 g of CrO_3 dissolved in 23 ml of conc. H_2SO_4 and diluted with H_2O to a volume of 100 ml) was added at –5° within 10 min. After stirring at –3° for 1 h, the mixture was filtered, and the solid was washed with acetone. Evaporation of the filtrate left a crystalline residue which was taken up in H_2O and AcOEt. The org. extracts were washed with H_2O, 1N $KHCO_3$, and brine, dried, and evaporated. The residue (1.3 g) was recrystallized from CH_2Cl_2/hexane to give 1.23 g (95%) of **21**. M.p. 170–172°. UV: 232 (15060), 249 (13800). IR: 1750*s*, 1725*s*, 1705*s*, 1490*s*, 1380*s*, 1350*s*, 1295*m*, 1235*s*, 1200*m*, 1155*m*, 1095*m*, 1040*m*, 1020*m*, 837*m*. ^{1}H-NMR (60 MHz): 0.98 (*t*, $J = 7$, 3 H); 4.10 (*q*, $J = 7$, 2 H); 7.25–7.83 (*m*, 9 arom. H). Anal. calc. for $C_{18}H_{14}ClN_3O_4$ (371.78): C 58.15, H 3.80, Cl 9.54, N 11.30; found: C 57.96, H 3.91, Cl 9.56, N 11.43.

Methyl 1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-4-methyl-5,6-dioxo-1,2,4-triazine-3-carboxylate (**28**). In the same way as described above, a soln. of 2.1 g (7.45 mmol) of **12b** in 210 ml of acetone was oxidized with 4.0 ml of *Jones* reagent. The crude product (2.2 g) was recrystallized from MeOH to give 1.78 g (81%) of **28**. M.p. 131–132°. UV: 229 (11600), 275 (11400). IR: 1760*s*, 1740*s*, 1710*s* (sh), 1500*s*, 1550*m*, 1370*s*, 1300–1260*s*, 1210*m*, 1190*m*, 1115*s*, 1110*s*, 1020*m*, 940*m*, 840*m*. ^{1}H-NMR (60 MHz): 3.61 (*s*, 3 H); 3.95 (*s*, 3 H); 7.20–7.70 (*m*, 4 arom. H). Anal. calc. for $C_{12}H_{10}ClN_3O_4$ (295.68): C 48.75, H 3.41, Cl 11.99, N 14.21; found: C 49.0, H 3.4, Cl 12.0, N 14.3.

Ammonolysis of **4b** *and* **12b**. *1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-5-oxo-4-phenyl-1,2,4-triazine-3-carboxamide* (**25**). A suspension of 2.25 g (6.3 mmol) of **4b** in 50 ml of 5M NH_3/MeOH was stirred at r.t. in a closed flask for 4 d. Evaporation of the mixture left a residue which was recrystallized from EtOH to give 1.72 g (83%) of **25**. M.p. 246–248°. IR (nujol): 3440*m*, 3280*w*, 3210*w* (br., NH, NH ass.), 1710*s* (C=O, lactam), 1690*s* (C=O, amide), 1595*m*, 1585*m*, 1490*s*, 1340*s*, 1260*s*, 995*m*, 815*m*, 760*m*, 695*m*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 4.44 (*s*, 2 H–C(6)); 7.21 (*d*, $J = 6$, 2 H); 2.30–2.55 (*m*, 7 arom. H, 1 H of NH_2); 8.10 (br. *s*, 1 H of NH_2). Anal. calc. for $C_{16}H_{13}ClN_4O_2$ (328.76): C 58.45, H 3.99, Cl 10.78, N 17.04; found: C 58.3, H 4.0, Cl 10.9, N 17.2.

1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-4-methyl-5-oxo-1,2,4-triazine-3-carboxamide (**33**). A suspension of 10.0 g (35.5 mmol) of **12b** in 350 ml of MeOH and 71 ml of conc. NH_3 was stirred at r.t. for 3 d and at 0° for 1 h. The crystalline product was filtered, washed with cold MeOH and hexane to give 8.45 gt (89%) of **33**. M.p. 227° (sint.), 230–232°. IR (nujol): 3400*m*, 3280*m*, 3210*m*, 1700*s* (sh), 1680*s*, 1600*m*, 1490*m*, 1465*s*, 1370*s*, 1290*m*, 1110*s*, 835*m*, 825*m*, 815*m*. ^{1}H-NMR (60 MHz, (D_6)DMSO): 3.21 (*s*, 3 H); 4.23 (*s*, 2 H–C(6)); 7.20–7.72 (*m*, 4 arom. H, 1 H of NH_2); 8.05 (br. *s*, 1 H of NH_2). Anal. calc. for $C_{11}H_{11}ClN_4O_2$ (266.69): C 49.54, H 4.16, Cl 13.29, N 21.01; found: C 49.6, H 4.3, Cl 13.2, N 20.9.

Bromination of **4b**. a) *Non-aqueous Workup. Ethyl 6-Bromo-1-(4-chlorophenyl)-1,4,5,6-tetrahydro-5-oxo-4-phenyl-1,2,4-triazine-3-carboxylate* (**22**). To a soln. of 2.11 g (5.9 mmol) of **4b** in 40 ml of AcOH, a soln. of 0.32 ml (0.99 g,. 6.2 mmol) of Br_2 in 5 ml of AcOH was added dropwise at 50–53°. After stirring for 90 min at 50°, 40 ml of toluene were added, and the mixture was evaporated. The residue was dissolved in 30 ml of toluene and evaporated. This was repeated twice to give 2.6 g of crude product as a foam. Crystallization from Et_2O/hexane gave 2.27 g (88%(of **22**. M.p. 113–115°. IR: 1745*s* (C=O, ester), 1725*s* (C=O, lactam), 1595*m*, 1490*s*, 1375*m*, 1350*m*, 1325*s*, 1245*m*, 1205*s*, 1195*s*, 1100*m*, 945*m*, 830*m*. ^{1}H-NMR (60 MHz): 1.01 (*t*, $J = 7$, 3 H); 4.14 (*q*, $J = 7$, 2 H); 7.05 (*s*,

H–C(6)); 7.15–7.60 (*m*, 9 arom. H). Anal. calc. for $C_{18}H_{15}BrClN_3O_3$ (436.69): C 49.51, H 3.46, Br 18.30, Cl 8.12, N 9.62; found: C 49.53, H 3.58, Br 18.13, Cl 8.05, N 9.61.

b) *Aqueous Workup. Ethyl 1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-6-hydroxy-5-oxo-4-phenyl-1,2,4-triazine-3-carboxylate* (**23**). Compound of **4b** (15.0 g, 42 mmol) were brominated as described above with 2.24 ml (7.04 g, 44 mmol) of Br_2. Evaporation of the mixture left a residue which was taken up in ice/H_2O and AcOEt. The org. extracts were washed with H_2O, cold 0.5N $KHCO_3$ (until the pH was 7), and brine, dried, and evaporated. The solid residue (16.1 g) was recrystallized from CH_2Cl_2/hexane to give 13.3 g (85%) of **23**. M.p. 146–148°. IR: 3580*w*, 3400*w* (br., OH ass.), 1750–1700*s*, 1600*m*, 1495*s*, 1345*s*, 1235*s*, 1195*m*, 1155*m*, 1110*m*, 1060*m*, 830*m*. ^{1}H-NMR (100 MHz): 1.02 (*t*, *J* = 7, 3 H); 4.04 (*q*, *J* = 7, 2 H); 4.75 (*d*, *J* = 5.5, exchangeable with D_2O, OH); 5.96 (*d*, *J* = 5.5, becomes *s* after exchange with D_2O, H–C(6)); 7.21–7.60 (*m*, 9 arom. H). Anal. calc. for $C_{18}H_{16}ClN_3O_4$ (373.80): C 57.84, H 4.32, Cl 9.49, N 11.24; found: C 57.8, H 4.4, Cl 9.5, N 11.4.

Ethyl 1-(4-Chlorophenyl)-6-ethoxy-5-oxo-4-phenyl-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (**24**). A soln. of 3.74 g (10 mmol) of **23** in 100 ml of EtOH was stirred at reflux for 1 h. After evaporation, the residue was dissolved in Et_2O and dried (Na_2SO_4). The drying agent was filtered off, and petroleum ether was added. After evaporation of part of the Et_2O and cooling the product crystallized. Filtration and washing with petroleum ether gave 3.1 g (77%) of **24**. M.p. 74–77°. IR: 1750–1710*s*, 1595*m*, 1445*s*, 1330*s*, 1295*m*, 1225*s*, 1190*m*, 1175*m*, 1095*m*, 1055*s*, 1005*m*, 830*m*. ^{1}H-NMR (60 MHz): 1.03 (*t*, *J* = 7, CH_3CH_2O); 1.20 (*t*, *J* = 7, CH_3CH_2OOC); 3.68 (*q*, *J* = 7, CH_3CH_2O); 4.10 (*q*, *J* = 7, CH_3CH_2OOC); 5.69 (*s*, H–C(6)); 7.20–7.62 (*m*, 9 arom. H). Anal. calc. for $C_{20}H_{20}ClN_3O_4$ (401.85): C 59.78, H 5.02, Cl 8.82; found: C 59.8, H 5.0, Cl 8.9, N 10.8.

$NaBH_4$ Reduction of **4b**. *Ethyl 1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-5-hydroxy-4-phenyl-1,2,4-triazine-3-carboxylate* (**26**). To a well stirred soln. of 4.62 g (12.9 mmol) of **4b** in 135 ml of EtOH and 70 ml of THF, 2.25 g (59.5 mmol) of $NaBH_4$ were added in 1 portion at r.t. Within 10 min, the temp. of the mixture reached 27°. A transient precipitate disappeared gradually during the next 180 min. The clear yellow soln. was cooled, and a mixture of 29 ml of 2N HCl and 100 ml of H_2O was added dropwise at 0–5° (final pH 4). The resulting mixture was evaporated, until the volume was *ca.* 100 ml. More H_2O (50 ml) was added, and the crystalline product was filtered, washed copiously with H_2O, Et_2O, hexane, and dried at 80°/0.05 Torr for 6 h to give 3.99 g (86%) of **26**. M.p. 158–160°. UV: 255 (10740), 344 (23000). IR: 3560–3300*w* (br., OH, OH ass.), 1725*s* (C=O, ester), 1595*s*, 1490*s*, 1380*m*, 1300–1250*s*, 1215*s*, 1155*s*, 1095*s*, 825*m*. ^{1}H-NMR (100 MHz): 1.04 (*t*, *J* = 7, CH_3CH_2OOC); 3.25 (*dd*, *J* = 2, 12, 1 H of 2 H–C(6)); 3.53 (*d*, *J* = 7, exchangeable with D_2O, OH); 4.07 (*dd*, *J* = 2, 12, 1 H of 2 H–C(6)); 4.12 (*q*, *J* = 7, CH_3CH_2OOC); 5.40 (*dt*, *J* = 2, 7, becomes *t* after exchange with D_2O, H–C(5)); 7.05–7.45 (*m*, 9 arom. H). Anal. calc. for $C_{18}H_{18}ClN_3O_3$ (359.81): C 60.09, H 5.04, Cl 9.85, N 11.68; found: C 59.97, H 5.12, Cl 9.93, N 11.82.

Ethyl 1-(4-Chlorophenyl)-5-methoxy-4-phenyl-1,4,5,6-tetrahydro-1,2,4-triazine-3-carboxylate (**27**). To a soln. of 520 mg (1.45 mmol) of **26** in 11 ml MeOH (dissolved at 50°, then cooled to r.t.), 2 mg of TsOH were added. After stirring for 30 min at r.t. (TLC: no trace of starting material) and addition of 3 mg of $NaHCO_3$, the mixture was evaporated to give a residue which was taken up in AcOEt and H_2O. The org. extracts were washed with cold 0.1N $KHCO_3$ and brine, dried, and evaporated to give 540 mg of crude product. Crystallization from i-PrOH gave 462 mg (85%) of **27**. M.p. 128–130°. UV: 253 (10800), 343 (26100). IR: 1725*s*, 1600*s*, 1495*s*, 1385*s*, 1300–1255*s*, 1220*s*, 1190*s*, 1180*s*, 1095*s*, 1005*m*, 830*m*. ^{1}H-NMR (60 MHz): 1.06 (*t*, *J* = 7, CH_3CH_2OOC); 3.25 (*dd*, *J* = 2, 12, *A* of *ABX*, 1 H of 2 H–C(6)); 3,55 (*s*, CH_3O); 3.95–4.33 (*q* and *dd*, CH_3CH_2OOC and *B* of *ABX*, 1 H of 2 H–C(6)); 4.97 (*t*, *J* = 2, *X* of *ABX*, H–C(5)); 6.90–7.45 (*m*, 9 arom. H). Anal. calc. for $C_{19}H_{20}ClN_3O_3$ (373.84): C 61.05, H 5.39, Cl 9.49, N 11.24; found: C 61.14, H 5.58, Cl 9.55, N 11.53.

Hydrolysis and Decarboxylation of **12b**. *1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-4-methyl-5-oxo-1,2,4-triazine-3-carboxylic Acid* (**29**). A suspension of 1.8 g (6.4 mmol) of **12b** and 1.06 g (10 mmol) of Na_2CO_3 in 26 ml of MeOH and 26 ml of H_2O was stirred at r.t. for 3 d. The MeOH was distilled off, and the residue was diluted with 50 ml of H_2O, filtered through a plug of cotton wool, and acidified at 5° by dropwise addition of 5N HCl (*ca.* 4 ml, final pH 2). After stirring at 5° for 1 h, the crystals were filtered, washed with H_2O and hexane, and dried at 80°/0.05 Torr for 16 h to give 1.64 g (96%) of **29**. M.p. 120–122° (recrystallizes after decarboxylation) then 165–168°. pK^* = 3.96 (equiv. mol.-weight: 272). UV: 245 (11920), 300 (sh), 337 (10300). IR (nujol): 3400–2400*w* (br., OH, ass.), 1690*s* (sh), 1680*s*, 1600*m*, 1495*m*, 1460*s*, 1425*m*, 1370*s*, 1345*m*, 1290*m*, 1180*m*, 1110*m*, 825*m*. ^{1}H-NMR (60 MHz, (D_6)DMSO): 3.29 (*s*, CH_3N); 4.29 (*s*, $CH_2(6)$); 7.44 (*s*, 4 arom. H). Anal. calc. for $C_{11}H_{10}ClN_3O_3$ (267.67): C 49.36, H 3.76, Cl 13.24, N 15.70; found: C 49.34, H 3.79, Cl 13.32, N 15.80.

1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-4-methyl-1,2,4-triazin-5-one (**30**). Acid **29** (1.5 g, 5.6 mmol) was heated at 180° for 12 min (cessation of CO_2 evolution). The cooled mixture was recrystallized from CH_2Cl_2/EtOH to give 1.18 g (94%) of **30**. M.p. 160° (sint.), 170–172°. UV: 249 (10680), 305 (8920), 325 (sh). IR: 1705*s* (C=O, lactam), 1635*w*, 1595*m*, 1490*s*, 1430*m*, 1390*m*, 1365*m*, 1300*s*, 1040*m*, 885*m*, 825*m*. ^{1}H-NMR (60 MHz): 3.19 (*s*, CH_3N); 4.10

(*s*, 2 H–C(6)); 6.75 (*s*, H–C(3)); 6.90–7.35 (*m*, 4 arom. H). Anal. calc. for $C_{10}H_{10}ClN_3O$ (223.66): C 53.70, H 4.51, Cl 15.85, N 18.79; found: C 53.78, H 4.54, Cl 15.92, N 18.65.

Bromination of **12b**. a) *Non-aqueous Workup. Methyl 6-Bromo-1-(4-chlorophenyl)-1,4,5,6-tetrahydro-4-methyl-5-oxo-1,2,4-triazine-3-carboxylate* (**31**). As described for **4b**, a soln. of 981 mg (3.48 mmol) of **12b** in 25 ml of AcOH was brominated with a soln. of 0.19 ml (583 mg, 3.65 mmol) of Br_2 in 5 ml of AcOH at 45° for 1 h. Workup by evaporation with toluene (3 ×) gave 1.35 g of crude solid product. Recrystallization from CH_2Cl_2/hexane furnished 1.07 g (85%) of **31**. M.p. 122–124°. IR: 1755*s* (C=O, ester), 1720*s* (C=O, lactam), 1500*s*, 1445*m*, 1390*m*, 1335*s*, 1225*s*, 1115*s*, 1100*s*, 1020*m*, 835*m*. ^{1}H-NMR (60 MHz): 3.43 (*s*, CH_3N); 3.95 (*s*, CH_3OOC); 6.95 (*s*, H–C(6)); 7.46 (*s*, 4 arom H). Anal. calc. for $C_{12}H_{11}BrClN_3O_3$ (360.60): C 39.97, H 3.08, Br 22.16, Cl 9.83, N 11.65; found: C 40.15, H 3.13, Br 21.78, Cl 9.95, N 11.86.

b) *Aqueous Workup. Methyl 1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-6-hydroxy-4-methyl-5-oxo-1,2,4-triazine-3-carboxylate* (**32**). Compound **12b** (90 g, 32 mmol) were brominated as described above with 1.72 ml (5.4 g, 33 mmol) of Br_2. After evaporation, the residue was taken up in ice/H_2O and AcOEt. The org. extracts were washed with H_2O, cold 0.5N $KHCO_3$ (until the pH was 7), and brine, dried, and evaporated. The solid residue (11.8 g) was recrystallized from CH_3CN to give 4.9 g (52%) of **32**. M.p. 151–153° (dec.). IR: 3550*w* (OH), 3450–3200*w* (OH ass.), 1735*s* (C=O, ester), 1710*s* (C=O, lactam), 1595*w*, 1490*s*, 1440*m*, 1335*m*, 1240*m*, 1165*m*, 1110*s*, 1015*m*, 925*m*, 865*m*, 830*m*. ^{1}H-NMR (60 MHz, $CDCl_3$ + (D_6)DMSO): 3.43 (*s*, CH_3N); 3.93 (*s*, CH_3OOC); 5.81 (*d*, J = 7.5, becomes *s* after exchange with D_2O, H–C(6)); 7.08 (*d*, J = 7.5, exchangeable with D_2O, OH); 7.25–7.50 (*m*, 4 arom. H). Anal. calc. for $C_{12}H_{12}ClN_3O_4$ (297.70): C 48.42, H 4.06, Cl 11.91, N 14.12; found: C 48.5, H 4.2, Cl 11.9, N 14.1.

$NaBH_4$ Reduction of **12b**. *1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-3-(hydroxymethyl)-4-methyl-1,2,4-triazin-5-one* (**34**). To a soln. of 1.41 g (5 mmol) of **12b** in 50 ml of MeOH and 58 ml of THF, 378 mg (10 mmol) of $NaBH_4$ were added in 1 portion at 5°. After stirring at r.t. for 2 h (TLC: starting material consumed), the mixture was cooled with ice/H_2O and 2N HCl was added dropwise, until the pH was 5. The mixture was diluted with 80 ml of H_2O and evaporated *in vacuo* at 50°, until pure H_2O distilled off. After standing for 1 h at 2°, the crystalline precipitate was filtered and washed with H_2O and hexane to give 0.99 g of crude product. TLC: mainly one spot with R_f (AcOEt/toluene 2:1) 0.52. Two recrystallizations from CH_2Cl_2/hexane gave 0.44 g (35%) of **34**. M.p. 149–151°. UV: 250 (11000), 304 (9260). IR: 3550–3250*w* (OH, OH ass.), 1705*s* (C=O, lactam), 1595*m*, 1495*s*, 1370*s*, 1265*s*, 1140*m*, 1095*m*, 1070*m*, 1005*m*, 840*m*, 825*m*. ^{1}H-NMR (250 MHz): 2.57 (br. *s*, exchangeable with D_2O, OH); 3.29 (*s*, CH_3N); 4.10 (*s*, 2 H–C(6)); 4.50 (*s*, CH_2OH); 7.07 (*d*, J = 9, 2 arom. H); 7.28 (*d*, J = 9, 2 arom. H). Anal. calc. for $C_{11}H_{12}ClN_3O_2$ (253.69): C 52.08, H 4.77, Cl 13.98, N 16.56; found: C 51.98, H 4.85, Cl 14.23, N 16.68.

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