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Regiospecific Syntheses of the Monomethylated 3-Phenyldihydro-1,2,4-triazin-6(1*H*)-ones

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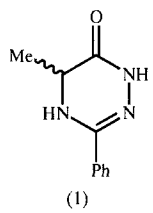
Unambiguous syntheses of four unreported monomethylated derivatives of 3-phenyldihydro-1,2,4-triazin-6(1*H*)-ones, namely, the 1-methyl (2), 2-methyl (3), 4-methyl (4) and the imidic *O*-methyl derivative (5), are described. Regioselectivity was achieved for the synthesis of (2) by addition of ethyl glycinate to the 1,3-dipolar nitrile imine derived from *N*-methylbenzohydrazonoyl bromide hydrobromide (8). The key step for the synthesis of (3) was addition of benzyl 3-methylcarbazate (14) to ethyl *N*-[chloro(phenyl)methylene]glycinate (15b). The 4-methyl compound (4) was prepared by cycloaddition of ethyl *N*-(thiobenzoyl)sarcosinate (21) with hydrazine hydrate, and the *O*-methyl compound (5) was prepared by reaction of sodium methoxide with 6-chloro-3-phenyl-4,5-dihydro-1,2,4-triazine (23).

Introduction

In regard to our investigation into the properties and chemistry of novel heterocyclic systems it was of interest to prepare and study the five monomethylated 3-phenyldihydro-1,2,4-triazin-6(1*H*)-ones (1)–(5). Four of these compounds are previously unreported. The syntheses of the *S*-enantiomer and of the racemic material of the C 5-methyl derivative (1) have been reported, by Anderson *et al.*[1] and Camparini *et al.*,[2] respectively.

There is some confusion in the literature concerning the synthesis of certain 4,5-dihydro-1,2,4-triazin-6(1*H*)-ones, due to possible formation of the isomeric five-membered ring 3-aminoimidazolones (6). In some cases incorrect assignment of structures has resulted; this problem has been discussed[3] by Mathis *et al.** and Hajjem *et al.* While it is possible to use an ambiguous synthetic route, and to separate and identify structural isomers, it is preferable to devise routes which are specific for both ring size and regiosubstitution on the dihydrotriazinone ring.

In this paper we report unambiguous syntheses of the new compounds (2)–(5).



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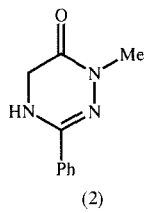

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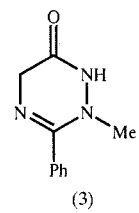

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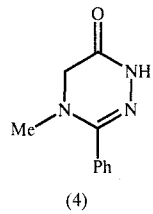

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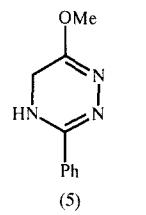

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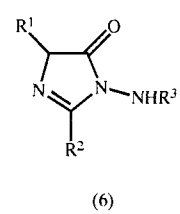

(6)

Results and Discussion

Synthesis of the 1-Methylated Dihydrotriazinone (2)

The synthesis of 1-methyl-3-phenyl-4,5-dihydro-1,2,4-triazin-6(1*H*)-one (2) is outlined in Scheme 1. Benzaldehyde methylhydrazone (7) was brominated at −15° in carbon tetrachloride to give a good yield (89%) of the hydrazonoyl bromide hydrobromide (8). Fliege *et al.*[4] reported the synthesis of the hydrazonoyl bromide hydrobromide (8) using acetic acid as solvent, but in our hands this method gave the desired hydrazonoyl bromide salt (8) contaminated with about 35% of the *N*-acylhydrazone (9).[5] Furthermore, Fliege *et al.*[4] reported that the hydrazonoyl bromide salt (8) was recrystallized from acetonitrile. Repeating this procedure gave only 43% of compound (8) due to its

* It should be noted that in the paper by Mathis *et al.*[3] the reported infrared spectrum of 1,3-diphenyl-4,5-dihydro-1,2,4-triazin-6(1*H*)-one has a carbonyl absorption and a C=C absorption at 1855 and 1520 cm^{-1}, respectively. These reported absorptions are evidently printing errors. We repeated the synthesis of 1,3-diphenyl-4,5-dihydro-1,2,4-triazin-6(1*H*)-one and found absorptions at 1655 and 1620 cm^{-1}.

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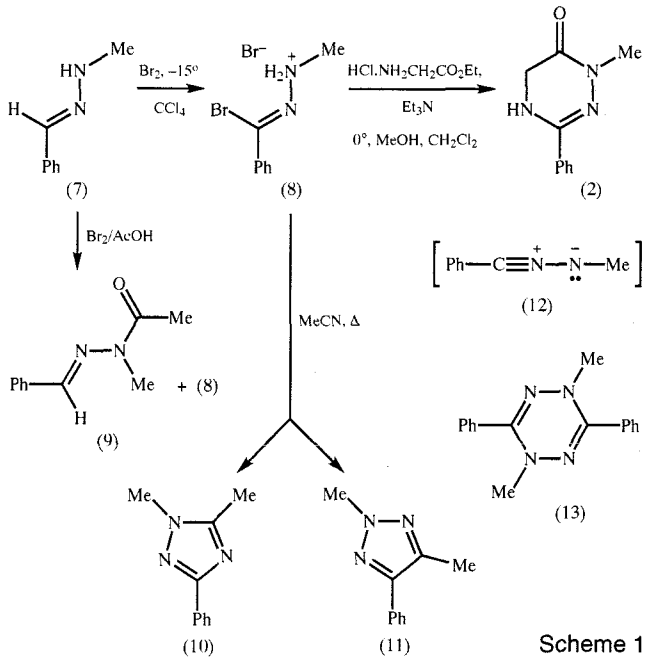
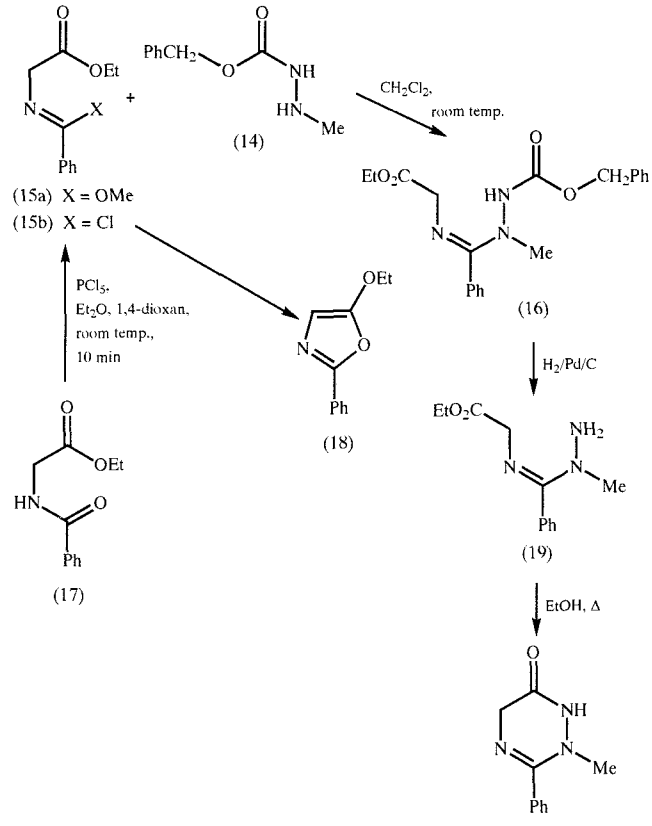


Scheme 1

partial conversion into a mixture of the cycloaddition products 1,5-dimethyl-3-phenyl-1*H*-1,2,4-triazole (10) and 2,4-dimethyl-5-phenyl-2*H*-1,2,3-triazole (11). Similarly, Frazer *et al.*[6] have reported preparing regioisomers of adducts from the cycloaddition of the nitrile imine (12) and benzonitrile. Analytical t.l.c. and g.l.c. analysis of the mixture of (10) and (11) gave only one spot and one peak, respectively. G.l.c.m.s. analysis of the mixture gave one peak corresponding to the ion $M^{+\bullet}$ of (10) and (11). ^1H and ^{13}C n.m.r. spectroscopy revealed a 60:40 mixture of the known compound (10) and the unreported regioisomer (11), respectively. The identity of 1,5-dimethyl-3-phenyl-1*H*-1,2,4-triazole (10) was confirmed by comparison of its spectroscopic data with those reported by Pérez *et al.*[7] The ^1H and ^{13}C n.m.r. resonances for 2,4-dimethyl-5-phenyl-2*H*-1,2,3-triazole (11) were derived by subtraction of the respective resonances for (10) from those of the mixture. The hydrazonoyl bromide salt (8) was best purified by trituration of the crude material with acetonitrile at room temperature. Under these conditions no cycloaddition products were formed. Addition of triethylamine to the hydrazonoyl bromide salt (8) generated the nitrile imine (12)[4] which cyclized with ethyl glycinate to afford the desired 1-methyl-3-phenyl-4,5-dihydro-1,2,4-triazin-6(1*H*)-one (2) in 83% yield. 1,4-Dimethyl-3,6-diphenyl-1,4-dihydro-1,2,4,5-tetrazine (13) was also isolated as a by-product from the dimerization of the intermediate nitrile imine (12). The spectral data for the symmetrical tetrazine (13) were identical with those reported.[4]

Synthesis of the 2-Methylated Dihydrotriazinone (3)

Cyclocondensation of amino acid-derived imidates with hydrazine hydrate affords the corresponding 4,5-dihydro-1,2,4-triazin-6(1*H*)-ones,[8] but the use of methylhydrazine introduces ambiguity. Indeed, Camparini *et al.*[2] reported that the reaction of methylhydrazine with amino acid-derived imidates gave mixtures of the regioisomeric N 1- and N 2-methyldihydrotriazinones. To obviate this, and to adapt this methodology for regiospecific synthesis of compound (3), it was necessary to choose a derivative of methylhydrazine in which the unmethylated nitrogen is rendered non-nucleophilic with a readily removable protecting group. Accordingly, the carbazate (14) was chosen, and used in a successful regiospecific synthesis of 2-methyl-3-phenyl-2,5-dihydro-1,2,4-triazin-6(1*H*)-one (3), as summarized in Scheme 2.



Scheme 2

The imidate (15a) has been reported by Shi *et al.*[9] but no specific preparative details were given. We now report that the imidate (15a) is conveniently prepared in good yield (81%) by reaction of the toluene-4-sulfonic acid salt of ethyl glycinate with methyl benzimidate in dichloromethane. The carbazate (14) was prepared as reported by Pederson.[10] It was originally expected that the glycine-derived imidate ester (15a) would react with the carbazate (14) to give the protected amidrazone (16). However, under a variety of conditions there was no reaction between the carbazate (14) and the glycine imidate ester (15a); under forcing conditions the imidate (15a) decomposed.

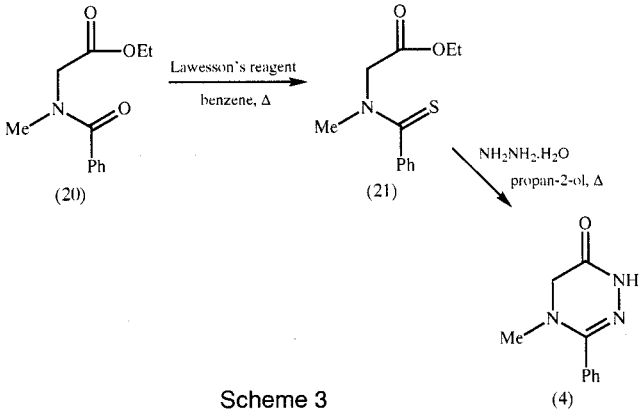
Attention was then turned to the imidoyl chloride (15b) which could be expected to be more reactive

than the corresponding imidate ester (15a) for both electronic and steric reasons. Cornforth[11] reported that treatment of ethyl *N*-benzoylglycinate (17) with phosphorus oxychloride gave 5-ethoxy-2-phenyloxazole (18), presumably via the unisolated imidoyl chloride (15b). We now report the first isolation of the imidoyl chloride (15b) (87% yield) and its use in the synthesis of (3). According to the general procedure reported by Sheehan and Corey[12] a solution of ethyl *N*-benzoylglycinate (17) in a mixture of anhydrous 1,4-dioxan and diethyl ether was treated with phosphorus pentachloride at room temperature for 10 min. With rapid, careful handling the imidoyl chloride (15b) was isolated, and its spectroscopic data were recorded. Not surprisingly (cf.[11]) it was found that the imidoyl chloride (15b) readily cyclized to 5-ethoxy-2-phenyloxazole (18) upon storage at room temperature, with brief heating, or upon treatment with base such as triethylamine or diisopropylamine.

Reaction of the freshly prepared imidoyl chloride (15b) with the carbazate (14) gave the amidrazone derivative (16) in 75% yield.* Hydrogenolysis of (16) over palladium/charcoal, and subsequent decarboxylation gave the free amidrazone (19) which was not isolated, but cyclized by heating in ethanol to give the desired 2-methyl-3-phenyl-2,5-dihydro-1,2,4-triazin-6(1*H*)-one (3) in 76% yield. The ^{1}H and ^{13}C n.m.r. spectra of (3) showed methyl resonances at 3·25 and 42·7 ppm, respectively.

Preparation of the 4-Methylated Dihydrotriazinone (4)

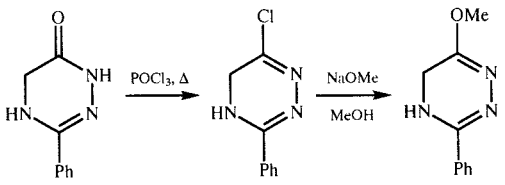
We prepared 4-methyl-3-phenyl-4,5-dihydro-1,2,4-triazin-6(1*H*)-one (4) (Scheme 3) by the general procedure of Anderson *et al.*[1] Thus, reaction of the amide (20) with Lawesson's reagent [2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetan 2,4-disulfide][13] gave the new thioamide (21) which was cyclized with hydrazine hydrate to give the desired 4-methyl-3-phenyl-4,5-dihydro-1,2,4-triazin-6(1*H*)-one (4). The ^{1}H and ^{13}C n.m.r. spectra of (4) showed methyl resonances at 2·77 and 39·5 ppm, respectively.



Scheme 3

Preparation of 6-Methoxy-3-phenyl-4,5-dihydro-1,2,4-triazine (5)

3-Phenyl-4,5-dihydro-1,2,4-triazin-6(1*H*)-one (22) was converted in good yield into the new chlorodihydrotriazine (23) by reaction with phosphorus oxychloride (Scheme 4). The infrared spectrum of the chlorodihydrotriazine (23) showed no carbonyl absorption in the region of 1670 cm^{-1} but a new band at 1639 cm^{-1} for C=N. The c.i. mass spectrum showed the expected molecular ion. Treatment of the chlorodihydrotriazine (23) with sodium methoxide in methanol afforded 6-methoxy-3-phenyl-4,5-dihydro-1,2,4-triazine (5) in excellent yield. The ^{1}H and ^{13}C n.m.r. spectra of (5) showed the methyl resonances at 3·73 and 53·2 ppm, respectively.



Scheme 4

Conclusion

The unambiguous syntheses reported above could have general applicability in the regiospecific synthesis of variously substituted dihydro-1,2,4-triazin-6(1*H*)-ones. The need for such unambiguous syntheses was shown by the fact that it would be quite difficult to conclusively assign structures (2)–(4) on the basis of their spectroscopic data alone. Studies of the physical properties and chemistry of the dihydrotriazinone ring system are in progress, and will be reported elsewhere.

Experimental

Melting points were determined on a Reichert hot-stage melting point apparatus and are uncorrected. Microanalyses were performed by the Research School of Chemistry, Australian National University, Canberra, or by National Analytical Laboratories, Melbourne. Infrared spectra were measured on a Perkin Elmer 842 spectrophotometer (cm^{-1}) with absorption intensities classified as br (broad), s (strong), m (medium) or w (weak). ^{1}H n.m.r. spectra were recorded at 200 MHz on a Bruker AC 200 or Varian Gemini spectrometer. ^{13}C n.m.r. spectra were recorded at 50·3 MHz on the above instruments. Chemical shifts (δ) are measured in ppm downfield from $SiMe_4$ as an internal standard, with multiplicities designated as s (singlet), d (doublet), t (triplet), q (quartet) or m (multiplet); (D)chloroform was used as the solvent unless otherwise stated. ^{13}C n.m.r. spectral assignments were derived from *J*-modulated spin echo experiments or DEPT experiments. High- and low-resolution chemical ionization (methane) mass spectra were performed on a Joel JMS-DX303 mass spectrometer, with only the M+1 ion (if observed) and principal ion peaks reported. G.l.c. was carried out on a Hewlett Packard 5890 gas chromatograph fitted with a flame ionization detector; helium was the carrier

* Against expectation, reaction of the imidoyl chloride (15b) with hydrazine hydrate in ethanol gave only 16–19% of 3-phenyl-4,5-dihydro-1,2,4-triazin-6(1*H*)-one (22), the remaining material being the oxazole (18).

gas, and an HP-1 25 m column was used. Injection port and detector temperatures were set at 100 and 254°, respectively. The program used involved an initial temperature of 50° for 1 min before increasing the temperature at a rate of 10°/min until it reached 254° where it was held for 15 min. Light petroleum refers to the fraction of b.p. 40–60°. All anhydrous reactions were performed under a dry argon atmosphere. All extracts were dried over magnesium sulfate monohydrate.

N-Methylbenzohydrazonoyl Bromide Hydrobromide (8)

Method (A) with CCl_4 as solvent. Benzaldehyde methylhydrazone (7)[14] (1·00 g, 7·45 mmol) was dissolved in anhydrous carbon tetrachloride (20 ml), and cooled to −15°. Bromine (310 μl) dissolved in anhydrous carbon tetrachloride (40 ml) was added dropwise while the temperature was maintained at −15°. The mixture was then allowed to warm up to room temperature and stirred for 2 h. The orange precipitate which formed was collected and washed with anhydrous carbon tetrachloride (20 ml), and triturated with anhydrous acetonitrile (20 ml) to give *N*-methylbenzohydrazonoyl bromide hydrobromide (8) as a white solid (1·6 g, 90%), m.p. 135–139° (lit.[4] 142–143°). Compound (8) reacted with $(CD_3)_2SO$ and was insoluble in $CDCl_3$, so n.m.r. data were not obtained.

Method (B) with acetic acid as solvent. Following the procedure of Fliege *et al.*[4] benzaldehyde methylhydrazone (7) (1·8 g, 13 mmol) was dissolved in anhydrous acetic acid (20 ml), and cooled to 8°. A solution of bromine (0·7 ml, 13 mmol) in anhydrous acetic acid (40 ml) was added dropwise while the temperature was kept at 8°. The mixture was then allowed to warm up to room temperature and stirred for 2 h. The orange precipitate which formed was collected and triturated with anhydrous diethyl ether. The ether extract was washed with water, saturated sodium chloride solution, dried and the solvent was evaporated to afford a white solid. Recrystallization of the solid from diethyl ether/light petroleum gave *N*-methyl-*N'*-(phenylmethylene)acetohydrazide (9) (827 mg, 35%), m.p. 83° (lit.[5] 80°). Recrystallization of the orange precipitate from anhydrous acetonitrile (20 ml) gave *N*-methylbenzohydrazonoyl bromide hydrobromide (8) as a white solid, (1·7 g, 43%), m.p. 135–139° (lit.[4] 142–143°). Evaporation of the mother liquor gave an oil. Purification of the residue by column chromatography over silica gave 1,5-dimethyl-3-phenyl-1*H*-1,2,4-triazole (10)[7] and 2,4-dimethyl-5-phenyl-2*H*-1,2,3-triazole (11) which could not be separated and gave one peak by g.l.c. analysis and one spot by t.l.c. analysis. G.l.c. R_t 12·9 min, 100%. ^{1}H n.m.r. of 60:40 mixture of (10) and (11): δ 2·28 and 2·67, both s, CMe; 3·52 and 3·61, both s, NMe; 7·19–7·65, m, Ar; 7·75–8·15, m, Ar. ^{13}C n.m.r. of (10) and (11): δ 18·1 and 18·2, CMe; 40·2 and 41·0, NMe; 128·8, 129·0, 130·2, 130·8, 132·9, 134·1, Ar; 155·1, 157·1, 161·2, 162·9, C=N.

1-Methyl-3-phenyl-4,5-dihydro-1,2,4-triazin-6(1H)-one (2)

A solution of anhydrous triethylamine (4·4 ml, 31·5 mmol) in anhydrous methanol (30 ml) was added dropwise to an ice-cold solution of *N*-methylbenzohydrazonoyl bromide hydrobromide (8) (1·54 g, 5·25 mmol) and ethyl glycinate hydrochloride (0·73 g, 5·25 mmol) in dry dichloromethane (50 ml) and anhydrous methanol (20 ml). The mixture was stirred overnight at room temperature, then the solvent was removed under reduced pressure. The residue was dissolved in diethyl ether (75 ml), and washed with water (50 ml). The aqueous layer was reextracted with diethyl ether (75 ml), and the combined extract was washed with saturated sodium chloride solution (30 ml), dried and evaporated. G.l.c. and ^{1}H n.m.r. spectroscopic analysis showed that the crude product contained the desired product (2) (85%) and the tetrazine (13) (7%). This material was triturated with light petroleum until the filtrate remained colourless. Recrystallization of the residue from ethyl acetate/cyclohexane afforded *1-methyl-3-phenyl-4,5-dihydro-1,2,4-triazin-6(1H)-one* (2) (0·82 g, 83%), g.l.c. R_t 15·5 min, 99%, m.p. 151° (Found: C, 63·2; H, 5·5; N, 22·0%; $[M+1]^{+\bullet}$, 190·098. $C_{10}H_{11}N_3O$ requires C, 63·5; H, 5·9; N, 22·2%; $[M+1]^{+\bullet}$, 190·099). ν_{max} (KBr) 3324s, 1650s, 1611s, 1545m, 1444m, 1394m, 1314w, 1047w, 979w, 927w, 780w, 762w, 695m cm^{-1}. ^{1}H n.m.r. δ 3·27, s, Me; 3·90, d, *J* 1·2 Hz, CH_2; 5·90, br s, NH (N4); 7·32–7·47, m, 3H, Ar; 7·55–7·75, m, 2H, Ar. ^{13}C n.m.r. δ 36·0, Me; 43·3, CH_2; 126·0, C2′,6′ or C3′,5′; 128·5, C2′,6′ or C3′,5′; 130·3, C4′; 131·9, C1′; 146·2, C=N; 158·7, C=O. Mass spectrum: *m/z* 190 ($[M+1]^{+\bullet}$, 100%), 160 (9). The light petroleum filtrates from the tituration were combined and recrystallized from methanol/light petroleum to afford the 1,4-dimethyl-3,6-diphenyl-1,4-dihydro-1,2,4,5-tetrazine (13) (96 mg) as a yellow solid, m.p. 98° (lit.[4] 98–99°).

Ethyl N-[Methoxy(phenyl)methylene]glycinate (15a)

The toluene-4-sulfonic acid salt of ethyl glycinate[15] (6·1 g, 22·2 mmol) was added to a solution of methyl benzimidate[16] (3·0 g, 22·2 mmol) in dichloromethane (15 ml) and the mixture was heated under reflux for 45 min. The cooled reaction mixture was then poured onto a short column of silica gel (80 ml). Elution with dichloromethane afforded the imidate (15a) (4·0 g, 81%) as a colourless oil. The product was not purified further and was used immediately. G.l.c. R_t 12·4 min, 97%. ν_{max} (film) 2984m, 2946m, 1746s, 1672s, 1602w, 1580w, 1530w, 1493w, 1435m, 1373m, 1348m, 1282s, 1190s, 1128m, 1085m, 1028m, 922w, 868w, 767m, 703m cm^{-1}. ^{1}H n.m.r. δ 1·20, t, *J* 7·1 Hz, OCH_2**Me**; 3·85, s, OMe; 4·05, s, NCH_2; 4·13, q, *J* 7·1 Hz, OC**H**$_2$Me; 7·25–7·39, m, Ar. ^{13}C n.m.r. δ 14·1, OCH_2**Me**; 52·1, NCH_2; 53·5, OMe; 60·7, O**C**H_2Me; 127·8, C2′,6′ or C3′,5′; 128·5, C2′,6′ or C3′,5′; 129·8, C4′; 131·5, C1′; 164·6, C=N; 171·2, C=O. Mass spectrum: *m/z* 222 ($[M+1]^{+\bullet}$, 100%), 190 (70), 155 (3), 148 (18), 135 (6), 118 (4), 104 (2), 86 (3).

Attempted Reaction of Ethyl N-[Methoxy(phenyl)methylene]-glycinate (15a) with Benzyl 3-Methylcarbazate (14)

One mole equivalent of each of the imidate derivative (15a) and benzyl 3-methylcarbazate (14) were dissolved in various solvents (dimethylformamide, ethanol or dichloromethane). These solutions, or neat mixtures, were heated from 25 to 150° under neutral or acidic conditions (10% mole equivalence of toluene-4-sulfonic acid or Amberlyst resin 15A). No reaction products were observed by ^{1}H or ^{13}C n.m.r. spectroscopic analysis. The imidate (15a) decomposed under forcing conditions.

Ethyl N-[Chloro(phenyl)methylene]glycinate (15b)

According to the general procedure reported by Sheehan and Corey,[12] ethyl *N*-benzoylglycinate (17)[1] (1·0 g, 4·8 mmol) was dissolved in anhydrous 1,4-dioxan (1·7 ml) and anhydrous diethyl ether (7 ml), then phosphorus pentachloride (1·0 g, 4·8 mmol) was added. The mixture was stirred at room temperature for 10 min and then the yellow solution was evaporated under reduced pressure (0·05 mmHg) at <25° to give ethyl *N*-[chloro(phenyl)methylene]glycinate (15b) (1·1 g, 87%), for which the ^{1}H n.m.r. spectrum showed >90% of (15b) and <10% of (17). This product was not purified further but used immediately. It spontaneously cyclized to 5-ethoxy-2-phenyloxazole (18) upon storage at room temperature, brief heating, or treatment with base. ^{1}H n.m.r. δ 1·30, t, *J* 7·2 Hz, CH_2**Me**; 4·25, q, *J* 7·2 Hz, C**H**$_2$Me; 4·52, s, NCH_2; 7·37–7·43, m, 3H, Ar; 7·92–8·13, m, 2H, Ar. ^{13}C n.m.r. δ 14·2, OCH_2**Me**; 55·4, NCH_2; 61·6, O**C**H_2Me; 128·3, C2′,6′ or C3′,5′; 129·1, C2′,6′ or C3′,5′; 131·9, C4′; 135·2, C1′; 147·1, C=N; 168·8, C=O.

Ethyl N-{*[2-(Benzyloxycarbonyl)-1-methylhydrazino]-(phenyl)methylene}glycinate (16)*

A solution of freshly prepared imidoyl chloride (15b) (510 mg, 2·26 mmol) in dichloromethane (30 ml) and benzyl 3-methylcarbazate[10] (14) (814 mg, 4·52 mmol) was stirred at room temperature overnight. The solvent was removed at reduced pressure and the residue was purified by column chromatography over silica [some decomposition and hydrolysis of (16) was observed]. Elution with dichloromethane/methanol mixtures gave the title amidrazone (16) (751 mg, 75%) as a colourless *oil* (Found: $[M+1]^{+\bullet}$, 370·175. $C_{20}H_{23}N_3O_4$ requires $[M+1]^{+\bullet}$, 370·175). ν_{max} (film) 3291m(br), 2985m, 1736s, 1629s, 1598m, 1495m, 1445m, 1376m, 1239s, 1191s, 1095s, 1028m, 913w, 855w, 772m, 738m, 701s cm^{-1}. ^1H n.m.r. δ 1·20, t, *J* 7·1 Hz, OCH_2**Me**; 3·14, s, NMe; 3·81, s, NCH_2; 4·15, q, *J* 7·1 Hz, OCH_2Me; 5·01, s, OCH_2Ar; 6·83–7·27, m, 11H, Ar and NH. ^{13}C n.m.r. δ 14·1, OCH_2**Me**; 39·1, NMe; 52·3, NCH_2; 60·6, OCH_2Me; 64·7, OCH_2Ar; 126·9, 127·3, 128·1, 128·4, 128·7, 129·3, aromatic carbons; 131·9, C1′; 136·1, C1″; 156·5, C=N or NCOO; 157·3, NCOO or C=N; 171·7, COEt. Mass spectrum: *m/z* 370 ($[M+1]^{+\bullet}$, 53%), 262 (5), 221 (7), 190 (9), 147 (3), 119 (4), 107 (37), 91 (100), 79 (26), 69 (6), 61 (19).

*2-Methyl-3-phenyl-2,5-dihydro-1,2,4-triazin-6(1*H*)-one (3)*

A suspension of 5% palladium/charcoal (100 mg) in a solution of the amidrazone derivative (16) (108 mg, 0·292 mmol) in ethanol (5 ml) was stirred at room temperature overnight in an atmosphere of hydrogen. Removal of the catalyst by filtration and washing with ethanol, and evaporation of the filtrate gave an oil. This was dissolved in ethanol and heated under reflux for 3 h. The solvent was evaporated at reduced pressure and the residue was chromatographed over silica gel. Gradient elution with methanol/dichloromethane (5:100) afforded *2-methyl-3-phenyl-2,5-dihydro-1,2,4-triazin-6(1*H*)-one* (3) (42 mg, 76%), m.p. 197° (dec.) (Found: C, 57·7; H, 6·3; N, 20·2%; $[M+1]^{+\bullet}$, 190·099. $C_{10}H_{11}N_3O+H_2O$ requires C, 58·0; H, 6·3; N, 20·3%; $[M+1]^{+\bullet}$, 190·098). ν_{max} (KBr) 3454m(br), 3133m(br), 2807m(br), 1639m, 1537s, 1497m, 1455m, 1414m, 1317m, 1192w, 1042w, 916w, 773m, 703m, 486w cm^{-1}. ^1H n.m.r. δ (CD_3OD) 3·25, s, NMe; 3·88, s, CH_2; 4·94, br s, NH; 7·62, s, 5H, Ar. ^{13}C n.m.r. δ (CD_3OD) 42·4, CH_2; 42·7, Me; 129·5, C1′; 130·1, C2′,6′ or C3′,5′; 130·5, C2′,6′ or C3′,5′; 133·5, C4′; 152·4, C=N; 165·6, C=O. Mass spectrum: *m/z* 190 ($[M+1]^{+\bullet}$, 100%), 175 (9), 150 (2), 118 (3), 104 (5). *m/z* (f.a.b.) 190 ($[M+1]^{+\bullet}$, 100%), 153 (11).

Ethyl N-*(Thiobenzoyl)sarcosinate (21)*

Lawesson's reagent* (1·8 g, 4·5 mmol)[13] was added to a solution of ethyl *N*-benzoylsarcosinate[17] (20) (2·0 g, 9·0 mmol) in dry benzene (20 ml), and the mixture was heated under reflux for 2 h. Removal of the solvent gave a red oil (2·06 g). Flash chromatography over silica gel and gradient elution with light petroleum/dichloromethane (10:1) mixtures afforded *ethyl* N-*(thiobenzoyl)sarcosinate* (21) (1·7 g, 81%) as a yellow oil. G.l.c. R_t 15·3 min, 100% (Found: C, 61·0; H, 6·5; N, 6·1%; $[M+1]^{+\bullet}$, 238·091. $C_{12}H_{15}NO_2S$ requires C, 60·7; H, 6·4; N, 5·9%; $[M+1]^{+\bullet}$, 238·090). ν_{max} (film) 2983w, 1744s, 1498s, 1209s cm^{-1}. ^1H n.m.r. δ 1·19, 1·26, 2×t, *J* 7·2 Hz, CH_2**Me**; 3·13, 3·50, 2×s, NMe; 4·00–4·28, m, C**H**$_2$Me; 4·12, 4·75, 2×s, NCH_2; 7·29, s, 5H, Ar. ^{13}C n.m.r. δ 14·2, 14·2, CH_2**Me**; 42·3, 43·5, NMe; 55·9, 57·0, NCH_2; 61·5, 61·9, **C**H_2Me; 125·4, 125·8, 128·3, 128·5, 128·8, C2′–6′; 142·9, 143·1, C1′; 167·2, 167·6, C=O; 203·4, C=S. Mass spectrum: *m/z* 238 ($[M+1]^{+\bullet}$, 100%), 222 (5), 208 (3), 192 (5), 180 (4), 152 (16), 121 (19), 118 (6), 105 (3).

*4-Methyl-3-phenyl-4,5-dihydro-1,2,4-triazin-6(1*H*)-one (4)*

A solution of ethyl *N*-(thiobenzoyl)sarcosinate (21) (1·0 g, 4·2 mmol) in propan-2-ol containing hydrazine monohydrate (99%, 0·4 ml, 7·6 mmol) was heated under reflux overnight. The solvent was evaporated in vacuum and the residue was purified by column chromatography over silica. Gradient elution with methanol/dichloromethane (1:100) afforded *4-methyl-3-phenyl-4,5-dihydro-1,2,4-triazin-6(1*H*)-one* (4) (479 mg, 60%), g.l.c. R_t 15·5 min, 100%, m.p. 134–135° (dec.) (Found: C, 63·2; H, 6·0; N, 22·1%; $[M+1]^{+\bullet}$, 190·097. $C_{10}H_{11}N_3O$ requires C, 63·5; H, 5·9; N, 22·2%; $[M+1]^{+\bullet}$, 190·098). ν_{max} (KBr) 3188m, 1666s, 1473m, 809m, 701m cm^{-1}. ^1H n.m.r. δ 2·77, s, NMe; 3·92, s, CH_2; 7·37, s, Ar. ^{13}C n.m.r. δ 39·5, NMe; 50·9, CH_2; 128·5, C2′,6′ or C3′,5′; 128·6, C2′,6′ or C3′,5′; 129·7, C4′; 132·4, C1′; 149·3, C=N; 161·3, C=O. Mass spectrum: *m/z* 190 ($[M+1]^{+\bullet}$, 100%), 160 (7).

6-Chloro-3-phenyl-4,5-dihydro-1,2,4-triazine (23)

3-Phenyl-4,5-dihydro-1,2,4-triazin-6(1*H*)-one[1] (22) (5·0 g, 28·5 mmol) was added to phosphorus oxychloride (50 ml), and the mixture was stirred and heated under reflux for 4 h. The reaction mixture was cooled and concentrated under vacuum; then dry toluene (20 ml) was added and the mixture was evaporated to dryness again. This process was repeated twice more. Then the reaction mixture was poured into a saturated solution of sodium hydrogen carbonate (500 ml). The aqueous layer was extracted with ethyl acetate (3×300 ml), and the combined organic layers were washed with saturated sodium chloride solution (50 ml), dried and concentrated to give a light yellow solid. Recrystallization from ethyl acetate/light petroleum gave *6-chloro-3-phenyl-4,5-dihydro-1,2,4-triazine* (23) (4·5 g, 99%), g.l.c. R_t 13·7 min, 93%, m.p. 128–129° (Found: C, 55·5; H, 4·3; N, 22·0%; $[M+1]^{+\bullet}$, 194·049. $C_9H_8ClN_3$ requires C, 55·8; H, 4·2; N, 21·7%; $[M+1]^{+\bullet}$, 194·049). ν_{max} (KBr) 3410s(br), 3100s(br), 2922s(br), 1639s, 1635s, 1474s, 1353m, 1305s, 1096s, 1030m, 984s, 783s, 696s cm^{-1}. ^1H n.m.r. δ [$CDCl_3$/$(CD_3)_2SO$] 4·20, s, CH_2; 7·28–7·57, m, 4H, Ar and NH; 7·72–7·91, m, 2H, Ar. ^{13}C n.m.r. δ [$CDCl_3$/$(CD_3)_2SO$] 49·0, CH_2; 126·4, C2′,6′ or C3′,5′; 127·9, C2′,6′ or C3′,5′; 130·3, C4′; 131·6, C1′; 137·6, C=N; 151·3, C–Cl. Mass spectrum: *m/z* 194 ($[M+1]^{+\bullet}$, 89%), 158 (44), 119 (11), 104 (100), 91 (8), 77 (9), 61 (5).

6-Methoxy-3-phenyl-4,5-dihydro-1,2,4-triazine (5)

The chlorotriazine (23) (2·0 g, 10·3 mmol) was added to freshly prepared sodium methoxide (785 mg, 20·7 mmol) in anhydrous methanol (10 ml). The solution was stirred at room temperature for 1 h, then the solvent was evaporated under reduced pressure. The residue was dissolved in ethyl acetate (100 ml), and washed with water (30 ml). The aqueous layer was extracted with ethyl acetate (50 ml); the combined extracts were washed with saturated sodium chloride solution, dried and evaporated to give a yellow solid which was recrystallized from ethyl acetate/light petroleum to afford *6-methoxy-3-phenyl-4,5-dihydro-1,2,4-triazine* (5) (1·9 g, 97%), g.l.c. R_t 13·7 min, 99%, m.p. 150–151° (Found: C, 63·6; H, 6·0; N, 22·4%; $[M+1]^{+\bullet}$, 190·096. $C_{10}H_{11}N_3O$ requires C, 63·5; H, 5·9; N, 22·2%; $[M+1]^{+\bullet}$, 190·096). ν_{max} (KBr) 3175m(br), 2947m, 1679s, 1630m, 1525m, 1437w, 1329s, 1266m, 1162w, 1018w, 983w, 778w, 699w cm^{-1}. ^1H n.m.r. δ [$CDCl_3$/$(CD_3)_2SO$] 3·73, s, OMe; 3·95, NH; 7·29–7·56, m, 3H, Ar; 7·73–7·96, m, 2H, Ar. ^{13}C n.m.r. δ [$CDCl_3$/$(CD_3)_2SO$] 42·6, CH_2; 53·2, OMe; 126·3, C2′,6′ or C3′,5′; 127·8, C2′,6′ or C3′,5′; 129·8, C4′; 132·7, C1′; 151·7, C=N or C–O; 152·3, C=N or C–O. Mass

* 2,4-Bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetan 2,4-disulfide.

spectrum: m/z 189 ($[M+1]^{+\bullet}$, 100%), 144 (9), 118 (16), 104 (74), 87 (5), 77 (7), 57 (16).

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