# Cycloadditions of 3*H*-Indoles[1]

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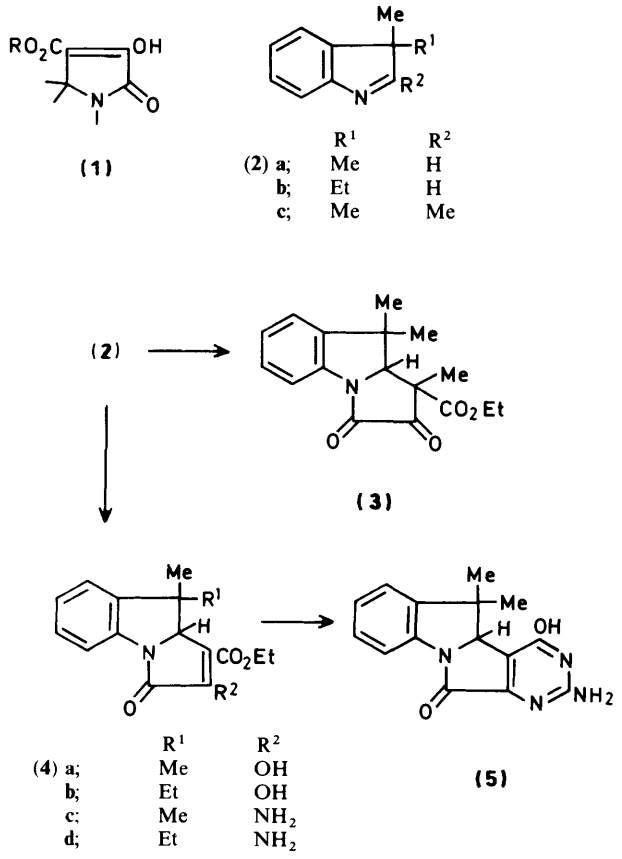
Treatment of 3*H*-indoles (indolenines) with diethyl oxaloacetate and diethyl oxalopropionate, respectively, yield the pyrrolidones (**4**) and (**3**) and with thiobenzoyl isocyanate the thiadiazine (**16**) is formed. The 1 : 2 product (**8**) is formed with dimethyl acetylenedicarboxylate whilst thiocyanates and alkyl isothiocyanates yield triazine derivatives (**11**). In contrast, and not in accord with literature precedence, aryl and acyl isothiocyanates produce the thiadiazine derivatives (**14**).

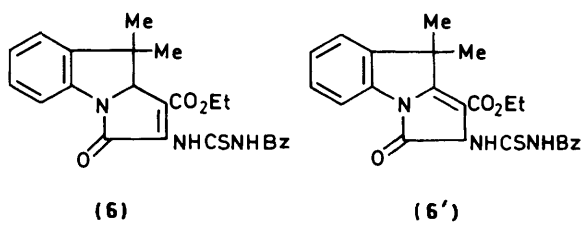
Our interest in the cycloadditions of 3*H*-indoles stemmed from the observation[2] that imines react with oxaloacetic esters to yield pyrrolidones of the general formula (**1**). Our desire to utilise this reaction and to extend its scope to the formation of fused analogues led us to investigate the addition to the readily available[3] 3,3-dialkyl-3*H*-indoles (**2**) (*cf.* Scheme) and we were




Scheme.

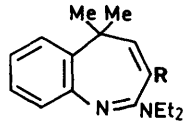
able to demonstrate that the treatment of compound (**2a**) with diethyl oxalopropionate and compounds (**2a**, **b**) with diethyl oxaloacetate yielded compounds (**3**) and (**4a**, **b**), respectively. The assigned structure of the cycloadduct (**3**) was supported by its i.r. spectrum which exhibited absorptions at 1 765, 1 740, and 1 695 $cm^{-1}$, consistent with the presence of ester, oxo, and amide groups. The behaviour of the oxaloacetate adducts was, however, a little more complex in that from the solid state spectra of compounds (**4a**) and (**4b**), it appeared that two structurally different products had been formed. Each product exhibited an amide absorption at 1 675 $cm^{-1}$, but whereas compound (**4a**) showed a second carbonyl frequency at 1 655 $cm^{-1}$, the ester carbonyl absorption for compound (**4b**) was observed at 1 708 $cm^{-1}$. However, in chloroform solution the spectra of the two compounds were almost superimposable, with ester and amidic carbonyl frequencies at 1 708 and 1 675 $cm^{-1}$, respectively. It was concluded from these data that in the solid state the ester group of compound (**4a**) is s-*trans* to the carbon–carbon double bond but s-*cis* in solution. Such changes in i.r. frequencies of carbonyl groups caused by changes in conformation have been observed previously.[4] These differences arise as a consequence of intermolecular hydrogen bonding by compound (**4a**) in the solid state with a predictable change to intramolecular hydrogen bonding between an s-*cis* ester carbonyl and the hydroxy group in solution.

Both compounds (**4a**) and (**4b**) possess enolisable carbonyl groups and accordingly both compounds were transformed into their respective amino derivatives (**4c**) and (**4d**) using ammonium formate. With this ready availability of a new enamino ester system, it was hoped to be able to prepare a number of cyclised derivatives using the methods described by Wamhoff,[5] however, we were to be disappointed. The ester (**4c**) failed to react with phenyl isocyanate and phenyl isothiocyanate or with dichlorotriphenylphosphorane. Treatment of compound (**4c**) with guanidine gave the very insoluble pyrimidine derivative (**5a**) in low yield and benzoyl isothiocyanate yielded the acylthiourea (**6a**). In compound (**6**) a 1,3-prototropic shift occurs, supported by the presence of a doublet at δ 5.95 for 1 H which collapses to a singlet at δ 5.9 upon addition of $CD_3CO_2D$, the singlet vanishing completely after about 1 h, suggesting the existence of the equilibrium (**6**) ⇌ (**6′**). Further evidence for the existence of this equilibrium was also forthcoming from the i.r. spectra of compound (**6**). Whereas the solution spectrum ($CHCl_3$) exhibited three carbonyl absorptions at 1 640, 1 685, and 1 730 $cm^{-1}$ consistent with the structure (**6**), the solid state spectrum, however, exhibited four absorptions at 1 645, 1 670, 1 695, and 1 730 $cm^{-1}$ consistent with the tautomer (**6′**) also being present.

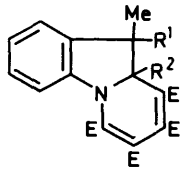



Although the reactivity of the enamino ester was disappointing, the formation of addition products encouraged us to investigate further cycloadditions of the 3*H*-indole system.

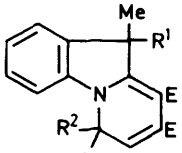
Although it has been known for some time that acid chlorides and acid anhydrides add across the imine double bond,[6] a reaction which has found synthetic utility[7] in the synthesis of gliotoxin analogues, few other investigations have been reported. The only direct cycloaddition of 3*H*-indoles which has come to our notice is the $BF_3$-catalysed nucleophilic addition of ynamines when the benzazepines (**7**) are formed.[8] Treatment of the C=N bond in benzothiazole, benzimidazole, and benzoxazole, respectively, with dimethylacetylenedicarboxylate has been reported[9] and consequently our initial investigations with compounds (**2a**) and (**2b**) were carried out with this same ester. According to the above cited work, the isolated product might have been expected to have any one of the structures (**8a, b**)—(**10a, b**). Of these alternative structures, (**9a, b**) were excluded on the basis of the lack of n.O.e. between protons on carbons 4 and 6. The structures (**10a, b**) were eliminated on mechanistic grounds (the rearrangement would require the generation of a dialkylphenyl carbanion) and from spectral evidence in support of the structure (**8c**). All the methyl signals in the $^1H$ n.m.r. spectrum were within the region 1—2 p.p.m. consistent with the assigned structure, whereas in structure (**10c**) a methyl signal at 2.5—3 p.p.m. would be expected.[10]



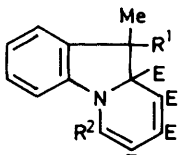
(**7**)



(**8**)



(**9**)



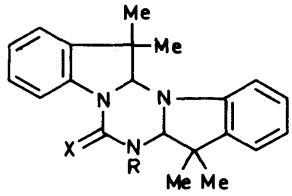
(**10**)

| | $R^1$ | $R^2$ |
|---|---|---|
| **a**; | Me | H |
| **b**; | Et | H |
| **c**; | Me | Me |

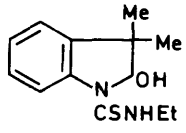
E = $CO_2Me$

We next extended this 1,4-dipolar cycloaddition[11] to the study of the reactions of the 3*H*-indoles (**2**) with heterocumulenes. In the reaction of the 3*H*-indoles (**2**) with dimethyl acetylenedicarboxylate, the only product isolated was the 1:2 adduct. Although reaction conditions were varied, we were unable to isolate any product with the inverse ratio of reactants as has been isolated for the 3,4-dihydroisoquinolines.[12] However, with isocyanates and isothiocyanates it was the 2:1 adducts which were isolated, *i.e.* the 3*H*-indole was acting as the nucleophile and as the dipolarophile. The product (**11a**), from the reaction of the 3*H*-indole (**2a**) with phenyl isocyanate, exhibited a typical triazinone carbonyl absorption[13] at 1 665 $cm^{-1}$ and the n.m.r. showed *inter alia* two singlets at 5.35 and 5.42 p.p.m. assigned to the protons at 7a and 13a. The aromatic protons gave a complex pattern of signals centred at 7.05 p.p.m. except one, the proton at C-4 which gave a signal at 7.8 p.p.m. This pattern of signals was a common feature of all the 1,4-dipolar cycloaddition products of the 3*H*-indoles (**2a, b**) with heterocumulenes. For the 7-ethyl analogue (**11b**), the two diastereoisomers were isolated. There were slight differences in the carbonyl frequencies (1 660 and 1 665 $cm^{-1}$) otherwise the i.r. spectra were superimposable. The 7a and 13a proton signals in the n.m.r. were also positioned differently, occurring at 5.0 and 5.15 p.p.m. and 4.7 and 4.9 p.p.m., respectively.

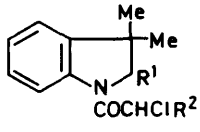
Isothiocyanates when treated with the 3*H*-indoles (**2a, b**) gave either the triazinethiones or iminothiadiazines, depending upon the nature of the moiety attached to the isothiocyanate group. With ethyl isothiocyanate, the triazine thione (**11c**) was isolated. The n.m.r. signal pattern confirmed the structural resemblance to the triazine ketone (**11a**) and the i.r. spectrum exhibited thiourea B and C absorption at 1 460 and 1 370 $cm^{-1}$, respectively, consistent with the assignments made by Huisgen *et al.*[14] for the cycloaddition products derived from 3,4-dihydroisoquinoline. In addition a significant amount of the thiourea (**12**) was isolated, which may well have arisen *via* a [2 + 2] cycloaddition followed by hydrolytic ring opening. This was the only evidence of a [2 + 2] cycloaddition to be found in this work. Attempts in this direction were made with the *in vitro* generation of ketenes but only the apparent acid chloride addition derived products (**13**) were isolated. Although [2 + 2] cycloadditions may have been involved, their involvement in the formation of products (**13**) must remain a matter of conjecture.

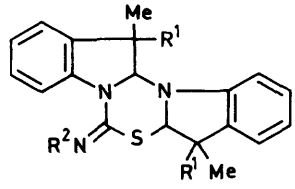


| | X | R |
|---|---|---|
| (**11**) **a**; | O | Ph |
| **b**; | O | Et |
| **c**; | S | Et |
| **d**; | O | Bz |



(**12**)





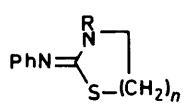
| | $R^1$ | $R^2$ |
|---|---|---|
| (**13**) **a**; | OH | Cl |
| **b**; | OH | H |
| **c**; | $OCOCH_2Cl$ | H |

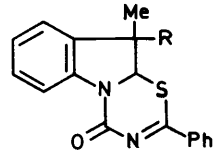
| | $R^1$ | $R^2$ |
|---|---|---|
| (**14**) **a**; | Me | Ph |
| **b**; | Et | Ph |
| **c**; | Me | Bz |
| **d**; | Et | Bz |
| **e**; | Me | $CO_2Et$ |
| **f**; | Et | $CO_2Et$ |

The products from the 3*H*-indoles (**2a**) and (**2b**) and phenyl isothiocyanate again showed n.m.r. spectra consistent with the pentacyclic system; however, the i.r. spectra where characterised by strong absorption at 1 560 and 1 575 $cm^{-1}$, respectively, together with a much enhanced phenyl absorption at 1 605 $cm^{-1}$. It is clear from the results of Huisgen *et al.*[14] and Jensen and Nielsen[15] acyclic or cyclic tetrasubstituted thioureas would not be expected to absorb above 1 500 $cm^{-1}$ whereas isothioureas substituted on the imino nitrogen by phenyl would exhibit doublets at *ca.* 1 600 $cm^{-1}$. These data are consistent with the iminothiadiazine structures (**14a, b**) for these new products. Further confirmation for the correctness of these assignments comes from the i.r. spectra of *N*-(4,5-dihydro-3-methyl-1,3-thiazol-2-ylidene)aniline (**15a**) and the corresponding 1,3-thiazine (**15b**). The relevant frequencies for these compounds were observed at 1 620 and 1 585 $cm^{-1}$ and 1 610 and 1 585

$cm^{-1}$, respectively. The enhancement of the phenyl absorption is certainly due to a coupling of the phenyl and imine vibrations.

It has been previously noted[16] that the cycloadditions of imines with acyl isocyanates and isothiocyanates proceed *via* an electrocyclic [4 + 2] cycloaddition rather than a 1,4-dipolar reaction, and in agreement we found that the treatment of the 3*H*-indole (**2a**) with thiobenzoyl isocyanate gave the [4 + 2] addition product (**16**). In contrast, however, acyl isocyanates





| | $R^1$ | *n* |
|---|---|---|
| (**15**) **a**; | Me | 1 |
| **b**; | H | 2 |

| | $R^1$ |
|---|---|
| (**16**) **a**; | Me |
| **b**; | Et |

and isothiocyanates gave 1,4-dipolar products, again with compound (**2a**) acting as both nucleophile and dipolarophile. Benzoyl isocyanate yielded the expected triazinone (**11d**) with the associated carbonyl frequencies 1 700 $cm^{-1}$ for the 7-benzoyl substituent and 1 660 $cm^{-1}$ for the ring carbonyl group. The corresponding triazine thione from benzoyl isothiocyanate would also be expected to have an i.r. frequency at *ca.* 1 700 $cm^{-1}$ for the benzoyl substituent but instead the products obtained exhibited strong absorptions at 1 615 and 1 495 $cm^{-1}$. The corresponding frequencies for the product from the 3*H*-indole (**2b**) were 1 625 and 1 500 $cm^{-1}$, respectively. Such frequencies are observed in heterocyclic acylimines[17] indicating that again it is the thiadiazines (**14c, d**) which are the preferred products. If this were so, then it would be expected that by replacement of the phenacyl group by ethoxycarbonyl an increase in these frequencies by approximately 40 and 20 $cm^{-1}$ would be observed,[18] as was indeed found. The reaction of the 3*H*-indoles (**2a, b**) with ethoxycarbonyl isothiocyanate yielded products with i.r. frequencies at 1 665 and 1 520 $cm^{-1}$ for compound (**14e**) and 1 665 and 1 515 $cm^{-1}$ for compound (**14f**).

It had been hoped to characterise the 1,4-dipolar cycloaddition products further by $^{13}C$ n.m.r. measurements on compounds (**11b, c**) and (**14a, c, e**), however, in solution dissociation was extensive which made signal assignment ambiguous. Of those signals which were clearly assignable, all spectra exhibited a signal at 179.5 p.p.m. for C-2 of the starting indole, whilst of the products derived from isothiocyanates only compound (**11c**) exhibited a signal at 199 p.p.m. attributed to a carbon–sulphur double bond. This confirms the conclusions of the i.r. studies, namely, the thiadiazines are alternative products to the usually observed triazinethiones in the reaction of imines with isothiocyanates.

## Experimental

M.p. are uncorrected. The n.m.r. spectra were measured in p.p.m. at 90 MHz on a Varian EM390 and i.r. spectra on a Perkin-Elmer 398 spectrophotometer; *J* was in Hz. Chromatography was carried out on 230—400 mesh ASTM silica gel using the appropriate eluant. Unless otherwise stated, all reactions were carried out in an argon atmosphere. The 3*H*-indoles were prepared by the method of Horishino.[3]

*Ethyl* 9,9a-*Dihydro*-1,9,9-*trimethyl*-2,3-*dioxo*-1H-*pyrrolo*[1,2-a]*indole*-1-*carboxylate* (**3**).—A solution of 3,3-dimethyl-3*H*-indole (3.6 g) and diethyloxalopropionate (5 g) in glacial acetic acid (80 ml) was set aside at ambient temperatures for 4 days. The red solution was evaporated to dryness under reduced pressure and the product was recrystallised from ethyl acetate–hexane to yield the *title compound* (**3**) (3.5 g, 47%), m.p. 129—131 °C (Found: C, 67.9; H, 6.5; N, 5.1. $C_{17}H_{19}NO_4$ requires C, 67.8; H, 6.3; N, 4.7%); $\nu_{max.}$(Nujol) 1 765 (C=O), 1 740 (C=O), and 1 695 $cm^{-1}$ (C=O); $\delta_H(CDCl_3)$ 1.08 (3 H, t, *J* 7.5), 1.11 (3 H, s), 1.55 (3 H, s), 1.6 (3 H, s), 4.06 (3 H, s), 7.2 (3 H, m), and 7.8 (1 H, m).

Similarly prepared were *ethyl* 9,9a-*dihydro*-2-*hydroxy*-9,9-*dimethyl*-3-*oxopyrrolo*[1,2-a]*indole*-1-*carboxylate* (**4a**) (45%), m.p. 150 °C (isopropyl alcohol) (Found: C, 67.0; H, 6.0; N, 4.7. $C_{16}H_{17}NO_4$ requires C, 66.9; H, 6.0; N, 4.9%); $\nu_{max.}$(Nujol) 3 160 (OH), 1 675 (C=O), and 1 655 $cm^{-1}$ (C=O); $\delta_H(CDCl_3)$ 0.80 (3 H, s), 1.38 (3 H, t, *J* 7.5), 1.60 (3 H, s), 4.3 (2 H, m), 4.7 (1 H, s), 7.18 (3 H, m), 7.57 (1 H, m), and 9.3 (1 H, s) and *ethyl* 9-*ethyl*-9,9a-*dihydro*-2-*hydroxy*-9-*methyl*-3-*oxopyrrolo*[1,2-a]-*indole*-1-*carboxylate*, (**4b**) (44%), m.p. 136 °C (isopropyl alcohol) (Found: C, 67.8; H, 6.4; N, 4.4. $C_{17}H_{19}NO_4$ requires C, 67.8; H, 6.35; N, 4.65%); $\nu_{max.}$(Nujol) 3 290 (OH), 1 708 (C=O), and 1 675 $cm^{-1}$ (C=O); $\delta_H(CDCl_3)$ 0.85 (3 H, s), 1.0 (3 H, t, *J* 7.5), 1.42 (3 H, t, *J* 7.5), 2.08 (2 H, m), 4.44 (2 H, q, *J* 7.5), 5.0 (1 H, s), and 7.45 (5 H, m).

*Ethyl* 2-*Amino*-9,9a-*dihydro*-9,9-*dimethyl*-3-*oxopyrrolo*-[1,2-a]*indole*-1-*carboxylate* (**4c**).—A mixture of compound (**4a**) (11.4 g) and ammonium formate (2.5 g) in 2-methoxyethanol (60 ml) was heated under reflux for 2 h. The solution was evaporated to dryness under reduced pressure and the residue was recrystallised from ethanol to give the *title compound* (**4c**) (4.9 g, 43%), m.p. 169 °C (Found: C, 66.7; H, 6.6; N, 9.8. $C_{18}H_{18}N_2O_3$ requires C, 67.1; H, 6.3; N, 9.8%); $\nu_{max.}$(Nujol) 3 400, 3 310 (NH), 1 705 (C=O), and 1 674 $cm^{-1}$ (C=O); $\delta_H(CDCl_3)$ 0.79 (3 H, s), 1.32 (3 H, t, *J* 7.5), 1.6 (3 H, s), 4.25 (2 H, m), 4.72 (1 H, s), 5.82 (2 H, s), and 7.32 (4 H, m).

Similarly prepared was *ethyl* 2-*amino*-9-*ethyl*-9,9a-*dihydro*-9-*methylpyrrolo*[1,2-a]*indole*-1-*carboxylate* (**4d**) (45%), m.p. 115 °C (ethanol) (Found: C, 67.6; H, 6.8; N, 9.1. $C_{17}H_{20}N_2O_3$ requires C, 68.0; H, 6.7; N, 9.3%); $\nu_{max.}$(Nujol) 3 390, 3 290 (NH), 1 705 (C=O), and 1 675 $cm^{-1}$ (C=O); $\delta_H(CDCl_3)$ 0.8 (3 H, s), 0.94 (3 H, t, *J* 7.5), 1.31 (3 H, t, *J* 7.5), 2.15 (2 H, m), 4.31 (2 H, q, *J* 7.5), 5.05 (1 H, s), 5.95 (2 H, s), and 7.4 (4 H, m).

2-*Amino*-4b,5-*dihydro*-4-*hydroxy*-5,5-*dimethyl*-11-*oxo*-*pyrimido*[5′,4′:3,4]*pyrrolo*[1,2-a]*indole* (**5**).—Guanidine hydrochloride (4.8 g) was added to a solution of sodium (1.4 g) in ethanol (50 ml). After the mixture had been stirred at room temperature for 30 min, compound (**4a**) (2.9 g) was added and the mixture then heated under reflux for 6 days. After filtration the solution was concentrated to *ca.* 15 ml and diluted with water (60 ml). The pH of the solution was adjusted to 6—7 and the precipitate was collected. Recrystallisation from aqueous dimethylformamide (DMF) yielded the *product* (**5**) (0.7 g, 15%), m.p. >360 °C (Found: C, 64.1; H, 5.1; N, 19.6. $C_{15}H_{14}N_4O_2$ requires C, 63.8; H, 5.0; N, 19.85%); $\nu_{max.}$(Nujol) 3 305, 3 130 (NH), and 1 660 $cm^{-1}$ (C=O).

*Reaction of Compound* (**4c**) *with Benzoyl Isothiocyanate.*—A solution of compound (**4c**) (0.3 g) and benzoyl isothiocyanate (1.5 ml) in acetonitrile (10 ml) was heated under reflux for 24 h. After evaporation and chromatography (2% ether in chloroform), the appropriate fraction was crystallised from ethanol to yield the *product* (**6**) (130 mg, 36%), m.p. 182—183 °C (Found: C, 63.7; H, 5.2; N, 9.4. $C_{24}H_{23}N_3O_4S$ requires C, 64.1; H, 5.1; N, 9.35%); $\nu_{max.}$(Nujol) 3 160, 3 230 (NH), 1 645, 1 670, 1 695, and 1 730 $cm^{-1}$ (C=O); $\delta_H[(CD_3)_2SO]$ 1.2 (3 H, t, *J* 8), 1.65 (6 H, s), 4.15 (2 H, m), 5.95 (1 H, d, *J* 8), 7.6 (9 H, m), 10.2 (1 H, s), and 11.3 (1 H, d, *J* 8).

*Tetramethyl* 9a,10-*Dihydro*-10,10-*dimethylpyrido*[1,2-a]-*indole*-6,7,8,9-*Tetracarboxylate* (**8a**).—A suspension of the 3*H*-

indole (**2a**) (0.5 g) in acetonitrile (10 ml) was treated dropwise at 0 °C with a solution of dimethyl acetylenedicarboxylate (1.5 g) in acetonitrile (5 ml). After cooling, the mixture was stirred at ambient temperatures for 20 h. The solvent was removed under reduced pressure and after chromatography (30% ethyl acetate in hexane) the main product was isolated as a yellow oil which gave the *title compound* (**8a**) as yellow crystals (0.7 g, 46%), m.p. 115—117 °C after crystallisation from toluene–ethyl acetate–hexane (Found: C, 61.9; H, 5.5; N, 2.9. $C_{22}H_{23}NO_8$ requires C, 61.5; H, 5.4; N, 3.3%); $\nu_{max.}$(Nujol) 1 690, 1 710, 1 770, and 1 735 $cm^{-1}$ (C=O); $\delta_H(CDCl_3)$ 1.3 (3 H, s), 1.5 (3 H, s), 3.64 (3 H, s), 3.71 (3 H, s), 3.80 (3 H, s), 3.87 (3 H, s), 5.2 (1 H, s), and 7.05 (4 H, m).

Similarly prepared were compounds (**8b**) (63%), m.p. 138—140 °C (Found: C, 62.3; H, 6.3; N, 2.9. $C_{23}H_{25}NO_8$ requires C, 62.3; H, 5.6; N, 3.2%); $\nu_{max.}$(Nujol) 1 690, 1 708, 1 728, and 1 735 $cm^{-1}$ (C=O); $\delta_H(CDCl_3)$ 0.54 (t, 3 H, *J* 7), 0.98 (3 H, s), 1.02 (3 H, s), 1.95 (2 H, q, *J* 7), 3.41 (3 H, s), 3.52 (3 H, s), 3.56 (3 H, s), 3.66 (3 H, s), 5.06 (1 H s), and 6.65 (4 H, m) and (**8c**) (35%), m.p. 165 °C (Found: C, 62.6; H, 5.9; N, 2.9. $C_{33}H_{25}NO_8$ requires C, 62.3; H, 5.6; N, 3.2%); $\nu_{max.}$(Nujol) 1 695, 1 720, and 1 740 $cm^{-1}$ (C=O); $\delta_H[(CD_3)_2SO]$ 1.14 (3 H, s), 1.4 (3 H, s), 1.51 (3 H, s), 3.29 (3 H, s), 3.60 (3 H, s), 3.98 (3 H, s), 6.67 (1 H, m), and 7.25 (3 H, m).

13a,14-*Dihydro*-8,8,14,14-*tetramethyl*-6-*oxo*-7-*phenyl*-6H,8H-[1,3,5]*triazino*[2,1-a:4,3-a′]*di-indole* (**11a**).—A mixture of the 3*H*-indole (**2a**) (0.21 g) and phenyl isocyanate (0.3 g) in acetonitrile (10 ml) was heated under reflux for 24 h, evaporated to dryness, and the residue recrystallised from acetonitrile to yield the *product* (**11a**) (0.25 g, 65%), m.p. 183—185 °C (Found: C, 79.3; H, 6.7; N, 10.3. $C_{27}H_{27}N_3O$ requires C, 79.3; H, 6.7; N, 10.3%); $\nu_{max.}$(Nujol) 1 665 $cm^{-1}$ (C=O); $\delta_H(CDCl_3)$ 0.8 (3 H, s), 1.28 (3 H, s), 1.31 (3 H, s), 1.48 (3 H, s), 5.35 (1 H, s), 5.42 (1 H, s), 7.05 (12 H, m), and 7.8 (1 H, m).

7-*Ethyl*-13a-14-*dihydro*-8,8,14,14-*tetramethyl*-6-*oxo*-6H,8H-[1,3,5]*triazino*[2,1-a:4.3-a′]*di-indole* (**11b**).—A solution of the 3*H*-indole (**2a**) (1 g) and ethyl isocyanate (5 ml) in acetonitrile (10 ml) was heated under reflux for 6 h. The solution was evaporated to dryness and the residue chromatographed (10% ethyl acetate in hexane) to give the *product* (**11b**) as two diastereoisomers (I) and (II).

Diastereoisomer (I) (0.51 g, 39%), m.p. 121—123 °C (cyclohexane) (Found: C, 76.4; H, 7.6; N, 11.4. $C_{23}H_{27}N_3O$ requires C, 76.5; H, 7.5; N, 11.6%); $\nu_{max.}$(Nujol) 1 660 $cm^{-1}$ (C=O); $\delta_H(CDCl_3)$ 1.3 (15 H, m), 3.15 (1 H, m), 3.90 (1 H, m), 5.0 (1 H, s), 5.15 (1 H, s), 7.0 (7 H, m), and 7.65 (1 H, m). Diastereoisomer (II) (0.54 g, 41%), m.p. 108—109 °C (hexane) (Found: C, 76.9; H, 7.7; N, 11.7. $C_{23}H_{27}N_3O$ requires C, 76.5; H, 7.5; N, 11.6%); $\nu_{max.}$(Nujol) 1 665 $cm^{-1}$ (C=O); $\delta_H(CDCl_3)$ 1.3 (15 H, m), 3.16 (1 H, m), 3.98 (1 H, m), 4.7 (1 H, s), 4.9 (1 H, s), 6.4 (1 H, m), 7.05 (6 H, m), and 7.68 (1 H, m).

*Reaction of the* 3H-*Indole* (**2a**) *with Ethyl Isothiocyanate*.—A solution of the 3*H*-indole (**2a**) (1 g) and ethyl isothiocyanate (4 ml) in acetonitrile (10 ml) was heated under reflux for 48 h. The reaction mixture was evaporated to dryness and chromatographed (5% ethyl acetate in hexane). The first fraction was recrystallised from cyclohexane to yield the *thiourea* (**12**) (120 mg, 6%), m.p. 113 °C (Found: C, 62.0; H, 7.3; N, 10.8; $C_{13}H_{18}N_2OS$ requires C, 62.4; H, 7.2; N, 11.2%); $\delta_H(CDCl_3)$ 1.3 (9 H, m), 3.8 (m, 2 H), 4.78 (1 H, s), 5.75 (1 H, s), 6.5 (1 H, s), and 7.2 (4 H, m).

The main fraction (800 mg, 61%) was crystallised from hexane to yield the *triazinethione* (**11c**), m.p. 154 °C (Found: C, 72.9; H, 7.2; N, 11.0. $C_{23}H_{27}N_3S$ requires C, 73.2; H, 7.2; N, 11.1%); $\nu_{max.}$(Nujol) 1 460 and 1 370 $cm^{-1}$; $\delta_H(CDCl_3)$ 1.45 (12 H, m), 1.75 (3 H, s), 3.2 (1 H, m), 4.65 (1 H, m), 4.85 (1 H, s), 4.95 (1 H, s), 6.0 (1 H, d), 6.9 (6 H, m), and 8.65 (1 H, m).

7-*Benzoyl*-13a,14-*dihydro*-8,8,14,14-*tetramethyl*-6-*oxo*-6H,8H-[1,3,5]*triazino*[2,1-a:4,3-a′]*di-indole* (**11d**).—A solution of the 3*H*-indole (**2a**) (1.5 g) and benzoyl isocyanate (1.5 g) in acetonitrile (20 ml) was heated under reflux for 6 h. On cooling, crystals of a non-indolic material separated out and were filtered off. Upon concentration of the mother liquor to 10 ml, the *product* (**11d**) separated (900 mg, 42%), m.p. 172—174 °C (from acetonitrile) (Found: C, 76.9; H, 6.3; N, 9.6. $C_{28}H_{27}N_3O_2$ requires C, 76.9; H, 6.2; N, 9.8%); $\nu_{max.}$(Nujol) 1 700 and 1 645 $cm^{-1}$ (C=O); $\delta_H$ 1.35 (3 H, s), 1.4 (3 H, s), 1.42 (3 H, s), 1.75 (3 H, s), 5.6 (1 H, s), 5.7 (1 H, s), 5.9 (1 H, d), 6.9 (7 H, m), and 7.25 (5 H, s).

1-(2,2-*Dichloroacetyl*)-2-*hydroxy*-3,3-*dimethyl*-3H-*indole* (**13a**).—A solution of the 3*H*-indole (**2a**) (0.5 g) was suspended in dimethoxyethane (10 ml) and treated with dichloroacetyl chloride (0.34 ml) at 0 °C. Triethylamine (0.48 ml) in dimethoxyethane (2 ml) was added and after 30 min the reaction was poured into brine (50 ml). The aqueous system was extracted with ethyl acetate (3 × 25 ml) and the organic extracts were washed with brine, dried, and evaporated to dryness. Chromatography (20% ethyl acetate in hexane) yielded an oil which crystallised from cyclohexane to yield the *product* (**13a**) (0.43 g, 39%), m.p. 126—128 °C (Found: C, 52.7; H, 4.4; Cl, 25.7; N, 4.7. $C_{12}H_{13}Cl_2NO_2$ requires C, 52.55; H, 4.4; Cl, 25.9; N, 5.1%); $\delta_H(CDCl_3)$ 1.26 (3 H, s), 1.46 (3 H, s), 3.48 (1 H, d, *J* 10), 5.52 (1 H, d, *J* 10), 6.6 (1 H, s), 7.22 (3 H, m), and 8.05 (1 H, m).

Similarly prepared (at −60 °C) was 1-(2-*chloroacetyl*)-2-*hydroxy*-3,3-*dimethyl*-3H-*indole* (**13b**) (43%), m.p. 115—117 °C (cyclohexane) (Found: C, 59.8; H, 6.0; Cl, 15.0; N, 5.8. $C_{12}H_{14}ClNO_2$ requires C, 60.1; H, 5.9; Cl, 14.8; N, 5.8%); $\delta_H(CDCl_3)$ 1.3 (3 H, s), 1.5 (3 H, s), 3.5 (1 H, s), 4.25 (1 H, d, *J* 13), 4.25 (1 H, d, *J* 13), 5.48 (1 H, d, *J* 10), 7.25 (3 H, m), and 8.1 (1 H, s). A second, minor product identified as 2-(2-*chloroacetoxy*)-1-(2-*chloroacetyl*)-3,3-*dimethyl*-3H-*indole* (**13c**) (9%) was isolated from the above reaction m.p. 135—136 °C (cyclohexane) (Found: C, 52.8; H, 4.3; Cl, 22.5; N, 4.5. $C_{14}H_{15}Cl_2NO_3$ requires C, 53.1; H, 4.7; Cl 22.45; N, 4.4%); $\delta_H(CDCl_3)$ 1.46 (6 H, m), 4.16 (2 H, s), 4.22 (1 H, d, *J* 14), 4.45 (1 H, d, *J* 14), 6.8 (1 H, s), 7.3 (3 H, m), and 8.15 (1 H, s).

13a-14-*Dihydro*-8,8,14,14-*tetramethyl*-6-*phenylimino*-6H,8H-[1,3,5]*thiadiazino*[3,2-a:5,4-a′]*di-indole* (**14a**).—A solution of phenyl isothiocyanate (1.35 g) and the 3*H*-indole (**2a**) (3.0 g) were heated under reflux for 16 h in acetonitrile (10 ml) when a further quantity of phenyl isothiocyanate (1.35 g) was added. The reaction mixture was heated for a further 48 h. Upon cooling the mixture was extracted with hexane (3 × 10 ml), evaporated to dryness under reduced pressure, and the residue recrystallised from acetonitrile to yield the *title compound* (**14a**) (1.3 g, 30%), m.p. 144 °C (Found: C, 76.6; H, 6.4; N, 9.9. $C_{27}H_{27}N_3S$ requires C, 76.2; H, 6.4; N, 9.9%); $\nu_{max.}$(Nujol) 1 605 (Ph) and 1 560 $cm^{-1}$ (C=N); $\delta_H(CDCl_3)$ 1.28 (3 H, s), 1.32 (6 H, s), 1.55 (3 H, s), 5.2 (2 H, s), 6.8 (12 H, m), and 8.2 (1 H, m). The products (**14b—f**) were prepared in a similar manner and their physical data are recorded in the Table.

9a,10-*Dihydro*-10,10-*dimethyl*-6-*oxo*-8-*phenyl*[1,3,5]*thiadiazino*[3,2-a]*indole* (**16a**).—A solution of thiobenzoyl isocyanate (0.33 g) in toluene[19,20] (1 ml) was added to a stirred suspension of the 3*H*-indole (**2a**) (0.25 g) in acetonitrile (10 ml). The mixture was stirred at room temperature for 20 h when a further quantity of thiobenzoyl isocyanate (0.28 g) was added. Stirring was continued for 5 h after which the reaction mixture was evaporated to dryness. After chromatography (10% ethyl

**Table.** 1,3,5-Thiadiazino[3,2-*a*:5,4-*a'*]di-indole (**14**)

| Compd. | $R^1$ | $R^2$ | M.p. (°C) | Yield (%) | Analysis (%) Found (calc.) C | H | N | $\nu_{max.}/cm^{-1}$ | $\delta_H$ |
|---|---|---|---|---|---|---|---|---|---|
| (**14b**) | Et | Ph | 137 | 32 | 76.7 | 6.8 | 9.4 | 1 605 | 1.3 (16 H, m), 5.4 (2 H, m), 6.6 (12 H, m), and 8.7 |
| | | | | | (76.5) | (6.6) | (9.6) | 1 575 | (1 H, m) |
| (**14c**) | Me | Bz | 160—161 | 65 | 74.1 | 6.0 | 9.1 | 1 615 | 1.35, 1.50, 1.55 (12 H, 3 × s), 5.12 (1 H, s), 5.3 (1 H, |
| | | | | | (74.2) | (6.0) | (9.3) | 1 495 | s), 7.0 (10 H, m), 8.25 (1 H, m), and 8.7 (1 H, m) |
| (**14d**) | Et | Bz | 140 | 61 | 74.9 | 6.7 | 8.9 | 1 625 | 1.4 (16 H, m), 5.2 (2 H, m), 6.95 (10 H, m), 8.15 (2 H, |
| | | | | | (74.8) | (6.4) | (8.7) | 1 500 | m), and 8.65 (1 H, m) |
| (**14e**) | Me | $CO_2Et$ | 173 | 49 | 68.2 | 6.5 | 10.0 | 1 665 | 1.3 (9 H, m), 1.55 (6 H, s), 4.2 (2 H, q), 5.18 (1 H, s), |
| | | | | | (68.4) | (6.4) | (10.0) | 1 520 | 5.23 (1 H, s), 6.95 (7 H, m), and 8.5 (1 H, m) |
| (**14f**) | Et | $CO_2Et$ | 117 | 56 | 69.5 | 7.2 | 9.7 | 1 665 | 1.3 (19 H, m), 3.86 (2 H, q), 5.3 (2 H, m), 6.9 (7 H, m), |
| | | | | | (69.5) | (6.9) | (9.3) | 1 515 | and 8.3 (1 H, m) |

acetate in hexane) the residue was crystallised from hexane to yield the *title compound* (**16a**) (0.28 g, 53%), m.p. 113—115 °C (Found: C, 69.8; H, 5.4; N, 9.1. $C_{18}H_{16}N_2OS$ requires C, 70.11; H, 5.23; N, 9.08%); $\nu_{max.}$(Nujol) 1 660 $cm^{-1}$ (C=O); $\delta_H(CDCl_3)$ 1.4 (3 H, s), 1.6 (3 H, s), 5.35 (1 H, s), 7.4 (6 H, m), and 8.3 (3 H, m).

Similarly prepared was 10-*ethyl*-9a,10-*dihydro*-10-*methyl*-6-*oxo*-8-*phenyl*[1,3,5]*thiadiazino*[3,2-a]*indole* (**16b**) (49%), m.p. 112—113 °C (from cyclohexane) (Found: C, 70.9; H, 5.5; N, 8.6. $C_{19}H_{18}N_2OS$ requires C, 70.8; H, 5.6; N, 8.7%); $\nu_{max.}$(Nujol) 1 660 $cm^{-1}$ (C=O); $\delta_H(CDCl_3)$ 0.96 (3 H, t), 1.45 (3 H, s), 1.52 (3 H, s), 1.8 (2 H, m), 5.32 and 5.44 (1 H, d), 7.5 (6 H, m), and 8.25 (3 H, m).

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1 This work formed the basis of a communication presented at the 10th International Conference of Heterocyclic Chemistry, Waterloo, Canada, 1985, and is taken from the Honours Degree in Applied Chemistry project thesis (A. P. M.) at Manchester Polytechnic.
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