Cyclisation of Heterocyclic Hydrazones prepared from Dimethyl Acetylenedicarboxylate

By **David J. Le Count** * and (in part) **Alexander T. Greer**, Imperial Chemical Industries Limited, Pharmaceuticals Division, Alderley Park, Macclesfield, Cheshire SK10 4TG

The cyclisation of a number of hydrazones prepared from cyclic aminoguanidines and amidrazones and dimethyl acetylenedicarboxylate has been studied. In many cases conditions have been found for cyclisation to either 1,2,4-triazin-5-ones or 5-hydroxypyrazoles (pyrazolin-5-ones). Individual tautomers of certain products may be isolated in the solid state.

THE reactions of acetylenic carbonyl compounds with hydrazines [1] and guanidines [2,3] have been investigated extensively but the corresponding reactions with aminoguanidines and amidrazones have received less attention. Sasaki [3] prepared the 1,2,4-triazin-5-one (1) from aminoguanidine and dimethyl acetylenedicarboxylate and Wamhoff [4] has investigated the reaction of the cyclic amidrazones (2; X = CH_2, n = 1—4) with dimethyl acetylenedicarboxylate and obtained the 1,2,4-triazin-5-ones (3; X = CH_2, n = 1—4). In this work 2-hydrazinopyridine was found to react exceptionally, the hydroxypyrazole (4; R = 2-pyridyl) being formed. Concurrent with the latter investigation we were studying the reaction of 2-hydrazino-Δ^2-imidazoline with dimethyl acetylenedicarboxylate; our

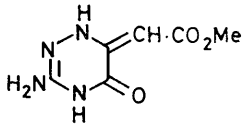
[1] R. Turner, 'Pyrazoles, Pyrazolines, Indazoles, and Condensed Rings,' ed. R. H. Wiley, Interscience, New York, 1967, p. 3; R. Fuks and H. G. Viehe, 'Chemistry of Acetylenes,' ed. H. G. Viehe, Dekker, New York, 1969, p. 556; S. J. Miller and R. Tanaka, 'Selective Organic Transformations,' ed. B. S. Thyagarajan, Interscience, New York, 1970, vol. 1, p. 143.

[2] A. A. Katner and E. A. Ziege, *Chem. Comm.*, 1971, 864.

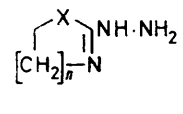
[3] H. Sasaki, H. Sakata, and Y. Iwanami, *J. Chem. Soc. Japan*, 1964, **85**, 704.

[4] M. Brügger, H. Wamhoff, and F. Korte, *Annalen*, 1972, **757**, 100.

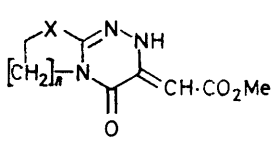
results prompted us to extend our investigations to other cyclic aminoguanidines and amidrazones. Part of this work has been reported briefly elsewhere.[5]



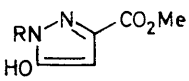
(1)



(2)



(3)



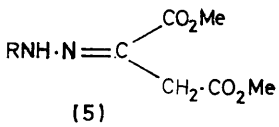
(4)

When a methanolic suspension of 2-hydrazino-Δ^2-imidazoline hydriodide was treated with dimethyl acetylenedicarboxylate the hydrazone (5; R = Δ^2-imidazolin-2-yl) was precipitated in low yield. Surprisingly, the product was isolated not as the salt but as the free base, and an examination of the reaction mother liquors showed that the hydrogen iodide had reacted with the ester to yield dimethyl iodofumarate. The side reaction was prevented by working in water containing triethylamine and a much higher yield of hydrazone was obtained. The product was relatively stable in organic solvents but in warm water it was converted rapidly into the pyrazolin-5-one (6; R = Δ^2-imidazolin-2-yl), $\nu_{max.}$ (KBr) 1721 and 1669 (C=O), 1628 (C=C), and 1565 cm^{-1} (C=N), τ [$(CD_3)_2SO$] 5·1 (olefinic singlet) and 6·25 (singlet) (integral ratio 1 : 7), in agreement with the proposed structure.

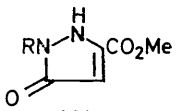
When the reaction was carried out in methanol containing triethylamine the isomeric triazinone (7; X = NH) was formed, $\nu_{max.}$ (KBr) 1732 and 1684 cm^{-1} (C=O). The n.m.r. spectrum [$(CD_3)_2SO$] showed two quartets centred at τ 5·95 and 6·35 and a singlet at τ 6·4, resolved into two singlets upon addition of trifluoroacetic acid. The *N*-methyl analogue (5; R = 1-methyl-Δ^2-imidazolin-2-yl) behaved similarly in that in the presence of triethylamine it cyclised to the triazinone (7; X = NMe). However, it was not possible to prepare the pyrazolin-5-one (6; R = 1-methyl-Δ^2-imidazolin-2-yl) under any conditions studied.

Cyclisation of the hydrazone (5; R = Δ^2-thiazolin-2-yl) proceeded differently in that the triazinone (3; X = S, n = 1) was precipitated from cold methanol–triethylamine. The i.r. absorptions [$\nu_{max.}$ (Nujol) 3150 (NH), 1695 (C=O), 1655 (C=O), and 1584 cm^{-1} (C=C)] compared well with those reported by Wamhoff[4] for (3; X = CH_2, n = 1) but we consider the ester carbonyl group to have the lower of the two carbonyl frequencies, not the higher as proposed by Wamhoff. Thus in warm methanol the triazinone (3; X = S, n = 1) tautomerises to (7; X = S), with carbonyl frequencies (Nujol) at 1735 and 1680 cm^{-1} [*cf.* (7; X = NH)]. This shift correlates well with the difference in ester carbonyl frequencies between compounds (8) (1740) and (9) (1639 cm^{-1}).[6]

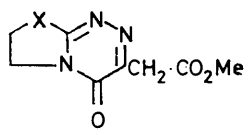
A similar result was obtained with the hydrazone (5; R = phthalazin-1-yl): the exocyclic tautomer (10) was prepared by cyclisation under basic conditions and the endocyclic tautomer (11) by thermal cyclisation, or by thermal tautomerisation of (10).



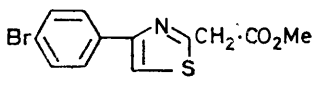
(5)



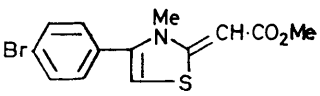
(6)



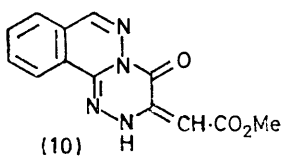
(7)



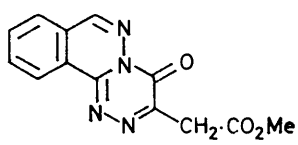
(8)



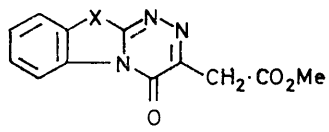
(9)



(10)



(11)



(12)

Thermal cyclisation of the hydrazone (5; R = benzothiazol-2-yl) from 2-hydrazinobenzothiazole was interesting in that the tautomeric forms of the resulting pyrazole were isolable. Recrystallisation of the product from aqueous solvents gave the pyrazolin-5-one (6; R = benzothiazol-2-yl) monohydrate. On heating *in vacuo* at 100° the water was lost and the 5-hydroxypyrazole (4; R = benzothiazol-2-yl) was obtained (ester carbonyl frequency shifted from 1715 to 1745 cm^{-1}).

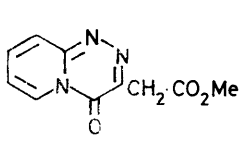
Cyclisation of the hydrazone (5; R = benzothiazol-2-yl) to the triazinone (12; X = S) by the methods previously used proved difficult, the 5-hydroxypyrazole usually being formed. When, however, acetic anhydride was used as solvent the desired product was isolated in good yield, only a minor amount of the *O*-acetyl derivative of (4; R = benzothiazol-2-yl) being formed. This cyclisation method also proved effective with (5; R = 2-pyridyl); we were thus able to prepare the elusive pyrido[2,1-*c*]triazinone (13).

Thermal cyclisation of the hydrazone (5; R = benzimidazol-2-yl) gave the pyrazolin-5-one (6; R = benzimidazol-2-yl) but the structure of the product was not immediately clear from the spectra. The ester

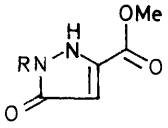
[5] D. J. Le Count and A. T. Greer, *Tetrahedron Letters*, 1973, 2905.

[6] P. J. Taylor, personal communication.

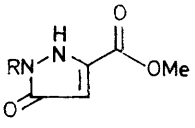
carbonyl frequency (1738 cm^{-1}) suggested that the product existed in the hydroxy-form, as did the n.m.r. signal for the olefinic proton (τ 4·2). The corresponding signals for compounds (4; R = 2-pyridyl) and (4; R = benzothiazol-2-yl) were at τ 3·9 and 3·95, respectively, and for (6; R = Δ^2-imidazolin-2-yl) the signal was at τ 5·1. However a strong band at 1655 cm^{-1} in the i.r. spectrum of the product was outside the range reported for the pyrazole ring system.[7] We consider the explanation to lie in the different stereochemistry of the products. The pyrazolin-5-one (6; R = benzimidazol-2-yl) probably assumes the *s-cis*-conformation (14), with its associated higher ester carbonyl frequency,[8] whereas the pyrazolin-5-one (6; R = Δ^2-imidazolin-2-yl) for example, assumes the *s-trans*-conformation (15). This explanation would also account for the downfield shift of the signal for the olefinic proton in (6; R = benzimidazol-2-yl). Support for this proposal came from the i.r. spectrum of (6; R = benzimidazol-2-yl) in dimethyl sulphoxide, which showed two ester carbonyl bands (1735 and 1719 cm^{-1}).



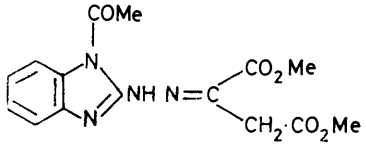
(13)



(14)



(15)



(16)

Surprisingly the hydrazone (5; R = benzimidazol-2-yl) was reluctant to cyclise to (12; X = NH). In methanol and triethylamine only small amounts of the latter were obtained, both at room temperature and at reflux. The main product was the hydroxypyrazole (3; R = benzimidazol-2-yl), obtained as its triethylamine salt, which was surprisingly stable. It could be recovered unchanged from solution and the i.r. spectra of the solid state and of a solution in chloroform were almost identical. Only when the salt was heated above 100° was the triethylamine slowly lost, giving (6; R = benzimidazol-2-yl). Heating the hydrazone (5; R = benzimidazol-2-yl) in acetic anhydride also failed to give the desired product, the amide (16) being obtained. The location of the acetyl group on a benzimidazole nitrogen atom is supported by the downfield shift of the n.m.r. signal for one of the benzenoid protons.

* This compound exhibited polymorphism. Some examples melted at 132° before resolidifying at 165°.

[7] P. E. Gagnon, J. L. Boivin, and R. J. Paquin, *Canad. J. Chem.*, 1953, **31**, 1025; F. G. Baddar, M. F. El-Newaihy, and M. R. Salem, *J. Chem. Soc.* (*C*), 1969, 836.

EXPERIMENTAL

N.m.r. spectra were measured at 60 MHz with tetramethylsilane as internal standard.

Dimethyl 2-(*Δ^2-Imidazolin-2-ylhydrazono*)*succinate* (5; R = Δ^2-imidazolin-2-yl).—Dimethyl acetylenedicarboxylate (4·2 g) was added to a solution of 2-hydrazino-Δ^2-imidazoline hydriodide [9] (6·9 g) and the mixture was stirred vigorously at 0 °C to produce an emulsion. Triethylamine (3 ml) was then added dropwise and stirring was continued for 2 min. The *product* (3·1 g), filtered off and recrystallised from chloroform, had m.p. 165° (resolidifies and remelts at 210°) * (Found: C, 44·6; H, 5·8; N, 22·8. $C_9H_{14}N_4O_4$ requires C, 44·6; H, 5·8; N, 23·15%), $\nu_{max.}$ (KBr) 1721 (C=O) and 1696 cm^{-1} (C=O), τ [$(CD_3)_2SO$] 6·30 (s), 6·39 (s), 6·42 (s), and 6·51 (s).

Similarly prepared were (a) *dimethyl* 2-(*1-methyl-Δ^2-imidazolin-2-ylhydrazono*)*succinate* (5; R = 1-methyl-Δ^2-imidazolin-2-yl), m.p. 88—90° (from propan-2-ol) (Found: C, 46·5; H, 6·1; N, 21·7. $C_{10}H_{16}N_4O_4$ requires C, 46·9; H, 6·2; N, 21·9%), $\nu_{max.}$ (KBr) 1731 (C=O), 1695 (C=O), and 1605 cm^{-1} (C=N), τ ($CDCl_3$) 6·21 (s), 6·24 (s), 6·37 (s), and 6·40 (s) (12H), and 7·1 (3H, s) [the *2-hydrazino-1-methyl-Δ^2-imidazoline hydriodide*, m.p. 182—184° (from EtOH) used as starting material was prepared [9] from 1-methyl-2-methylthio-Δ^2-imidazoline hydriodide [10] (Found: C, 19·8; H, 4·6; N, 23·1. $C_4H_{10}N_4$,HI requires C, 19·8; H, 4·55; N, 23·15%)]; (b) *dimethyl* 2-(*phthalazin-1-ylhydrazono*)*succinate* (5; R = phthalazin-2-yl), m.p. 160° (from propan-2-ol) (Found: C, 56·0; H, 4·5; N, 18·4. $C_{14}H_{14}N_4O_4$ requires C, 56·0; H, 4·5; N, 18·4%), $\nu_{max.}$ (KBr) 1730 (C=O) and 1700 cm^{-1} (C=O), τ [$(CD_3)_2SO$] 1·6—2·08 (5H, m), 6·05 (2H, s), 6·14 (3H, s), and 6·36 (3H, s).

Methyl 1-(*Δ^2-Imidazolin-2-yl*)-5-*oxo*-*Δ^3-pyrazoline*-3-*carboxylate* (6; R = Δ^2-imidazolin-2-yl).—A solution of the hydrazone (5; R = Δ^2-imidazolin-2-yl) (1 g) in water (25 ml) was heated under reflux for 1 h, then concentrated to *ca.* 10 ml, and cooled to yield the *product* (0·7 g), m.p. 265° (Found: C, 46·0; H, 4·7; N, 26·6. $C_8H_{10}N_4O_3$ requires C, 45·7; H, 4·8; N, 26·65%).

Methyl 2-(*4,6,7,8-Tetrahydro-4-oxoimidazo*[2,1-c][1,2,4]-*triazin-3-yl*)*acetate* (7; X = NH).—A solution of 2-hydrazino-Δ^2-imidazoline hydriodide (2·3 g), dimethyl acetylenedicarboxylate (1·4 g), and triethylamine (1 ml) in methanol (15 ml) was kept at room temperature for 24 h. The *product* (0·8 g), collected and recrystallised from propan-2-ol, had m.p. 202° (Found: C, 45·6; H, 4·8; N, 26·4. $C_8H_{10}N_7O_3$ requires C, 45·7; H, 4·8; N, 26·6%).

Methyl 2-(*4,6,7,8-Tetrahydro-8-methyl-4-oxoimidazo*[2,1-c]-[1,2,4]*triazin-3-yl*)*acetate* (7; R = NMe).—A solution of the hydrazone (5; R = 1-methyl-Δ^2-imidazolin-2-yl) (1 g) in methanol (10 ml) containing triethylamine (1 ml) was heated under reflux for 5 h, then evaporated to dryness. The *product* (0·78 g), crystallised from ethyl acetate–light petroleum, had m.p. 98—99° (Found: C, 48·3; H, 5·3; N, 24·8. $C_9H_{12}N_4O_3$ requires C, 48·2; H, 5·35; N, 25·0%), $\nu_{max.}$ (KBr) 1730 (C=O), 1682 (C=O), and 1610 cm^{-1} (C=N), τ ($CDCl_3$) 5·77 (m), 6·25 (m), 6·20 (s), 6·24 (s), and 6·88 (s).

[8] A. R. Katritzky and P. J. Taylor, 'Physical Methods in Heterocyclic Chemistry,' ed. A. R. Katritzky, Academic Press, New York and London, vol. 4, p. 417.

[9] W. G. Finnegan, R. A. Henry, and E. Lieber, *J. Org. Chem.*, 1953, **18**, 779.

[10] A. F. McKay and M. E. Kreling, *J. Org. Chem.*, 1957, **22**, 1581.

Dimethyl 2-(4,5-*Dihydrothiazol*-2-*ylhydrazono*)*succinate* (5; R = 4,5-dihydrothiazol-2-yl).—An ice-cold solution of 2-hydrazino-4,5-dihydrothiazole hydrobromide [11] (4 g) in water (50 ml) containing sodium hydroxide (0·8 g) was treated dropwise with dimethyl acetylenedicarboxylate (2·8 g) and the mixture was stirred until the oil which separated had crystallised. Filtration and recrystallisation of the solid from ethyl acetate–light petroleum afforded the *product* (3·5 g), m.p. 85—87° (Found: C, 42·0; H, 5·2; N, 16·1. $C_9H_{13}N_3O_4S$ requires C, 41·7; H, 5·0; N, 16·2%), $\nu_{max.}$ (KBr) 1717 (C=O), 1705 (C=O), and 1603 cm^{-1} (C=N), τ [$(CD_3)_2SO$] 6·28 (s), 6·30 (s), 6·42 (s), 6·32 (m), and 6·71 (m).

Methyl 2-(3,4,6,7-*Tetrahydro*-4-*oxo*-2H-*thiazolo*[2,3-c]-[1,2,4]*triazin*-3-*ylidene*)*acetate* (3; X = S, *n* = 1).—The foregoing product (2·5 g) was stirred in methanol (25 ml) containing triethylamine (2·5 ml) for 0·75 h. The *product* (1·8 g), filtered off and recrystallised rapidly from cold chloroform–light petroleum, had m.p. 153—156° (Found: C, 42·2; H, 4·0; N, 18·3. $C_8H_9N_3O_3S$ requires C, 42·3; H, 4·0; N, 18·5%).

Methyl 2-(6,7-*Dihydro*-4-*oxo*-4H-*thiazolo*[2,3-c][1,2,4]*triazin*-3-*yl*)*acetate* (7; X = S).—A solution of compound (3; X = S, *n* = 1) (1 g) in methanol (50 ml) was heated under reflux for 1 h and evaporated to dryness to give a *solid* (1 g), m.p. 121—123° (Found: C, 42·3; H, 4·0; N, 18·3. $C_8H_9N_3O_3S$ requires C, 42·3; H, 4·0; N, 18·5%), τ [$(CD_3)_2SO$] 5·62 (m), 6·50 (m), 6·23 (s), and 6·38 (s).

Methyl 2-(3,4-*Dihydro*-4-*oxo*-2H-[1,2,4]*triazino*[3,4-a]-*phthalazin*-3-*ylidine*)*acetate* (10).—A solution of the hydrazone (5; R = phthalazin-1-yl) (1·9 g) in methanol (100 ml) containing triethylamine (5 ml) was heated under reflux for 0·5 h; the *product* (1·3 g) was filtered off; m.p. 217—218° (Found: C, 57·9; H, 3·8; N, 20·5. $C_{13}H_{10}N_4O_3$ requires C, 57·8; H, 3·7; N, 20·7%), $\nu_{max.}$ (Nujol) 3250 (N–H), 1712 (C=O), and 1650 cm^{-1} (C=O).

Methyl 2-(4-*Oxo*-4H-[1,2,4]*triazino*[3,4-a]*phthalazin*-3-*yl*)-*acetate* (11).—(*a*) The hydrazone (5; R = phthalazin-1-yl) (0·6 g) was placed in an oil-bath at 160° and the temperature was raised to 180° during 10 min. After cooling, the resulting *solid* was recrystallised frim methanol–propan-2-ol; yield 0·3 g, m.p. 217—218° (Found: C, 57·8; H, 3·7; N, 20·8. $C_{13}H_{10}N_4O_3$ requires C, 57·8; H, 3·7; N, 20·7%), $\nu_{max.}$ (Nujol) 1738 (C=O) and 1690 cm^{-1} (C=O), τ [$(CD_3)_2SO$] 0·74—1·9 (5H, m), 5·95 (2H, s), and 6·27 (3H, s).

(*b*). A stirred suspension of (5; R = phthalazin-1-yl) (2 g) in water (100 ml) was heated under reflux for 30 h. The resulting solution was cooled and the product, identical with the product from method (*a*), was collected (1·0 g.).

(*c*) A solution of compound (10) (1·9 g) in dimethyl sulphoxide (75 ml) was heated on a steam-bath for 2 h, then diluted with water (750 ml.). The suspension was filtered to give a solid (1·4 g), identical with the products prepared by methods (*a*) and (*b*).

Dimethyl 2-(*Benzothiazol*-2-*ylhydrazono*)*succinate* (5; R = benzothiazol-2-yl).—A stirred, ice-cold suspension of 2-hydrazinobenzothiazole [12] (3·3 g) in ethanol (20 ml) was treated dropwise with dimethyl acetylenedicarboxylate (2·85 g) in ethanol (5 ml) and stirring was continued for a further 3 h. The suspension was then filtered to yield the yellow *product*, m.p. 162° (Found: C, 50·7; H, 4·4; N, 13·5. $C_{13}H_{13}N_3O_4S$ requires C, 50·8; H, 4·2; N, 13·7%), $\nu_{max.}$ (KBr) 1738 (C=O) and 1712 cm^{-1} (C=O), τ [$(CD_3)_2SO$] 2·1—2·55 (4H, m), 6·2 (5H, s), and 6·35 (3H, s).

Similarly prepared was *dimethyl* 2-(*benzimidazol*-2-*ylhydrazono*)*succinate* (5; R = benzimidazol-2-yl), m.p. 260° (from ethyl acetate–light petroleum), from 2-hydrazinobenzimidazole [12] (Found: C, 51·1; H, 5·2; N, 18·0. $C_{13}H_{14}N_4O_4,H_2O$ requires C, 50·7; H, 5·2; N, 18·2%), $\nu_{max.}$ (KBr) 1734 (C=O) and 1708 cm^{-1} (C=O), τ [$(CD_3)_2SO$] 2·5—3·1 (4H, m), 6·12 (5H, s), and 6·30 (3H, s).

Drying the hydrazone (5; R = benzimidazol-2-yl) *in vacuo* at 110° (P_2O_5) for 5 h gave *methyl* 1-(*benzimidazol*-2-*yl*)-5-*oxo*-Δ^3-*pyrazolin*-3-*carboxylate* (6; R = benzimidazol-2-yl), m.p. 264° (Found: C, 55·6; H, 4·0; N, 21·8. $C_{12}H_{10}N_4O_3$ requires C, 55·8; H, 3·9; N, 21·7%), $\nu_{max.}$ (KBr) 3230 (N–H), 1738 (C=O), and 1655 cm^{-1} (C=O), τ [$(CD_3)_2SO$] 2·2—2·75 (4H, m), 4·2 (1H, s), and 6·1 (3H, s).

Thermal Cyclisation of the Hydrazone (5; R = benzothiazol-2-yl).—The hydrazone (1 g) was heated at 175° (oil-bath) until effervescence ceased. After the resulting solid had cooled it was recrystallised from aqueous ethanol to yield *methyl* 1-(*benzothiazol*-2-*yl*)-5-*oxo*-Δ^3-*pyrazolin*-3-*carboxylate monohydrate* (6; R = benzothiazol-2-yl) (0·6 g), m.p. 161° (Found: C, 48·9; H, 3·7; N, 14·3. $C_{12}H_9N_3O_3S,H_2O$ requires C, 49·2; H, 3·7; N, 14·3%), $\nu_{max.}$ (Nujol) 3500, 3300, 2500 (H-bonded H_2O), 1715 (C=O), 1605, and 1580 cm^{-1}, τ [$(CD_3)_2SO$] 1·7—2·75 (4H, m), 3·95 (1H, s), and 6·08 (3H, s).

The pyrazolinone monohydrate was heated *in vacuo* at 110° (P_2O_5) for 3 h to yield *methyl* 1-(*benzothiazol*-2-*yl*)-5-*hydroxypyrazole*-3-*carboxylate* (4; R = benzothiazol-2-yl), m.p. 161° (Found: C, 52·7; H, 3·3; N, 15·3. $C_{12}H_9N_3O_3S$ requires C, 52·4; H, 3·6; N, 15·3%), $\nu_{max.}$ (KBr) 1745 (C=O) and 1620 cm^{-1} (C=N). Both compounds showed $\nu_{max.}$ ($CHCl_3$) 1730 (C=O) and 1630 cm^{-1} (C=N).

Methyl 2-(4-*Oxo*-4H-[1,2,4]*triazolo*[3,4-b]*benzothiazol*-3-*yl*)-*acetate* (12; X = S).—A solution of the hydrazone (5; R = benzothiazol-2-yl) (10 g) in acetic anhydride (50 ml) was heated under reflux for 1·75 h, then cooled, and the *product* (5·8 g) was filtered off; m.p. 223° (from chloroform–petroleum) (Found: C, 52·0; H, 3·4; N, 15·1. $C_{12}H_9N_3O_3S$ requires C, 52·4; H, 3·6; N, 15·3%), $\nu_{max.}$ (KBr) 1725 (C=O) and 1680 cm^{-1} (C=O), $\nu_{max.}$ ($CHCl_3$) 1740 and 1690 cm^{-1}, τ ($CDCl_3$) 1·1 (1H, m), 2·45 (3H, m), 6·0 (2H, s), and 6·3 (3H, s).

The mother liquors were evaporated to dryness and the residue was washed with hot methanol. The insoluble material was recrystallised from chloroform–petroleum to yield *methyl* 5-*acetoxy*-1-(*benzothiazol*-2-*yl*)*pyrazole*-3-*carboxylate* (163 mg), m.p. 172—174° (Found: C, 52·9; H, 3·6; N, 13·5. $C_{14}H_{11}N_3O_4S$ requires C, 53·0; H, 3·5; N, 13·2%), $\nu_{max.}$ (KBr) 1780 (C=O) and 1720 cm^{-1} (C=O), τ ($CDCl_3$) 2·0—2·8 (4H, m), 3·88 (1H, s), 6·14 (3H, s), and 7·5 (3H, s).

Acetylation of the Pyrazolinone (6; R = benzothiazol-2-yl) *Hydrate*.—A solution of the hydrate (3·1 g) in acetic anhydride (15 ml) was heated under reflux for 2·5 h, then allowed to cool to room temperature. The crystals of methyl 5-acetoxy-1-(benzothiazol-2-yl)pyrazole-3-carboxylate, identical with those just described, were filtered off.

Methyl 2-(4-*Oxo*-4H-*pyrido*[2,1-c][1,2,4]*triazin*-3-*yl*)*acetate* (13).—A mixture of dimethyl 2-(2-pyridylhydrazono)-succinate [5] (7 g) and acetic anhydride (25 ml) was heated on a steam-bath for 2 h. The resulting purple solution was evaporated to dryness, methanol (10 ml) was added, and the suspension was cooled to *ca.* −15° and filtered. The crystals were washed with ice-cold ethyl acetate. Recrystallisation from methanol yielded the *product*

[11] T. P. Johnston, C. R. Stringfellow, and A. Gallagher, *J. Org. Chem.*, 1965, **30**, 2073.
[12] B.P. 2,073,600/1937.

(2·5 g), m.p. 171—173° (Found: C, 54·7; H, 4·3; N, 18·8. $C_{10}H_9N_3O_3$ requires C, 54·8; H, 4·1; N, 19·2%), $\nu_{max.}$ (KBr) 1735 (C=O), 1682 (C=O), 1630 (C=N), and 1540 cm^{-1} (C=N), τ ($CDCl_3$) 1·25 (1H, d), 2·21 (1H, s), 2·28 (1H, s), 2·8 (1H, m)), 5·9 (2H, s), and 6·26 (3H, s).

Cyclisation of Dimethyl 3-(*Benzimidazol-2-ylhydrazono*)-*succinate* (5; R = benzimidazol-2-yl) *with Triethylamine.*—A solution of the hydrazone (1·5 g) in methanol (15 ml) containing triethylamine (1·5 ml) was heated under reflux for 2·5 h, cooled, and filtered. The crystals (0·3 g) were recrystallised from aqueous dimethylformamide to yield *methyl* 2-(4,10-*Dihydro*-4-*oxo*[1,2,4]*triazino*[4,3-a]*benzimidazol*-3-*yl*)*acetate* (12; X = NH), m.p. 286° (Found: C, 55·5; H, 3·9; N, 21·4. $C_{12}H_{10}N_4O_3$ requires C, 55·8; H, 3·9; N, 21·7%), $\nu_{max.}$ (KBr) 1740 (C=O) and 1693 cm^{-1} (C=O), τ [$(CD_3)_2SO$] 1·65—2·9 (4H, m), 6·15 (2H, s), and 6·34 (3H, s).

The mother liquor from the filtration was evaporated to dryness and the residue was recrystallised from chloroform–light petroleum to give *methyl* 1-(*benzimidazol-2-yl*)-5-*hydroxypyrazole*-3-*carboxylate triethylamine salt* (620 mg), m.p. 264° (Found: C, 59·8; H, 6·9; N, 19·4. $C_{18}H_{19}N_5O_3$ requires C, 60·2; H, 7·0; N, 19·5%), $\nu_{max.}$ (KBr) 1725 (C=O) and 1612 cm^{-1} (C=N), $\nu_{max.}$ ($CHCl_3$) 1718 (C=O) and 1615 cm^{-1} (C=N), τ [$(CD_3)_2SO$] 1·65—2·9 (m), 4·71 (1H, s), 6·18 (3H, s), 6·72 (6H, q), and 8·88 (9H, t).

Acetylation of the Hydrazone (5; R = benzimidazol-2-yl).—A solution of the hydrazone (2·85 g) in acetic anhydride (100 ml) was heated on a steam-bath for 2 h. Crystals, which separated on cooling, were collected to afford *dimethyl* 2-(1-*acetylbenzimidazol*-2-*ylhydrazono*)*succinate* (16) (2·05 g), m.p. 177—178° (Found: C, 52·5; H, 4·9; N, 17·1. $C_{13}H_{16}N_4O_5$,0·25H_2O requires C, 53·5; H, 4·9; N, 16·7%), $\nu_{max.}$ (KBr) 1722 (C=O), 1712 (C=O), and 1700 cm^{-1} (C=O), τ 1·85 (1H, m), 2·78 (3H, m), 6·16 (s), 6·22 (s), and 6·39 (s) (8H), and 7·28 (3H, s).

We thank Mr. P. J. Taylor for discussions on the i.r. spectra and the Management of Rhein Pharma Arzneimittelwerk Plankstadt, nr. Heidelberg, in whose laboratories this work was initiated, for facilities.

[3/1698 *Received*, 10*th August*, 1973]