Addition Reactions of Heterocyclic Compounds. Part LVIII.[1] Reactions of Nitrogenous Heterocycles with Acetylacetylene

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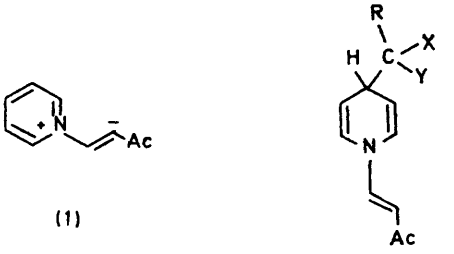
Simple pyridines react with acetylacetylene and proton donors at −20° to give high yields of (*E*)-1-(3-oxobut-1-enyl)-1.4-dihydropyridines. while in the absence of such donors low yields of other compounds are isolated. Acetylacetylene reacts with 4-aminopyridine to give 4-[(*E*)-3-oxobut-1-enylimino]-1.4-dihydropyridine, imidazoles give the 1-[(*E*)-3-oxobut-1-enyl] derivatives, methyl 2-pyridylacetate yields quinolizines, and pyrrole the 2-[(*E*)-3-oxobut-1-enyl] derivative and 4.6-diacetylindole. The structures of these products and of minor components, are deduced mainly from their n.m.r. spectra.

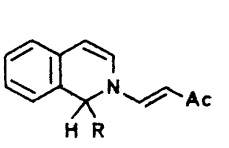
ALTHOUGH many reactions between acetylene-mono- and -di-carboxylic esters and nitrogen-containing heterocycles in the presence and absence of proton donors have been investigated,[2,3] there are very few reports of the use of other activated acetylenes in such reactions. Acetylacetylene, readily available [4] from the oxidation of but-3-yn-2-ol, has been used in typical Diels–Alder reactions,[5] and with acetylene itself, acetylcyclo-octatetraene is obtained.[6] The carbonyl group undergoes photocyclisations with isobutene to give ethynyloxetans,[7] and a number of Michael-type additions to the triple bond have been reported, including the formation of (*E*)-1-(3-oxobut-1-enyl)benzotriazole from benzotriazole,[8] and of 2-amino-4-methylpyrimidine from guanidine [9] by addition and cyclisation. It was therefore of interest to explore the reactions of acetylacetylene with heterocycles, and to see if the activated methyl group would become involved.

Acetylacetylene reacted with pyridines in the presence of proton donors at 0° to give strongly coloured tars, from which no crystalline material could be extracted, but at −20° 1 : 1 : 1 molar adducts (2)—(12), involving nitromethane or other compounds possessing active

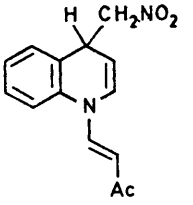


(1)

		R	X	Y
(2)		H	H	NO_2
(3)	3-Me	H	H	NO_2
(4)	3,5-Me_2	H	H	NO_2
(5)		H	Me	NO_2
(6)		Me	Ac	Ac



(7) R = CH_2NO_2
(8) R = $CHAc_2$
(9) R = CHECN
(10) R = $CH(CN)_2$
(11) R = OMe



(12)

E = CO_2Me throughout

hydrogen atoms, could be isolated, sometimes in high yield. These products are presumably formed *via* an

[1] Part LVII, R. M. Acheson and J. Woollard, preceding paper.
[2] R. M. Acheson and M. S. Verlander, *J.C.S. Perkin I*, 1974, 430, and previous papers in the series.
[3] R. M. Acheson, *Adv. Heterocyclic Chem.*, 1963, **1**, 125.
[4] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 1946, 39.
[5] A. A. Petrov and B. V. Turmanova, *Zhur. obschei. Khim.*, 1956, **26**, 2744, and earlier papers.
[6] A. C. Cope and R. M. Pike, *J. Amer. Chem. Soc.*, 1953, **75**, 3220.
[7] M. J. Jorgensen, *Tetrahedron Letters*, 1966, 5811.
[8] S. Hoffmann and E. Mühle, *Z. Chem.*, 1968, **8**, 419.
[9] Soc. Usines Chim. Rhône-Poulenc, B.P. 595,738 (*Chem. Abs.*, 1948, **42**, 3439).

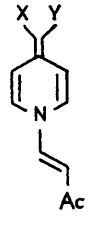
intermediate ion [*e.g.* (1)] abstracting a proton from the donor, followed by combination of the resulting two ions, as reported[1,10] for similar compounds obtained from methyl propiolate. Their n.m.r. spectra (Table 1) all showed AB quartets (J *ca.* 14 Hz) indicating a *trans*-vinyl group, and closely resembled those of their analogues in the propiolate[1,10] series. The spectrum of (9) showed two sets of signals corresponding to the two sets of diastereoisomers. The 1 : 1 : 1 adduct expected from 2-methylpyridine and nitromethane could not be detected, but the oxidation product (14) was obtained. No attempt had been made to exclude air from the reaction vessels and compound (16) was obtained along with (5) from pyridine, the ester, and nitroethane. 4-Nitroso-*NN*-dimethylaniline oxidised compounds (2) and (3) to (13) and (15) respectively.

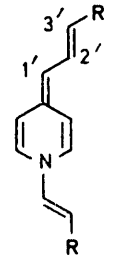
TABLE 1

^{1}H N.m.r. spectra (60 MHz; τ values; J in Hz) for solutions in $CDCl_3$ with tetramethylsilane as internal standard

Compound	Proton resonances	CH_3CO
(2)	2,6-H_2, 3·61d; 3,5-H_2, 5·06q; 4-H, 6·12m; 4-CH_2, 5·68d, J 6·3; $J_{2,3}$ 7·8; $J_{3,4}$ 3·9; H_a, 2·85d; H_b, 4·44d; J 13·5	7·84
(6)	2,6-H_2, 3·69d; 3,5-H_2, 5·32q; 4-H, 5·82t; $J_{2,3}$ 8·2; $J_{3,4}$ 3·7; H_a 2·87d; H_b, 4·51d, J 13·8; 4-CMe, 8·66; 4-CAc_2, 7·92	7·85
(9)	Ar-H_4, 2·7—2·95m; 1-H, 4·48br, d; 4-H, 4·00d; $J_{1,3}$ 1·0; $J_{3,4}$ 7·5 set (a): 1-C*H*, 6·15d, J 6·0; 1-CE, 6·39; 3-H, 5·50q; H_a, 2·56d; H_b, 4·32d, J 14·0 set (b): 1-C*H*, 6·05d, J 6·2; 1-CE, 6·24; 3-H, 3·58q; H_a, 2·65d; H_b, 4·39d, J 13·9	7·82
(11)	Ar-H_4, 2·7m; 1-H, 3·90br; 1-OMe, 7·02; 3-H, 3·35d;[a] 4-H, 4·06d; $J_{3,4}$ 7·5; H_a, 2·43d; H_b, 4·16, J 13·8	7·79
(14)[b]	2-Me, 7·03; 3,5-H_2 1·82m; 6-H, 1·07d; 4-CH_2, 4·12; $J_{5,6}$ 7·5; H_a, 1·69d; H_b, 2·86d, J 13·8	
(17)[c]	2,6-H_2, 2·82d; 3,5-H_2, 2·19d; $J_{2,3}$ 8·1; H_a, 2·21d; H_b, 3·55d, J 14·5; 4-CAc_2, 7·82	7·76
(18)[d]	2,6-H_2, 2·64m; 3-H, 3·16d;[a] 5-H, 3·77d;[a] $J_{2,3}$ 8; H_a, 2·30d; H_b, 3·75d, J 14·5; 1′-H, 4·34d, J 12; 2′-H, 2·33q; 3′-H, 4·12d, J 15	7·80, 7·80
(18)[b]	2,6-H_2, 1·08d; 3,5-H_2, 1·87d; $J_{2,3}$ 7·2; H_a, 1·69d; H_b, 2·76d; J 14·5; 1′-H, 3·20d, J 15·6; 2′-H, 2·62;[e] 3′-H_2, 6·18d, J 6·6	7·38, 7·56
(20)[d]	Ar-H_3, 3-H, 2·2—2·7m; 4-H, 3·29d; 8-H, 1·54d;[a] $J_{3,4}$ 7·8; $J_{7,8}$ 8; H_a 1·34d; H_b, 3·69d, J 15·1	7·59
(21)	Ar-H_4, 2·4—3·0m; 2-Me, 8·11; 2-CC*H*, 7·28; 4-H, 2·58; 6-H, 3·65d; 7-H, 4·27d; $J_{6,7}$ 7·8; 11b-H, 3·43	7·71
(23)	1-H, 3·37; 4-H, 1·52; 6-H, 2·30q; 7-H, 3·4m; 8,9-H_2, 1·96m; $J_{6,7}$ 9·6; $J_{6,8}$ 1·0	7·23
(25)	1-E, 6·23; 2-H, 2·06d; 4-H, 4·06q;[a] 4-CH_2, 6·90q, 7·75q, J 18; 6-H, 2·05d; 7-H, 3·31;[e] 8-H, 2·58m; 9-H, 1·29d,[a] $J_{2,4}$ 1·0; $J_{a,b}$ 9·6; $J_{a,c}$ 2·4; $J_{6,7}$ 6·6; $J_{7,8}$ 6·6; $J_{8,9}$ 9	7·73, 8·03
(25)[b]	1-CO_2Me, 5·90; 2-H, 1·47; 4-H, 3·52br, d; 4-CH_2, 6·33q, 7·05q; 6-H, 1·05d; 7-H, 2·25;[e] 8-H, 1·62d; 9-H, 1·17d; $J_{a,b}$ 8·4; $J_{a,c}$ 2, $J_{b,c}$ 18; $J_{6,7}$ 6; $J_{6,8}$ 2; $J_{7,8}$ 6·6; $J_{8,9}$ 6	7·55, 7·72
(29)	1-E, 6·24; 2-H, 2·68; 4-H, 4·46q; 4-CH_2, 6·80q, 7·70q, $J_{b,c}$ 18·3; 6-H, 2·26q; 7-H, 3·42;[e] 8-H, 2·68m; 9-H, 1·33q; $J_{a,b}$ 9; $J_{a,c}$ 2·1; $J_{6,7}$ 6·6; $J_{6,8}$ 1·2; $J_{7,8}$ 6·6; $J_{7,9}$ 1·5; $J_{8,9}$ 9·0; vinyl H_a, 2·78d; vinyl-H_b, 4·20d, J 16·1	7·76, 7·99
(30)[c]	2,6-H_2, 1·67d;[a] 3,5-H_2, 2·93d;[a] $J_{2,3}$ 5·1; NH, 0·0br; H_a, 2·03d; H_b, 4·40d, J 12·7	7·82
(31)[f]	Ar-H_4, 2·1—2·7m; 2-H, 0·70; H_a, 3·05d; H_b, 4·02d, J 10·4	7·70
(32)	Ar-H_4, 2·1—2·7m; 2-H, 1·79; H_a, 1·93d; H_b, 3·32d, J 14·7	7·64
(33)	2-H, 2·18br; 4-H, 2·75m; 5-H, 2·83br; H_a, 2·18d; H_b, 3·63d, J 14·7	7·69
(35)	1-H, 0·45br; 3-H, 3·45m, Σ J 6·6; 4-H, 3·77m, Σ J 9; 5-H, 3·05m, Σ J 6·3; H_a, 2·58d; H_b, 3·60d; J 15·7	7·72
(36)	1-H, −0·5br; 2-H, 2·76m; 3-H, 3·57t, J 3·0; 5, 7-H_2, 2·28	7·29, 7·29
(A)	4-H, 1·66d;[g] 6-H, 1·87d;[g] $J_{4,6}$ 1·6; 1-CO_2Me 6·09; 2-Me, 7·42[h]	7·39, 7·41[h]

[a] With further splitting. [b] Solvent, trifluoroacetic acid. [c] Solvent, [$^2H_6$]dimethyl sulphoxide. [d] Measured at 100 MHz. [e] Six lines. [f] As a mixture with (32). [g] Assignments could be interchanged. [h] As for *g*. A = Methyl 3,5-diacetyl-2-methylbenzoate.





		X	Y
(13)		H	NO_2
(14)	2-Me	H	NO_2
(15)	3-Me	H	NO_2
(16)		Me	NO_2
(17)		Ac	Ac

(18) R = Ac
(19) R = E

The n.m.r. spectrum of the pyridine (14) in [$^2H_6$]dimethyl sulphoxide showed the presence of both geometrical isomers, but compound (15) was too insoluble for the spectrum to be recorded. Trifluoroacetic acid protonated both compounds to give the expected pyridinium salt in each case.

Comparison of the n.m.r. spectrum of the quinoline adduct (12) with those of other quinolines,[11] and the fact that the coupling constant[11-13] for the olefinic heterocyclic protons (8 Hz) is in agreement with a 1,4- but not a 1,2-dihydro-structure, shows that the nitromethyl anion added to position 4 as for other quinolinium derivatives.[12,13]

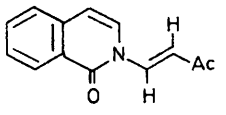
The only isolable product from the reaction between 4-methylpyridine, acetylacetylene, and nitromethane was the dihydropyridine (18), whose spectra closely

[10] R. M. Acheson and M. S. Verlander, *J. Chem. Soc.* (*C*), 1969, 2311.
[11] J. D. Baty, G. Jones, and C. Moore, *J. Org. Chem.*, 1969, **34**, 3295.
[12] H. Albrecht and F. Kröhnke, *Annalen*, 1968, **717**, 96.
[13] R. Branley and M. D. Johnson, *J. Chem. Soc.*, 1965, 1372.

resembled those of the corresponding compound (19) from methyl propiolate,[14] except in acidified methanol. In trifluoroacetic acid the n.m.r. spectra of compounds (18) and (19) showed apparent complete protonation at position 3'. 3,5-Dimethylpyridine with the acetylene and acetylacetone gave an unstable colourless solid which yielded only 1,3,5-triacetylbenzene on attempted purification. This product was also obtained from 3-methylpyridine with methyl acetoacetate, but in addition some methyl 3,5-diacetyl-2-methylbenzoate was formed and identified from its spectra; a similar compound is formed in reactions of ethyl propiolate.[15] Isoquinoline with methanol and the acetylene gave an excellent yield of the dihydro-derivative (11), but corresponding compounds from the alkylpyridines were not isolable.

In dry ether, in the absence of proton donors, acetylacetylene with 3,5-dimethylpyridine gave only 1,3,5-triacetylbenzene which had been obtained previously from the acetylene with triethylamine.[16]

With isoquinoline in acetonitrile, which is not sufficiently acidic to provide a proton under these conditions, a low yield of the isoquinoline (20) was obtained and identified from its n.m.r. spectrum and comparison of this with that of 2-allylisoquinolin-1(2*H*)-one.[17] Traces of water, and aerial oxidation could account for its formation from the expected intermediate zwitterion [*cf.* (1)]. With ether as solvent the product was the oxazinoisoquinoline (21), presumably formed from the zwitterion by cycloaddition to the carbonyl function of the acetylene; a similar sequence gives the oxazinophenanthridine (22).[18]



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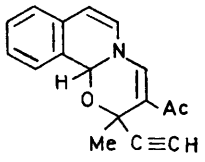

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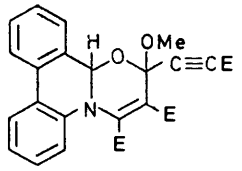
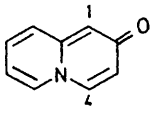
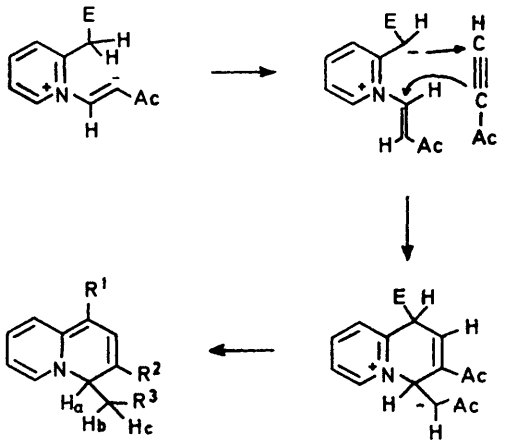


(22)



(23) 3-Ac
(24) 3,4-E_2

Acetylacetylene with methyl 2-pyridylacetate in ether gave compounds (23) and (25). The quinolizone (23) could be formed [19] in the same way as (24), and these compounds had similar n.m.r. spectra except that (23) lacked a low-field 6-proton. The 4*H*-quinolizine (25) could be formed as shown in Scheme 1, and was unaffected by 4-nitroso-*NN*-dimethylaniline in boiling methanol. The 4*H*-quinolizine (26) was the only product from 1-(2-pyridyl)butan-2-one. The n.m.r. spectra for



(25) R^1 = E, R^2 = R^3 = Ac
(26) R^1 = CO·Et, R^2 = R^3 = Ac
(27) R^1 = R^2 = R^3 = E

SCHEME 1

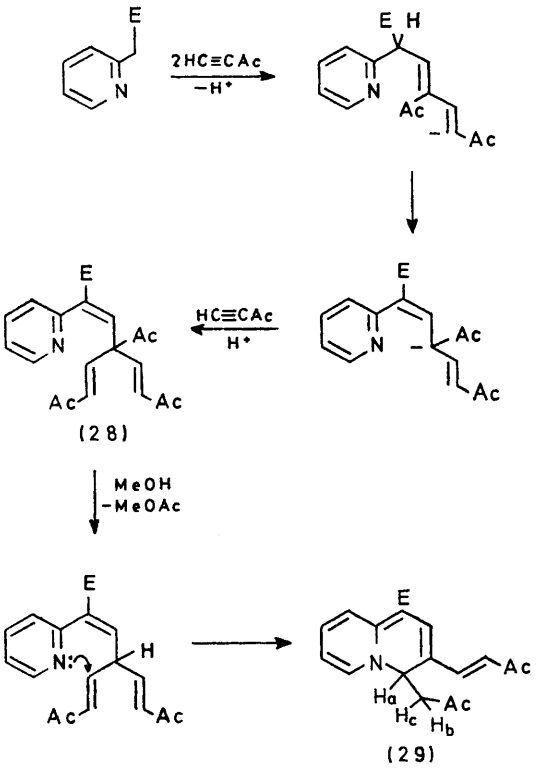
compounds (25)—(27) [20] are closely similar and indicate the structures of the first two compounds, and their u.v. spectra resemble that of tetramethyl 4*H*-quinolizine-1,2,3,4-tetracarboxylate.[21] Reaction between the acetylene and methyl 2-pyridylacetate in methanol gave compounds (25) and (29); a possible route to (29) is indicated in Scheme 2, the intermediate triketone (28) undergoing a reverse Claisen reaction.

4-Aminopyridine with the acetylene gave a 1 : 1 molar adduct, which showed a broad N–H absorption [22] in the i.r., including maxima at 3320, 3270, 3260, and 3170 cm^{-1}, and an A_2B_2 system, and an AX system with J 12·6 Hz in its n.m.r. spectrum. These data are consistent with structure (30), for a greater coupling constant would have been expected of a *trans*-vinyl group attached to a ring nitrogen atom.[23]

Since the stereochemistry of the addition of secondary amines to triple bonds is solvent-dependent,[24,25] it was hoped that benzimidazole with acetylacetylene in benzene would produce the *cis*-adduct (31) instead of the previously reported *trans*-isomer (32).[8] The n.m.r. spectrum of the product showed that some (31) was formed, but it isomerised faster than it could be isolated. In toluene both imidazole and 2-methylimidazole gave the *trans*-adducts (33) and (34) exclusively, the latter existing in two crystalline forms.

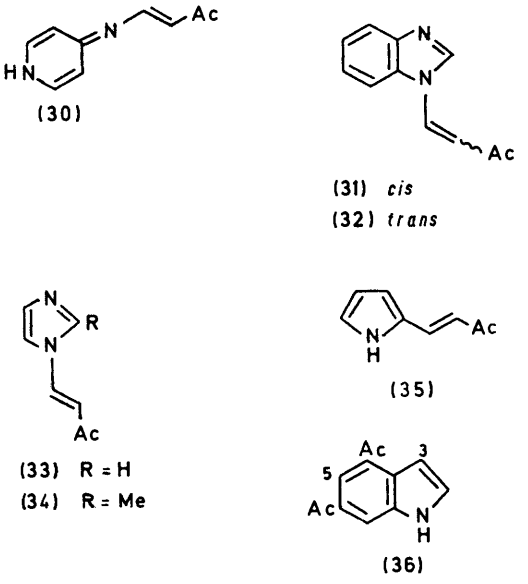
[14] R. M. Acheson and D. A. Robinson, *J. Chem. Soc.* (*C*), 1968, 1633.
[15] V. Boekelheide and J. E. Nottke, *J. Org. Chem.*, 1969, **34**, 4134.
[16] F. Wille and F. Knorr, *Chem. Ber.*, 1952, **85**, 841.
[17] H. Winn and H. Tiekelmann, *J. Org. Chem.*, 1967, **32**, 59.
[18] R. M. Acheson and A. O. Plunkett, *J. Chem. Soc.*, 1962, 3758.
[19] R. M. Acheson and D. A. Robinson, *J. Chem. Soc.* (*C*), 1968, 1629.
[20] J. M. Woollard, D.Phil. Thesis, Oxford University, 1973.
[21] R. M. Acheson and G. A. Taylor, *J. Chem. Soc.*, 1960, 1691.
[22] C. L. Angyal and R. L. Werner, *J. Chem. Soc.*, 1952, 2911.
[23] J. G. Wilson and W. Bottomley, *J. Heterocyclic Chem.*, 1967, **4**, 361.
[24] S. Toppet, E. Van Loock, G. L'abbe, and G. Smets, *Chem. and Ind.*, 1971, 703.
[25] C. H. McMullen and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1966, 1217.

Pyrrole with acetylacetylene yielded 1,3,5-triacetylbenzene, the pyrrole (35) which could be formed by the



SCHEME 2

well known Michael-type additions [26,27] of pyrroles at the 2-position to acetylenes, and 5,7-diacetylindole (36).



The spectra of (36) showed it to be an indole, and comparison of its n.m.r. spectrum with those of indole-carboxylic esters [28] left no doubt concerning the position of the acetyl groups; the 3- and 7-protons are strongly deshielded. The indole could be formed from (35) *via* a Diels–Alder addition and dehydrogenation sequence, for which there are analogies [29] and which we have demonstrated, but other routes to (36) are possible.

In most of the above reactions acetylacetylene behaved like methyl propiolate. However, loss of the acetylenic proton to give a carbanion which would add like the methoxycarbonylacetylide ion from methyl propiolate to various pyridinium type salts, did not occur. No evidence for proton loss from the methyl group was found.

EXPERIMENTAL

The instruments and chromatographic procedures [30] have been described in earlier papers in the series, but toluene was used in place of benzene for chromatography. All analyses for new compounds were within accepted limits for C, H, and N, and are available as Supplementary Publication No. SUP 21192 (10 pp., 1 microfiche),* which also gives details of i.r., u.v., and n.m.r. spectra not described in the paper. Acetylacetylene was prepared as described.[4] N.m.r. spectra are recorded for $CDCl_3$ solutions with tetramethylsilane as internal standard. Peaks $<10\%$ of the base peak are not recorded for mass spectra.

General Procedure for Reactions with Proton Donors.— The proton donor (0·05 mol) and the pyridine (0·02 mol) in ether (35 ml) were cooled to −20°. Acetylacetylene (1·36 g, 0·02 mol) was added, and the mixture kept at −20° for several days. If no solid precipitated, the solvent was evaporated and the residue chromatographed. The results are given in Table 2; for compound (18); *m/e* 230 (15%), 229 (M^+, 92), 228 (18), 215 (15), 214 (100), 212 (11), 186 (28), 147 (14), 146 (25), 118 (20), 117 (29), 90 (13), and 89 (14) (other peaks $<11\%$), *m** 227 (229 ⟶ 228), 200 (229 ⟶ 214), 196·5 (229 ⟶ 212), 162 (214 ⟶ 186), 151 (229 ⟶ 186), and 99·5 (214 ⟶ 146).

1,4-Dihydro-4-nitromethylene-1-[(E)-3-oxobut-1-enyl]pyridine (13). 4-Nitroso-*NN*-dimethylaniline (300 mg, 0·02 mol) in methanol (15 ml) was added to 1,4-dihydro-4-nitromethyl-1-[(*E*)-3-oxobut-1-enyl]pyridine (2) (312 mg, 0·015 mol) in methanol (10 ml). Refluxing for 10 min and followed by cooling precipitated compound (13) (173 mg, 58%), as yellow micro-needles, purple by reflected light, m.p. 214—218°.

1,4-Dihydro-3-methyl-4-nitromethylene-1-[(E)-3-oxobut-1-enyl]pyridine (15). The 3-methyl-4-nitromethyl compound (3) (333 mg, 0·015 mol) similarly gave compound (15) (40 mg, 17%), as yellow crystals, purple by reflected light, m.p. 252—257°; this was too insoluble for satisfactory recrystallisation.

Methyl acetoacetate, acetylacetylene, and 3-methylpyridine. 1,3,5-Triacetylbenzene precipitated from the ether, and chromatography (twice) of the remaining material, gave first *methyl 3,5-diacetyl-2-methylbenzoate*, as needles (from toluene–petroleum), m.p. 78—80°, followed by more

* For details of Supplementary Publications, see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1973, Index issue.

[26] O. Diels and K. Alder, *Annalen*, 1932, **498**, 1.
[27] R. M. Acheson and J. M. Vernon, *J. Chem. Soc.*, 1963, 1008.
[28] R. M. Acheson, *J. Chem. Soc.*, 1965, 2630.
[29] W. E. Noland, W. C. Kuryla, and R. F. Lange, *J. Amer. Chem. Soc.*, 1959, **81**, 6010.
[30] R. M. Acheson, J. M. F. Gagan, and D. R. Harrison, *J. Chem. Soc.* (*C*), 1968, 362.

1,3,5-triacetylbenzene, as needles (from methanol), m.p. 160—162° (lit.,[31] 161—162°), $\nu_{max.}$ 1692, 1589, and 1421 cm^{-1}, τ 1·30 (3H) and 7·32 (9H).

Acetylacetylene with 3,5-dimethylpyridine. (i) Acetylacetylene (4·08 g) was added to 3,5-dimethylpyridine (3·21 g) in ether (20 ml) at room temperature. The mixture became warm and the residue, after removal of the solvent, was dissolved in a minimum of chloroform. Chromatography gave 1,3,5-triacetylbenzene.

(ii) Reaction at −18° gave identical results, and at −60° with boron trifluoride a black mixture was obtained.

TABLE 2

Preparations

Product	Notes	Crystallisation solvent	M.p. (°C)	Appearance	Yield (%)
(2)	*a*		100—106	Yellow-green	54
(3)	*a*		60—65	Yellow	36
(4)		Et_2O–$MeNO_2$	116—118	Yellow needles	44
(5)	*b*		Gum	Red	
(6)		PhMe–petroleum	112—115	Pale yellow	74
(7)	*b,c*	MeOH	97 [d]	Yellow	44
(8)		PhMe–$CHCl_3$	106—109	Colourless	63
(9)	*b,c*	MeOH	111—116	Colourless	77
(10)		MeOH	111—113	Pale yellow	44
(11)		PhMe–trace MeOH	90—93	Colourless	87
(12)	*b,e*	PhMe–$CHCl_3$	112—114·5	Colourless	2
(14)	*b,f*	MeOH–$CHCl_3$	185—187	Violet [g]	2
(16)	*b,f,h*	aq. MeOH	230—235	Purple [i]	
(17)		MeOH	179—181	Yellow needles	4
(18)	*f,j*	MeOH–$CHCl_3$	198—201	Maroon needles	39
(21)	*b*	MeOH–$CHCl_3$	230—232	Colourless	1

[a] Decomposed on storage or attempted crystallisation. [b] Obtained by chromatography of filtrate from *c* or of whole reaction mixture. [c] Filtered off from reaction mixture. [d] Solidified and re-melted at 134—136°. [e] From second yellow band from column. [f] Solidified on trituration with MeOH–EtOH. [g] Yellow under microscope. [h] $EtNO_2$ (25 ml) + Et_2O (15 ml) were used in the synthesis. [i] Orange under microscope. [j] $MeNO_2$ used as solvent.

Acetylacetylene with isoquinoline. (i) Acetylacetylene (1·35 g) was added to isoquinoline (2·58 g) in acetonitrile (25 ml) at room temperature. After 2 days, evaporation and chromatography gave (E)-2-(3-*oxobut*-1-*enyl*)*isoquinolin*-1(2H)-*one* (20) (10 mg), as needles (from methanol), m.p. 149—151°, *m/e* 213 (M^+, 6%), 198 (23), 171 (11), 170 (100), and 128 (13), *m** 135·5 (213 ⟶ 170), 112 (146 ⟶ 128), and 96·5 (170 ⟶ 128).

(ii) With ether as reaction solvent, chromatography gave, from the first fraction, 3-*acetyl*-2-*ethynyl*-2-*methyl*-2H,11bH-[1,3]*oxazino*[2,3-a]*isoquinoline* (21) (11 mg), as white crystals (from methanol–chloroform), m.p. 230—232°, *m/e* 265 (M^+, 56%), 264 (11), 250 (25), 224 (18), 223 (20), 222 (100), 194 (14), 146 (11), 145 (37), 130 (55), and 129 (90), *m** 263 (265 ⟶ 264), 196·5 (250 ⟶ 222), 186·5 (264 ⟶ 222), and 169 (222 ⟶ 194).

Acetylacetylene with methyl 2-pyridylacetate. (i) Acetylacetylene (2·04 g) was added to methyl 2-pyridylacetate (4·53 g) in ether (25 ml) at room temperature. After 8 days 3-*acetylquinolizin*-2-*one* (23) (616 mg, 11%) was filtered off, as yellow needles (from ethyl acetate–methanol), m.p. 190—193°. Evaporation of the filtrate and trituration with methanol gave *methyl* 3-*acetyl*-4-*acetonyl*-4H-*quinolizine*-1-*carboxylate* (25), as orange crystals (from methanol), m.p. 147—149°. The filtrate was chromatographed, and a red band eluted with ether gave more (25) (total yield 1·08 g, 25%).

(ii) The reaction was repeated using methanol (5 ml) and ether (20 ml) as solvent. After 8 days compound (25) (63%) was filtered off and the residue chromatographed. Elution of a red band with ether gave more (25). The mother liquors of this showed a second component (t.l.c.), and chromatography gave *methyl* 4-*acetonyl*-3-[(E)-3-*oxobut*-1-*enyl*]-4H-*quinolizine*-1-*carboxylate* (29) (33 mg), as crimson rhombs (from methanol), m.p. 156—159°, *m/e* 313 (M^+, 12%), 257 (18), 256 (100), and 155 (10), *m** 209 (313 ⟶ 256) and 196 (256 ⟶ 224).

3-*Acetyl*-4-*acetonyl*-1-*propionyl*-4H-*quinolizine* (26). Acetylacetylene (2·04 g) was added to 1-(2-pyridyl)butan-2-one (2·0 g) in ether (25 ml) at room temperature. After 5 days the solvent was evaporated off and trituration with methanol gave the 4H-*quinolizine* (26), as orange rhombs (from methanol), m.p. 175—177°. Chromatography of the filtrate gave 1,3,5-triacetylbenzene (86 mg), and more (26) (total yield 505 mg, 14%).

Acetylacetylene with 4-aminopyridine. The acetylene (1·36 g) and the pyridine (1·88 g) were mixed in ether (25 ml). After 2 days the solvent was evaporated off and the residue chromatographed. Elution with ether gave 1,4-*dihydro*-4-[(E)-3-*oxobut*-1-*enylimino*]*pyridine* (30) (1·05 g, 45%), as white needles (sublimed), m.p. 138—141°, *m/e* 162 (M^+, 65%), 149 (45), 147 (100), and 119 (15) (others <15%), *m** 133·5 (162 ⟶ 147), followed by unchanged 4-aminopyridine (510 mg).

Refluxing acetylacetylene for several hours with 2-acetylpyridine, ethyl 2-pyridinecarboxylate, ethyl (*E*)-3-(2-pyridyl)acrylate, and indole gave small amounts of 1,3,5-triacetylbenzene but no other crystalline compound.

(E)-1-(3-*Oxobut*-1-*enyl*)*benzimidazole* (32).—(i) Benzimidazole (2·36 g) and acetylacetylene (1·36 g) were refluxed for 2 h in dry benzene (10 ml). Cooling gave compound (32) (69%), m.p. 120—122° (from petroleum–toluene) (lit.,[8] for a different procedure, 121—122°). The filtrate was chromatographed and gave sticky solids, the n.m.r. spectra of which showed signals assignable to the *cis*-isomer (31) in addition to those of (32). Attempted isolation of (31) was unsuccessful, for it slowly isomerised to pure (32) in solution.

(ii) Replacing the benzene by methanol gave compound (32) (3·10 g, 84%), and evaporation of the filtrate showed (n.m.r.) no trace of (31).

(E)-1-(3-*Oxobut*-1-*enyl*)*imidazole* (33). Acetylacetylene (1·36 g) was added to imidazole (1·36 g) in dry toluene (10 ml) at room temperature. After 15 min the mixture had become pale red and warm, and all the solid had dissolved. As the mixture cooled to room temperature, compound (33) precipitated (50%), as white needles, m.p. 112—114° (from petroleum–toluene) (lit.,[8] 117—118°).

2-*Methyl*-1-[(E)-3-*oxobut*-1-*enyl*]*imidazole* (34). Acetylacetylene (1·36 g) was warmed with 2-methylimidazole (1·64 g) in benzene (10 ml) until a vigorous reaction began. As the mixture cooled the imidazole (34) precipitated and afforded crystals (from petroleum–toluene), m.p. 59°, followed by solidification and re-melting at 69—71°, $\nu_{max.}$ 1686, 1665, 1649, 1540, 1500, 1420, and 1402 cm^{-1}, *m/e* 150 (M^+, 94%), 135 (100), 109 (43), 107 (65), 80 (29), and 68 (29) (others

[31] Z. I. Shramova and A. P. Skoldinev, *J. Org. Chem.* (*U.S.S.R.*), 1963, **33**, 172.

<5%), *m** 121·5 (150 → 135), 85 (135 → 107), 79 (150 → 109), and 60 (107 → 80).

Acetylacetylene with Pyrrole. The acetylene (1·36 g) was refluxed with pyrrole (1·34 g) for 3·5 h and the resulting tar was chromatographed. The first yellow band gave a pale yellow, solid mixture (55 mg). Rechromatography starting with 50% petroleum–toluene as eluant gave, from the first half of the yellow band, **4,6-*diacetylindole*** (**36**), as pale yellow needles (from toluene–petroleum), m.p. 154—155·5°. The second half of the band was a mixture containing 1,3,5-triacetylbenzene. The third, brown band on the original column gave (*E*)-2-(3-oxobut-1-enyl)pyrrole (**35**) (395 mg, 15%), as cream needles (from toluene–petroleum), m.p. 114—115·5° (lit.,[32] 112—114°).

Acetylacetylene with the pyrrole (**35**). The pyrrole (**35**) (170 mg) was refluxed for 90 min with acetylacetylene (0·45 g). Chromatography gave a crystalline solid (24 mg) whose n.m.r. spectrum showed it to be a 2 : 3 mixture of 4,6-diacetylindole and 1,3,5-triacetylbenzene, followed by unchanged (**35**).

We thank Mrs. E. E. Richards for the 100 MHz n.m.r. spectra, Dr. N. M. Sinclair for the mass spectra, and the S.R.C. for a Studentship (to J. W.).

[4/1065 *Received*, 31*st May*, 1974]

[32] R. A. Jones and J. A. Lindner, *Austral. J. Chem.*, 1965, **18**, 875.