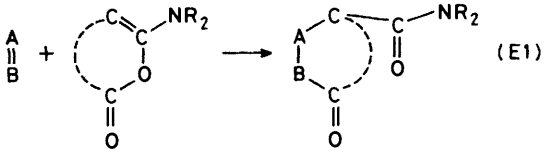
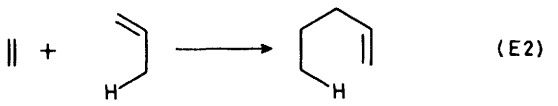
Ene-type Reactions involving Transfer of Acyl Groups. Addition of 4-Phenyl-1,2,4-triazoline-3,5-dione to Various Unsaturated Compounds

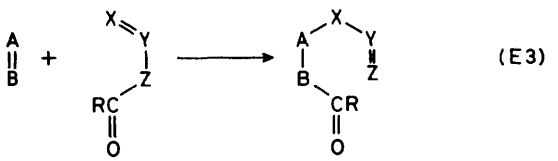
By **William E. Bottomley, Gerhard V. Boyd,* and René L. Monteil,** Department of Chemistry, Chelsea College, London SW3 6LX

4-Phenyl-1,2,4-triazoline-3,5-dione adds to α-angelica lactone and 2-methylisoquinolin-1-one to yield products of an ene-type reaction in which acyl groups are transferred, to the mixed anhydride of benzoic and piperidine-1-dithiocarboxylic acids to give a product from which sulphur has been extruded, and to 4,4-dimethyl-3-piperidinocyclobut-2-enone which undergoes Michael addition.

We recently described [1] the reactions of enol lactones bearing dialkylamino-substituents with various unsaturated compounds A=B to yield products resulting from addition and transfer of an acyl group from one component to the other [equation (E-1)] and we pointed out the formal analogy of this process to the ene synthesis, in which a hydrogen atom migrates [equation (E-2)].[2] Previous examples of the 'acyl-ene reaction' include the addition of benzene to α-ethoxyvinyl acetate,[3] of *N*-phenyltriazolinedione [4] and aldehydes [5] to enol esters, and of aldehydes and imines to 2-phenyl-2-oxazolin-5-one hydroperchlorate.[6] These reactions may







be expressed by the general equation (E3), in which Z is oxygen, Y carbon, and X represents either carbon or nitrogen. We have sought to extend the scope of the synthesis by varying X, Y, and Z and we now report on the reaction of the potent enophile 4-phenyl-1,2,4-triazoline-3,5-dione (1) [7] with unsaturated acyl compounds of diverse types.

RESULTS AND DISCUSSION

5-Methylfuran-2(3*H*)-one (α-angelica lactone) (2) reacted with the triazolinedione somewhat more slowly than the unsaturated lactones of equation (E1). An adduct was formed, whose properties, particularly the appearance of signals due to adjacent methine and methylene protons in its ^{1}H n.m.r. spectrum, accord with the proposed structure (3). 2-Methylisoquinolin-1-one (4), which contains the grouping C=C–N–CO, slowly gave a colourless product (5), whose u.v. spectrum closely resembled that of the adduct (6) of the triazolinedione to 3-morpholino-2-benzopyran-1-one; [1] the i.r. spectrum was also consistent with formula (5). The compound dissolved in aqueous alkali with a red colour, due, presumably, to the anion (7), and was recovered on acidification. Because of its sparing solubility in common organic solvents its n.m.r. spectrum had to be determined for a solution in deuteriotrifluoroacetic acid. In this solvent the compound appeared to exist as the salt of the tetracyclic form (8), since the spectrum did not contain a signal attributable to a methine proton.

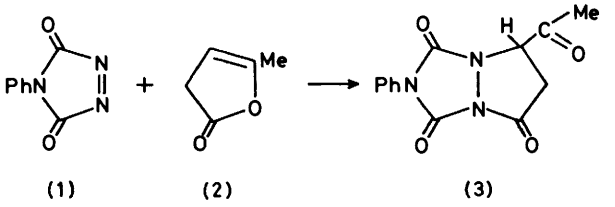
The fast reaction of phenyltriazolinedione with *S*-benzoylpiperidine-1-dithiocarboxylic acid (9) [8] gave a product whose composition corresponded to that of an adduct lacking one atom of sulphur. Its i.r. and ^{1}H n.m.r. spectra support structure (12). We suggest that the compound is formed from the initial adduct (10) *via* the thia-aziridinium sulphide (11) as shown.

The atom Z in the 'acyl-ene' component X=Y–Z–COR of this and previous reports is either oxygen, nitrogen, or sulphur. We were interested to find an example of an all-carbon system that would undergo the reaction and we considered that the dimethylpiperidinocyclobutenone (13) [9] might be suitable because it contains an activating dialkylamino-substituent, the double bond is fixed, and ring-strain would favour carbon–carbon bond fission. Treatment of the cyclobutenone with phenyltriazolinedione resulted in an instantaneous discharge of the red colour of the latter and the formation of an adduct in almost quantitative yield. The compound was evidently not the product (14) of an 'acyl-ene' reaction, since its ^{1}H n.m.r. spectrum showed the presence of an NH group and the absence of a methine proton. The i.r. spectrum contained a broad band at *ca.* 3 000 cm^{-1} and the u.v. spectrum exhibited absorptions due to piperidinocyclobutenone and phenylurazole (16) chromophores at 261 and 225 nm, respectively. The product is accordingly formulated as the Michael adduct (15).

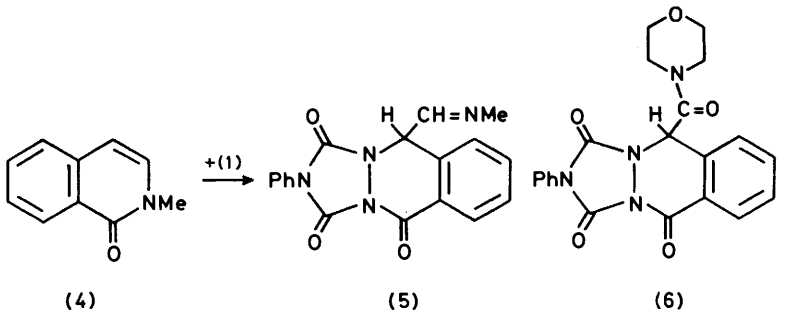
EXPERIMENTAL

In preliminary experiments, 0.1M solutions of 4-phenyl-1,2,4-triazoline-3,5-dione [7] in dichloromethane were mixed with similar solutions of (*a*) 3-morpholino-2-benzopyran-1-

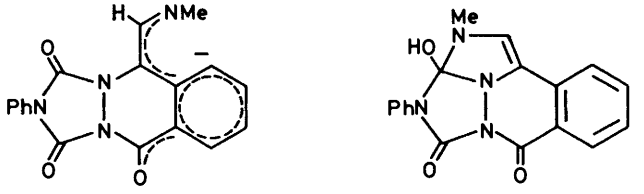
one,[10] (*b*) 5-methylfuran-2(3*H*)-one (α-angelica lactone), (*c*) 2-methylisoquinolin-1-one, and (*d*) *S*-benzoylpiperidine-1-dithiocarboxylic acid [8] at room temperature and the times



(1) (2) (3)



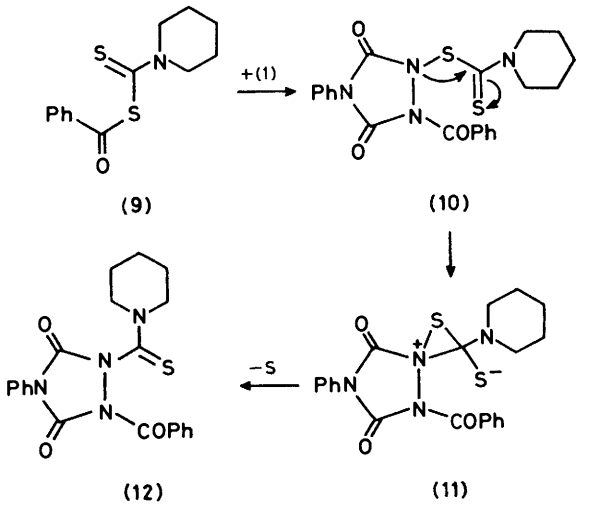
(4) (5) (6)



(7) (8)

required for the discharge of the red colour were noted: (*a*) 6 s, (*b*) 36 min, (*c*) 45 min, and (*d*) 6 min.

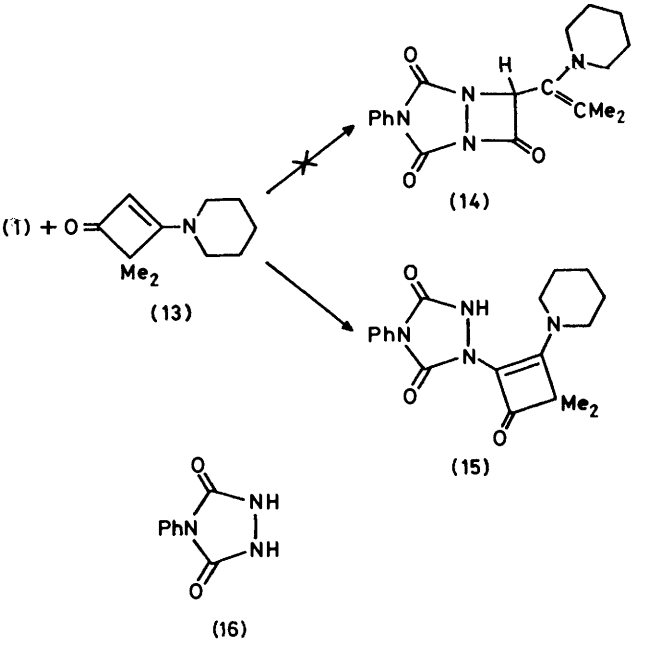
*7-Acetyl-6,7-dihydro-2-phenyl-*2H*-pyrazolo*[1,2-a]*-1,2,4-triazole-1,3,5-trione* (3).—A solution of 4-phenyl-1,2,4-triazoline-3,5-dione (0.35 g, 0.002M) and freshly distilled



(9) (10) (11) (12)

α-angelica lactone (0.3 g, 1.53 mol equiv.) in dichloromethane (20 ml) was stirred under nitrogen for 10 h. The solvent was removed and the residue was recrystallised from benzene–dichloromethane to give the *adduct* (0.4 g, 81%), m.p. 166.5—167.5 °C, $\nu_{max.}$ (CH_2Cl_2) 1 829, 1 762, and 1 730) cm^{-1}; δ (CD_3CN) 7.0 (m, Ph), 4.95 (t, CH), 3.30 (d, CH_2), and 2.4 (s, Me); *m/e* 273 (M^+) and 230 (M^+ — Ac) (Found: C, 57.4; H, 3.95; N, 15.1. $C_{13}H_{11}N_3O_4$ requires C, 57.15, H, 4.05; N, 15.4%).

*2,10-Dihydro-10-(methyliminomethyl)-2-phenyl-*1,2,4-



(13) (14) (15) (16)

triazolo[1,2-b]*phthalazine*-1,3,5-*trione* (5).—A solution of the phenyltriazolinedione (0.795 g, 0.005M) and 2-methylisoquinolin-1-one (0.87 g, 1 mol equiv.) in dichloromethane (50 ml) was refluxed in an atmosphere of nitrogen for 5 h. Evaporation of the solvent and trituration of the residue with ether gave the *adduct* (0.5 g, 30%), m.p. 304—305 °C (from acetic acid–ether); $\nu_{max.}$ (Nujol) 1 760, 1 700, 1 670, 1 640, and 1 600 cm^{-1}; $\delta(CF_3CO_2D)$ 8.60—7.60 (m, Ar and =CH), 7.55 (s, NPh), and 3.84 (s, Me); $\lambda_{max.}$ (EtOH) 230, 250sh, and 295 nm [$\lambda_{max.}$ for compound (6), 228, 240, 255sh, and 282 nm]; *m/e* 336 (M^+) (Found: C, 64.9; H, 4.35; N, 16.5. $C_{18}H_{14}N_4O_3$ requires C, 64.7; H, 4.4; N, 16.75%).

1-*Benzoyl*-2-(*piperidine*-1-*thiocarbonyl*)-4-*phenyl*-1,2,4-*triazolidine*-3,5-*dione* (12).—A solution of the phenyltriazolinedione (0.35 g, 0.002M) and *S*-benzoylpiperidine-1-dithiocarboxylic acid (0.51 g, 1.1 mol equiv.) in dichloromethane (20 ml) was stirred under nitrogen for 1 h. The solvent was removed and the residue was washed with ether to give the *product* (0.45 g, 60%), m.p. 245—245.5 °C (decomp.) (from acetone–ether); $\nu_{max.}$ (Nujol) 1 810, 1 755, 1 705, and 1 600 cm^{-1}; $\delta(CDCl_3)$ 8.95—7.30 (m, 2 Ph), 4.60—3.70 (m, 4 H) and 2.15—1.40 (m, 6 H) (piperidino); *m/e* 408 (M^+), 128 ($C_5H_{10}NCS^+$), and 105 ($PhCO^+$) (Found: C, 61,6; H, 4.9; N, 13.7; S, 7.9. $C_{21}H_{20}N_4O_3S$ requires C, 61.75; H, 4.95; N, 13.7; S, 7.85%).

1-(3,3-*Dimethyl*-4-*oxo*-2-*piperidinocyclobut*-1-*enyl*)-4-*phenyl*-1,2,4-*triazolidine*-3,5-*dione* (15).—A stirred solution of 4,4-dimethyl-3-piperidinocyclobut-2-en-1-one [9] (0.12 g, 0.006 7M) in acetonitrile (5 ml) was treated dropwise with a solution of the phenyltriazolinedione (0.117 g, 1 mol equiv.) in acetonitrile (5 ml). Immediate decolourisation occurred and the product (0.22 g, 93%) separated. It had m.p. 229—230 °C (from acetonitrile); $\nu_{max.}$ ($CHCl_3$) 3 000 (br), 1 775, 1 760, 1 710, and 1 600 cm^{-1}; $\delta(CDCl_3)$ 10.0 (br, NH), 7.35 (m, Ph), 3.40 (m, 4 H) and 1.60 (m, 6 H) (piperidino), and 1.35 (s, 2 Me); $\lambda_{max.}$ (MeCN) 225 and 261 nm; *m/e* 354 (M^+), 178 (phenyltriazolinedione$^+$), and 84 ($C_5H_{10}N^+$) (Found: C, 64,4; H, 64.5; N, 15.9. $C_{19}H_{22}N_4O_3$ requires C, 64.4; H, 6.25; N, 15.8%).

We thank the S.R.C. and the Governors of this College for studentships (to W. E. B. and R. L. M., respectively) and May and Baker Ltd. for their interest.

[9/759 *Received*, 16*th May*, 1979]

REFERENCES

[1] G. V. Boyd, R. L. Monteil, P. F. Lindley, and M. M. Mahmoud, *J.C.S. Perkin I*, 1978, 1351; A. E. Baydar and G. V. Boyd, *ibid.*, p. 1360.
[2] K. Alder, F. Pascher, and A. Schmitz, *Ber.*, 1943, **76**, 27.
[3] H. H. Wasserman and J. Solodar, *J. Amer. Chem. Soc.*, 1965, **87**, 4002.
[4] K. B. Wagener, S. R. Turner, and G. Butler, *J. Org. Chem.*, 1972, **37**, 1454.
[5] H. H. Wasserman and S. H. Wentland, *Chem. Comm.*, 1969, 1216; T. Mukaiyama, J. Hanna, T. Inoue, and T. Sato, *Chem. Letters*, 1974, 381.
[6] A. M. Knowles, A. Lawson, G. V. Boyd, and R. A. Newberry, *Tetrahedron Letters*, 1971, 485.
[7] R. C. Cookson, S. S. Gupte, I. D. R. Stevens, and C. T. Watts, *Org. Synth.*, 1971, **51**, 121.
[8] D. S. Tarbell and R. P. F. Scharrer, *J. Org. Chem.*, 1962, **27**, 1972.
[9] R. H. Hasek, P. G. Gott, and J. C. Martin, *J. Org. Chem.*, 1964, **29**, 2510.
[10] G. V. Boyd and R. L. Monteil, *J.C.S. Perkin I*, 1978, 1338.