Formation and Acid-catalysed Rearrangement of 1,2-Diazepin-5-ones

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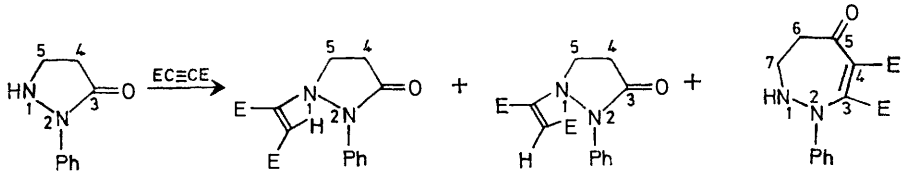
Dimethyl acetylenedicarboxylate reacts with 2-phenylpyrazolidin-3-ones (1)—(3) to give tetrahydro-1,2-diazepin-5-ones (9)—(11) as well as Michael addition products, the oxopyrazolidinyl-maleates and -fumarates (4)—(8). The structure of dimethyl 1,2,6,7-tetrahydro-7,7-dimethyl-5-oxo-2-phenyl-1,2-diazepine-3,4-dicarboxylate (10) was confirmed by *X*-ray crystallographic analysis. The diazepinones undergo ring contraction reactions in acid to yield 1-phenylpyrazole derivatives (12)—(21).

DIMETHYL ACETYLENEDICARBOXYLATE reacts with a variety of heterocyclic compounds thermally, as demonstrated chiefly by the work of Acheson,[1] and photochemically [2] to give new ring systems incorporating one or more molecules of the ester. We reported recently [3] that the ester also reacts with 2-phenylpyrazolidin-3-ones (1)—(3) to give tetrahydro-1,2-diazepin-5-ones (9)—(11) (Scheme 1). The diazepinones in turn undergo acid-catalysed rearrangements to pyrazoles, a ring contraction reaction of a general type that has been observed for 1,2-diazepines.[4]



SCHEME 1 E = CO_2Me throughout

The reaction of dimethyl acetylenedicarboxylate with pyrazoles,[5] aziridine,[6] and other secondary amines such as piperidine [7,8] has been shown to give Michael addition products, amino-maleic and -fumaric esters. The stereochemistry of the products varies with the nature of the amine and of the solvent.[6,9] If α-amino-ketones are used, the carbanionic intermediate from the nucleophilic attack of the amine on the acetylenic ester reacts with the carbonyl group to give pyrrole derivatives.[10]

Our interest in the reaction of pyrazolidinones with dimethyl acetylenedicarboxylate arose from our investigation of the ester as a possible trap for 1,3-dipolar intermediates in photochemical reactions of heterocyclic compounds. An investigation of the thermal reactions of pyrazolidinones with acetylenic esters showed that the pyrazolidinone (1) did not react with methyl propiolate under conditions that led to two types of product from the reaction of dimethyl acetylenedicarboxylate with all three pyrazolidinones (1)—(3).

Spectra established that the early fractions from chromatographic separations of the reaction products were mixtures of compounds which were chiefly the oxopyrazolidinylmaleic esters (4)—(6) with some of the corresponding fumaric esters (7) and (8) present also. Extensive chromatography was used to obtain a pure sample of the maleic ester (4), and its structure was assigned on spectroscopic evidence. Its i.r. spectrum has a broad carbonyl absorption centred at 1 720 with shoulders at 1 740 and 1 700 cm^{-1}. Huisgen [7,11] reports absorptions at 1 736—1 744 cm^{-1} for the ester group α to the nitrogen atom, and at 1 692—1 705 cm^{-1} for the one β to the nitrogen atom in similar compounds. The stereochemistry assigned is confirmed by the fact that the vinyl proton absorbs at δ 4.8 whereas that of the minor component of the original mixture, the compound given the fumarate structure (7), resonates further downfield at δ 5.8.[6,8] The ^{13}C n.m.r. spectrum of the maleic ester (4) clearly shows the retention of the pyrazolidinone nucleus (Figure 1) and the presence of two unsaturated carbon

[1] R. M. Acheson, *Adv. Heterocyclic Chem.*, 1963, **1**, 125; R. M. Acheson, G. Paglietti, and P. A. Tasker, *J.C.S. Perkin I*, 1974, 2496, and previous papers; H. Pleininger and D. Wild, *Chem. Ber.*, 1966, **99**, 3070; F. Fried, J. B. Taylor, and R. Westwood, *Chem. Comm.*, 1971, 1226; M.-S. Lin and V. Snieckus, *J. Org. Chem.*, 1971, **36**, 645; F. Troxler, H. P. Weber, A. Jaunin, and H.-R. Loosli, *Helv. Chim. Acta*, 1974, **57**, 750.

[2] R. P. Gandhi and V. K. Chadha, *Indian J. Chem.*, 1971, **9**, 304.

[3] S. N. Eğe, E. Y. Tsui, R. L. Spencer, B. E. Potter, B. K. Eagleson, and H. Z. Friedman, *J.C.S. Chem. Comm.*, 1974, 216.

[4] D. J. Harris, M. T. Thomas, V. Snieckus, and E. Klingsberg, *Canad. J. Chem.*, 1974, **52**, 2805.

[5] H. Reimlinger and C. H. Moussebois, *Chem. Ber.*, 1965, **98**, 1805; R. M. Acheson and P. W. Poulter, *J. Chem. Soc.*, 1960, 2138.

[6] J. E. Dolfini, *J. Org. Chem.*, 1965, **30**, 1298.

[7] R. Huisgen, K. Herbig, A. Siegel, and H. Huber, *Chem. Ber.*, 1966, **99**, 2526.

[8] K. Herbig, R. Huisgen, and H. Huber, *Chem. Ber.*, 1966, **99**, 2546.

[9] R. Huisgen, B. Giese, and H. Huber, *Tetrahedron Letters*, 1967, 1883.

[10] D. S. James and P. E. Fanta, *J. Org. Chem.*, 1962, **27**, 3346; J. B. Hendrickson, R. Rees, and J. F. Templeton, *J. Amer. Chem. Soc.*, 1964, **86**, 107; U. K. Pandit and H. O. Huisman, *Rec. Trav. chim.*, 1966, **85**, 311.

[11] R. Huisgen and K. Herbig, *Annalen*, 1965, **688**, 98.

atoms, one of which (δ_C 98.83) is β to a nitrogen atom.[12]

The other products from the reaction, compounds (9)—(11), are yellow, crystalline substances shown by their

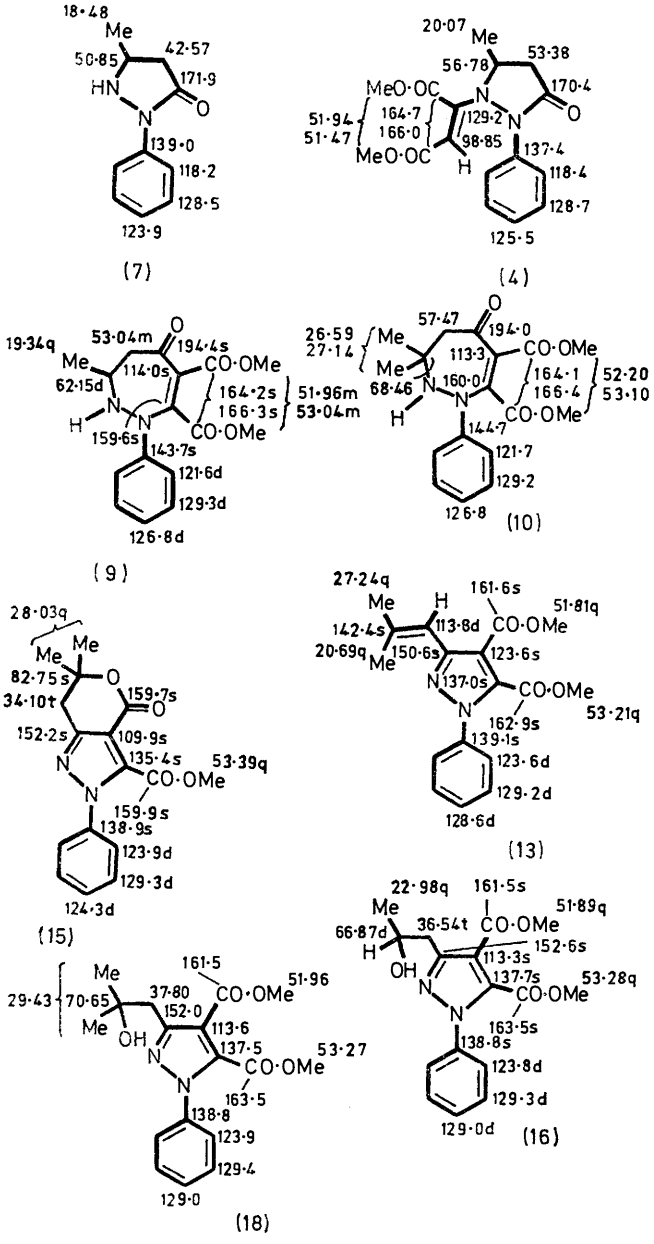
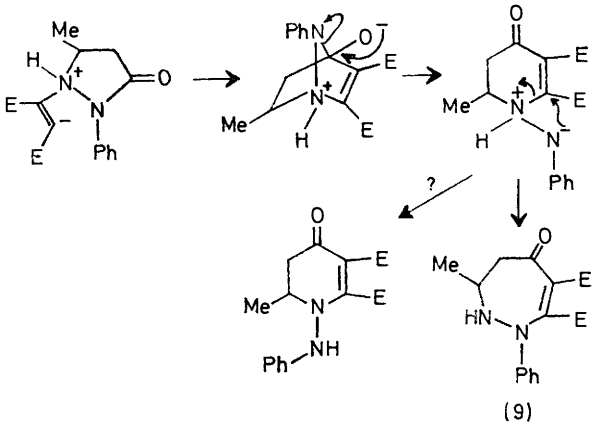


FIGURE 1 25.2 MHz ^{13}C N.m.r. spectra at 27 °C of representative pyrazolidinones, tetrahydrodiazepinones, and substituted pyrazoles (in deuteriochloroform); chemical shifts are in p.p.m. downfield from tetramethylsilane

mass spectra to be 1 : 1 adducts of the pyrazolidinones and the acetylenic ester. All three have i.r. spectra that are similar, with a weak absorption at 3 300 cm^{-1} attributed to NH stretching, and a broad complex of bands in the carbonyl region centred at 1 748 and 1 655 cm^{-1} when the spectra are taken in chloroform. When the spectrum of compound (9) is taken in a potassium bromide pellet, however, the carbonyl region shows three absorptions at 1 730, 1 695, and 1 670 cm^{-1}, the first two of which were assigned to unsaturated ester groups α and β to a nitrogen atom and the third to a ketone function conjugated with a nitrogen atom.[13] The absorption near δ_C 194 in the ^{13}C n.m.r. spectrum of the products (9) and (10) (Figure 1) confirms the presence of an αβ-unsaturated carbonyl group. In addition, the band appearing at 114.01 for (9) and at 113.35 for (10) could be assigned to an unsaturated carbon atom β to a nitrogen atom and also substituted by carbonyl groups.[12] The ^1H n.m.r. spectra of the compounds indicate that no rearrangement has occurred in the carbon skeleton of the pyrazolidinones, a fact confirmed by metastable ions in the mass spectra of compounds (9) and (11) at 239.5 corresponding to 318 ⟶ 276 (M − 42), and at 229.5 for (10) [332 ⟶ 276 (M − 56)], signalling the loss of propene and butene respectively from the parent ions. All three compounds exhibit a one-proton band between δ 4.4 and 5.1, removed by deuterium oxide, the multiplicity of which is related to the substitution at C-5 of the parent pyrazolidinone [doublet for compound (9), singlet for (10), and broad multiplet for (11)].

All these facts point strongly to the tetrahydro-1,2-diazepin-5-one structures shown, which necessitates an unusual insertion of the acetylenic ester into the amide bond of the pyrazolidinones. It appears that as long as there is not easy exchange of protons in the reaction medium, the carbanionic intermediate from the Michael addition of N-1 of the pyrazolidinone to the ester can attack the carbonyl group across the ring to give a bicyclic amino-acetal intermediate (Scheme 2) which can



SCHEME 2

open to a zwitterion reminiscent of the pyridinium ions shown to undergo photochemical ring expansion to diazepines by Streith [14] and Snieckus.[15] This raises the

[12] J. B. Stothers, ' C-13 Nuclear Magnetic Resonance Spectroscopy,' Academic Press, New York, 1972.

[13] N. H. Cromwell, F. A. Miller, A. R. Johnson, R. L. Frank, and D. J. Wallace, *J. Amer. Chem. Soc.*, 1949, **71**, 3337; J. Weinstein and G. M. Wyman, *J. Org. Chem.*, 1958, **23**, 1618; J. Dabrowski, *Spectrochim. Acta*, 1963, **19**, 475.

[14] J. Streith and J. M. Cassal, *Angew. Chem. Internat. Edn.*, 1968, **7**, 129; J. Streith, J. P. Luttringer, and M. Natasi, *J. Org. Chem.*, 1971, **36**, 2962.

[15] A. Balasubramanian, J. M. McIntosh, and V. Snieckus, *J. Org. Chem.*, 1970, **35**, 433.

possibility that the products might be the *N*-anilino-4-pyridone derivatives that would result from the shift of a proton from one nitrogen atom to the other. Several pieces of evidence speak against this. Hardest to reconcile with such a structure are the multiplicities for the exchangeable protons in the ^{1}H n.m.r. spectra, which strongly suggest that the NH is adjacent to the carbon bearing the methyl group in the example shown in Scheme 2. The ^{13}C n.m.r. spectra also indicate that the aromatic carbon atoms on N-1 resemble those in acetanilide more than they resemble those in aniline.[12] In addition, compounds (9)—(11) do not dissolve in dilute, aqueous acid, *i.e.* they display very little basicity.

The unusual nature of the reaction led us to seek confirmation of the structure of these diazepinones by an *X*-ray crystallographic structure determination. The diazepinone (10) was chosen for the analysis. The structure of the molecule is shown in Figure 2, and bond distances and angles are in Figure 3. An analysis of the conformation of the seven-membered ring shows that the carbonyl group is not coplanar with the carbon–carbon double bond, the dihedral angle between the planes O(10), C(5), C(6) and C(5), C(6), C(7) being 19.4(2)°. The shortest transannular distances are N(1)–C(4) [2.793(4)] and N(2)–C(5) [2.856(4) Å]. Models show that if the carbonyl group and the double bond were coplanar, these distances would be *ca.* 2.5 and 3.3 Å, respectively, if we assume normal bond distances and angles in the ring. Thus the out-of-plane bending of the carbonyl group is accompanied by relief of an otherwise very short N(1)–C(4) approach, and by shortening of N(2)–C(5) by *ca.* 0.4 Å.

During an attempt to record the ^{1}H n.m.r. spectra of the diazepinones (9) and (10) in trifluoroacetic acid, it

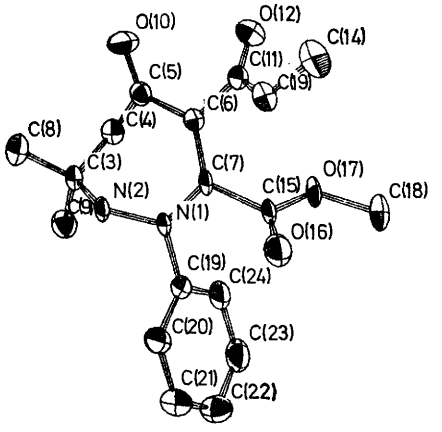


FIGURE 2 Thermal ellipsoid plot of the molecular structure of the diazepinone (10) showing the crystallographic numbering; hydrogen atoms have been omitted

became evident that the compounds were undergoing chemical reaction in the acidic solvent. The products from the reaction with trifluoroacetic acid, and later with toluene-*p*-sulphonic acid, displayed in every case a brilliant blue fluorescence, a property typical of many pyrazoles, and especially of 1-phenylpyrazoles with

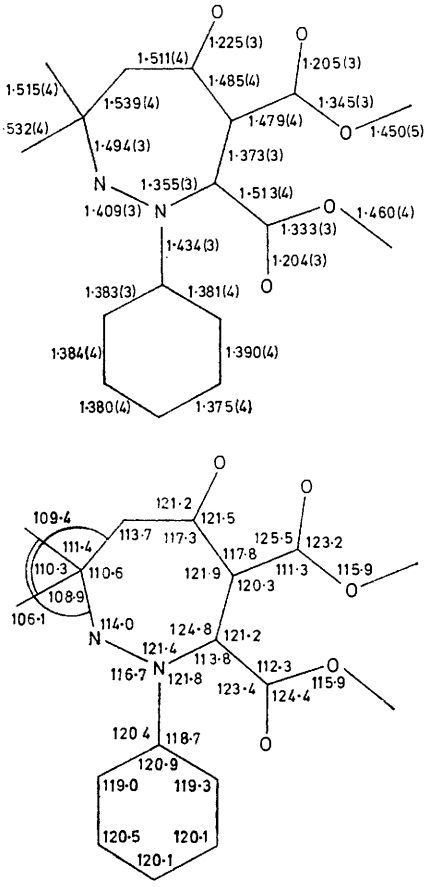


FIGURE 3 Bond lengths (top) with standard deviations in parentheses, and bond angles ($\sigma = 0.2°$) (bottom) for the diazepinone (10)

ketone, acid, or ester substituents in the 4- and 5-positions,[16] as well as of 1-phenyl-Δ^2-pyrazolines.[17] The products were characterized as those of ring-contraction resulting from transannular interaction between the carbonyl group and N-2 of the diazepinones (Scheme 3). Moore [18] has demonstrated that 1,2-diazepin-4-ones undergo a variety of ring contraction and transformation reactions under acidic and basic conditions, and Snieckus [4] has shown that pyrazoles and pyridines result from acid-catalysed rearrangements of 1,2-diazepines with fragmentation of the ring. In the case of the tetrahydro-1,2-diazepin-5-ones (9) and (10), all the carbon atoms of the ring are retained as substituted pyrazoles are formed.

Four products were obtained from the reaction of the diazepinone (9) with trifluoroacetic acid, with their relative amounts varying somewhat with the quality of the trifluoroacetic acid and with how long the reaction mixture is left in water after quenching. The first fraction from chromatography of the reaction mixture on

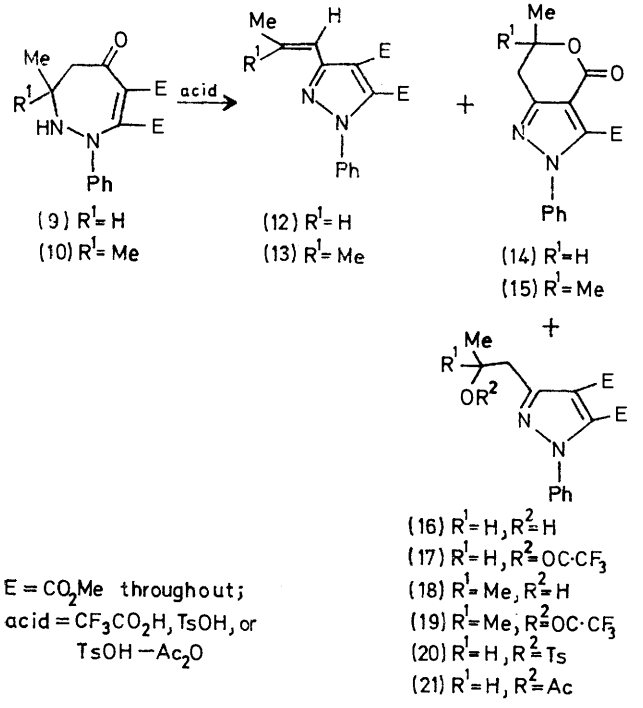
[16] I. I. Grandberg, S. V. Tabak, and A. N. Kost, *J. Gen. Chem.* (*U.S.S.R.*), 1963, **33**, 517.

[17] F. Straus, *Ber.*, 1918, **51**, 1457; W. Reid and G. Dankert, *Chem. Ber.*, 1957, **90**, 2707.

[18] O. S. Rothenberg and J. A. Moore, *J. Org. Chem.*, 1972, **37**, 2796; S. M. Rosen and J. A. Moore, *ibid.*, p. 3770, and previous papers.

silica gel consisted of a mixture of the propenylpyrazole (12) and the corresponding trifluoroacetate (17). This is evident from the ^{1}H n.m.r. spectra, which exhibit varying intensities for bands for the methyl protons, a multiplet at δ 1.9 for (12) and a doublet at δ 1.4 for (17), as well as the presence of a very low field multiplet, δ 5.6, attributed to the methine proton in (17). T.l.c. of this fraction on alumina, silica, and acid-washed alumina established that one component of the mixture was being converted into a much more polar substance on alumina, but not on silica and acidic alumina. Chromatography on alumina gave the propenylpyrazole (12) and the pyrazole alcohol (16).

Elemental analysis and the mass spectrum of (12) established that it was formed by formal loss of water from the diazepinone (9). The ^{1}H n.m.r. spectrum indicates the presence of two vinyl protons as a multiplet at



SCHEME 3

δ 6.7, and the position and multiplicity of the methyl band at δ 1.9 establishes the nature of the propenyl side chain. The aryl band is a singlet, a characteristic of 1-phenylpyrazoles with substituents in the 5-position when spectra are taken in deuteriochloroform.[19,20] The i.r. spectrum in chloroform shows the presence of two ester functions at 1 750 and 1 725 cm^{-1}. The ester carbonyl band in the i.r. spectrum of a liquid film of diethyl 1-phenylpyrazole-4,5-dicarboxylate is reported at 1 725 cm^{-1}, whereas dimethyl 1-phenylpyrazole-3,4-dicarboxylate has two bands, at 1 770 and 1 725 cm^{-1}.[19] A variety of dimethyl 3-aryl-1-*p*-nitrophenylpyrazole-4,5-dicarboxylates have been shown to have two carbonyl absorptions at 1 735—1 715 cm^{-1} when studied in potassium bromide disc, whereas other similar compounds had single absorptions at 1 730—1 725 cm^{-1}.[21] Crown ether-catalysed permanganate oxidation[22] of the propenylpyrazole (12) and esterification of the resulting 1-phenylpyrazole-3,4,5-tricarboxylic acid 4,5-dimethyl ester yielded the known[21,23] trimethyl 1-phenylpyrazole-3,4,5-tricarboxylate, which shows a single carbonyl band at 1 745 cm^{-1} in chloroform solution; a single absorption at 1 730 cm^{-1} was reported[21,23] for it in potassium bromide. There does not seem, therefore, to be a discernible correlation between structure, and number and frequency of carbonyl absorptions to be expected for pyrazolepolycarboxylic acid esters.

The ^{1}H n.m.r. spectra of the next two compounds to be isolated by chromatography of the original acid reaction mixture, the pyrazole lactone (14) and the pyrazole alcohol (16), show that they are closely related. Both have doublets for the methyl protons, at δ 1.3 for (16) and 1.6 for (14), and methine proton signals appear at δ 4.1 for (16) and (downfield) at δ 4.8 for (14). Both spectra also show a singlet for the aryl protons. The i.r. spectrum of the lactone (14) shows a single rather broad absorption at 1 745 cm^{-1}, whereas that of the pyrazole alcohol (16) has two bands, at 1 745 and 1 720 cm^{-1}. The presence of the hydroxy-group in (16) is indicated by absorption at 3 450 cm^{-1}.

The ^{1}H n.m.r. and mass spectra show that the pyrazole alcohol (16) is an isomer of the diazepinone (9), whereas the lactone (14) has been formed by loss of methanol as well as rearrangement. The mass spectra of (14) and (16) both have *m/e* 242 as the base peak, and the spectra at masses lower than that are practically identical. The mass spectrum of the lactone (14) has a metastable ion at 204.8 (286 ⟶ 242; $M - 44$) for the decomposition of the parent ion to the base peak, whereas in the alcohol (16) loss of 44 mass units precedes loss of methanol to give the base peak, *m** 213.7 (274 ⟶ 242). Possible paths of fragmentation are depicted in Scheme 4.[24]

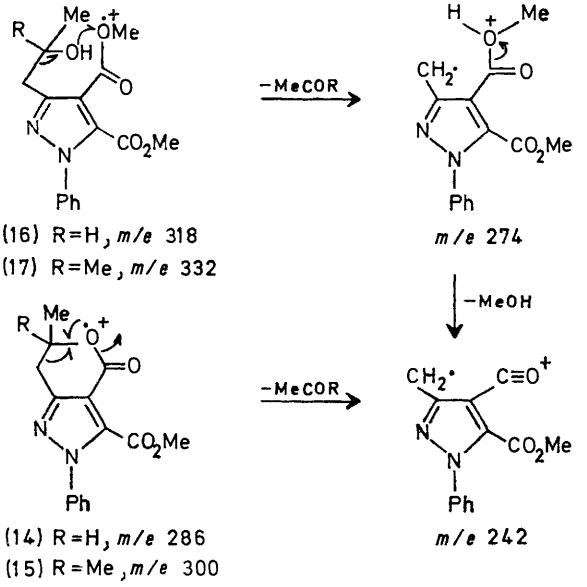
The ^{13}C n.m.r. spectrum of the pyrazole-alcohol (16) (Figure 1) is in accord[12] with the assigned structure. Although our sample of the lactone (14) was not large enough for a complete ^{13}C n.m.r. spectrum to be obtained, it was possible to see the downfield shift of the secondary carbon signal from δ_C 66.87 in the spectrum of (16) to 77.42 in that of (14). The structural relationship of the lactone (14) to the alcohol (16) was confirmed by methanolysis of (14) to give (16).

When toluene-*p*-sulphonic acid was used, the diazepinone (9) yielded the tosyl ester (20) of the pyrazole alcohol (16), along with some propenylpyrazole (12). The

[19] L. Bauer and C. S. Mahajanshetti, *J. Heterocyclic Chem.*, 1967, **4**, 325.
[20] G. Coispeau, J. Elguero, and R. Jacquier, *Bull. Soc. chim. France*, 1969, 2061.
[21] H. Ogura, K. Kubo, Y. Watanabe, and T. Itoh, *Chem. and Pharm. Bull. (Japan)*, 1973, **21**, 2026.
[22] D. J. Sam and H. E. Simmons, *J. Amer. Chem. Soc.*, 1972, **94**, 4024.
[23] M. K. Saxena, M. N. Gudi, and M. V. George, *Tetrahedron*, 1973, **29**, 101.
[24] F. W. McLafferty, 'Interpretation of Mass Spectra,' Benjamin, Reading, 1973, Second edn., p. 136.

structure of (20) was determined by analysis as well as by the characteristic blue fluorescence the compound exhibits, and by evidence in its ^{1}H n.m.r. and i.r. spectra of the incorporation of a tosyl group: aryl nine-proton multiplet at δ 7.4, three-proton singlet at δ 2.4 for the aryl methyl group, and the downfield shift of the methine multiplet of (16) to δ 5.1; and sulphonate ester bands in the i.r. at 1 375 and 1 180 cm^{-1}.[25] If acetic anhydride was present when the rearrangement of the diazepinone (9) with toluene-*p*-sulphonic acid was carried out, then the acetate ester (21) of the pyrazole alcohol (16) was the main product, characterized by a three-proton singlet at δ 2.0 in a ^{1}H n.m.r. spectrum that was otherwise very similar to that of the trifluoroacetate ester (17), which was converted into the alcohol (16) on the alumina column.

The similarity of the products from the ring contraction reaction of the diazepinone (10) in trifluoroacetic acid to those from (9) was evident from their i.r. spectra; in



SCHEME 4

every case the i.r. spectrum of a compound in one series is very similar to that of the corresponding compound in the other. The trifluoroacetate ester (19) present as impurity in the propenylpyrazole (13) was not hydrolysed on an alumina column with the same ease as was the ester (17). The propenylpyrazole (13) was prepared for characterization by toluene-*p*-sulphonic acid-catalysed rearrangement of the diazepinone (10), no tosylate ester of the corresponding pyrazole alcohol (18) being formed in this case and some pyrazole lactone (15) being obtained instead.

In this series as well, the pyrazole lactone (15) and the pyrazole alcohol (18) show a close structural relationship, both giving *m/e* 242 as the base peak in their mass spectra, with metastable ions at 195.2 (300 ⟶ 242) for (15) and 213.7 (274 ⟶ 242) for (18), corresponding to the fragmentation discussed for the lactone and the alcohol in the other series (Scheme 4).

The assignments made to the bands in the ^{13}C n.m.r. spectra of the products from the rearrangement of the diazepinones shown in Figure 1 require comment only in the case of the propenylpyrazole (13), where the off-resonance decoupled spectrum showed the absorption at δ_C 113.8 to be a doublet and thus necessitated that it be assigned to the olefinic carbon atom next to the pyrazole ring; splitting of the band at δ_C 123.6 assigned to the *ortho*-carbon atoms in the phenyl ring revealed another singlet underneath, which was assigned to C-4 in the pyrazole ring. A chemical shift of δ_C 113.8 for an alkene carbon atom is more typical of β-carbon atoms in styrenes than of α-carbon atoms.[12] This shift seems to resemble those for the α-carbon atoms (δ_C 102, 108) of acrylonitriles.[12] The corresponding bands in the spectrum of the propenylpyrazole (12) appear to be at δ_C 120.1 for the carbon atom on the side chain, and 123.9 for C-4 of the pyrazole ring. In any case, in both of these compounds, C-4 is more deshielded than in the other pyrazoles where its chemical shift ranges from δ_C 109.9 to 113.6.

The differences between the products from the acid-catalysed rearrangement of the diazepinones (9) and (10) reflect the added substitution at C-7 of the diazepinone (10). The greater ease with which the lactone (15) is formed can be traced to the greater likelihood that a carbocation at C-7 is formed at some stage after attack of N-1 on the protonated carbonyl group of the diazepinone. Similarly, the greater steric hindrance at that carbon atom prevents attack by tosylate anion so that the tosylate ester (20) obtained from (9) is absent among products from (10). Similarly, the easy hydrolysis of the trifluoroacetate ester (17) to the alcohol (16) is not seen for the ester (19).

The ring expansion reaction reported here for pyrazolidinones with dimethyl acetylenedicarboxylate appears to have some generality. Preliminary results indicate that the corresponding six-membered ring compound, 6-methyl-2-phenyltetrahydropyridazin-3(2*H*)-one gives dimethyl 1-anilino-3,4,5,6-tetrahydro-7-methyl-4-oxoazepine-2,3-dicarboxylate upon reaction with the acetylenic ester.[26] In this case the zwitterionic intermediate postulated in Scheme 2 seems to stabilize itself by proton transfer.

EXPERIMENTAL

M.p.s were determined for samples in capillaries with a Thomas–Hoover apparatus. I.r. spectra were recorded with a Perkin-Elmer 237B spectrophotometer. ^{1}H N.m.r. spectra were recorded with a Varian T-60 spectrometer; ^{13}C n.m.r. spectra were obtained with a PFT 100 25.2 MHz Fourier transform n.m.r. spectrometer (tetramethylsilane internal standard for both). Mass spectra were obtained with an A.E.I. MS 902 spectrometer.

For chromatographic separations, silica gel refers to Grace grade 923, 100—200 mesh, and alumina to Woelm neutral alumina, grade II, unless otherwise specified. Analytical

[25] R. M. Silverstein, G. C. Bassler, and T. C. Morrill, 'Spectrometric Identification of Organic Compounds,' Wiley, New York, 1974, 3rd edn., p. 114.

[26] S. N. Eğe and M. L. C. Carter, unpublished data.

t.l.c. was carried out on Eastman Chromagram Sheets of silica gel and alumina, with and without fluorescent indicator. Solvents were all reagent grade. All evaporations were carried out with a rotary evaporator under vacuum.

Reactions of the Pyrazolidinones (1)—(3) *with Dimethyl Acetylendicarboxylate.*—(a) *Formation of dimethyl* 1,2,6,7-*tetrahydro*-7-*methyl*-5-*oxo*-2-*phenyl*-1,2-*diazepine*-3,4-*dicarboxylate* (9).—The diazepinone (9) was formed when the pyrazolidinone (1) [27] was treated with dimethyl acetylenedicarboxylate in a variety of solvents. Acetone, ether, benzene, toluene, acetonitrile, and absolute ethanol were tried. The best results were obtained in polar but non-protic solvents such as acetone and acetonitrile. Very little diazepinone was formed in ethanol.

Typically the pyrazolidinone (1) (3.52 g, 0.020 mol) and the acetylenic ester (3.00 g, 0.021 mol) were refluxed in acetonitrile (50 ml; distilled from calcium hydride) for 3.5 h. The next morning, after addition of 20 drops of ester, the mixture was refluxed for 6.5 h, and this procedure was repeated the following day. Removal of the solvent gave an oil, which crystallized when dissolved in methanol to give the *diazepinone* (9), bright yellow prisms, m.p. 177.5—178.5° (from methanol) (Found: C, 60.5; H, 5.7; N, 8.8. $C_{16}H_{18}N_2O_5$ requires C, 60.4; H, 5.7, N, 8.8%); *m/e* 318 (M^+), 287, 276, 259, 245, 227, 202, 144, 143, 91, and 77 (base); *m** 259 (318 ⟶ 287), 239.5 (318 ⟶ 276), 217.5 (276 ⟶ 245), 210.9 (318 ⟶ 259), 198.9 (259 ⟶ 227), and 162 (318 ⟶ 227); $\nu_{max.}$ ($CHCl_3$) 3 300, 1 748, 1 655, 1 590, 1 525, 1 510, and 1 175 cm^{-1}; $\nu_{max.}$ (KBr) 1 730, 1 695, and 1 670 cm^{-1}; δ ($CDCl_3$) 1.1 (3 H, d, *J* 7 Hz), 2.9 (2 H, m), 3.5 (3 H, s), 3.7 (3 H, s), 4.1 (1 H, m), 4.8 (1 H, d, *J* 8 Hz, exchangeable), and 7.3 (5 H, s); for ^{13}C n.m.r. data see Figure 1.

Chromatography of the residue from the crystallization [an oil (4.54 g)] on alumina, grade IV (125 g), gave a crude separation of the other products [eluted with benzene (600 ml)] from another 0.53 g of (9) [eluted with benzene–ether (9 : 1; 600 ml)]. The total yield of (9) was 3.54 g (56%).

The early fractions from the chromatography of the residue from the crystallization of the diazepinone (9) contained a mixture which appeared from n.m.r. spectra to be the isomeric oxopyrazolidinyl-maleic and -fumaric esters (4) and (7). The major component, the maleic ester (4), could be obtained in a reasonably pure state by extensive chromatography. In a typical experiment, when 495 mg of residue was chromatographed on alumina, grade IV (30 g), the combined first three (20 ml) fractions [183 mg (eluted with benzene)], were rechromatographed on alumina (20 g).

The ester (4) (58 mg) was isolated as an oil in the first eight fractions (30 ml) (eluted with benzene); $\nu_{max.}$ ($CHCl_3$) 1 740, 1 720, 1 700, 1625, 1 600, 1 500, 1 445, 1 370, 1 350, and 1 150 cm^{-1}; δ (CCl_4) 1.2 (3 H, d, *J* 6 Hz), 2.5 (2 H, m), 3.5 (3 H, s), 3.9 (3 H, s), 4.1 (1 H, m), 4.8 (1 H, s), and 7.4 (5 H, m); for ^{13}C n.m.r. data see Figure 1.

Later fractions from the chromatography had similar i.r. spectra with differences in the relative intensities of some bands and n.m.r. spectra that were a superposition of the spectrum of various quantities of fumaric ester (7), δ (CCl_4) 1.4 (3 H, d, *J* 6 Hz), 3.6 (3 H, s), 3.7 (3 H, s), 5.8 (1 H, s), on that of the ester (4).

No reaction was observed when the pyrazolidinone (1) was refluxed with an equimolar amount of methyl propiolate in acetonitrile for 9 h.

[27] L. Knorr and P. Duden, *Ber.*, 1892, **25**, 759.
[28] B. Prentice, *Annalen*, 1896, **292**, 272.

(b) *Formation of dimethyl* 1,2,6,7-*tetrahydro*-7,7-*dimethyl*-5-*oxo*-2-*phenyl*-1,2-*diazepine*-3,4-*dicarboxylate* (10). The pyrazolidinone (2) [28] (3.80 g, 0.02 mol) and the acetylenic ester (2.92 g, 0.02 mol) were refluxed in acetonitrile (50 ml; distilled from calcium hydride) for 4 h; the mixture was set aside overnight, and then refluxed for 5 h after addition of 20 drops of ester. The addition of more ester and the reflux were repeated for 4 more days. Evaporation of the solvent, and dissolution of the oil that remained in methanol (15 ml), gave the *diazepinone* (10), yellow crystals (1.63 g, 25%), m.p. 162.5—163° (from methanol) (Found: C, 61.3; H, 6.3; N, 8.3. $C_{17}H_{20}N_2O_5$ requires C, 61.4; H, 6.1; N, 8.4%); *m/e* 332 (M^+), 300, 276, 245, 241, 202, 160, 144, 143, 91, and 77 (base); *m** 229.5 (332 ⟶ 276) and 217.5 (276 ⟶ 245); $\nu_{max.}$ ($CHCl_3$) 3 300, 1 748, 1 655, 1 525, 1 510, 1 450, 1 390, 1 375, 1 325, and 1 120 cm^{-1}; δ ($CDCl_3$) 1.1 (6 H, s), 2.9 (2 H, s), 3.6 (3 H, s), 3.8 (3 H, s), 4.4 (1 H, s, exchangeable), and 7.3 (5 H, s); for ^{13}C n.m.r. data see Figure 1.

Chromatography of the residue from the crystallization of (10) on alumina (grade IV) gave a series of fractions which from their n.m.r. spectra seemed to be mixtures of the esters (5) and (8), δ (CCl_4) 5.3 and 6.1 (vinyl protons). Further purification of these compounds was not attempted.

(c) *Formation of dimethyl* 1,2,6,7-*tetrahydro*-6-*methyl*-5-*oxo*-2-*phenyl*-1,2-*diazepine*-3,4-*dicarboxylate* (11). The pyrazolidinone (3) [29] (181 mg, 1.03 mmol) and the acetylenic ester (150 mg, 1.05 mmol) were heated in acetonitrile (5 ml) for 6 h, and then set aside overnight. Evaporation, and chromatography of the residue on alumina, [grade IV (20 g)] gave the maleic ester (6), an oil (193 mg) [eluted with benzene (100 ml)], δ (CCl_4) 1.2 (3 H, d, *J* 6 Hz), 3.0 (2 H, m), 3.5 (3 H, s), 3.9 (3 H, s), 4.1 (1 H, m), 4.9 (1 H, s), and 7.4 (5 H, m), and the *diazepinone* (11) (108 mg, 34%) [eluted by benzene–ether (9 : 1; 150 ml)], bright yellow prisms, m.p. 136—137.5° (from methanol) (Found: C, 60.4; H, 5.7; N, 8.7. $C_{16}H_{18}N_2O_5$ requires C, 60.4; H, 5.7; N, 8.8%); *m/e* 318 (M^+), 286, 276, 275, 245, 202, 160, 144, 143, 91, and 77 (base); *m** 239.5 (318 ⟶ 276) and 217.5 (276 ⟶ 245); $\nu_{max.}$ ($CHCl_3$) 3 300, 1 745, 1 655, 1 600, 1 525, 1 510, 1 170, and 1 126 cm^{-1}; δ ($CDCl_3$) 1.0 (3 H, d, *J* 5 Hz), 3.1—4.1 (3 H, m), 3.5 (3 H, s), 3.6 (3 H, s), 5.1 (1 H, m, exchangeable), and 7.3 (5 H, s).

Acid-catalysed Rearrangement of the Diazepinone (10).—(a) *Trifluoroacetic acid.* The diazepinone (10) (360 mg) was dissolved in trifluoroacetic acid in an n.m.r. tube and inspected at intervals. In 15 min a second singlet in the methyl region was apparent; in 2 h the new compound comprised about half the mixture and a second product was present; in 4 h the diazepinone (10) was a minor component of the mixture, which now had five different methyl absorptions. The mixture was quenched with water after 6 h and left in water overnight. The organic layer, an oil, was taken up in methylene chloride; the solution was washed with aqueous 5% sodium hydrogen carbonate, then water, dried ($MgSO_4$), and evaporated. T.l.c. of the oil on silica gel (methylene chloride) showed three spots, all displaying a brilliant blue fluorescence.

Chromatography of the oil (368 mg) on silica gel (40 g) gave three major fractions. The first, an oil (217 mg) [eluted with benzene–ether (9 : 1; 100 ml and 4 : 1 ; 100 ml) after development with benzene (100 ml)] was a mixture of the propenylpyrazole (13) and the trifluoroacetyl ester (19) of the pyrazole alcohol (18), $\nu_{max.}$ ($CHCl_3$) 1 775 cm^{-1}, δ

[29] A. Vystrčil and Z. Stejskal, *Casopis Českého Lékárnictva*, 1950, **63**, 75 (*Chem. Abs.*, 1952, **46**, 7566*d*).

($CDCl_3$) 1.6 (6 H, s), 3.7 (2 H, s), 3.9 (6 H, s), and 7.5 (5 H, s). Extensive chromatography on silica gel and on alumina changed the ratio of the components but did not effect complete separation. The pyrazole (13) was eventually prepared by another method (below) for characterization.

The second fraction [19 mg; eluted with benzene–ether (1 : 1; 100 ml)] was *methyl* 2,4,6,7-*tetrahydro*-6,6-*dimethyl*-4-*oxo*-2-*phenylpyrano*[4,3-c]*pyrazole*-3-*carboxylate* (15), white crystals, m.p. 148—149° (from carbon tetrachloride) (Found: C, 63.9; H, 5.3; N, 9.3. $C_{16}H_{16}N_2O_4$ requires C, 64.0; H, 5.4; N, 9.3%); *m/e* 300 (M^+), 285, 269, 242 (base), 225, 184, 155, 144, 143, 129, 105, 91, 77, 65, 59, and 51; *m** 241.2 (300 ⟶ 269), 195.2 (300 ⟶ 242), and 139.9 (242 ⟶ 184); $\nu_{max.}$ ($CHCl_3$) 1 730, 1 330, 1 075, and 1 050 cm^{-1}; δ ($CDCl_3$) 1.6 (6 H, s), 3.1 (2 H, s), 3.9 (3 H, s), and 7.5 (5 H, s); for ^{13}C n.m.r. data see Figure 1.

The third fraction [120 mg; eluted partly with benzene–ether (1 : 1) and with benzene–ether (3 : 7; 100 ml)] was *dimethyl* 3-(2-*hydroxy*-2-*methylpropyl*)-1-*phenylpyrazole*-4,5-*dicarboxylate* (18), white crystals, m.p. 91—91.5° (from carbon tetrachloride) (Found: C, 61.4; H, 6.2; H, 8.4. $C_{17}H_{20}N_2O_5$ requires C, 61.4; H, 6.1; N, 8.4%); *m/e* 332 (M^+), 317, 314, 285, 274, 242 (base), 184, 158, 144, 143, 105, 77, 59, and 51; *m** 256.2 (317 ⟶ 285), 213.7 (274 ⟶ 242), and 139.9 (242 ⟶ 184); $\nu_{max.}$ (CCl_4) 3 500, 1 750, 1 725, 1 600, 1 545, 1 510, 1 480, 1 260, and 1 225 cm^{-1}; δ ($CDCl_3$) 1.3 (6 H, s), 3.1 (2 H, s), 3.6 (1 H, s, exchangeable), 3.8 (6 H, s), and 7.4 (5 H, s); for ^{13}C n.m.r. data see Figure 1.

(b) *Toluene*-p-*sulphonic acid*. The diazepinone (10) (670 mg, 2 mmol) was refluxed with toluene-*p*-sulphonic acid monohydrate (386 mg, 2 mmol) in benzene (75 ml) for 0.5 h, after which the yellow colour of (10) was gone and t.l.c. on alumina (benzene) showed the presence of two compounds. The mixture was washed once with water, twice with aqueous 5% sodium hydrogen carbonate, and once again with water, dried ($MgSO_4$), and evaporated. The light yellow oil (621 mg) obtained was chromatographed on alumina (62 g) to give *dimethyl* 3-(2-*methylpropenyl*)-1-*phenylpyrazole*-4,5-*dicarboxylate* (13) (353 mg) [eluted by benzene (330 ml)], m.p. 60.5—62° (from pentane) (Found: C, 64.9; H, 5.8; N, 8.9. $C_{17}H_{18}N_2O_4$ requires C, 64.9; H, 5.8; N, 8.9%); *m/e* 314 (M^+), 282, 224, 196, 195, 144, 143, 119, 93, 77 (base), and 51; *m** 177.9 (282 ⟶ 224), 171.5 (224 ⟶ 196), and 136.2 (282 ⟶ 196); $\nu_{max.}$ ($CHCl_3$) 1 745, 1 720, 1 600, 1 545, 1 500, 1 470, 1 450, and 1 255 cm^{-1}; δ ($CDCl_3$) 2.1 (6 H, m), 3.9 (6 H, s), 6.7 (1 H, m), and 7.5 (5 H, s); for ^{13}C n.m.r. data see Figure 1.

The other component of the mixture [eluted by benzene–ether (9 : 1; 600 ml)] was the pyrazole lactone (15), (87 mg).

Acid-catalysed Rearrangement of the Diazepinone (9).—(a) *Trifluoroacetic acid*. The diazepinone (9) (636 mg, 2 mmol) was dissolved in trifluoroacetic acid (5 ml) and left at room temperature for 69 h, after which t.l.c. on silica gel (chloroform) showed three spots which displayed strong blue fluorescence. The mixture was diluted with water and set aside for 5 h, then extracted with methylene chloride. The organic layer was washed with aqueous 5% sodium hydrogen carbonate, then water, and dried ($MgSO_4$). Evaporation gave a yellow oil (650 mg). Chromatography of the oil on silica gel [80 g; column developed with benzene (200 ml)] gave three fractions. The first, an oil (380 mg) [eluted by benzene–ether (4 : 1; 200 ml)] was a mixture, showing n.m.r. bands at δ (CCl_4) 1.4 (3 H, d, *J* 6 Hz), 3.3 (2 H, d, *J* 6 Hz), 3.8 (6 H, s), 5.6 (1 H, m), and 7.4 (5 H, m) attributed to the trifluoroacetyl ester (17) of the pyrazole alcohol (16), besides the bands eventually assigned to the propenylpyrazole (12) (below). T.l.c. of similar fractions on silica gel and on acidic alumina, made by soaking alumina sheets in 95% ethanol (35 ml)–acetic acid (1 ml), and drying at 100 °C for 0.5 h, with benzene as solvent, showed only one spot. T.l.c. on untreated alumina (benzene) showed two components.

Rechromatography of this fraction on alumina (55 g) gave *dimethyl* 1-*phenyl*-3-*propenylpyrazole*-4,5-*dicarboxylate* (12), an oil (168 mg) [eluted by benzene (350 ml)], purified by Kugelrohr distillation (Found: C, 64.1; H, 5.2; N, 9.5. $C_{16}H_{16}N_2O_4$ requires C, 64.0; H, 5.4; N, 9.3%); *m/e* 300 (M^+), 268, 210, 182, 144, 143, 105, 91, 77 (base), and 51; *m** 239 (300 ⟶ 268), 164.6 (268 ⟶ 210), 157.7 (210 ⟶ 182), and 123.5 (268 ⟶ 182); $\nu_{max.}$ (CCl_4) 1 750, 1 725, 1 600, 1 535, 1 510, 1 470, 1 270, 1 225, and 1 100 cm^{-1}; δ_H (CCl_4) 1.9 (3 H, m), 3.8 (6 H, s), 6.7 (2 H, m), and 7.4 (5 H, m); δ_C 18.62, 51.79, 53.14, 120.1, 124.0, 128.8, 129.2, 131.8, 139.0, 150.5, 161.4, and 162.9.

Ether (150 ml) eluted the pyrazole alcohol (16) (84 mg), identified by n.m.r. comparison with an authentic sample (below).

The second fraction from the original chromatography on silica gel was *methyl* 2,4,6,7-*tetrahydro*-6-*methyl*-4-*oxo*-2-*phenylpyrano*[4,3-c]*pyrazole*-3-*carboxylate* (14) (57 mg) [eluted by benzene–ether (1 : 1; 200 ml)], white crystals, m.p. 130—131.5° (from carbon tetrachloride) (Found: C, 62.9; H, 5.0; N, 9.8. $C_{15}H_{14}N_2O_4$ requires C, 62.9; H, 4.9; N, 9.8%); *m/e* 286 (M^+), 271, 243, 242 (base), 184, 156, 155, 144, 143, 105, 77, and 51; *m** 217.7 (271 ⟶ 243), 204.8 (286 ⟶ 242), 139.9 (242 ⟶ 184), 132.3 (184 ⟶ 156), 84.5 (242 ⟶ 143), and 71.5 (286 ⟶ 143); $\nu_{max.}$ ($CHCl_3$) 1 745, 1 595, 1 565, 1 510, 1 325, 1 080, and 1 045 cm^{-1}; δ ($CDCl_3$) 1.6 (3 H, d, *J* 6 Hz), 3.0 (2 H, m), 3.6 (6 H, s), 4.8 (1 H, m), and 7.4 (5 H, s); δ_C (partial) 20.93, 29.67, 53.39, 77.42, 124.4, 129.3, 139.4, and 152.7.

The final fraction from the chromatography on silica gel was *dimethyl* 3-(2-*hydroxypropyl*)-1-*phenylpyrazole*-4,5-*dicarboxylate* (16) (142 mg) [eluted by ether (400 ml)], white crystals, m.p. 81.5—82° (from carbon tetrachloride) (Found: C, 60.4; H, 5.6; N, 8.8. $C_{16}H_{18}N_2O_5$ requires C, 60.4; H, 5.7; N, 8.8%); *m/e* 318 (M^+), 303, 274, 243, 242 (base), 184, 158, 144, 143, 105, 77, and 51; *m** 213.7 (274 ⟶ 242) and 139.9 (242 ⟶ 184); $\nu_{max.}$ ($CHCl_3$) 3 450, 1 745, 1 720, 1 603, 1 545, 1 510, 1 375, 1 270, and 1 100 cm^{-1}; δ ($CDCl_3$) 1.3 (3 H, d, J 6 Hz), 3.1 (3 H, m), 3.8 (6 H, s), 4.1 (1 H, m), and 7.4 (5 H, s); for ^{13}C n.m.r. data see Figure 1.

(b) *Toluene*-p-*sulphonic acid*. The diazepinone (9) (363 mg, 1.14 mmol) was heated with toluene-*p*-sulphonic acid monohydrate (218 mg, 1.14 mmol) in benzene (25 ml) for 1.5 h. T.l.c. on alumina (benzene) showed the presence of the propenylpyrazole (12) and a new compound. The mixture was diluted with ether and water, and the organic layer washed with water, aqueous 5% sodium hydrogen carbonate, and water again, and dried ($MgSO_4$). Removal of the solvent left an oil (420 mg), which on chromatography on alumina (21 g) gave compound (12) (88 mg) [eluted by benzene (200 ml)] and *dimethyl* 1-*phenyl*-3-(2-*tosyloxypropyl*)-*pyrazole*-4,5-*dicarboxylate* (20) (179 mg) [eluted partly by benzene, partly by benzene-ether (9 : 1; 200 ml)] and the pyrazole alcohol (16) (12 mg) [eluted by ether (60 ml)]. The tosylate (20) gave white crystals, m.p. 97—98° (from carbon tetrachloride) (Found: C, 58.6, H, 5.2; N, 5.9. $C_{23}H_{24}N_2O_7S$ requires C, 58.5; H, 5.1; N, 5.9%); $\nu_{max.}$ ($CHCl_3$) 1 745, 1 720, 1 603, 1 375, 1 265, 1 180, 1 100, and

925 cm^{-1}; δ ($CDCl_3$) 1.5 (3 H, d, *J* 6 Hz), 2.4 (3 H, s), 3.3 (2 H, m), 3.9 (6 H, 2s), 5.1 (1 H, m), and 7.4 (9 H, m).

If the reaction of the diazepinone (9) (318 mg, 1 mmol) with toluene-*p*-sulphonic acid monohydrate (190 mg, 1 mmol) was carried out in acetic anhydride (50 ml) and the anhydride was distilled off after 1 h, chromatography of the residue after the usual work-up, on alumina, gave mostly the acetyl derivative (21) of the pyrazole alcohol (16), an oil (231 mg), δ (CCl_4) 1.3 (3 H, d, *J* 6 Hz), 2.0 (3 H, s), 3.1 (2 H, d, *J* 7 Hz), 3.9 (6 H, s), 5.2 (1 H, m), and 7.5 (5 H, m).

Conversion of the Pyrazole Lactones (14) *and* (15) *into the Pyrazole Alcohols* (16) *and* (18).—When the pyrazole lactones (14) and (15) were kept at room temperature in methanol in the presence of toluene-*p*-sulphonic acid for several days, t.l.c. on silica gel [benzene–chloroform (4 : 1) or chloroform] showed the presence of the pyrazole alcohols (16) and (18), respectively. Chromatography gave samples of (16) and (18) which had i.r. spectra identical with those of analytical samples of the pyrazole alcohols.

Oxidation of the Propenylpyrazole (12).—The propenylpyrazole (12) (248 mg, 0.83 mmol), potassium permanganate (348 mg, 2.2 mmol), and dicyclohexyl-18-crown-6 (3 drops; Aldrich) were stirred in benzene (13 ml) for 1.5 h. The mixture was set aside overnight, and the solid was filtered off and rinsed with benzene. The solid was then shaken with water, filtered (suction) through Hy-Flo Supercel, and washed with successive 10 ml portions of water until the washings (100 ml) showed no fluorescence when spotted on a t.l.c. plate. The filtrate was allowed to evaporate, and the crystalline solid that remained was treated with concentrated hydrochloric acid (5 ml); the resulting slurry was extracted with ether until the extracts showed no fluorescence. The combined extracts (75 ml) were dried ($MgSO_4$) and evaporated to leave white crystals (215 mg), δ ($CDCl_3$) 3.9 (3 H, s), 4.0 (3 H, s), 7.6 (5 H, s), and 11.0 (1 H, s). 4,5-Bismethoxycarbonyl-1-phenylpyrazole-3-carboxylic acid was dissolved in 2,2-dimethoxypropane (5 ml), a drop of concentrated hydrochloric acid was added, and the mixture was kept at room temperature for a week, after which t.l.c. on alumina (chloroform) showed the presence of a new, less polar component. Removal of solvent and chromatography of the brown oil that resulted on alumina (11.0 g) gave trimethyl 1-phenylpyrazole-3,4,5-tricarboxylate, white crystals [66 mg; eluted by benzene (150 ml)], m.p. 88° (from methanol) (lit.,[21] 88°; lit.,[23] 89°), $\nu_{max.}$ ($CHCl_3$) 1 745 cm^{-1}; δ ($CDCl_3$) 3.8 (3 H, s), 3.9 (6 H, s), and 7.4 (5 H, s).[23]

Crystal Structure Determination of the Diazepinone (10).—A crystal of dimensions 0.3 × 0.3 × 0.4 mm, grown from methanolic solution, was selected. Cell dimensions were

TABLE 1

Atomic co-ordinates with standard deviations in parentheses; the first two digits of the hydrogen numbers correspond to the number of the atom to which the hydrogen is bonded

	x/a	*y/b*	*z/c*
N(1)	0.638 40(15)	0.656 58(6)	0.584 60(26)
N(2)	0.527 71(15)	0.639 31(7)	0.583 81(27)
C(3)	0.505 81(20)	0.616 98(9)	0.799 60(31)
C(4)	0.600 10(24)	0.575 97(10)	0.906 37(33)
C(5)	0.639 33(20)	0.533 07(9)	0.747 96(32)
C(6)	0.713 07(19)	0.556 93(8)	0.601 54(31)
C(7)	0.717 03(19)	0.616 45(9)	0.554 68(31)
C(8)	0.396 52(26)	0.584 09(12)	0.752 47(44)
C(9)	0.496 64(32)	0.670 11(11)	0.950 07(42)
O(10)	0.613 85(15)	0.480 39(6)	0.745 36(26)
C(11)	0.787 83(20)	0.514 79(8)	0.515 38(34)
O(12)	0.834 95(15)	0.473 64(6)	0.614 88(26)
O(13)	0.797 25(13)	0.527 85(6)	0.307 39(23)
C(14)	0.874 86(32)	0.491 79(15)	0.211 65(53)
C(15)	0.806 26(19)	0.641 47(8)	0.438 79(34)
O(16)	0.786 85(14)	0.669 07(7)	0.270 35(24)
O(17)	0.907 74(13)	0.629 07(6)	0.543 80(24)
C(18)	0.998 77(24)	0.646 05(11)	0.431 50(47)
C(19)	0.662 42(21)	0.718 81(8)	0.609 08(32)
C(20)	0.595 01(21)	0.760 14(9)	0.486 78(35)
C(21)	0.621 12(24)	0.819 83(10)	0.512 49(40)
C(22)	0.712 74(24)	0.837 89(9)	0.658 63(42)
C(23)	0.778 90(22)	0.796 53(11)	0.780 53(40)
C(24)	0.753 23(21)	0.736 45(9)	0.758 29(36)
H(02)	0.515(2)	0.609(1)	0.482(4)
H(041)	0.659(2)	0.600(1)	−0.038(3)
H(042)	0.572(2)	0.553(1)	0.023(4)
H(081)	0.406(2)	0.551(1)	0.671(4)
H(082)	0.373(2)	0.571(1)	0.885(4)
H(083)	0.334(2)	0.609(1)	0.668(5)
H(091)	0.479(2)	0.656(1)	0.093(5)
H(092)	0.573(2)	0.692(1)	0.978(4)
H(093)	0.431(3)	0.695(1)	0.878(4)
H(141)	0.953(3)	0.500(2)	0.303(6)
H(142)	0.853(3)	0.446(2)	0.218(5)
H(143)	0.875(3)	0.507(2)	0.085(7)
H(181)	0.987(3)	0.625(2)	0.289(6)
H(182)	1.001(3)	0.685(1)	0.417(5)
H(183)	1.067(4)	0.635(2)	0.527(8)
H(20)	0.531(2)	0.747(1)	0.386(3)
H(21)	0.574(2)	0.848(1)	0.426(4)
H(22)	0.730(2)	0.879(1)	0.680(4)
H(23)	0.842(2)	0.806(1)	0.889(4)
H(24)	0.801(2)	0.707(1)	0.851(3)

TABLE 2

Anisotropic* (× 10^4) and isotropic (Å^2) thermal parameters of the non-hydrogen and hydrogen atoms, respectively; standard deviations are given in parentheses

	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N(1)	9(2)	24(1)	38(1)	1(1)	8(1)	3(1)
N(2)	10(2)	30(1)	29(1)	−1(1)	5(1)	1(1)
C(3)	16(2)	33(1)	29(1)	−1(1)	10(1)	0(1)
C(4)	28(2)	35(1)	27(1)	0(1)	8(1)	2(1)
C(5)	24(2)	31(1)	30(1)	3(1)	5(1)	5(1)
C(6)	21(2)	25(1)	29(1)	1(1)	7(1)	2(1)
C(7)	8(2)	31(1)	29(1)	−1(1)	5(1)	0(1)
C(8)	29(3)	53(2)	40(2)	−14(2)	10(1)	3(1)
C(9)	38(3)	42(2)	41(2)	3(2)	16(2)	−8(1)
O(10)	61(2)	29(1)	52(1)	−7(1)	29(1)	4(1)
C(11)	20(2)	28(1)	37(1)	−4(1)	7(1)	−1(1)
O(12)	42(2)	38(1)	55(1)	16(1)	13(1)	10(1)
O(13)	28(2)	40(1)	35(1)	7(1)	11(1)	−3(1)
C(14)	43(3)	66(2)	51(2)	15(2)	22(2)	−13(2)
C(15)	9(2)	29(1)	38(1)	−1(1)	10(1)	−4(1)
O(16)	34(2)	49(1)	40(1)	3(1)	13(1)	15(1)
O(17)	8(1)	45(1)	47(1)	−1(1)	9(1)	5(1)
C(18)	18(2)	62(2)	78(2)	−9(2)	31(2)	7(2)
C(19)	23(2)	24(1)	35(1)	−4(1)	14(1)	−1(1)
C(20)	34(2)	29(1)	39(1)	3(1)	8(1)	2(1)
C(21)	49(2)	31(1)	55(2)	6(1)	20(2)	6(1)
C(22)	56(3)	29(1)	65(2)	−8(1)	35(2)	−8(1)
C(23)	29(3)	46(2)	59(2)	−13(1)	18(2)	−17(1)
C(24)	22(2)	38(1)	44(1)	−3(1)	10(1)	−4(1)

	B		*B*		*B*
H(02)	2.7(5)	H(092)	4.5(7)	H(183)	14.8(15)
H(041)	2.6(5)	H(093)	5.2(7)	H(20)	2.6(5)
H(042)	3.6(5)	H(141)	8.5(11)	H(21)	5.0(6)
H(081)	4.6(7)	H(142)	7.8(9)	H(22)	6.0(7)
H(082)	3.9(6)	H(143)	9.0(12)	H(23)	6.1(7)
H(083)	4.8(7)	H(181)	9.2(10)	H(24)	3.4(5)
H(091)	5.5(7)	H(182)	7.9(9)		

* The anisotropic thermal parameters U_{ij} (Å^2) are those of the temperature factor exp $[-2\pi^2(U_{11}a^{*2}h^2 + \ldots 2U_{12}a^*b^*hk + \ldots)]$.

derived from least-squares analysis of fifteen carefully centred Cu-K_{α_1} diffraction peaks, measured with a Syntex P1 diffractometer at room temperature.

Crystal Data.—$C_{17}H_{20}N_2O_5$, $M = 332.37$. Monoclinic, $a = 12.25(2)$, $b = 22.51(3)$, $c = 6.196(5)$ Å, $\beta = 99.61(8)°$, $U = 1\ 684(2)$ Å^3, $Z = 4$, $D_c = 1.311$ g cm^{-3}, $F(000) = 704$, space group $P2_1/n$. Cu-K$_\alpha$ radiation, $\lambda = 1.5418$ Å, μ(Cu-K_α) = 8.2 cm^{-1}.

The intensities of the 1 760 unique reflections with $2\theta \leqslant 118.6°$ were measured with monochromated Cu-K_α radiation on the Syntex diffractometer. Data were collected by the θ—2θ scan mode with a scan speed which was variable (2—24° min^{-1}) depending on the intensity of the reflection. The scans extended from one degree below $2\theta(K_{\alpha 1})$ to one degree above 2θ ($K_{\alpha 2}$). Background measurements were made at each end of the scan for one half the time of the scan. The intensities of three check reflections were re-measured at regular intervals during the data collection. No systematic trend was detected. Of the 1 760 reflections measured, 157 had $I \leqslant 3\sigma_I$, with σ values based on counting statistics. These were regarded as ' unobserved ' and were excluded from the subsequent least-squares refinement. The data were reduced to normalised structure factors in the usual way. No correction for absorption was deemed necessary.

The 116 reflections with $E > 1.80$ were used to solve the structure by means of the MULTAN program.[30] The resulting E map revealed all 24 non-hydrogen atoms. The co-ordinates and thermal parameters of these atoms were refined with the least-squares program CLS [31] in the block-diagonal mode, employing weights deduced from counting statistics. Isotropic, followed by two cycles of anisotropic refinement brought the R value to 0.117. Ten strong reflections which clearly suffered from extinction were deleted from subsequent refinement.

A difference electron density map then revealed all the hydrogen atoms. Thirteen additional reflections (23 total) were given zero weight on account of extinction, the rejection criterion being that of highest expected secondary extinction.[32] Continued refinement of all atoms, with isotropic thermal parameters for the hydrogens, gave an R value of 0.085.

A trend in $\Sigma w(\Delta F)^2$ with $|F_o|$ then indicated that the weighting $(\sigma^2|F_o|)^{-1}$, based on counting statistics, had produced an overweighting of the strongest reflections. To overcome this, weights of $(\sigma^2|F_o| + KF_o^2)^{-1}$ were introduced, where K = 0.0001 was found satisfactorily to eliminate the trend in $\Sigma w(\Delta F)^2$. Four cycles of refinement under this weight scheme brought R to 0.039. A final difference map showed no significant features. Observed and final calculated structure factors are available as Supplementary Publication No. SUP 21676 (11 pp., 1 microfiche).*

The final atomic co-ordinates are given in Table 1 and the thermal parameters in Table 2. Figure 2 shows a thermal-ellipsoid plot of the molecular structure and indicates the atom numbering. Bond distances and selected angles are given in Figure 3.

[5/1998 *Received*, 13*th October*, 1975

* For details of Supplementary Publications, see Notice to Authors, No. 7, *J.C.S. Perkin I*, 1975, Index issue.

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