Cycloadditions. Part II.[1] A Steric Effect in the 1,3-Dipolar Addition of 2-Diazopropane to Methyl But-2-ynoate

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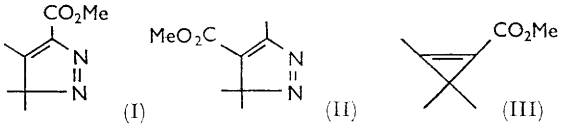
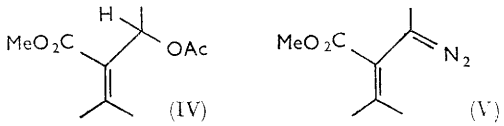
The predominant mode of 1,3-dipolar addition of 2-diazopropane to methyl but-2-ynoate is the opposite of that predicted on electronic grounds, 4-methoxycarbonyl-3,3,5-trimethyl-3*H*-pyrazole and 5-methoxycarbonyl-3,3,4-trimethyl-3*H*-pyrazole being obtained in the ratio 6 : 1. In contrast, methyl propiolate behaves normally with 2-diazopropane, giving solely 3,3-dimethyl-5-methoxycarbonyl-3*H*-pyrazole. The preference for reverse addition to methyl but-2-ynoate is attributed to steric factors in the transition states for cycloaddition.

The structures of the 3*H*-pyrazoles were established by photolysis, the diazoalkenes initially generated being trapped with acetic acid as acetoxy-esters. In the absence of acetic acid, the diazo-intermediates underwent further photolysis to cyclopropenes.

In connection with other work on cycloadditions,[2] we required an authentic sample of the 3*H*-pyrazole (I). Following our usual procedure,[3] we treated methyl but-2-ynoate with 2-diazopropane. It was expected on electronic grounds [4] that the reaction should give a single adduct (I), but there was obtained a mixture (82%) of two isomeric adducts, *A* and *B*, in the ratio 6 : 1. Both compounds showed the expected [3] spectroscopic properties for 3*H*-pyrazoles (see Experimental section) and were evidently the isomers (I) and (II). Isomer *B* had u.v. bands at 245 and 360 mμ (ε 4250 and 153, respectively). The corresponding bands for *A* occurred at longer wavelengths (257 and 381 mμ, ε 4640 and 144, respectively), and since the 3*H*-pyrazole (II) contains the more extended conjugated system, this structure was tentatively assigned to isomer *A*. In agreement with this, the carbonyl stretching frequency for *A* was 13 cm.$^{-1}$ lower than that for *B*. However, in absence of adequate models for the 3*H*-pyrazoles (I) and (II), the assignments are not unambiguous, and chemical evidence was sought.



On photolysis, the adducts showed behaviour characteristic of 3*H*-pyrazoles,[3a,5] both isomers giving the cyclopropene (III) *via* intermediate diazoalkenes. As in a previous example,[3a] the diazoalkene (red, $\lambda_{max.}$ 492 mμ) from isomer *A* could be trapped as an acetoxy-compound (51%) by photolysis of *A* in 2% ethereal acetic acid. The product is formulated as the diester (IV) on the basis of its n.m.r. spectrum, which indicated



the presence of a methyl group (τ 8·56) coupled (*J* 7 c./sec.) to an adjacent methine proton at τ 4·22, in addition to two allylic methyl groups (τ 8·15), acetate (τ 7·99) and methoxycarbonyl (τ 6·23). The ester (IV) must have been formed from the diazoalkene (V), the intermediate expected from the 3*H*-pyrazole (II).

[1] (*a*) Part I, S. D. Andrews, A. C. Day, and A. N. McDonald, *J. Chem. Soc.* (*C*), 1969, 787; (*b*) the present paper is also regarded as Part V of 'Photochemistry of Organic Nitrogen Compounds;' Part IV, S. D. Andrews and A. C. Day, *J. Chem. Soc.* (*B*), 1968, 1271.

[2] S. D. Andrews and A. C. Day, *Chem. Comm.*, 1967, 902; S. D. Andrews, A. C. Day, and R. N. Inwood, to be published.

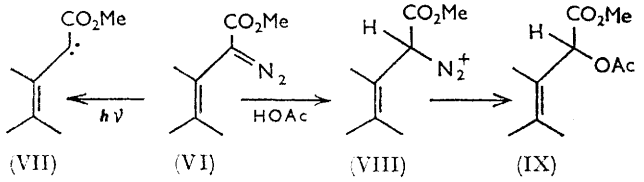
[3] A. C. Day and M. C. Whiting, (*a*) *J. Chem. Soc.* (*C*), 1966, 1719; (*b*) *J. Chem. Soc.* (*B*), 1967, 991.

[4] R. Huisgen, R. Grashey, and J. Sauer in 'The Chemistry of Alkenes,' ed. S. Patai, Interscience, New York, 1964, p. 826; R. Huisgen, *Angew. Chem. Internat. Edn.*, 1963, **2**, 565, 633.

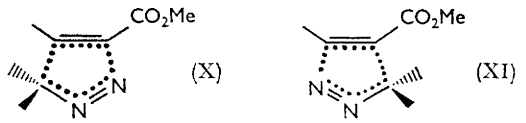
[5] G. L. Closs and W. A. Böll, *J. Amer. Chem. Soc.*, 1963, **85**, 3904; *Angew. Chem. Internat. Edn.*, 1963, **2**, 399; G. Ege, *Tetrahedron Letters*, 1963, 1667; R. Anet and F. A. L. Anet, *J. Amer. Chem. Soc.*, 1964, **86**, 525; but see ref. 3*b*.

The adducts *A* and *B* therefore have structures (II) and (I), respectively.

The photolytic intermediate from *B* [≡ (*I*)] was yellow ($\lambda_{max.}$ 422 mμ), and much less reactive to acid than that from the 3*H*-pyrazole (II). At the light intensity used for the latter, photolysis of isomer (I) in ethereal acetic acid gave solely the cyclopropene (III), even at high acid concentration (25%). In this case, the intermediate is an α-diazoester (VI), and it is well-known that such compounds are much less readily protonated than simple diazoalkanes.[6] To facilitate protonation [(VI) ⟶ (VIII); non-photochemical] at the expense of carbenoid decomposition [(VI) ⟶ (VII) ⟶ (III); mainly photochemical [3a]], photolysis of the 3*H*-pyrazole (I) was conducted at greatly reduced light intensity. Carbenoid decomposition was, in this way, partially suppressed, and there was now obtained, in addition to the cyclopropene (III), a low yield (17%) of the expected diester (IX), the formation of which affords independent proof that isomer *B* has structure (I).

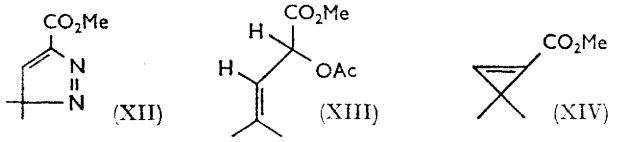


The reaction of 2-diazopropane with methyl but-2-ynoate thus gives predominantly (86%) the product (II) of reverse addition to the acetylenic bond. Such reversals in the addition of diazoalkanes to conjugated acetylenes have previously been observed only for highly phenylated systems where steric effects might be expected to be severe, *e.g.* the addition of diphenyldiazomethane to phenylpropiolic ester.[7] Though our example contains much less bulky groups, it seems that here too the reversal is steric in origin. The transition states for normal (X) and reverse (XI) addition both contain two gauche interactions involving the *gem*-dimethyl group and, respectively,



methyl and methoxycarbonyl groups. Conformational studies of cyclohexanes suggest that the methoxycarbonyl group is effectively smaller than the methyl group,[8] so that, sterically, reverse addition (XI) is favoured; apparently the steric effect is large enough to outweigh the electronic preference for orientation (X). With diazomethane steric effects are insignificant, for von Auwers and Ungemach [9] obtained only the electronically favoured adduct from diazomethane and ethyl but-2-ynoate.

As expected on this basis, methyl propiolate reacted with 2-diazopropane to give solely the 5-methoxycarbonyl-3*H*-pyrazole (XII), the adduct preferred both sterically and electronically. The structure of this compound was established by its photolytic conversion in ethereal acetic acid into the acetoxy-compound



(XIII), which gave n.m.r. signals for a vinyl proton at τ 4·73 coupled (*J* 9 c./sec.) to a methine proton at τ 4·31. Photolysis of (XII) in ether alone gave the unstable cyclopropene (XIV).

Similar reversals of orientation have been observed in the reactions of diazoalkanes with simple, conjugated ethylenic [1a] and allenic [2] esters and related compounds.[10] Such effects are also found with other 1,3-dipolar reagents.[4]

EXPERIMENTAL

General experimental procedures were as described in Part I,[1a] except that n.m.r. spectra were run in deuteriochloroform unless otherwise stated (*J* in c./sec.).

The Reaction of 2-Diazopropane with Methyl But-2-ynoate.—A solution of methyl but-2-ynoate [11] (1·2 g.) and 2-diazopropane [12] (7 g.) in ether (250 ml.) was kept at 0° overnight. Distillation gave an oil (1·78 g.), b.p. 98—110°/0·2 mm., containing two components (by t.l.c.). Chromatography on silica gel (80 g.) and elution with ether–light petroleum (1 : 4) (450 ml.) gave an oil which on distillation yielded 4-*methoxycarbonyl*-3,3,5-*trimethyl*-3H-*pyrazole* (II) (1·45 g., 70%), b.p. 95—100°/0·2 mm., n_D^{24} 1·4650 (Found: C, 57·3; H, 7·5; N, 16·4. $C_8H_{12}N_2O_2$ requires C, 57·1; H, 7·2; N, 16·7%); *m/e* 168 (M^+); $\nu_{max.}$ 1715s (C=O) and 1642m cm.$^{-1}$ (N=N); $\lambda_{max.}$ 257 and 381 mμ (ε 4640 and 144, respectively); $\lambda_{max.}$ (EtOH) 262 and 369 mμ (ε 4540 and 142, respectively); n.m.r. τ 8·48 [6H, s, C(3)-methyls], 7·31 [3H, s, C(5)-methyl], and 6·14 (3H, s, CO_2Me). Further elution of the column with ether–light petroleum (1 : 1) (100 ml.) then ether (300 ml.) gave solid 5-*methoxycarbonyl*-3,3,4-*trimethyl*-3H-*pyrazole* (I) (0·24 g., 12%) which recrystallised from pentane as needles, m.p. 41—41·5° (Found: C, 56·9; H, 7·4; N, 16·8%); *m/e* 168 (M^+); $\nu_{max.}$ 1728s (C=O) and 1638m cm.$^{-1}$ (N=N); $\lambda_{max.}$ 245 and 360 mμ (ε 4250 and 153, respectively); $\lambda_{max.}$ (EtOH) 252 and 345 mμ (ε 4330 and 184, respectively); n.m.r., τ 8·61 [6H, s, C(3)-methyls], 7·69 [3H, s, C(4)-methyl], and 6·02 (3H, s, CO_2Me).

Photolysis of 4-*Methoxycarbonyl*-3,3,5-*trimethyl*-3H-*pyrazole* (II).—(i) A solution of the 3*H*-pyrazole (120 mg.) in ether (25 ml.) was irradiated under reflux in a Pyrex

[6] H. Zollinger, 'Azo and Diazo Chemistry,' Interscience, London, 1961, pp. 102 *et seq.*

[7] R. Hüttel, J. Riedl, H. Martin, and K. Franke, *Chem. Ber.*, 1960, **93**, 1425.

[8] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, 'Conformational Analysis,' Wiley, New York, 1965, pp. 44 and 433—444.

[9] K. von Auwers and O. Ungemach, *Ber.*, 1933, **66**, 1205.

[10] Literature cited in refs. 1*a* and 2.

[11] I. N. Nazarov, S. N. Ananchenko, and I. V. Torgov, *Bull. Acad. Sci. U.S.S.R.*, 1959, 84.

[12] A. C. Day, P. Raymond, R. M. Southam, and M. C. Whiting, *J. Chem. Soc.* (*C*), 1966, 467; S. D. Andrews, A. C. Day, P. Raymond, and M. C. Whiting, *Org. Synth.*, in the press.

flask with an external Hanovia 450-w medium-pressure mercury lamp placed 5-cm. below the flask. The absorption band at 380 mμ rapidly decreased and the solution became pink ($\lambda_{max.}$ 492 mμ). The band at 492 mμ reached a maximum intensity after 65 min. and was indistinguishable from the base-line after 190 min. Distillation of the colourless solution gave 2-methoxycarbonyl-1,3,3-trimethylcyclopropene (III) (80 mg., 80%), b.p. 80—90° (bath)/27 mm. (lit.,[13] b.p. 57°/15 mm.), n_D^{26} 1·4370 (Found: C, 68·2; H, 8·8. Calc. for $C_8H_{12}O_2$: C, 68·5; H, 8·6%); *m/e* 140 (M^+); $\nu_{max.}$ 1840s (C=C) and 1712s cm.$^{-1}$ (C=O); $\lambda_{max.}$ 230 mμ (ε 6850); n.m.r., τ 8·80 [6H, s, C(3)-methyls], 7·77 [3H, s, C(1)-methyl], and 6·24 (3H, s, CO_2Me).

(ii) (In acetic acid). The 3*H*-pyrazole (200 mg.) was photolysed as above in ether (49 ml.) and acetic acid (1 ml.). No absorption band at 492 mμ was detected during photolysis, which was complete after 2 hr. The solution was washed with 2N-sodium carbonate solution then with brine, dried ($MgSO_4$), evaporated, and chromatographed on silica gel (30 g.). Elution with ether–light petroleum (1 : 4) (200 ml.) gave an oil (methyl 2-isopropylidenebut-3-enoate or methyl 2-ethylidene-3-methylbut-3-enoate) (39 mg., 23%), b.p. 70—80° (bath)/0·2 mm.; $\nu_{max.}$ 1723 (C=O) and 925s cm.$^{-1}$; $\lambda_{max.}$ 220 mμ (ε 4800); n.m.r. (CCl_4), τ 8·14 (6H, broadened), 6·27 (3H, s, CO_2Me), 5·20 and 5·12 (2H, multiplets), and 4·85 (1H, m). Further elution with the same solvent (125 ml.) gave *methyl 3-acetoxy-2-isopropylidenebutanoate* (IV) (121 mg., 51%), b.p. 70—80° (bath)/0·2 mm., n_D^{19} 1·4505 (Found: C, 59·95; H, 8·10. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·05%); *m/e* 200 (M^+); $\nu_{max.}$ 1742s and 1242s (OAc) and 1735s cm.$^{-1}$ (CO_2Me); n.m.r., τ 8·56 [3H, d, *J* 7, C(4)-protons], 8·15 (6H, two overlapping signals, Me_2C=), 7·99 (3H, s, OAc), 6·23 (3H, s, CO_2Me), and 4·22 [1H, q, *J* 7, C(3)-H].

Photolysis of 5-Methoxycarbonyl-3,3,4-trimethyl-3H-pyrazole (I).—(i) The 3*H*-pyrazole (190 mg.) in ether (50 ml.) was photolysed as described for the isomer (II). As the absorption band at 350 mμ decreased, a yellow colour ($\lambda_{max.}$ 422 mμ) developed, reaching its maximum intensity after 2 hr. and becoming indistinguishable from the base line after 6 hr. Distillation gave the cyclopropene (III) (140 mg., 88%), b.p. 80—90° (bath)/27 mm. n_D^{26} 1·4370 (Found: C, 68·5; H, 8·5%). The product was identical (n_D, i.r., u.v., n.m.r., and mass spectra) with the sample prepared from the isomeric 3*H*-pyrazole (II).

(ii) (In acetic acid). The 3*H*-pyrazole (290 mg.) was irradiated in ether (48 ml.) and acetic acid (12 ml.) with the lamp *ca.* 10 cm. below the flask, a fine wire gauge being interposed to reduce the light intensity incident on the flask. The heat of the lamp was sufficient to maintain very gentle boiling. Irradiation was continued for 48 hr.; then the light yellow-brown solution was washed successively with 2N-sodium carbonate solution and brine, dried ($MgSO_4$), and evaporated. The oil (290 mg.) contained some cyclopropene (III) ($\nu_{max.}$ 1840 cm.$^{-1}$), which was removed under reduced pressure. The residue was chromatographed on silica gel (35 g.). Elution with ether–light petroleum (1 : 99) (150 ml.) gave an oil (20 mg.) ($\nu_{max.}$ 1715s, 1626w, 1605w, 908w, and 880w cm.$^{-1}$). Elution with ether–light petroleum (1 : 19) (250 ml.) gave *methyl 2-acetoxy-3,4-dimethylpent-3-enoate* (IX) (60 mg., 17%), b.p. 80—90° (bath)/1 mm. (Found: C, 59·85; H, 7·7. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·05%); $\nu_{max.}$ 1754s and 1236s (OAc) and 1735sh cm.$^{-1}$ (CO_2Me); n.m.r. (CCl_4), τ 8·40, 8·28, and 8·18 (signals of approximately equal intensity; $W_{\frac{1}{2}}$ 4, 2, and 3 c./sec., respectively; 9H, C-methyls); 7·93 (3H, s, OAc), 6·33 (3H, s, CO_2Me), and 4·22 [1H, $W_{\frac{1}{2}}$ 2 c./sec.; C(2)-H]; weak signals at τ 8·51, 8·04, 6·38, and 4·28 and a slight shoulder at 7·90 suggested the presence of a trace of methyl 4-acetoxy-3,4-dimethylpent-2-enoate, the allylic isomer of diester (IX). Elution of the column with more polar solvents (up to ether alone) gave traces of yellow material [$\lambda_{max.}$ 245 mμ (intense); shoulder >300 mμ].

Photolysis in ethereal acetic acid as described for the 4-methoxycarbonyl-3*H*-pyrazole (II) (*i.e.*, full lamp intensity, *ca.* 5 cm. from the flask) gave solely the cyclopropene (III), even at acetic acid concentrations up to 25%.

3,3-Dimethyl-5-methoxycarbonyl-3H-pyrazole (XII).—A solution of methyl propiolate (1 g.) and 2-diazopropane (3 g.) in ether (70 ml.) was kept at 0° overnight. Partial evaporation and cooling gave the 3H-*pyrazole* (XII) (1·25 g., 70%), m.p. 95° (from Et_2O) (Found: C, 54·6; H, 6·8; N, 18·0. $C_7H_{10}N_2O_2$ requires C, 54·5; H, 6·5; N, 18·2%); *m/e* 154 (M^+); $\nu_{max.}$ 1755 and 1735s (C=O) and 1624s cm.$^{-1}$ (N=N); $\lambda_{max.}$ 232 and 367, λ_{infl} 270 mμ (ε 3480, 119, and 730, respectively); $\lambda_{max.}$ (EtOH) 235 and 353 mμ (ε 3100 and 135, respectively); n.m.r., τ 8·50 [6H, s, C(3)-methyls], 6·02 (3H, s, CO_2Me), and 2·69 [1H, s, C(4)-H]. Though the crude reaction mixture was carefully investigated, no other adducts could be detected.

Photolysis of 3,3-Dimethyl-5-methoxycarbonyl-3H-pyrazole (XII).—(i) The 3*H*-pyrazole (XII) (500 mg.) in ether (85 ml.) was photolysed under reflux in the usual way. A yellow colour ($\lambda_{max.}$ 440 mμ) developed, reaching its maximum intensity after 45 min., and after 2 hr. the solution was again colourless. Evaporation gave *3,3-dimethyl-1-methoxycarbonylcyclopropene* (XIV), b.p. 60° (bath)/20 mm., n_D^{21} 1·4500 (Found: C, 66·5; H, 7·8. $C_7H_{10}O_2$ requires C, 66·6; H, 8·0%; $\nu_{max.}$ 1760s (C=C) and 1708s cm.$^{-1}$ (C=O); n.m.r. (CCl_4), τ 8·72 (6H, s, *gem*-dimethyl), 6·25 (3H, s, CO_2Me), and 2·15 [1H, s, C(2)-H]. The compound was stable in cold, dilute ethereal solution, but polymerised rapidly in the pure state, and on slow distillation, to give dimeric material (*m/e* 252) and an involatile solid, m.p. 80—85°.

(ii) The 3*H*-pyrazole (XII) (200 mg.) was photolysed in ether (45 ml.) and acetic acid (5 ml.) essentially as described for the homologue (I). A transient yellow colour ($\lambda_{max.}$ 440 mμ) developed, then faded during 1 hr. The solution was washed with 2N-sodium carbonate solution and then with brine, dried ($MgSO_4$), evaporated, and chromatographed on silica gel (30 g.). Elution with ether–light petroleum (1 : 4) (150 ml.) gave mixed fractions (29 mg.), b.p. 60—70° (bath)/0·2 mm., then (with 250 ml. solvent) *methyl 2-acetoxy-4-methylpent-3-enoate* (XIII) (85 mg., 35%), b.p. 60—70° (bath)/0·2 mm. (Found: C, 59·1; H, 7·8. $C_9H_{14}O_4$ requires C, 58·05; H, 7·6%); *m/e* 186; $\nu_{max.}$ 1768s and 1236s (OAc) and 1750s cm.$^{-1}$ (CO_2Me); u.v., end-absorption only; n.m.r. τ 8·19 [6H, broadened, C(4)-methyls], 7·87 (3H, s, OAc), 6·26 (3H, s, CO_2Me), 4·73 [1H, d, (*J* 9) of multiplets, C(3)-H], and 4·31 [1H, d, 9, C(2)-H].

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[13] G. L. Closs and L. E. Closs, *J. Amer. Chem. Soc.*, 1963, **85**, 99.