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Reaction of 3,3-Pentamethylenediaziridine with Diphenylcyclopropenone

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3,3-Pentamethylenediaziridine reacts with diphenylcyclopropenone in methanol to give two isomeric 1:1 adducts. One of these is 1,2-dihydro-4,5-diphenylpyridazine-3-spirocyclohexan-6-one and to the second is tentatively ascribed the structure 2", 3"-diphenylcyclohexanespiro-2'-oxadiazolidine-5'-spirocyclopropene on the basis of its conversion by a novel rearrangement back into an acylated diaziridine structure.

OUR interest in the addition reactions of small ring compounds ^{1,2} as a route to medium-sized heterocycles led us to examine the reaction of a diaziridine with diphenylcyclopropenone (DPP).^{3,4} 3,3-Pentamethylenediaziridine⁵ reacts with DPP in methanol at room temperature during 3 days. [Elevated temperatures increase the rate of reaction but also lead to rapid solvolytic cleavage of the DPP to form methyl (E)diphenylacrylate.] An oil resulted, chromatography of which yielded a pale yellow solid product in modest yield. This contained two isomeric 1:1 adducts, one of which (A) was separable and readily characterised as a dihydropyridazone as described later.

The n.m.r. spectra of both (A) and (B) show two broad exchangeable singlets and no vinyl proton; ¹ J. W. Lown, R. K. Smalley, and G. Dallas, Chem. Comm.,

1968, 1543. ² J. W. Lown and R. K. Smalley, Tetrahedron Letters, 1969, 169.

³ R. Breslow, R. Haynie, and J. Mirra, J. Amer. Chem. Soc., 1959, **81**, 247.

therefore the possible structures for these isomers are (I) - (IV).



⁴ (a) M. E. Vol'pin, Yu. D. Koreshkov, and D. N. Kursanov, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1959, **3**, 560; (b) D. N. Kursanov, M. E. Vol'pin, and Yu. D. Koreshkov, J. Gen. Chem. U.S.S.R., 1960, **30**, 2855. ⁵ E. Schmitz and R. Ohme, Chem. Ber., 1961, **94**, 2166.

Org.

Structure (IV) may reasonably be discounted since reaction (1) is mechanistically unattractive. Such



behaviour would be uncharacteristic of a diaziridine; once the nitrogen is quaternised the adjacent C-N bond is much more likely to break than is the N-N bond.⁶ Structure (II) would also result from N-N bond cleavage by cycloaddition to the C=C bond of the DPP. To test for such a reaction, the diaziridine was treated with maleic anhydride. The resultant NN'-bimaleimide (V) arises from nucleophilic attack by the nitrogen on the anhydride carbonyl followed by C-N cleavage. A more



satisfactory mode of reaction of the diaziridine with DPP is through the common intermediate (VI), which would lead naturally to (I) and (III).



Structure (I) is assigned to compound (A), which shows the typical reaction with phosphoryl chloride ⁷ to give the chlorodihydropyridazine, which crystallised from water as the hydrochloride dihydrate (VII). Izzo and Kende have reported the formation of a 4-pyridazone by the action of diazomethane on diphenylcyclopropenone.8

Attempts to obtain isomerically pure (B) showed it to be labile; it rearranged when heated in polar solvents such as acetone or ethyl acetate, to give compound (VIII). The rearrangement is catalysed by nucleophiles such as thiocyanate and by Meerwein's reagent, triethoxonium fluoroborate. The product (VIII) shows the characteristic reaction⁶ of a monosubstituted diaziridine in the immediate quantitative release of iodine (2 equiv.) from acidified potassium iodide solution.

7 T. L. Jacobs, 'Heterocyclic Compounds,' ed. R. C. Elderfield, Wiley, New York, 1957, vol. 6, p. 108.

This shows that the two nitrogen atoms are still bonded together in the primary adduct (B). Therefore we



suggest structure (III) for (B), analogous to that of the dimer of diphenylcyclopropenone.⁹

Compounds (IX) and (X) may reasonably be discounted as intermediates in the rearrangement of (III)



to (VIII), since (IX) and the N-acetyl derivative of (X) did not rearrange in the presence of nucleophiles. However, (X) itself was not available for comparison.

The overall reaction of DPP on 3,3-pentamethylenediaziridine via (III) to (VIII) is a mild monoacylation. The course of this reaction contrasts with the direct



acylation brought about by (E)-diphenylacryloyl chloride, which gave (XI), presumably via the labile acylated oxadiazoline intermediate.⁶

EXPERIMENTAL

M.p.s. were determined with a Fisher-Johns apparatus. I.r. spectra were recorded with a Perkin-Elmer model 421 spectrophotometer. N.m.r. spectra were recorded with a Varian A-60 analytical spectrometer for *ca*. 10–15% (w/v) solutions; line positions are reported in p.p.m. from tetramethylsilane. Mass spectra were determined with an A.E.I. MS9 double-focusing high-resolution mass spectrometer (ionisation energy usually 70 ev). Peak measurements were made by comparison with perfluorotributylamine at a resolving power of 15,000. Kieselgel DF-5 (Camag Switzerland) and Eastman-Kodak pre-coated silica sheets were used for t.l.c. Microanalyses were carried out by Mrs. D. Mahlow of this department.

Reaction of Pentamethylenediaziridine with Diphenylcyclopropenone.---A solution of pentamethylenediaziridine (8.2 g.) and diphenylcyclopropenone (15 g.) in cold methanol (100 ml.) was set aside at room temperature for 3 days. The resulting orange solution was concentrated in vacuo to

E. Schmitz, Adv. Heterocyclic Chem., 1963, 2, 121.

 ⁸ P. T. Izzo and A. S. Kende, *Chem. and Ind.*, 1964, 839.
⁹ R. Breslow, T. Eicher, A. Krebs, R. A. Peterson, and J. Posner, J. Amer. Chem. Soc., 1965, 87, 1320.

an orange-red oil, which was chromatographed on Fisher grade 1 alumina with benzene as eluant, to give a pale yellow solid (3.609 g., 15.6% based on initial diphenylcyclopropenone). Recrystallisation from ethyl acetate and acetone effected separation into two fractions: pure (A), and (B) contaminated with (A). The former (1.50 g.), m.p. 238° (decomp.) was 1,2-dihydro-4,5-diphenylpyridazine-3-spirocyclohexan-6-one [Found: C, 79.1; H, 7.1; N, 8.9%, M (mass spectrum), 318. C₂₁H₂₂N₂O requires C, 79·2; H, 7.0; N, 8.8%; M, 318], $\nu_{max.}$ (CHCl₃) 1640s (C=O) and 3280br and 3430 (sharp) (NH and OH) cm.⁻¹, δ (CDCl₃) 1.15-2.31 (10H, cyclohexyl H), 4.63br and 5.86br (each 1H, exchangeable NH), and 6.80-7.46 (10H, aryl H). The purity of this sample was proved by comparison with a sample of unchanged (A), m.p. 238°, remaining after the selective removal of (B) by rearrangement from a mixture of (A) and (B) (see later).

The second fraction consisted largely of 2",3"-diphenylcyclohexanespiro-2'-oxadiazolidine-5'-spirocyclopropane (B) (2.10 g.), m.p. 228° (decomp.) [Found: C, 79.0; H, 6.7; N, 8.6%; M (mass spectrum), 318. $C_{21}H_{22}N_2O$ requires C, 79·2; H, 6·9; N, 8·8%; M, 318], ν_{max} 1630s and 3410 (sharp, NH) cm.⁻¹, δ (CDCl₃) 1·15—2·25 (10H, cyclohexyl H), 4.55br and 5.82br (each 1H, exchangeable NH), and 6.80-7.38 (10H, aryl H). That these spectral data may be ascribed to (B) and not to the small quantity of (A) present is confirmed by the isolation of a pure sample of (B) during a trial rearrangement. [In nearly all thiocyanate-catalysed rearrangements a mixture of (B) with the rearrangement product was obtained.] Compound (B) (0.201 g.) and potassium thiocyanate (27 mg.) in acetone (10 ml.) were heated under reflux for 24 hr.; crystals of pure (B) separated (35 mg.), m.p. 240°, $\nu_{max.}$ (CHCl₃) 1630s and 3410 (sharp NH) cm.⁻¹, δ [(CD₃)₂SO] 1·15—2·25 (10H, cyclohexyl H), 6.90br (2H, NH), and 6.95-7.35 (10H, aryl H). Recrystallisation of this sample by prolonged heating in ethyl acetate (10 ml.) produced 1-(2,3-diphenylacryloyl)pentamethylenediaziridine (see later) (33 mg.), m.p. 147-148° (from benzene-light petroleum).

Thiocyanate-catalysed Rearrangement of Compound (B).— A solution of the compound (B) (0.873 g.) and potassium thiocyanate (0.065 g.) in acetone (35 ml.) was heated under reflux for 3 days and allowed to cool; crystals which separated (0.712 g.) gave a white powder, m.p. 148—149° (decomp.) (from ethyl acetate).

Diaziridine ring estimation. The product releases iodine from potassium iodide-acetic acid equivalent to 3.45 ml. of 0.1n-sodium thiosulphate, 97.5% of the theoretical amount predicted on the basis of one diaziridine ring and M = 318. Microanalysis produced variable results, since the product, being a diaziridine, incorporated varying amounts of water. However the C: N ratio agreed with the formula $C_{21}H_{22}N_2O, xH_2O$ and the parent peak of the mass spectrum corresponded to C₂₁H₂₂N₂O, *i.e.* an isomer of the starting material, 1-(2,3-diphenylacryloyl)pentamethylenediaziridine [Found: C, 70.5; H, 6.7; N, 7.8%; M (mass spectrum), 318.1731 (calc. 318.1732) C: N ratio 9.00. $C_{21}H_{22}N_2O, xH_2O$ requires C: N 9.00; M, 318], $\nu_{\rm max.}~({\rm CHCl_3})~1680{\rm s}~({\rm C=O})~{\rm and}~3380{\rm br}~{\rm and}~3200{\rm br}~({\rm NH}~{\rm and}~{\rm OH})~{\rm cm.^{-1}};~\delta~({\rm CDCl_3})~0.97{\rm --1.25}~(10{\rm H},~{\rm cyclohexyl}~{\rm H})~{\rm and}$ 6·90—7·95 (11H, aryl H and CH=C), $\lambda_{max.}$ (MeCN) 245 mµ (c 11,830).

Meerwein Reagent-catalysed Rearrangement of Compound (B).—A solution of compound (B) (0.859 g.) in dry methylene chloride (35 ml.) was treated dropwise with stirring with

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a solution of freshly prepared triethoxonium fluoroborate (2.86 g.) in dry methylene chloride (40 ml.) during 5 min. The mixture was stirred at room temperature for 7 days then treated cautiously with 50% aqueous potassium carbonate solution. The filtered organic layer was dried (MgSO₄). Evaporation of the solvent left an oil, trituration of which with ethyl acetate gave a white solid (0.8 g.), m.p. 142—143° identical with the product obtained from the thiocyanate-catalysed rearrangement.

Reaction of Pentamethylenediaziridine with (E)-2,3-Diphenylacryloyl Chloride.---A solution of freshly prepared 2,3-diphenylacryloyl chloride (3.38 g., 0.00718 mole) in dry pyridine (10 ml.) was added dropwise to a rapidly stirred solution of the resublimed diaziridine (1.57 g., 0.00718 mole) in dry pyridine (15 ml.) during 20 min. The mixture was then stirred for 3 hr. and set aside at room temperature overnight. Precipitated pyridine hydrochloride was collected and the filtrate was poured into water (50 ml.), acidified with 2N-hydrochloric acid, and extracted with benzene. The benzene layer was washed with aqueous sodium hydrogen carbonate then water and dried $(MgSO_4)$. Evaporation of the benzene solution left a red oil which was chromatographed on alumina with benzene as eluant; the main fraction, recrystallised from light petroleum, gave (E)-cyclohexanone NN-bis-(2,3-diphenylacryloyl)hydrazone (1.219 g., 33.5%), m.p. 176° [Found: C, 82·3; H, 6·2; N, 5·4%; M (osmometric), 538; (mass spectrum), 524. $C_{36}H_{32}N_2O_2$ requires C, 82·4; H, 6·2; N, $5\cdot3\%$; *M*, 524], ν_{max}. (CHCl₃) 1630s cm.⁻¹ (C=O), δ (CDCl₃) 1·26--3·24 (10H, cyclohexyl H) and 6·82---7·60 (22H, aryl and vinyl H). The product does not release iodine from acidified potassium iodide; the diaziridine ring is therefore no longer intact. In [2H5]pyridine the vinyl proton signals are selectively shifted beyond the aryl envelope and are clearly visible at δ 7.61].

(E)-2,3-*Diphenylacrylohydrazide*.—A solution of (E)-2,3diphenylacryloyl chloride [from the pure acid (5.5 g., 0.0246 mole) and thionyl chloride] in ether (50 ml.) was added dropwise with rapid stirring to a solution of hydrazine (8.5 g., 0.265 mole) in absolute ethanol (100 ml.) cooled in ice. A white solid separated; after 12 min. the mixture was poured into water, and the product gave (from ethyl acetate) (E)-2,3-*diphenylacrylohydrazide* (4.8 g., 82%), m.p. 134° [Found: C, 75.8; H, 6.2; N, 11.8%; M (osmometric), 240; (mass spectrum), 238. C₁₅H₁₄N₂O requires C, 75.6; H, 5.9; N, 11.8%; M, 238], v_{max} . (CHCl₃) 1660s (C=O) and 3330 and 3430 (NH and NH₂) cm.⁻¹, δ (CDCl₃) 3.90br (3H, exchanged by D₂O, NH·NH₂), 6.80—7.52 (10H, aryl H), and 7.86 (1H, vinyl H).

(E)-Cyclohexanone 2,3-Diphenylacryloylhydrazone. A mixture of cyclohexanone (1.03 g.) and (E)-2,3-diphenylacrylohydrazide (2.30 g.) in ethanol (10 ml.) was heated under reflux on a steam-bath for 8 hr., allowed to cool, and poured into water, affording a yellow gum which crystallised on trituration with ethyl acetate, and gave the hydrazone (2.19 g., 69%), m.p. 142° (from benzene-light petroleum) [Found: C, 79.1; H, 7.3; N, 8.7%; M (mass spectrum), 318; (osmometric), 305. $C_{21}H_{22}N_2O$ requires C, 79.2; H, 7.0; N, 8.80%; M, 318], v_{max} (CHCl₃) 1695s (C=O) and 3230br (NH) cm.⁻¹, δ (CDCl₃) 1.25—2.57 (10H, cyclohexyl H), 6.82—7.54 (10H, aryl H), 7.89 (1H, vinyl H), and 8.11br (1H, NH), λ_{max} (MeCN) 286 mµ (ε 24,000). (E)-3'-Acetyl-5'-(1,2-diphenylvinyl)cyclohexanespiro-2'-

(E)-3'-Acetyl-5'-($\overline{1}, \overline{2}$ -diphenylvinyl)cyclohexanespiro-2'oxadiazoline.—(E)-Cyclohexane 2,3-diphenylacryloylhydrazone (1·34 g.) in acetic anhydride (2·8 g.) was heated under reflux for 1 hr. then allowed to cool; water (30 ml.) was added and the mixture was neutralised with solid potassium carbonate. The residual oil crystallised when chilled and (from light petroleum) gave the oxadiazoline as a pale yellow amorphous powder (0.843 g., 55%), m.p. 165° [Found: C, 76.5; H, 6.6; N, 7.7%; *M* (osmometric), 363; (mass spectrum), 360. $C_{23}H_{24}N_2O_2$ requires C, 76.6; H, 6.7; N, 7.8%; *M*, 360], ν_{max} (CHCl₃) 1655s (Ac) and 1640 (oxadiazoline ¹⁰) cm.⁻¹, δ (CDCl₃) 1.17—2.00 (10H, cyclohexyl H), 2.07 (3H, Ac), and 2.0—7.65 (11H, aryl and vinyl H), λ_{max} 324 m μ (ϵ 22,200).

Reaction of 1,2-Dihydro-4,5-diphenylpyridazine-3-spirocyclohexan-6-one with Phosphoryl Chloride.-A solution of the compound (0.247 g.) in phosphoryl chloride (5 ml.) was heated under reflux for 90 min. then allowed to cool, and the excess of phosphoryl chloride was removed in vacuo. The residual yellow oil was treated with cold water, chilled, and triturated with ethyl acetate to afford bright yellow crystals (0.243 g., 94%) of 6-chloro-4,5-diphenyl-2Hpyridazinium-3-spirocyclohexane hydrochloride dihydrate, m.p. 138° (from water) [Found: Cl, 17.2; N, 6.6%; M (base peak mass spectrum), 336·1395 (calc. 336·1394 for ³⁵Cl). $C_{21}H_{22}Cl_2N_2, 2H_2O$ requires Cl, 17·3; N, 6·8%], (CHCl₃) 3100br cm.⁻¹ (NH), no C=O absorption, $v_{max.}$ δ (CDCl₃) 1·17-2·18 (10H, cyclohexyl H) and 6·74-7·77 (11H, aryl H and NH), λ_{max} 372 mµ (ϵ 4820). Attempted Thiocyanate-catalysed Rearrangements.—(a) (E)-

Attempted Thiocyanate-catalysed Rearrangements.—(a) (E)-Cyclohexanone 2,3-diphenylacryloylhydrazone (0.80 g.) and potassium thiocyanate (0.087 g.) were dissolved in acetone (35 ml.); the solution was heated under reflux for 72 hr. and allowed to cool. The solvents were evaporated off to leave a white gum (0.71 g.). Chromatography on grade 1 alumina in benzene gave (i) unchanged hydrazone (0.46 g.); (ii) (E)-2,3-diphenylacrylohydrazide (0.091 g.), m.p. 133°, mixed m.p. with authentic hydrazide 134°; and (iii) (E)acetone 2,3-diphenylacryloylhydrazone (0.2267 g.), m.p. 164° [Found: C, 77.6; H, 6.5; N, 9.9%; M (mass spectrum),

¹⁰ R. Breslow, C. Yaroslavsky, and S. Yaroslavsky, *Chem. and Ind.*, 1961, 1961.

278. $C_{18}H_{18}N_2O$ requires C, 77.7; H, 6.5; N, 10.0%; M, 278].

(b) (E)-3'-Acetyl-5'-(1,2-diphenylvinyl)cyclohexanespiro-2'-oxadiazoline (0.50 g.) and potassium thiocyanate (0.084 g.) in acetone (15 ml.) were heated under reflux for 14 hr., then allowed to cool. The solvent was allowed to evaporate to leave unchanged oxadiazoline (0.473 g.), m.p. 165°. The i.r. spectrum of the residue was identical with that of starting material.

(c) 1,2-Dihydro-4,5-diphenylpyridazine-3-spirocyclo-

hexan-6-one (A) (0.223 g.) and potassium thiocyanate (0.051 g.) in a mixture of dry acetone (10 ml.) and tetrahydrofuran (15 ml.) were heated under reflux for 72 hr. then allowed to cool. The solvents were evaporated off. The residual crystalline solid (0.24 g.), m.p. 235.8°, was identical (i.r.) with the starting material.

A similar experiment in which a suspension of the pyridazone in dry acetone containing a catalytic quantity of potassium thiocyanate was heated under reflux for several days, also produced no evidence of rearrangement.

Reaction of 3,3-Pentamethylenediaziridine with Maleic Anhydride.—3,3-Pentamethylenediaziridine (1.92 g.) was treated with maleic anhydride (3.36 g.) in ethyl acetate (50 ml.). The solution turned yellow and heat was evolved. It was warmed for 30 min. then set aside at room temperature for 2 days; the yellow solid deposited, m.p. 165° (decomp.), was NN'-bimaleimide containing a little maleic anhydride. The imide gave white crystals (1.57 g., 48%), m.p. 176° (decomp.) (from methanol) (lit.,¹¹ 176°) [Found: N, 14.3%; *M* (mass spectrum), 192. $C_8H_4N_2O_4$ requires N, 14.6%; *M*, 192], ν_{max} (Nujol) 1707 cm.⁻¹ (C=O), δ [(CD₃)₂SO], 6.37 (4H, s), vinyl H).

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¹¹ E. Hedaya, R. L. Hinman, and S. Theodoropulos, J. Org. Chem., 1966, **31**, 1311.