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PYRIDAZINES BY ADDITION OF DIAZOALKANES TO 1-BROMO- AND 1,2-DIBROMOCYCLOPROPENES

Ahmad R. Al Dulayymi and Mark S.Baird,

Department of Chemistry, University of Wales, Bangor, Gwynedd, LL57 2UW

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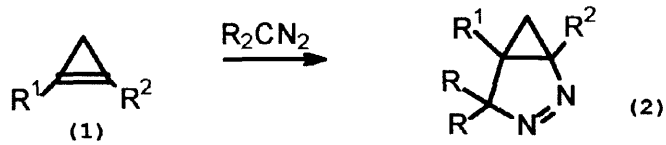
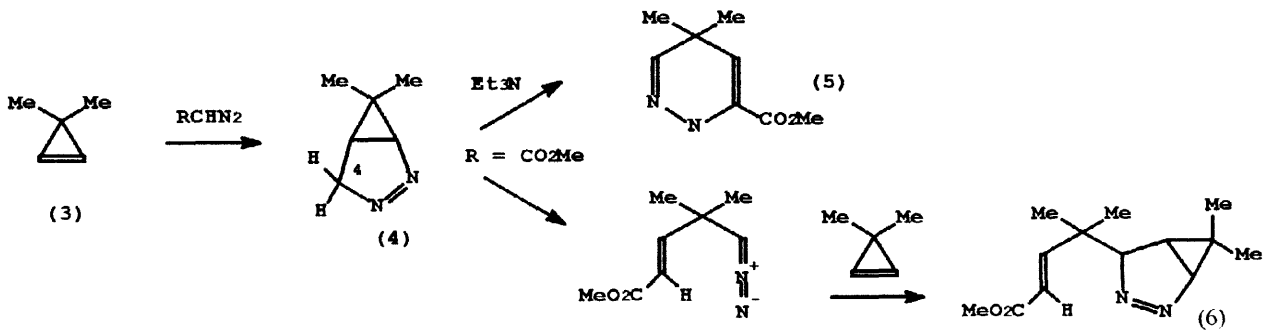
Abstract: Reaction of a range of 1-bromocyclopropenes with diazo-compounds leads to pyrazoles which ring-open to pyridazines in reasonable yield.

Diazoalkanes are known to undergo 1,3-dipolar cycloaddition to cyclopropenes under very mild conditions leading initially to pyrazolines.[1] The reactivity of alkylcyclopropenes towards diazoalkanes decreases with increasing substitution, and this has been explained in terms of steric effects.[2] The addition can show high regioselectivity, e.g., treatment of (**1**, R^1 = H, R^2 = $POPh_2$) with diazopropane leads only to (**2**, R^1 = H, R^2 = $POPh_2$), [3] while the cyclo-propene (**1**, R^1 = H, R^2 = COOMe) reacts with diazomethane to give only one regioisomeric adduct (**2**, R^1 = H, R^2 = COOMe).[4] In other cases, less selectivity is observed, eg., reaction of 1-t-butoxycarbonyl-2-phenyl-3,3-dimethylcyclopropene with diazomethane gave two regioisomers in a ratio of *ca.* 1:1.[5]



Although some pyrazolines (**2**) can be isolated, a number of others cannot be identified and rearrange rapidly under the reaction conditions.[2] In some cases they are sensitive to base or acid and rearrange to dihydropyridazines.[1,6,7,8] In other cases, they rearrange to diazoalkenes. Thus, while reaction of 3,3-dimethylcyclopropene with diazomethane leads to pyrazoline (**4**, R = H) as a stable compound, with methyl diazoacetate, it gives a mixture of products (**5**) and (**6**) originating from the initial adduct (**4**, R = COOMe).[2]



The instability of (**4**) was explained by the presence of the electron withdrawing group at C_4, facilitating its rearrangement to the diazo-derivative. This in turn undergoes a 1,3-dipolar addition with a second molecule of cyclopropene to give (**6**). The formation of dihydropyridazine (**5**) was again explained by the presence of the

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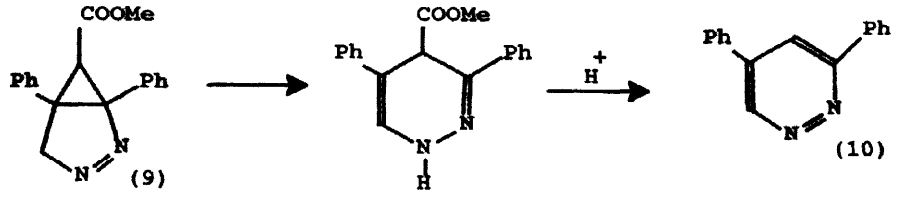
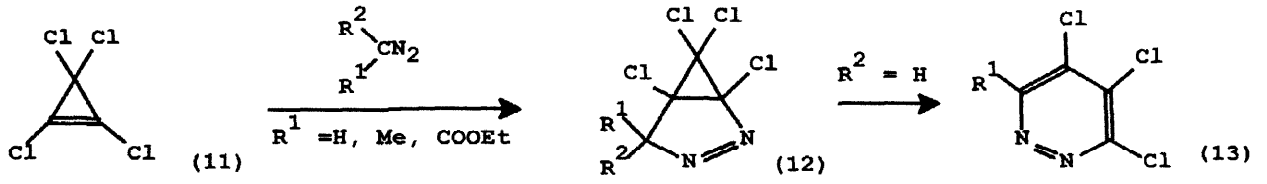
electron withdrawing group at C_4 in (4), and it also seems possible that the excess of diazoacetate ester may act as a basic catalyst in this rearrangement. This is supported by the exclusive formation of (5), when the reaction is run in the presence of triethylamine.[2]

Thermal decomposition of pyrazolines has also been reported. In some cases, this leads to the formation of bicyclo[1.1.0]butanes;[4] in others, complex products are obtained which are consistent with rearrangement of the pyrazoline to a diazo-compound which can eliminate nitrogen to produce a carbene, which in turn can undergo various intramolecular reactions.[9,4] The cycloadduct (9) is converted by alkali or acid into 3,5-diphenylpyridazine (10) by aromatisation of the intermediate dihydropyridazine with the loss of HCOOMe.[6,10]

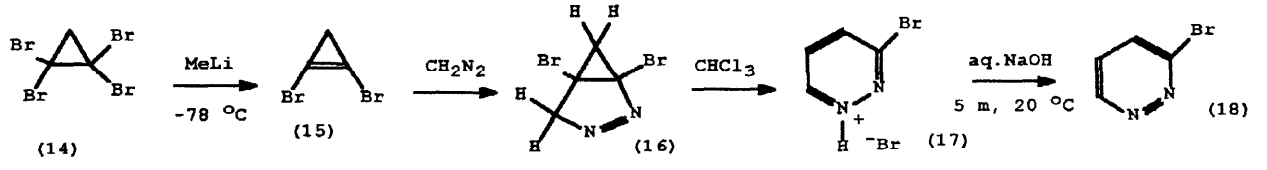


Similarly tetrachlorocyclopropene (11) reacts with an alkyl diazomethane to give the pyridazines (13) without isolation of the intermediate (12), the final step involving aromatisation of an intermediate dihydropyridazine, by loss of HCl.[11]



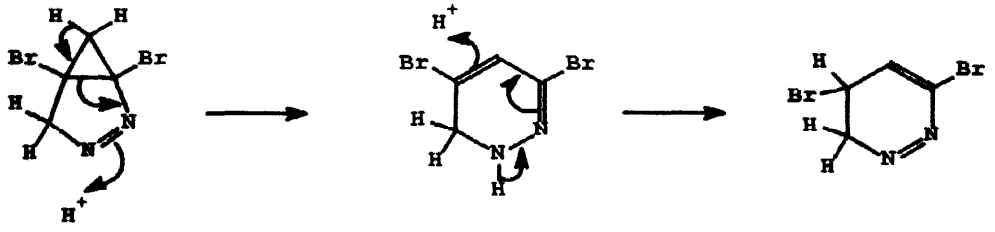
We now report the preparation of a number of pyridazines by related additions of diazo-compounds to 1-bromo- and 1,2-dibromocyclopropenes.

Cyclopropene (15), prepared in ether solution by treatment of the tetrabromocyclopropane (14) with 1 mololecular equivalents of methylithium at -78 °C,[12] was treated with an excess of diazomethane at 0 °C. A rapid reaction occurred leading to the pyrazoline (16) (85 %).The ^{1}H n.m.r spectrum of (16) showed the geminal hydrogens next to nitrogen as two doublets (J 19.8 Hz), while the methylene of the cyclopropane appeared as two doublets at δ 2.0 and 1.2 (J 7.7 Hz).

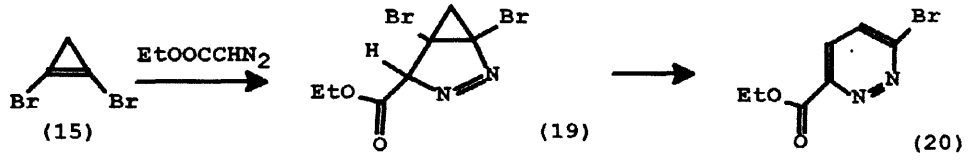


The pyrazoline (16) was relatively stable at 0-5 °C as a neat liquid. However it completely rearranged to (17) in 82 % yield when allowed to stand in chloroform for 1 h. The ^{1}H n.m.r spectrum of this showed a double doublet (1 H) at δ 9.1 (J 1.4 and 4.9 Hz), together with two doublets of doublets at δ 8.1 (J 1.4, 8.7 Hz) and 7.7 (J 4.9, 8.7 Hz), while the ^{13}C n.m.r. spectrum gave four signals in the aromatic region. Treatment of the salt (17) with base at room temperature for 5 min gave the free pyridazine (18) (67 %).[13] The ^{1}H n.m.r spectrum of this showed the expected three doublets of doublets at δ 9.1, 7.7 and 7.3. It could be distinguished from the

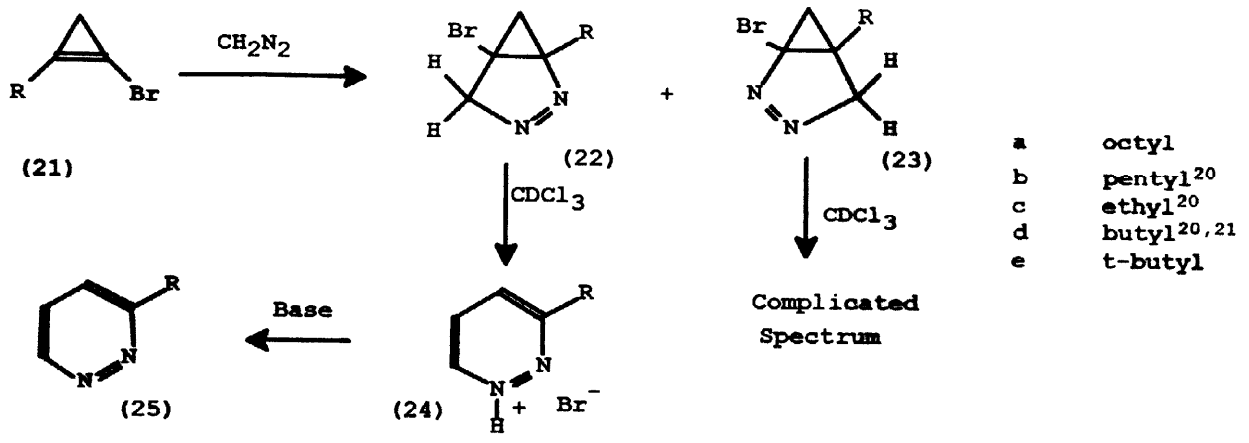
4-isomer because there was only one hydrogen at about δ 9. Thus 3-methylpyridazine is known to show two protons at δ 7.3 and one at 9.0,[7] while the 4-isomer shows one proton at δ 7.3 and two at 9.0 and 9.04 respectively.[8] Moreover, the carbon chemical shifts of C-3 and C-6 of these pyridazines occur at δ 149 - 160, whereas those of C-4 and C-5 occur at δ 127 - 138,[7,8] allowing them to be distinguished by means of DEPT spectra. The formation of (17) may involve protonation at one of the nitrogens followed by or concurrent with ring opening of the cyclopropane as shown below and then aromatisation. Clearly, whatever the detailed mechanism, the bromine at C-5 is selectively lost in this reaction:



Reaction of 1,2-dibromocyclopropene (**15**)[12] with ethyl diazoacetate was slow compared to that with diazomethane. After 38 h, a solid was obtained which on treatment with sodium bicarbonate gave the free pyridazine (**20**) in 52 % yield. The product (**20**) gave an ^{1}H n.m.r spectrum which included two doublets at δ 8.0 and 7.8 (J 8.8 Hz), while the ^{13}C spectrum included the carbonyl carbon at δ 163.5 and four aromatic carbons.[14] The formation of (**20**) presumably again involves an initial 1,3-dipolar addition to give the unstable pyrazoline (**19**) which undergoes a rapid rearrangement to (**20**) by a mechanism similar to that above.

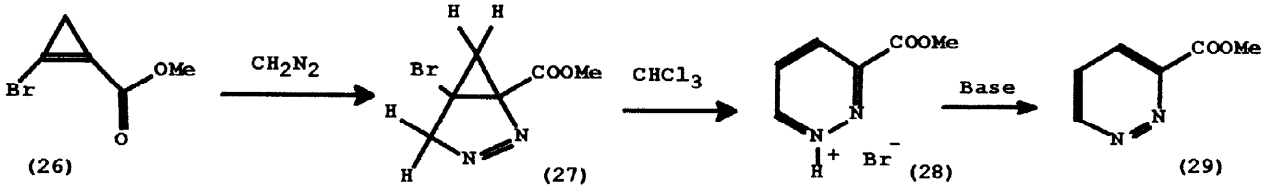


The reaction of a 1-bromo-2-alkylcyclopropenes (**21**)[15] with an excess of diazomethane was found to be less selective, leading to a mixture of two regioisomers in a ratio of *ca* 1- 2 : 1 which could generally be separated by column chromatography on silica. In the case of the octyl derivative, the ^{1}H n.m.r spectrum of the major isomer (**22a**) showed an AB pattern for the methylene group with a coupling constant of 19.4 Hz, and two double double doublets for the -CH_2- next to the ring at δ 2.3 (J 5.3, 10.4, 14.5 Hz) and 1.8 (J 5.3, 10.4, 15.8 Hz), two doublets for the methylene of the cyclopropane with a coupling constant of 6.4 Hz, a multiplet at δ 1.5 integrating for two protons and a broad singlet at δ 1.2 integrating for ten protons, together with a triplet for the methyl group. The minor isomer (**23a**) showed a very similar spectrum apart from the methylene group adjacent to nitrogen which appeared at a higher field by 0.3 ppm due to the shielding of the alkyl group.

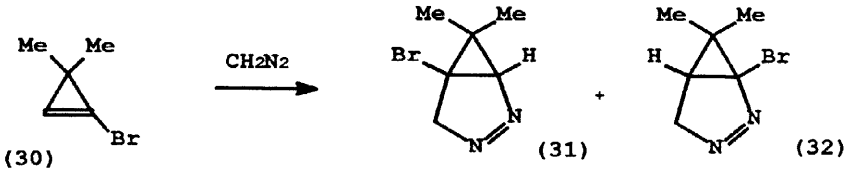


Under the same conditions, the major isomer rearranged to 3-octylpyridazine hydrobromide (**24a**) in a moderate yield. When this was treated with sodium bicarbonate it gave the free pyridazine (**25a**).

Addition of an excess of diazomethane in ether solution to methyl 1-bromocyclopropenecarboxylate (**26**) at -50 °C,[14] followed by stirring at room temperature for 2 h, gave the pyrazoline (**27**), which rearranged rapidly in chloroform or benzene to a brown solid (**28**) (56 %). The ^{1}H n.m.r spectrum included three double doublets in the aromatic region resonating at δ 9.4, 8.5 and 8.2, distinguishing it from the regioisomeric 4-ester.[7] Treatment of the methyl 3-pyridazine hydrobromide (**28**) with base gave the free pyridazine (**29**) in 45 % yield.[16]



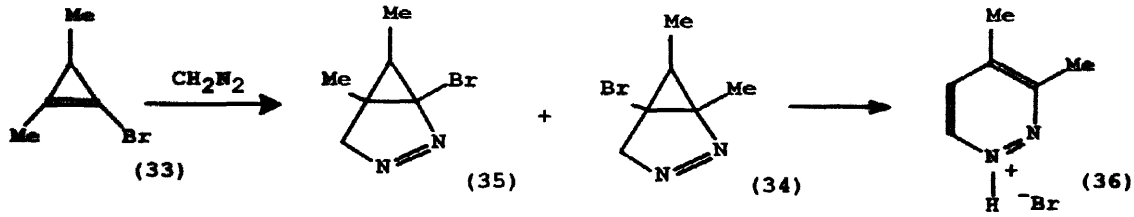
As noted above, the addition of diazomethane to 3,3-dimethylcyclopropene led to a stable pyrazoline. However, the cyclopropene (**30**)[15] gave a pyrazoline which showed less stability. Addition of diazomethane in ether solution at 0 °C, showed low selectivity and produced a mixture of two isomers (**31**) and (**32**) in ratio 2.2:1.



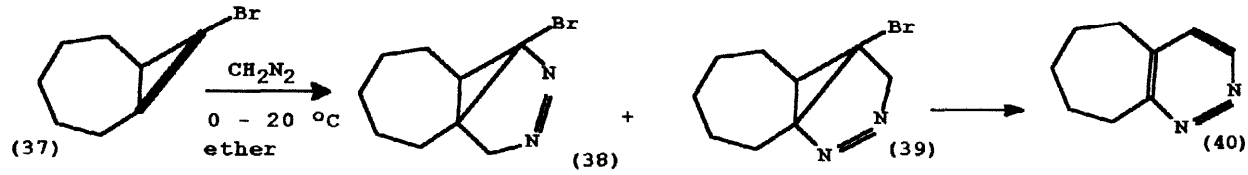
The ^{1}H n.m.r spectrum of the pyrazoline (**31**) showed a doublet at δ 4.7 with geminal coupling (J19.9 Hz), a doublet for the proton of the cyclopropane ring (J 2.5 Hz), and a double doublet at δ 4.5 with coupling constants of 19.9 and 2.5 Hz (the latter presumably being an allylic coupling). The second isomer (**32**) showed three double doublets for the ring hydrogens and two singlets for the methyl group. When the two isomers were allowed to stand in $CDCl_3$ a complicated mixture was obtained in each case and no pyridazine could be separated.

Moreover, reaction of diazomethane with 1-bromo-2,3-dimethylcyclopropene (**33**)[17] in ether solution at

0 to 20 °C for 2 h, led to the two pyrazolines (**34**) and (**35**) in a ratio of 4:3. The first isomer (**34**) showed an AB pattern for the methylene group with a coupling constant of 19.3 Hz and one singlet for the methyl group at δ 1.7 together with a doublet at δ 1.1 integrating to three protons and a quartet at δ 0.5 for the cyclopropane proton. When this isomer was allowed to stand in $CDCl_3$ for 10 h, 3,4-dimethylpyridazine hydrobromide (**36**) was obtained which showed two doublets in the aromatic region with coupling constant of 5.3 Hz. However, the second isomer (**35**) decomposed to a complicated mixture when allowed to stand in $CDCl_3$.



Addition of a diazoalkane to a cyclopropene fused to a second ring was also investigated. When diazomethane was allowed to react with the unstable 1-bromobicyclo [5.1.0]oct-8-ene (**37**).[18] The crude product was a mixture of two components (**38**) and (**39**) in a ratio of 1:1. Chromatography on silica eluting with petrol and ether (5:2) and a few drops of triethylamine gave a brown solid (**40**) in 35 % yield. The ^1H n.m.r spectrum of the pyridazine (**40**) showed two doublets in the aromatic region (J 5.3 Hz), two multiplets integrating for four protons at δ 3.5 and 3.1, together with another multiplet at δ 1.8 for (6 H).



Given the ready availability of 1-bromocyclopropenes, the above results may offer a useful route to a number of pyridazines which are difficult to obtain by other methods.

Experimental Section

Reagents were obtained from commercial suppliers and used without further purification unless stated. Dichloromethane was distilled over calcium hydride. Diethyl ether was distilled over sodium wire. Petroleum was either of boiling point 40 - 60 or 60 - 80 °C and was distilled. Reactions requiring anhydrous conditions were performed using oven dried glassware (250 °C) cooled under dry nitrogen and the experiments were conducted under a positive atmosphere of dry nitrogen. Organic solutions were dried over anhydrous magnesium sulphate, and, unless stated, were evaporated at 14 mmHg. Yields quoted are for the purified compounds unless stated.

All new compounds were homogeneous by tlc or by glc. Glc was conducted using a Perkin-Elmer Model F17 F.I.D. on a capillary column (30 m x 0.32 mm id Phase, DB5 split ratio of 50:1) using nitrogen as carrier gas. Tlc was performed using Aldrich silica gel 60 plates (F254). Compounds were visualised either under an ultraviolet source or by exposure to iodine vapour. Column chromatography was conducted with Merck 7736 silica gel under medium pressure. Melting points are uncorrected. Infrared spectra were obtained as KBr discs or as liquid films on a Perkin-Elmer 1600 FTIR spectrometer. Low resolution mass spectra were obtained using

a Finnigan Mat 1020 spectrometer. Mass measurements refer to ^{79}Br and ^{35}Cl isotopes unless stated and were obtained from the Swansea Mass Spectrometry Service. Microanalyses were performed with a Carlo-Erba Model 1106 CHN analyser. Nmr spectra were recorded on a Bruker AC250 at 250 MHz for protons and 62.5 MHz for carbon and in the latter case were either broad-band or gated decoupled.

Reactions of 1,2-dibromocyclopropene

With diazomethane: An excess of diazomethane in ether (20 ml) was added to a stirred solution of 1,2-dibromocyclopropene at 0 °C (which was prepared by the addition of methyllithium (8.7 mmol, 5.86 ml) to a stirred solution of 1,1,2,2-tetrabromocyclopropane (3.0 g, 8.3 mmol) in dry ether (40 ml) at -78 °C).[12,19] The reaction was stirred for 5 min at this temperature before quenching with water (2 ml). The ether layer was decanted from the ice. This was washed with ether (2 x 20 ml). The combined ether layers were allowed to reach room temperature and stirred for 2 h, when TLC showed no starting material. The solvent and diazomethane were removed at 0 °C and 14 mm Hg to give a yellow oil, *1,5-dibromo-2,3-diazabicyclo[3.1.0]hex-2-ene* (**16**) (1.7 g, 85 %) which showed δ_H: 4.9 (1 H, d, J 19.8 Hz), 4.8 (1 H, d, J 19.7 Hz), 2.0 (1 H, d, J 7.7 Hz), 1.2 (1 H, d, J 7.7 Hz); δ_C: 85.8, 75.0, 34.1, 31.9.

When compound (**16**) was allowed to stand in $CHCl_3$ at room temperature for 1 h, a brown solid was formed which was identified as *3-bromopyridazine hydrobromide* (**17**) (1.64 g, 82 %) (Found: C 20.2, H 1.8, N 11.5. $C_4H_4Br_2N_2$ requires: C 20.03, H 1.68, N 11.68) which showed δ_H: 9.1 (1 H, dd, J 1.4, 4.9 Hz), 8.1 (1 H, dd, J 1.4, 8.7 Hz), 7.7 (1 H, dd, J 4.9, 8.7 Hz); δ_C: 150.4, 148.5, 135.4, 131.4. Hydrobromide (**17**) (1.4 g) was treated with sodium hydroxide (2 g) in water (2 ml) for 5 min, extracted with ether (5 x 10 ml), and the combined ether layers were dried, and evaporated to give *3-bromopyridazine* (**18**)[13] (0.62 g, 67 %) as yellow crystals, m.p. 80-82 °C (dec.) (Found: C 30.1, H 1.6, N 17.3.$C_4H_3N_2Br$ requires: C 30.2, H 1.9, N 17.6) which showed δ_H: 9.1 (1 H, dd, J 1.3, 4.7 Hz), 7.7 (1 H, dd, J 1.3, 8.6 Hz), 7.3 (1 H, dd, 4.7, 8.6 Hz); δ_C: 150.6, 148.6, 131.7, 128.3.

With ethyl diazoacetate: Diazoester (0.9 ml, 8.5 mmol) was added to a stirred ether solution of 1,2-dibromocyclopropene at 0 °C and the mixture stirred for 38 h at room temperature. When TLC showed no starting material, the solvent was removed at 14 mm Hg to give a yellow oil (1.88 g) which became a semi-solid on standing for 24 h; this was treated with petroleum and the solid was filtered off (0.9 g). The solvent was removed from the filtrate; after 2 h the residue was treated again with petroleum ether. The solid which formed was again filtered off (0.5 g). The combined solids were treated with $CHCl_3$ and aq.sodium bicarbonate to give a brown solid, *ethyl 3-bromo-6-pyridazinecarboxylate* (**20**) (1.9 g, 51 %), which was recrystallized from petrol and ether to give white crystals, m.p. 143-145 °C (Found: N 12.3, C 36.8, H 3.1. $C_7H_7N_2O_2Br$ requires: N 12.1, C 36.4, H 3.1) which showed δ_H: 8.0 (1 H, d, J 8.8 Hz), 7.8 (1H , d, J 8.8 Hz), 4.5 (2 H, q, J 7.1 Hz), 1.4 (3 H, t, J 7.1 Hz); δ_C: 163.5, 151.1, 150.9, 132.1, 129.2, 62.9, 14.2; υ_{max}: 1727, 1548, 788 cm^{-1}.

Reaction of 1-bromo-2-alkylcyclopropenes with diazomethane

General Procedure: An excess of diazomethane in ether (7 ml) was added to a stirred solution of a 1-bromo-2-alkylcyclopropene in ether at 0 °C (which was prepared by the addition of methyllithium (1.02 ml, 1.2 eq) to a stirred solution of 1,1,2-tribromo-2-alkylcyclopropane (0.5 g, 1.2 mmol) in dry ether (10 ml) under nitrogen at -78 °C).[15] The mixture was allowed to reach -30 °C and then quenched with water (2 ml). The aq. layer was extracted with ether (2 x 10 ml), then the ether layers were combined. The reaction was allowed to reach room temperature and stirred for 24 h, when TLC showed no starting material was left; the excess of diazomethane and ether were removed at 0 °C and 14 mm Hg to give a yellow oil.

(a) **1-Bromo-2-octylcyclopropene**: Reaction as above gave two components in a ratio of *ca* 2:1, *5-bromo-1-octyl-2,3-diazabicyclo[3.1.0]hex-2-ene* and *1-bromo-5-octyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (**22a**, **23a**), which were separated by rapid column chromatography on silica gel eluting with petroleum and ether (5:0.5). The first isomer (0.27 g, 39 %) showed δ_H: 4.7 (1 H, d, J 19.4 H z), 4.6 (1 H, d, J 19.4 Hz), 2.3 (1 H, ddd, J 5.3, 10.4, 14.5 Hz), 1.8 (1 H, ddd, J 5.3, 10.4, 15.8 Hz), 1.5 (2 H, m), 1.4 (1 H, d, J 6.4 Hz), 1.2 (10 H, br, s), 0.3 (3 H, t, J 6.8 Hz), 0.6 (1 H, d, J 6.4 Hz). The second isomer (0.2 g, 29 %) showed δ_H: 4.5 (1 H, d, J 19.3 Hz), 4.3 (1 H, d, J 19.3 Hz), 2.3 (1 H, ddd, J 4.0, 9.3, 14.3 Hz), 1.8 (1 H, ddd, J 4.0, 9.3, 14.8 Hz), 1.5-0.7 (16 H, m, including a doublet at 1.4 with coupling constant 6.0 Hz), 0.6 (1 H, d, J 6.0 Hz). When this isomer was allowed to stand in $CDCl_3$ for 24 h at room temperature, a complex ^1H nmr spectrum was obtained. Under the same conditions the first isomer decomposed to give to a brown solid; removal of the solvent gave *3-octylpyridazine hydrobromide* (**24a**) (0.26 g, 38 %) (Found: C 52.9, H 8.0, N 10.1. $C_{12}H_{21}N_2Br$ requires C 52.8, H 7.8, N 10.3) which showed δ_H: 9.5 (1 H, br.d, J 5.0 Hz), 8.6 (1 H, dd, J 5.0, 8.5 Hz), 8.3 (1 H, dd, J 1.2, 8.5 Hz), 3.2 (2 H, t, J 7.8 H z), 1.7 (2 H, pent, J 7.8 Hz), 1.1 (10 H, br, s), 0.7 (3 H, t, J 7.0 Hz); δ_C: 156.3, 149.2, 136.4, 136.3, 33.6, 31.7, 29.1, 29.0, 22.5, 14.0; ν_{max}: 1622 cm^{-1}. The hydrobromide was treated with sat.aq.sodium bicarbonate (2 ml) and extracted with ether (2 x 10 ml), dried and evaporated to give *3-octylpyridazine* (**25a**) (0.14 g, 78 %) (Found M^+: 192.1626. $C_{12}H_{20}N_2$ requires: 192.1626) which gave a single peak on GLC and showed δ_H: 9.0 (1 H, dd, J 1.8, 4.6 Hz), 7.35 (1 H, dd, J 4.6, 8.4 Hz), 7.29 (1 H, dd, J 1.8, 8.4 Hz), 2.94 (2 H, complex), 1.74 (2 H, pent, J 7.5 Hz), 1.23 (10 H, br, s), 0.81 (3 H, t, J 7.0 Hz); δ_C: 163.2, 149.5, 126.3, 126.1, 36.4, 32.0, 29.6, 29.3, 29.2, 29.1, 22.6, 14.0; υ_{max}: 1586, 1463, 1437, 909, 732 cm^{-1}.

(b) **1-Bromo-2-pentylcyclopropene** : Reaction as above gave two isomers in a ratio of 3:2, *5-bromo-1-pentyl-2,3-diazabicyclo[3.1.0]hex-2-ene and 1-bromo-5-pentyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (**22b**, **23b**); δ_H (for mixture): 4.7 (1 H, d, J 19.4 Hz), 4.6 (1 H, d, J 19.4 Hz), 4.5 (1 H, d, J19.4 Hz), 4.3 (1 H, d, J 19.4 Hz), 2.4 (2 H, m), 1.9 (2 H, m), 1.6-1.2 (14 H, m), 0.9 (6 H, m), 0.62 (1 H, d, J 6.1 Hz), 0.58 (1 H, d, J 6.1 Hz). Rapid chromotography eluting with petroleum and ether (5:2) gave *3-pentylpyridazine hydrobromide* (**24b**) (0.35 g, 35 %) (Found: C 46.7, H 6.4, N 12.1. $C_9H_{15}BrN_2$ requires: C 46.8, H 6.5, N 12.1) which showed δ_H: 9.6 (1 H, dd, J 1.4, 5.0 Hz), 8.7 (1 H, dd, J 5.0, 8.6 Hz), 8.4 (1 H, dd, J 1.4, 8.6 Hz), 3.3 (2 H, t, J 7.6 Hz), 1.8 (2 H, pent, J 7.5 Hz), 1.3 (4 H, br , s), 0.8 (3 H, t, J 7.0 Hz); δ_C: 165.4, 150.0, 136.5, 136.37, 33.7, 31.0, 28.5, 22.2, 13.8; ν_{max}: 3415, 1618 cm^{-1}. The second isomer gave a complex ^1H nmr spectrum.

The hydrobromide above was treated with sat.aq. sodium bicarbonate (2 ml) as above to give *3-pentylpyridazine* (**25b**)[20] (0.1 g, 83 %) (Found M^+:150.1157; $C_9H_{14}N_2$ requires: 150.1157). This gave a single peak on GLC and showed δ_H: 9.0 (1 H, dd, J 1.9, 4.7 Hz), 7.37 (1 H, dd, J 4.7, 8.5 Hz), 7.3 (1 H, dd, J 1.9, 8.5 Hz), 2.94 (2 H, complex), 1.74 (2 H, pent, J 7.5 Hz), 1.32 (4 H, br, s), 0.86 (3 H, t, J 7 Hz); δ_C: 164.0, 150.9, 126.3, 126.2, 36.3, 31.3, 29.8, 22.4, 13.9; υ_{max}: 2233, 1597, 1456, 912, 732 cm^{-1}.

(c) **1-Bromo-2-ethylcyclopropene**: Reaction as above gave *5-bromo-1-ethyl-2,3-diazabicyclo[3.1.0]hex-2-ene* and *1-bromo-5-ethyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (**22c**, **23c**) in a ratioof 5:4. Chromatography as above gave the first isomer (0.3 g, 49 %) which showed δ_H: 4.8 (1 H, d, J 19.4 Hz), 4.7 (1 H, d, J 19.4 Hz), 2.4 (1 H ,dq, J 7.5,14.9 Hz), 1.9 (1 H, dq, J 7.4, 14.9 Hz), 1.4 (1 H, d, J 6.4 Hz), 1.2 (3 H, t, J 7.4 Hz), 0.6 (1 H, d, J 6.4 Hz). The second isomer (0.26 g, 42 %) showed δ_H: 4.5 (1 H, d, J 19.4 Hz), 4.3 (1 H, d, J 19.4 Hz), 1.6 (2 H, q, J 7.5 Hz), 1.4 (1 H, d, J 6.1 Hz), 1.0 (3 H, t, J 7.5 Hz), 0.6 (1 H, d, J 6.1 Hz).

When compound (**23c**) was allowed to stand in $CDCl_3$ for 24 h at 20 °C, decomposition led to a complicated ^1H n.m.r. spectrum. Under the same conditions, compound (**22c**) gave a brown solid, *3-ethylpyridazine hydrobromide* (**24c**) (0.28 g, 46 %) (Found: C 38.0, H 5.2, N 15.0. $C_6H_9BrN_2$ requires: C 38.1, H 4.8, N 14.8)

which showed δ_H: 9.6 (1 H d, J 4.9 Hz), 8.5 (1 H, dd, J 4.9, 8.5 Hz), 8.3 (1 H, d, J 8.5 Hz), 3.4 (2 H, q, J 7.5 Hz), 1.48 (3 H, t, J 7.5 Hz); δ_C: 164.9, 149.5, 126.5, 125.8, 29.5, 13.6; ν_{max}: 3420, 1621 cm^{-1}. The hydrobromide was treated with sat.aq.sodium bicarbonate (2 ml) as above to give *3-ethylpyridazine* (**25c**)[20] (0.09 g, 69 %) (Found M^+: 108.0687. $C_6H_8N_2$ requires: 108.0687) which gave a single peak on GLC and showed δ_H: 8.95 (1 H, dd, J 2.0, 4.6 Hz), 7.33 (1 H, dd, J 4.6, 8.4 Hz), 7.27 (1 H, dd, 2.0, 8.4 Hz), 2.9 (2 H, q, J 7.6 Hz), 1.28 (3 H, t, J 7.6 Hz); δ_C: 164.9, 149.5, 126.5, 125.8, 29.5, 13.6; υ_{max}: 2235, 1670, 1598, 911 cm^{-1}.

(d) **1-Bromo-2-butylcyclopropene**: Reaction as above gave *5-bromo-1-butyl-2,3-diazabicyclo[3.1.0]hex-2-ene* and *1-bromo-5-butyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (**22d, 23d**) in a ratio of *ca* 3:2. Chromatography as above gave the first isomer (0.5g, 39 %) which showed δ_H: 4.8 (1 H, d, J 19.6 Hz), 4.7 (1 H, d, J 19.6 Hz), 2.3 (1 H, ddd, J 5.3, 10.4, 14.5 Hz), 1.8 (1 H, ddd, J 5.3, 10.2, 15.5 Hz), 1.6 (2 H, m), 1.4 (1 H, d, J 6.4 Hz), 1.3 (2 H, m), 0.92 (3 H, t, J 7.2 Hz), 0.6 (1 H, d, J 6.4 Hz). The second isomer (0.4 g, 31 %) showed δ_H: 4.5 (1 H, d, J 19.3 Hz), 4.4 (1 H, d, J 19.3 Hz), 1.6 (2 H, m), 1.4 (1 H, d, J 6.0 Hz), 1.3 (4 H, br, m), 0.8 (3 H, t, J 7.0 Hz), 0.6 (1 H, d, J 6.0 Hz); when this isomer was allowed to stand in $CDCl_3$ for 24 h at room temperature complete decomposition occurred to give a mixture showing a complex ^1H n.m.r. spectrum.

Under the same conditions, compound (**22d**) was completely changed and gave a brown solid, *3-butylpyridazine hydrobromide* (**24d**) (0.45 g, 35 %) (Found: C 44.3, H 5.8, N 12.8. $C_8H_{13}BrN_2$ requires: C 44.3, H 6.0, N 12.9) which showed δ_H: 9.6 (1 H, dd, J 3.8, 5.0 Hz), 8.7 (1 H, dd, J 5.0, 8.6 Hz), 8.4 (1 H, dd, J 1.35, 8.6 Hz), 3.3 (2 H, t, J 7.6 Hz), 1.8 (2 H, pent, J 7.2 Hz), 1.4 (2 H, m), 0.9 (3 H, t, J 7.2 Hz); δ_C: 165.4, 149.1, 136.1, 136.1, 33.3, 31.0, 22.2, 20.3, 13.6. The hydrobromide was treated as above with sat.aq. sodium bicarbonate to give *3-butylpyridazine* (**25d**)[21] (0.23 g, 82 %) (Found M^+: 136.1000, $C_8H_{12}N_2$ requires: 136.1001) which gave a single peak on GLC and showed δ_H: 9.0 (1 H, dd, J 1.9, 4.7 Hz), 7.35 (1 H, dd, J 4.7, 8.4 Hz), 7.28 (1 H, dd, J 1.9, 8.4 Hz), 2.94 (2 H, complex), 1.72 (2 H, pent, J 7.2 Hz), 1.2 (2 H, m), 0.9 (3 H, t, J 7.2 Hz); δ_C: 164.1, 149.5, 126.3, 126.1, 36.1, 31.7, 22.3, 13.8; υ_{max}: 2235, 1670, 1599 cm^{-1}.

(e) **1-Bromo-2-t-butylcyclopropene**: Reaction as above gave one major component, *5-bromo-1-t-butyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (**22e**) by n.m.r., together with minor signals which may have corresponded to *1-bromo-5-t-butyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (**23e**). Chromatography as above gave the first isomer (0.05 g, 42 %) showed δ_H: 4.86 (1 H, d, J 19.5 Hz), 4.7 (1 H, d J 19.5 Hz), 1.8 (1 H, d, J 6.5 Hz), 1.3 (9 H, s), 0.47 (1 H, d, J 6.5 Hz). The second isomer (0.03 g, 25 %) decomposed fast and gave a complicated ^1H nmr spectrum. When compound (**22e**) was allowed to stand in $CDCl_3$ for 24 h at room temperature, it gave a brown solid. Evaporation of the solvent gave *3-t-butylpyridazine hydrobromide* (**24e**) (0.035 g, 29.4 %) (Found: C 44.6, H 6.4, N 12.3. $C_8H_{13}BrN_2$ requires: C44.4, H 6.0, N 12.9); δ_H: 9.9 (1 H, d, J 4.6 Hz), 8.7 (1 H, dd, J 4.6, 8.5 Hz), 8.5 (1 H, d, J 8.4 Hz), 1.5 (9 H, s); δ_C: 173.7, 145.8, 134.9, 134.3, 38.1, 29.5; υ_{max}: 1608 cm^{-1}. The hydrobromide was treated with sat.aq. sodium bicarbonate (2 ml) as above to give *3-t-butylpyridazine* (**25e**) (0.01 g, 55.5 %) (Found: M^+ 136.1001, $C_8H_{12}N_2$ requires 136.1000), which gave a single peak on GLC (δ_H: 9.0 (1 H, dd, J 1.7, 4.7 Hz), 7.4 (1 H, dd, J 1.7, 8.7 Hz), 7.3 (1 H, dd, J 4.7, 8.6 Hz), 1.4 (9 H, s); δ_C: 170.3, 149.2, 126.2, 123.0, 37.0, 29.9; ν_{max}: 1636 cm^{-1}).

Reaction of 1-bromo-3,3-dimethylcyclopropene with diazomethane

An excess of diazomethane in ether (10 ml) was added to a stirred solution of 1-bromo-3,3-dimethylcyclopropene in ether (20 ml) at 0 °C. The mixture was stirred at room temperature for 3 h when TLC showed no starting material. The solvent and excess of diazomethane were removed at 0 °C and 14 mm Hg to give a yellow oil which was a mixture of two isomers in a ratio of 2.2 : 1, *5-bromo-6,6-dimethyl-2,3-diazabicyclo-*

[3.1.0]hex-2-ene and *1-bromo-6,6-dimethyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (**31, 32**). These were separated by rapid chromatography on silica eluting with petroleum and ether (5:2). The first isomer (**32**) (0.35 g, 24 %) showed δ_H: 4.7 (1 H, d, J 19.9 Hz), 4.6 (1 H, d, J 2.5 Hz), 4.5 (1 H, dd, J 2.5, 19.9 Hz), 1.4 (3 H, s), 0.6 (3 H, s). The second, (**31**) (0.42 g, 29 %) showed δ_H: 4.7 (1 H, dd, J 6.2, 19.8 Hz), 4.1 (1 H, dd, J 1.3, 19.8 Hz), 1.6 (1 H, dd, J 1.3, 6.2 Hz), 1.4 (3 H, s), 0.6 (3 H, s); δc: 86.4, 76.3, 33.3, 27.7, 24.7, 12.3; ν_{max}: 1608 cm^{-1}. When either isomer was allowed to stand in $CDCl_3$ at room temperature decomposition occurred to a mixture which showed a complicated ^1H n.m.r. spectrum; for the first isomer this occurred within 1 h, for the second it occurred over 4 days.

Reaction of 1-bromo-2,3-dimethylcyclopropene

An excess of diazomethane in ether (10 ml) was added with stirring to 1-bromo-2,3-dimethylcyclopropene in ether (20 ml) at 0 °C. The mixture was stirred at room temperature for 2 h when TLC showed no starting material; the solvent and excess of diazomethane were removed at 0° C and 14 mm Hg to give a mixture of *5-bromo-1,6-dimethyl-2,3-diazabicyclo[3.1.0]hex-2-ene* and *1-bromo-5,6-dimethyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (**34, 35**) in a ratio of 4:3, which were separated by rapid chromatography eluting with petrolum and ether (5:2). The first isomer (0.1 g, 33 %) showed δ_H: 4.8 (1 H, d, J 19.3 Hz), 4.7 (1 H, d, J 19.3 Hz), 1.7 (3 H, s), 1.1 (3 H, d, J 6.3 Hz), 0.5 (1 H, q, J 6.3 Hz). When allowed to stand in $CDCl_3$ at 20 °C for 10 h, this was completely changed to give *3,4-dimethylpyridazine hydrobromide* (**36**)[23] (0.07 g, 23 %) which showed δ_H: 9.4 (1 H, d, J 5.3 Hz), 8.2 (1 H, d, J 5.3 Hz), 3.0 (3 H, s), 2.6 (3 H, s); δc: 147.6, 134.1, 38.1, 31.2, 19.4, 18.7; ν_{max}: 1626 cm^{-1}. The second isomer (0.06 g, 20 %),δ_H: 4.4 (1 H, d, J 19.6 Hz), 4.2 (1 H, d, J 19.6 Hz), 1.85 (3 H, s), 0.85 (1 H, q, J 6.4 Hz), 0.6 (3 H, d, J 6.4 Hz), decomposed rapidly in $CDCl_3$ but led to a complicated ^1H nmr spectrum.

Reaction of methyl 1-bromo-2-cyclopropene carboxylate with diazomethane

An excess of diazomethane in ether (7 ml) was added to a stirred solution of methyl 1-bromo-2-cyclopropene-carboxylate in ether (15 ml) at -50 °C. The mixture was allowed to reach room temperature for 2 h, then the solvent was removed at 0 °C and 14 mm Hg to give a brown oil which decomposed very quickly in benzene or chloroform, to give a brown solid, *methyl 3-pyridazinecarboxylate hydrobromide* (**28**) (0.4 g, 56 %) which showed δ_H (D_2O): 9.4 (1 H, dd, J 1.6, 5.2 Hz), 8.5 (1 H, dd, J 1.6, 8.6 Hz), 8.2 (1 H, dd, J 5.2, 8.6 Hz), 4.0 (3 H, s); δ_C: 163.8, 152.3, 151.5, 132.4, 132.1, 53.9. The hydrobromide (0.5 g) was treated with sat. aq. sodium bicarbonate (2 ml) for 10 min, and extracted with ether (5 x 10 ml) as above to give a brown solid, *methyl 3-pyridazinecarboxylate* (**29**)[16,22] (0.2 g, 45%), m.p. 130-132 °C (Found M^+: 138.0429. $C_6H_6O_2N_2$ requires: 138.0429) which showed δ_H: 9.4 (1 H, dd, J 1.7, 5.0 Hz), 8.24 (1 H, dd, J 1.7, 8.4 Hz), 7.7 (1 H, dd, J 5.0, 8.4 Hz), 4.1 (3 H, s); δ_C: 156.4, 153.1, 151.6, 127.6, 127.0, 53.4; υ_{max}: 1718, 1447, 767 cm^{-1}.

Reactions of 8-bromobicyclo[5.1.0]oct-1-(8)-ene with diazomethane

An excess of diazomethane in ether (10 ml) was added to a stirred solution of 8-bromobicyclo[5.1.0]oct-1(8)-ene[18] in ether (20 ml) at 0 °C. After 2 h at 20 °C,TLC showed no starting material. The solvent and excess of diazomethane were evaporated to give a 1:1 mixture of (**38**) and (**39**) which showed δ_H: 4.8 (1 H, d, J 19.3 Hz) and 4.7 (1 H, d, J 19.3 Hz) (for the first isomer), 4.5 (1 H, d, J 19.2 Hz) and 4.4 (1 H, d, J 19.2 Hz) (for the second isomer), and 2.6 - 1.0 (20 H, m), 0.5 (2 H, m) (both isomers). Chromatography eluting with petrol and ether (5:2) and a few drops of triethylamine gave a brown solid, *8,9-diazabicyclo[5.4.0]undeca-7,9,11-triene*

(40) (0.28 g, 35 %), m.p. 195-197 °C (Found M^+: 148.1000. $C_9H_{12}N_2$ requires 148.1001) which showed δ_H: 9.4 (1 H, d, J 5.3 Hz), 8.3 (1 H, d, J 5.3 Hz), 3.56 (2 H, m), 3.16 (2 H, m), 1.8 (6 H, m); δ_C: 166.7, 154.0, 148.3, 133.8, 35.1, 34.0, 31.3, 26.3, 25.4; υ_{max}: 1583, 1534, 1449, 962, 714 cm^{-1}. Neither pyrazoline was recovered in pure form.

References:

1. Baird, M. S. 'Cyclopropanes from Cyclopropenes' in *Three- and Four-Membered Carbocyclic Compounds: Houben-Weyl E17e*, Ed. de Meijere, A., 1996, 581-588., 1991, **1**, 65.
2. Aue, D.H., Lorens, R.B., Helwig G.S., *J.Org.Chem.*, 1979, 44, 1202; Latypova, M.M., Plemenkov, V.V., Bolesov, I.G., *Dokl.Akad.Nauk SSSR, Ser.Khim.*, 1983, 268, 627.
3. Heydt, H., Bush, K., Regitz, M. *Annalen.*, 1980, 590.
4. Baird, M.S., Hussain, H.H. *Tetrahedron*, 1987, 215.
5. Norden, W., Sander, V., Weyerstahl, P. *Chem. Ber.*, 1983, **116**, 3097.
6. Komendantov, M.I., Bekmukhametov, R.R. *Zh. Org. Khim.*, 1971, **7**, 423.
7. Kuroda, Y., Fujiwara, Y., Matsushifa, K. *J. Chem. Soc., Perkin Trans.*II, 1985, 1533; Tsuchiya, T., Arai, H., Igeta, H. *Chem. Pharm. Bull.*, 1972, **20**, 273.
8. Tsujimoto, T., Nomura, T., Iifuru, M.,Sasaki Y., *Chem.Pharm.Bull.*, 1979, **27**, 1169.
9. Schneider, M., Csacsko, B. *Angew.Chem.Int.Edn.Engl.*, 1977, **16**, 867; Eaton, D.F., Bergman, R.G., Hammond, G.S. *J.Amer.Chem.Soc.*,1972, **94**, 1351; Franck-Newmann, M., Buchcker, C. *Tetrahedron Lett.*,1969, 2659.
10. Komendantov, M.I., Bekmukhametov, R.R., Novinskii, V.G. *Zh. Org.Khim.*, 1976, **12**, 801.
11. Dehmlow, E.V. and Naser-ud-Din, *J. Chem. Res., (S)*, 1978, 40; (M), 1978, 582.
12. Al Dulayymi, J.R., Baird, M.S. *Tetrahedron Letters*, 1995, **36**, 3933.
13. Grundmann, G. *Chem.Ber.*, 1948, **1**, 81; Counotte-Potman, A., van der Plas, H.C. *J.Het.Chem*, 1983, **20**, 1259.
14. Barlin, G.B., Yap, C.Y. *Aust.J.Chem.*, 1977, **30**, 2319,2320.
15. Baird, M.S., Hussain, H.H., Nethercott, W. *J Chem Soc, Perkin Trans 1*, 1986, 1845-53.
16. Leanza, W.J, Becher, H.J., Rogers,E.F. *J.Am.Chem.Soc.*, 1953, **75**, 4086; Haider,N., Heinisch, G. and Kemetmuller, G. *J.Het.Chem.*, 1990, **27**, 1645; Heinisch, G., Pittenauer,E. *Sci.Pharm.*, 1991, **59**, 111.
17. Baird, M.S., Fitton, H.L., Clegg, W., McCamley, A. *J Chem Soc, Perkin Trans. 1*, 1993, 321.
18. Baird, M.S., Nethercott, W. *Tetrahedron Lett.*, 1983, 605-8.
19. Al Dulayymi, A.R., Al Dulayymi, J.R., Baird, M.S., Gerrard,M.E., Koza, G., Harkins, S.M., Roberts, E. *Tetrahedron*, 1996, **52**, 3409.
20. Levisalles, J. *Bull.Soc.Chim.Fr.*, 1957, 997, 1004, 1009.
21. Letsinger, R.L., Lasco, K. *J.Org.Chem.*, 1956, **21**, 812.
22. Dobba, M. *Ann.Chim.*, 1960, **5**, 531.
23. Horning, R.H., Amstutz, E.D. *J.Org.Chem.*, 1955, **20**, 707,708; Heinisch, G., Loetsch, G. *Heterocycles*, 1984, **8**, 1395.