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THE SYNTHESES, SPECTRA, AND SOME REACTIONS OF 2-PHTHALIMIDYL- AND 2-PHTHALIMIDYL-4,5-DICHLORO-5-AZABICYCLO[2.1.0]PENTANE[1,2]

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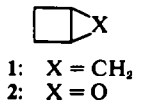
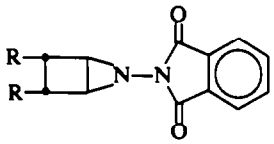
Abstract—Cyclobutene has been prepared by an improved method. The reaction of N-aminophthalimide with cyclobutene or *cis*-3,4-dichlorocyclobutene in the presence of lead tetraacetate gives 2-phthalimidyl- (**5**) or 2-phthalimidyl-4,5-dichloro-5-azabicyclo[2.1.0]pentane (**6**), respectively. The NMR spectra of **6** showed the presence of *exo* (**9**) and *endo* (**10**) isomers. The effect of ring size on the chemical shift of the bridgehead hydrogen absorption in a series of azabicyclo[n.1.0]alkanes was examined. Several reactions of **5** and **6** and alternative syntheses of the azabicyclo[2.1.0]pentane system were investigated.

As part of a study on the synthesis and properties of strained heterocyclic molecules[4] we have investigated synthetic routes to the 5-azabicyclo[2.1.0]-pentane structure (**4**) and some properties and reactions of two derivatives (**5, 6**) of the parent compound. The corresponding hydrocarbon (**1**)[5] and the oxygen (**2**)[6] and sulfur (**3**)[7] analogs are known and, subsequent to our preliminary communication,[2] perfluorotri- and tetracyclic compounds containing the ring system[8] and the 5-carboethoxy-1,4-dimethyl derivative[9] have been reported.

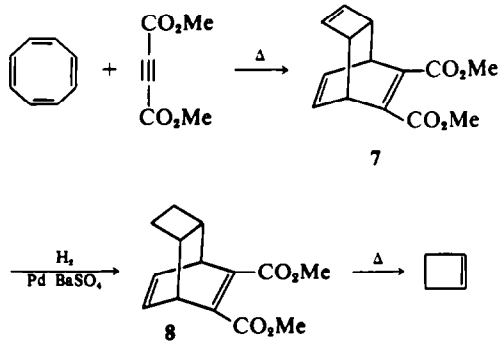


1: X = CH_2
2: X = O
3: X = S
4: X = NH



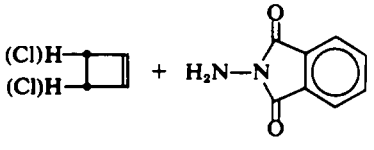
5: R = H
6: R = Cl

The successful path to **5** and **6** required cyclobutene and an improved preparation of this which gave 34–39% overall yield (59–66% conversion) based on cyclooctatetraene was found (Scheme I).* The yield of intermediate **7** (82%) and also its purity were markedly enhanced, and the amount of dimethyl phthalate by-product substantially reduced relative to previous results[11] by carrying out the addition at a lower temperature (100°) for a longer period (two weeks) and omitting vacuum distillation. A Pd.$BaSO_4$ catalyst was found to be superior to Pd.C, Rh.Al_2O_3, or $(Ph_3P)_3RhCl_2$ for the conversion of **7** to **8**.



SCHEME I

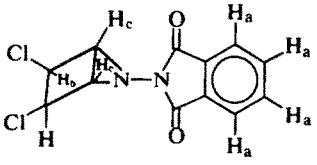
Reaction of N-aminophthalimide with cyclobutene or *cis*-3,4-dichlorocyclobutene[12] in the presence of lead tetraacetate gave **5** or **6** in 18–22% and 9–12% yields, respectively (Eq. 1), as crystalline solids.



$\xrightarrow{Pb(OAc)_4}$ **5** or **6** (1)

*After the present work was completed, the preparation of *cis*-3,4-dideuteriocyclobutene was reported[10] by the same route, but details and yields were not given. The present procedures are expected to be superior to those of Fleming and Wildsmith, especially with respect to the amount of dimethyl phthalate by-product and the selectivity of the partial hydrogenation.

The NMR spectrum of **6** was indicative of two isomers in a ratio of 4:1. Variations in relative peak intensities in fractions obtained from column chromatograms and a spin decoupling experiment confirmed the presence of isomers. Analysis of the spectrum was consistent with representation of the isomers as **9** and **10**.* That hydrogens above the plane of a cyclopropane ring are shielded has been clearly demonstrated[13] and this long range anisotropy effect has been found for oxirane and aziridine rings.[14] On this basis the further upfield signals (δ 3·82) for the nonbridgehead hydrogens (H_b) on the cyclobutane ring were assigned to the *exo* structure (**9**) and those relatively downfield (δ 4·51) to H_b in the *endo* structure (**10**). The decoupling experiment (irradiation of H_c at δ 4·33) produced a singlet for H_b at δ 3·82 (**9**), but did not alter the peaks at δ 4·51. The bridgehead hydrogens (H_c) signal for **9** was therefore the one at δ 4·33 and the corresponding H_c signal for **10** was the one at δ 4·12. The aromatic hydrogen absorption (H_a) appeared at δ 7·92.† The isomer ratio (**9**/**10** > 1) was consistent with the expectation that steric repulsion between the chlorine substituents and the aminophthalimide in the transition state for the formation of **10** would favor **9** as the major product.



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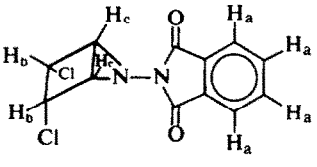

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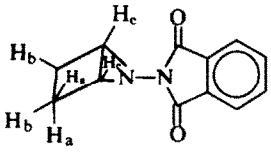
The UV and IR spectra of **5** and **6** showed absorption characteristic for N-aminophthalimides[15] but not for phthalhydrazides.[16] The NMR spectrum of **5** contained signals at δ 1·40 (H_a) and δ 2·18 (H_b) which also were consistent with the shielding effect (0·78 ppm, which is in agreement with the difference of 0·76 ppm for the corresponding hydrogens in **9** and **10** and with data in the literature)[13] of the aziridine ring on the *endo* hydrogens. A sample spectrally characterized as slightly impure **11** (prepared from the reaction of cyclobutene with N-benzenesulfonoxyurethane and triethylamine) showed corresponding absorption for the *exo* hydrogens (H_b δ 2·12) but at δ 1·77 for the *endo* hydrogens (H_a).‡ The lesser shielding effect (0·35 ppm) in **11** was attributed to the greater withdrawal of the nitrogen lone pair by the carboethoxy group. The azabicyclo[3.1.0]hexane homolog of **11** was also prepared.



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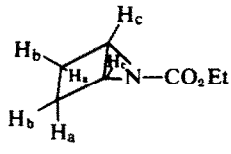
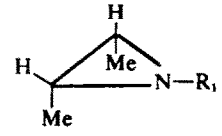


11

The NMR absorption at 50 Hz sweep width of the multiplets for **6** at δ 3·82 and 4·33 (the aliphatic hydrogens) revealed that these were mirror images. Six peaks for each multiplet were discernable but the resolution did not permit further analysis. The pattern resembled that of an AA'BB' system ($J_{AB} \neq J_{A'B'}$). The bridgehead hydrogen signal for **5** was 0·7 ppm downfield from the corresponding signal for 1-phthalimido-*cis*-2,3-dimethylaziridine (**12**),[18] and comparison of **5** and **11** with their next two higher homologs, and of the two known corresponding members of the parent system showed a consistent shift in the signal for the bridgehead hydrogens with the change in ring size. This might be caused by the differences in spatial relationships, or the concomitant change in the pi-bond



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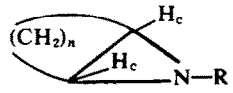
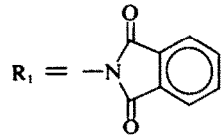


	δH_c		
n	R_1	R_2	R_3
2	3·34 (**5**)	3·05 (**11**)	–
3	3·14	2·85	2·35[21]
4	2·70[19]	2·53[20]	2·07[21]
5	2·67		
6	2·49		



R_2 = —CO_2Et

R_3 = H

*The finding of a single NMR absorption for the bridgehead hydrogen for **5**, and also for the ring hydrogens of **12**,[18] shows that only the less crowded invertomer is present for these compounds, and therefore also for **6**.

†The possibility of a phthalhydrazide structure was contraindicated by the observation that phthalhydrazide showed a multiplet at δ 7·6–8·2 whereas N-aminophthalimide showed a singlet at δ 7·8.

‡Absorption for hydrogen on unsubstituted cyclobutane is at δ 1·96 ppm.[17]

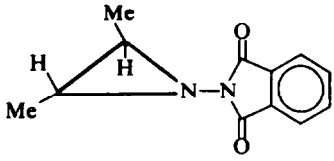
character of the bridging bond, or both. The shift was found to be small for n = 5 (R_1) and then to be larger again for n = 6.

The mass spectrum of **5** showed, unexpectedly, a P-2 peak of ten times the intensity of that (P) of the parent ion. That dehydrogenation to 1-phthalimidopyrrole and not disproportionation had occurred was shown by the fact that the intensity of the P + 2 peak was normal relative to that of P and the appearance of base peaks for the pyrrole ($C_4H_4N^+$) and phthalimido fragments. The phthalimido ion was not a significant participant in the dehydrogenation as the 147 and 146 peaks were of the expected relative amplitudes. In contrast, the 147 peak was quite intense and the 146 peak weak in the spectrum of **6**. Also, no major peaks for any of the possible 1-substituted pyrroles were observed, although strong P–Cl and P–2Cl peaks were present.

The mass spectrum of the labile product from the reaction of **5** with bromine showed the presence of a dibromide. The NMR spectrum of this product was consistent with that expected for *trans* addition to the bridging bond. The effect of the phthalimidyl group would make all the hydrogens nonequivalent, with a relatively slow inversion rate, and give two broad multiplets, as observed, for the aliphatic hydrogens.*

An attempt to convert **6** to the corresponding azabicyclopentene by dehalogenation through reaction with Cr(II) was not successful.† Phthalimide, which could be accounted for by a radical fragmentation scheme,‡ was isolated but none of the alternative 1-phthalimidopyrrole was detected.

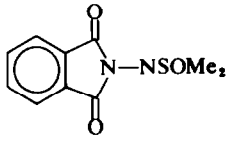
The stability of aziridines to acid has been found to be quite sensitive to steric factors. For example,



13

solvolytic cleavage of the aziridine ring of 1-phthalimido-*trans*-2,3-dimethylaziridine (**13**) by acetic acid was observed at room temperature whereas the *cis* isomer (**10**) was unreactive.[18] After **6** was heated with acetic acid for 24 hr, 28% was recovered unchanged. The bicyclic structure in **6** thus provides steric hindrance to the cleavage by acid.

Photolysis of the phthalimidosulfoximine (**14**)[22] in the presence of *cis*-3,4-dichlorocyclobutene

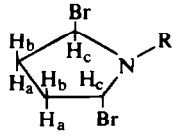


14

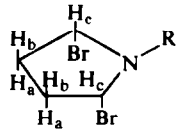
afforded only small amounts of **6**. The reason for the low yield was found to be the senstivity of **6** to UV radiation, perhaps due to the presence of the phthalimido moiety.

Exposure of **6** to sodium deuteroxide in D_2O-DMSO-d_6 at room temperature for several weeks resulted in the appearance of a new singlet at δ 7·57 but no apparent H-D exchange. Heating the solution caused slow exchange of the bridgehead and

cis*-Addition would be expected to yield the less crowded invertomer with the original bridgehead hydrogens (H_c) now identical and split by nonequivalent methylene hydrogens (H_b and H_a). The expected spectrum would then resemble that of **5 (a narrow H_c multiplet and two methylene multiplets).



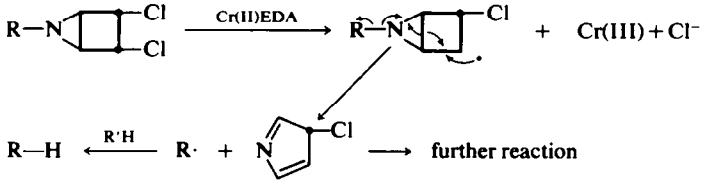
trans-addition product



cis-addition product

†Treatment of **6** with lithium, lithium amalgam, sodium iodide, or potassium t-butoxide also failed to effect dehalogenation. The last reagent formed a product (probably a salt) which reacted with water to reform **6**.

‡The suggested scheme is:

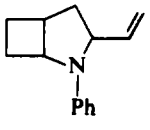


R = N-phthalimido; R'H = EDA or 3-chloropyrrole

methine hydrogens at equal rates, and the phthalimido singlet at δ 7·92 was gradually replaced by the peak at δ 7·57. The IR spectrum of the crude product responsible for the δ 7·57 absorption was similar to that of 3-hydroxyphthalimidine,[23] the aromatic hydrogens of which also absorbed at δ 7·57. The product was therefore thought to be formed by the reduction of one CO group in **6**. In a separate experiment it was found that phthalimide was readily reduced by lithium borohydride to 3-hydroxyphthalimidine.

When **5** was heated in DMSO-d_6, phthalimide and pyrrole were formed but no 1-phthalimidopyrrole, which was shown to be stable under the reaction conditions, was detected.* This reaction accounted for the decomposition of **5** in attempted deuterium exchange experiments.

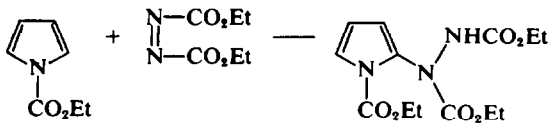
Attempts to isolate the parent compound by removal of the phthalimidyl group (e.g. with sodium hydrosulfite or hydrazine) from **5** and **6** were unsuccessful. The reaction of cyclobutene with phenyl azide produced a compound in low yield spectrally identified as a 2 : 1 adduct (**15**) instead of the hoped for phenylazabicyclopentane, and this reaction with 3,4-dichlorocyclobutene was also unsuccessful.



15

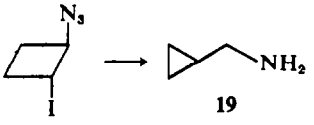
The Diels–Alder addition of the pyrrole ring and an azo compound, reduction, and subsequent loss of the azo moiety as nitrogen would lead to the desired azabicyclopentane system. However, the reactions of 4-phenyl-1,2,4-triazoline-3-5-dione[24] with pyrrole and 1-carboethoxypyrrole (**16**) were unsuccessful, and the latter plus ethyl azodiformate gave only the substitution product (**17**) in good yield (Eq. 2).

Hassner *et al.*[21] have prepared a number of unsubstituted azabicycloalkanes by the reduction of β-iodo azides with LAH. In a qualitative investigation of this method as a route to **4**, the addition of iodine azide to cyclobutene gave a labile product[21] having IR and NMR spectra in agreement with



16 **17** (2)

structure **18**. Spectral (NMR) analysis of the impure compound obtained by hydride reduction of **18** indicated that rearrangement to cyclopropylcarbinylamine **19** (Eq. 3) had occurred; no **4** or cyclobutylamine were detected. Attempts to form **4** by conversion of **18** (e.g. with diborane[21]) to the corresponding amine and then cyclization by treatment with potassium *t*-butoxide were unsuccessful.



18 **19**

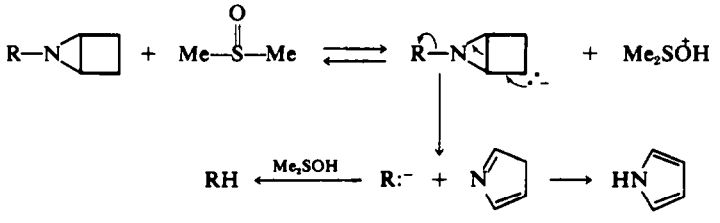
The success of the nitrene addition to form **5** and **6**, in contrast to the failure of the other routes, suggests that the former could be used to prepare other sterically strained aziridines.

EXPERIMENTAL

Lead tetraacetate (Arapahoe Chemical Co. or Alfa Inorganics) was recrystallized from glacial AcOH and dried. Cyclooctatetraene was provided by the BASF Corporation. NMR spectra were recorded on Varian HA-60, A-60, or T-60 spectrometers with TMS as an internal standard. UV spectra were recorded on a Cary Model 14 spectrophotometer and IR spectra were taken with Perkin Elmer Model 137 or 225 instruments. Mass spectra were recorded on an AEI MS-9 spectrometer (70 eV).

Cyclobutene. A mixture of 52 g (0·5 mol) of cyclooctatetraene and 71 g (0·5 mol) dimethyl acetylenedicarboxylate was stirred at 100° under N_2 for 2 weeks, after which the pressure was reduced and unchanged cyclooctatetraene (*ca* 17%) separated by distillation. The cooled residue was dissolved in MeOH (*ca* 150 ml) and the colorless ppt which formed was separated by filtration (sintered glass). The solvent was removed from the filtrate under aspirator pressure at room temp and then at *ca* 0·1

*An ionic fragmentation process is suggested (R = N-phthalimido):



mm for 10 hr with magnetic stirring. Solns of 12–25 g portions of the crude residual triene adduct (7) in 2:1 benzene–MeOH were treated with H_2 at 1 atm over 8% Pd · $BaSO_4$ until 0·9–1·0 equivs of H_2 was taken up. The mixture was filtered through Celite and the solvent removed as before.

The pyrolysis of 7 was affected at 200° (100 mm) and the cyclobutene collected in a cold (liquid N_2) trap before being distilled into a cold storage tube fitted with a stopcock: yield 9·2–10·5 g (34–39%). The NMR spectrum and VPC analysis of the product indicated it to be pure. A small residue in the trap was identified (NMR) as dimethyl phthalate.

General procedure for N-*phthalimidioazabicyclo compounds.** To a stirred mixture of 1·05 g (6·48 mmol) N-aminophthalimide, the alkene (25 mmol), and 20 ml dry dichloromethane was added 2·76 g (6·25 mmol) lead tetraacetate in portions over a 10 min period. After an additional 10–20 min, precipitated inorganic salts were removed by filtration and the solvent was removed under reduced pressure (aspirator). Residual AcOH was removed by the addition and evaporation of two 25-ml portions of dry benzene. The yellow, crystalline material thus obtained was chromatographed on silica gel (200–325 mesh, 6·7 × 13·5 cm column) with 3:1 petroleum ether–acetone as the eluent.

5-*Phthalimido*-5-*azabicyclo*[2.1.0]*pentane* (5). Recrystallization from MeOH or CCl_4 gave 0·24–0·30 g (18–22%) of yellow crystals: m.p. 114–116°; NMR (DMSO-d_6) δ 7·75 (s, 4), 3·44 (m, 2), 3·18 (m, 2) and 2·40 ppm (m, 2); IR (CH_2Cl_2) 1770 and 1710 cm^{-1}; UV (EtOH) 234 (4·57), 295 (3·08), 304 (3·04), and 330 nm (sh, log ε 2·57); mass spectrum *m/e* 214·0747 (M, calcd. 214·0741), 212 (M-2, rel intensity 10), 146 ($C_4H_8NO_2$), 91 (C_6H_5N) and 66 (C_4H_4N) base peak. The substance darkened on standing and was best stored in dry vials which had been washed with 5% KOH and then several times with distilled H_2O. (Found: C, 67·11; H, 4·72; N, 12·99. Calc. for $C_{12}H_{10}N_2O_2$: C, 67·28; H, 4·70; N, 13·08%).

Reaction of 100 mg of 5 with 100 mg of Br_2 in 1 ml dry dichloromethane gave 16·3 mg phthalimide and 64·8 mg of a viscous, pale yellow, labile oil: mass spectrum *m/e* 371·8890 (M, calc. for $C_{12}H_{10}N_2O_2Br_2$: 371·9115), no higher peaks up to *m/e* 800; NMR ($CDCl_3$) δ 7·73 (m, 4), 4·17 (br m, 2), and 2·13 ppm (br m, 4), multiplet widths *ca* 38 Hz (4·17) and *ca* 56 Hz (2·13). The material discolored rapidly even in a desiccator under an inert atmosphere.

2,3-*Dichloro*-5-*phthalimido*-5-*azabicyclo*[2.1.0]*pentane* (6). The progress of the product on the chromatographic column was followed with UV light. The yield was 0·16–021 g (9–12%), m.p. 165–170° (dec). Rechromatography gave pale yellow crystals, m.p. 165–170° (dec); NMR (acetone-d_6) δ 7·83 (s, 4), 4·51 (m, 0·2), 4·33 (m, 0·8), 4·12 (m, 0·2), and 3·82 ppm (m, 0·8) corresponding to a mixture of 9 and 10 in a ratio of 4:1. Spin decoupling by irradiation at δ 4·33 produced a singlet at δ 3·82 with peaks at δ 4·51 unchanged. Chromatographic fractions were obtained with isomeric peak ratios (3·82: 4·51 and 4·33: 4·12 varying from 2:1 to 6:1. UV (CH_3CN) 231 (3·4), 295 (2·15), and 305 nm (log ε 2·11); IR (CH_2Cl_2) 1770 and 1710 cm^{-1}; mass spectrum *m/e* 281·9944 (M, calcd 281·9962), 284 (0·6 intensity of M), 247 (M—Cl), 212 (M—2Cl), 184 (M—$C_2H_4Cl_2$), 147, 91, 76 plus P+2 peaks of correct intensities for these. The crystals darkened on standing and were best stored as described for 5. Attempted separation of the isomers by TLC on silica gel or alumina (2:1 to 5:1 light petroleum-acetone) and by recrystallization from CH_2Cl_2, light petroleum-acetone, CCl_4, or CH_3OH was unsuccessful. (Found: C, 51·08; H, 3·01; N, 9·60. Calc. for $C_{12}H_8Cl_2N_2O_2$: C, 50·91, H; 2·85; N, 9·90%).

6-*Phthalimido*-6-*azabicyclo*[3.1.0]*hexane*. The yield of yellow crystals was 0·7 g (49%); m.p. 119–26° and 126–128·5° after recrystallization from CCl_4-light petroleum; NMR (CH_2Cl_2 or $CDCl_3$) δ 7·69 (s, 4), 3·14 (m, 2), and 2·50–1·13 ppm (m, 4). (Found: C, 68·28; H, 5·37; N, 12·40. Calc. for $C_{13}H_{12}N_2O_2$: C, 68·41; H, 5·30; N, 12·27%).

7-*Phthalimido*-7-*azabicyclo*[4.1.0]*heptane*. This compound, 0·55 g (36%), was obtained as yellow crystals, m.p. 132–134°, and 133–136° (lit[16] 137°) after recrystallization from MeOH: NMR (CH_2Cl_2) δ 7·65 (s, 4), 2·70 (m, 2), 2·07 (br m, 4) and 132 ppm (m, 4); mass spectrum *m/e* 242·1100 (M, calcd 242·1055).

8-*Phthalimido*-8-*azabicyclo*[5.1.0]*octane*. The yield of yellow crystals, m.p. 122·5–125°, was 0·45 g (27%); NMR ($CDCl_3$) δ 7·73 (s, 4), 2·67 (m, 2), 2·14 (m, 4), and 1·55 ppm (m, 6). (Found: C, 69·97; H, 6·47; N, 10·70. Calc. for $C_{15}H_{16}N_2O_2$: C, 70·29; H, 6·29; N, 10·93%).

9-*Phthalimido*-9-*azabicyclo*[6.1.0]*nonane*. The yield of pale yellow crystals, m.p. 87–89°, was 0·4 g (24%); NMR ($CDCl_3$) δ 7·69 (s, 4), 2·58 (broad s, 2), 2·49 (s, 2), and 1·52 ppm (m, 10). (Found: C, 71·12; H, 6·85; N, 10·05. Calc. for $C_{16}H_{18}N_2O_2$: C, 71·09; H, 6·71; N, 10·36%).

6-*Carboethoxy*-6-*azabicyclo*[3.1.0]*hexane*. 6-Azabicyclo[3.1.0]hexane,[21] 0·86 g (10·3 mmol), was added to a stirred mixture of 1·09 g (10 mmol) ethyl chloroformate, 0·4 g (10 mmol) NaOH, 15 ml benzene, and 20 g ice at 7° (ice bath). After 1 hr, the temp had dropped to 4° and remained so for 1 hr. The mixture was poured into 20 ml of H_2O, the separated aqueous layer extracted twice with ether, and the combined benzene and ether layers dried ($MgSO_4$). This soln was combined with that from a run twice as large and the solvents removed by distillation (column packed with metal helices). Vacuum distillation of the residue gave 1·4 g (30%) of colorless oil: b.p. 110–112° (60 mm); NMR (CCl_4) δ 4·03 (q, J = 7 Hz, 2), 2·85 (s, 2), 1·33 (t, J = 7 Hz, 3) superimposed on 1·0–2·2 ppm (m, 6). Preparative TLC on silica gel with 5:1 light petroleum-acetone using I_2 vapor to visualize the edges afforded the analytical sample. (Found: C, 62·18; H, 8·62; N, 9·21. Calc. for $C_8H_{13}NO_2$: C, 61·91; H, 8·44; N, 9·04%).

Reaction of carboethoxynitrene with cyclobutene. To a cold (ice–salt bath), stirred mixture of 2·3 g (42 mmol) cyclobutene, 1·4 ml (1·1 g, 10 mmol) triethylamine, and 3 ml dry dichloromethane under N_2 was added dropwise a soln of 2·45 g (10 mmol) ethyl N-carboxy-O-phenylsulfonylhydroxylaminet in 7 ml dry dichloromethane over a period of 30 min. After 1·5 hr, the cooling bath was allowed to melt. Stirring was continued overnight, 5 ml of dry light petroleum was added, and the precipitated salts removed by filtration. Careful evaporation of the solvent and then distillation at 0·05 mm and 40° gave 104 mg (collected in liquid N_2 cooled trap) of crude product. TLC on HF_{254} silica gel with 4:1 light petroleum-acetone yielded 21 mg (1·5%) of material considered to be primarily 9: NMR (CCl_4) δ 4·17 (q, J = 7 Hz, 2), 3·07 (s, 2), 2·12 (m, 2), 1·77 (m, 2) and 1·13 ppm (5, J = 7, 3).

*A modification of the procedure given in ref. 19.

†Prepared[25] in 66% yield: m.p. 88–93° after recrystallization from benzene; IR ($CHCl_3$) 1730 and 3300 cm^{-1}; NMR (acetone) δ 10·2, (s, 1), 7·89 (m, 2), 7·60 (m, 3), 4·0 (q, J = 7 Hz, 2) and 1·07 ppm (t, J = 7 Hz, 3); mass spectrum *m/e* 245·0346 (M, calcd for $C_9H_{11}NO_5S$ 245·0358).

Treatment of 2,3-*dichloro*-5-*phthalimido*-5-*azabicyclo*-[2.1.0]*pentane* (**6**) *with acetic acid.* A mixture of 42·5 mg (0·15 mmol) of **6** and 5 ml glacial AcOH was heated on a steam bath for 24 hr. It was then poured into 20 ml H_2O and extracted with ether. Chromatography of the residue from the separated, washed ($NaHCO_3$), and dried ether layer on silica gel (3:1 light petroleum-acetone) gave 11·7 mg (28%) of unchanged **6** (identified by TLC and NMR).

Photolysis of N-*phthalimidodimethylsulfoximine* (**14**) *with* 3,4-*dichlorocyclobutene.* A soln of 0·83 g (3·5 mmol) of **14** and 1 g (8·1 mmol) 3,4-dichlorocyclobutene[12] in 100 ml dry acetonitrile was irradiated with a 450 watt Hi-pressure Hanovia lamp, type 679-1, through a Vycor filter under N_2. After 72 hr the solvent was removed (rotary evaporator) from the red-brown soln and chromatography (HF_{254} silica gel plates with 5:1 light petroleum-acetone) yielded 2·5 mg (0·3%) of **6** (characterized by NMR).*

Deuterium exchange of 2,3-*dichloro*-5-*phthalimido*-5-*azabicyclo*[2.1.0]*pentane* (**6**). The soln from the reaction of a small piece of clean Na and 50 μl of D_2O was added to a soln of **6** in DMSO-d_6 in an NMR tube. No change other than the appearance of a new, small singlet at δ 7·57 occurred on standing for several weeks at room temp. The mixture was then heated at 112–115° and the spectrum recorded after 35 min, 155 min, and 21·5 hr. The relative intensities of aliphatic and aromatic hydrogens corresponded to the spectrum for **6** after 35 min, but after 155 min the aliphatic signals corresponded to 41% of the phthalimido signals and to 26% of the total absorption in the aromatic region. The ratio of bridgehead to methine ring hydrogens remained constant at 1:1. After 21·5 hr, the only appreciable signal was the singlet at δ 7·57 which was attributed to 3-hydroxyphthalimidine.[23]

Reduction of phthalimide with lithium borohydride. Phthalimide, 2·94 g (20 mmol), was stirred with 0·64 g (30 mmol) of $LiBH_4$ in 170 ml of dry THF for 3 days. The soln was poured in 100 ml of satd NaCl aq, the separated H_2O layer extracted with Et_2O, and the solvent removed from the combined, dried ($MgSO_4$) organic solns. Recrystallization of the pale yellow solid from water gave 2 g (66%) of 3-hydroxyphthalimidine as colorless needles, m.p. 175–176° (lit[23] 179°): NMR (DMSO-d_6) δ 8·75 (br s, 1), 7·57 (s, 4), 6·30 (d, J = 9 Hz, 1), and 5·85 ppm (d, J = 9 Hz, 1); IR (KBr) 3310, 3170, and 1695 cm^{-1}.[17]

Reaction of 2,3-*dichloro*-5-*phthalimido*-5-*azabicyclo*-[2.1.0]*pentane* (**6**) *with* Cr(II).[26] Oxygen-free N_2 was bubbled through a stirred soln of 0·5 ml (7·5 mmol) of ethylenediamine and 5 ml of *ca* 0·8 N chromous chloride in 40 ml dry DMF. To this was added (syringe) a soln of 140 mg (0·5 mmol) of **6** in 2 ml DMF. After 30 min, NMR analysis of the residue from the ether extract of a 5 ml aliquot showed the presence of phthalimide: δ 7·9 (s). Preparative TLC (silica gel, 2 5:1 light petroleum-acetone) of the concentrate of the mixture afforded phthalimide (NMR δ 8·0 (s, 4) and 4·0 (br s, 1)) and two unidentified bands. No 1-phthalimidopyrrole was detected.

Reaction of phenyl azide with cyclobutene. A soln of 1·8 g (33 mmol) cyclobutene and 1 g (8·4 mmol) phenyl azide in 15 ml dichloromethane was allowed to stand in a stoppered flask at −20° for 4 mo. (no apparent decrease in IR absorption for azide). The mixture was then allowed to stand at room temp in a sealed vial for 5 weeks (small decrease in IR absorption for azide). Vacuum (*ca* 0·01 mm) distillation at room temp removed unchanged phenyl azide and cyclobutene and chromatography (TLC on HF_{254} silica gel with 6:1 light petroleum-acetone) of the residue twice gave *ca* 0·1 g of an oil spectrally characterized as **15**: NMR (CCl_4) δ 6·90 (m, 5), 5·87 (m, 1), 4·87 (m, 2), 4·03 (m, 2), 2·30 (m, 1) and 1·50 (m, 6); UV (EtOH) 246 (4·82) and 285 mm (log ϵ 3·87); mass spectrum *m/e* 199·1376 (M, calcd 199·1360); IR (CCl_4) 3050, 2940, 1640, 1600, 1490, 1330, 1290, 1180, 995, 915 and 690 cm^{-1}.

Ethyl pyrrole-1-*carboxylate* (**16**). The method in the literature for the preparation of t-butyl pyrrole-1-carboxylate[27] was used with the substitution of ethyl azidoformate for t-butyl azidoformate and gave 8·1 g (58%) of **16**: b.p. 67–68° (9 mm) (lit[28] 75° at 13 mm); NMR (CCl_4) δ 7·17 (t, J = 2 Hz, 2), 6·10 (t, J = 2 Hz, 2), 4·14 (q, J = 7 Hz, 2) and 1·40 ppm (t, J = 7 Hz, 3).

Reaction of ethyl pyrrole-1-*carboxylate* (**16**) *with diethyl azodiformate. Diethyl* N-2-(1-*carboethoxy*)*pyrrolyl*-N,N′-*hydrazodicarboxylate* (**17**). A mixture of 1·39 g (10 mmol) **16**, 1·74 g (10 mmol) diethyl azodiformate, and 15 ml dry THF was stirred under anhydrous conditions for 38 days at which time TLC analysis of an aliquot showed products plus unchanged reactants. The latter were removed by distillation at *ca* 10^{-6} mm (liquid N_2 cooled receiver) and preparative TLC (HF_{254} silica gel with 4:1 light petroleum-acetone) of the viscous orange oil residue (2·2 g) gave 1·1 g (35%) of **17** as a yellow oil: NMR (CCl_4) δ 7·54 (br s, 1), 7·12 (d of d, J = 2 and 4 Hz, 1), 6·32 (d of d, J = 2 and 4 Hz, 1), 6·08 (t, J = 4 Hz, 1), 4·24 (sextuplet, J = 7 Hz, 6) and 1·22 ppm (m, 9). Rechromatography using dry dichloromethane and separating the center of the band gave an analytical sample which exhibited the same NMR spectrum except that the absorption for N—H had shifted to δ 7·14 from δ 7·54. (Found: C, 49·97; H, 6·22; N, 13·53. Calc. for $C_{13}H_{19}N_3O_6$: C, 49·84; H, 6·11; N, 13·41%).

Reaction of cyclobutene with iodine azide. To a cold (ice–salt bath) soln of 0·456 g (27 mmol) iodine azide in 50 ml dry acetonitrile was added 1·5 g (27·7 mmol) cyclobutene in 10 ml dichloromethane. The mixture was worked up in the prescribed manner[21] and the dried organic layer yielded *ca* 4·4 g (73%) of **18** as a labile, orange-red oil containing iodine and nitrogen (Na fusion). The IR spectrum showed the absence of vinylic hydrogens and a strong absorption at *ca* 2100 cm^{-1};[21] NMR (CCl_4) δ 1·2 (m, 1), 2·2 (m, 3), 5·9 and 6·2 (m,m, 2).

Reaction of crude 1-*azido*-2-*iodocyclobutane* (**18**) *with* LAH. A soln of 3·8 g (17 mmol) crude **18** in 8 ml dry ether was added dropwise to a cold (ice bath), stirred suspension of 1·25 g (33 mmol) LAH in 50 ml dry ether. A green color which appeared faded as the mixture came to room temp. After being stirred for 6 hr and standing for 5 days, the mixture was hydrolyzed with 5 ml 40% KOH. The colorless ppt which was separated gave a positive test for iodide. Careful removal (slow distillation through a 22 cm glass helices-packed column with a total reflux head take off) left *ca* 2 g of crude liquid product containing some ether. TLC analysis showed traces of starting material but no cyclobutylamine. The NMR (CCl_4) of a basic pro-

*TLC analyses of the reaction mixture during photolysis showed the early presence of a small amount of **6** which did not increase appreciably with time. The yield of material which remained near the origin and fluoresced orange under UV irradiation increased with time. In a separate experiment, irradiation of **6** in acetonitrile in the same manner for 4 hr gave product(s) with the same characteristics.

duct separated by preparative VPC was in agreement with that expected for **19**: δ 2·8 (br s, 2, NH_2), 2·58 (d, J = 6 Hz, 2, CH_2NH_2), 0·9 (m, 1, CH), and 0·5 (m, 4, CH_2CH_2); irradiation at δ 2·58 simplified the multiplet at δ 0·9 but not the one at δ 0·5.

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