

Reactions of Nitrenes with Strained Olefins. Nitrene Additions
to the Bicyclo[2.2.1]hept-2-ene System

G. Richard Meyer and Nancy A. Rao (1)

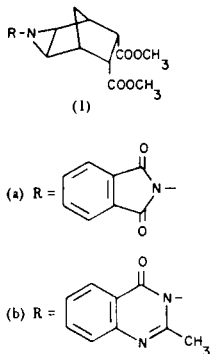
Department of Chemistry, University of St. Thomas, Houston, Texas 77006

Received October 10, 1976

The synthesis of two examples of the 3-azatricyclo[3.2.1.0^{2,4}]octane ring system is described. The product azabicycles are obtained in low yields and are stable in refluxing chlorobenzene. The lead tetraacetate oxidation of 3-amino-2-methyl-4-quinazolone leads to high yields of the deaminated compound.

J. Heterocyclic Chem., **14**, 335 (1977).

We wish to report the use of the method of Rees and coworkers (2) to synthesize two examples of the 3-azatricyclo[3.2.1.0^{2,4}]octane ring system (3). Thus reaction of *N*-aminophthalimide with *endo*, *cis*-dimethylbicyclo[2.2.1]hept-2-ene-5,6-dicarboxylate in the presence of lead tetraacetate in dichloromethane solvent yields *endo*, *cis*-dimethyl-3-aza-3-phthalimidyltricyclo[3.2.1.0^{2,4}]octane-6,7-dicarboxylate (1a) in a 10.5% isolated yield. Hoesch and Dreiding have shown that lead tetraacetate oxidizes *N*-aminophthalimide to phthalimide in the absence of olefin (4). Accordingly, we have isolated phthalimide in approximately 8% yield in the above reaction. Obviously the lead tetraacetate oxidation of *N*-aminophthalimide to phthalimide is a competing reaction pathway.



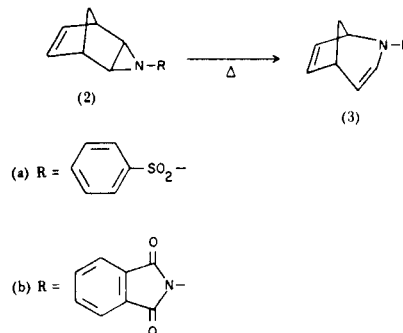
The other new aziridine synthesized is *endo*, *cis*-dimethyl-3-aza-3-(2-methyl-4-quinazolyl)tricyclo[3.2.1.0^{2,4}]octane-6,7-dicarboxylate (1b). This compound was prepared by a procedure analogous to that used in the preparation of 1a, using 3-amino-2-methyl-4-quinazolone as the nitrene precursor. The aziridine was obtained in 5-6% yields. 2-Methyl-4-quinazolone was also isolated in a 24% yield from each reaction mixture. In analogy with the results obtained by Hoesch and Dreiding,

we have found that the reaction of 0.5 mole of lead tetraacetate with 3-amino-2-methyl-4-quinazolone in the absence of olefin leads to high yields (about 80%) of the deaminated compound, 2-methyl-4-quinazolone (5). Thus apparently there is a side reaction involving the lead tetraacetate oxidation of 3-amino-2-methyl-4-quinazolone in the aziridine synthesis reaction.

The two new aziridines were found to be remarkably stable for a 3-azatricyclo[3.2.1.0^{2,4}]octane ring system. Unsaturated analogs of the system have been found not to be particularly stable. Thus 3-benzenesulfonyloxy-3-azatricyclo[3.2.1.0^{2,4}]oct-6-ene (2a) is unstable (6-8) and 3-phthalimidyl-3-azatricyclo[3.2.1.0^{2,4}]oct-6-ene (2b) rearranged after heating for 40 minutes at 120° (4). Both compounds rearrange to the corresponding 2-azabicyclo[3.2.1]octa-3,6-diene (3). The aziridines (1a) and (1b) were found to be stable after refluxing for 24 hours in carbon tetrachloride and in chlorobenzene (b.p. 132°).

Acknowledgements.

The generous support of this work by the Robert A. Welch Foundation is gratefully acknowledged. We would also like to thank Mr. Peter Cipolla for the lead tetraacetate-quinazolone reactions, Dr. J. E. Hudson at Rice University for the mass spectra and the University of Houston for the nmr spectra.



EXPERIMENTAL

Melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. Ir spectra were recorded on a Perkin-Elmer Model 237 B grating infrared spectrophotometer. Nmr spectra (in deuteriochloroform with tetramethylsilane as internal standard) were measured on a Varian T-60 spectrometer. The elemental analyses were performed by Galbraith Laboratories.

The lead tetraacetate was obtained from G. Frederick Smith Chemical Company. It was not recrystallized, but the acetic acid was removed under vacuum to give a white, powdery material before use. The dichloromethane was washed with concentrated sulfuric acid and 10% potassium hydroxide, stored over solid sodium hydroxide overnight and distilled. It was stored over molecular sieves in brown bottles. The carbon tetrachloride and chlorobenzene were reagent grade and were used without further purification.

The 3-amino-2-methyl-4-quinazolone was prepared as described by Rees, *et al.* (2).

Synthesis of *endo, cis*-Dimethylbicyclo[2.2.1]hept-2-ene-5,6-dicarboxylate.

The diester was prepared *via* Fisher esterification of the diacid (9).

Synthesis of *endo, cis*-Dimethyl-3-aza-3-phthalimidyltricyclo[3.2.1.0^{2,4}]octane-6,7-dicarboxylate (**2a**).

To a solution of 1.01 g. (6.2 mmoles) of *N*-aminophthalimide and 3.95 g. (18.8 mmoles) of *endo, cis*-dimethylbicyclo[2.2.1]hept-2-ene-5,6-dicarboxylate in dry dichloromethane (18 ml.) was added 2.79 g. (6.3 mmoles) of lead tetraacetate over a period of 12 minutes in the dark. After stirring for an additional 15 minutes, the reaction mixture was filtered and the solid washed with additional dichloromethane (20 ml.) and ether (20 ml.). The combined organic layers were washed with 1% sodium hydroxide and water, dried over anhydrous magnesium sulfate and then evaporated to dryness on a rotary evaporator. The residue was treated with several portions of benzene to remove the acetic acid. The benzene was removed to leave a yellow solid. Recrystallization from denatured alcohol gave compound **2a** (0.24 g., 10.5% yield) as yellow crystals, m.p. 186-188° and phthalimide (0.15 g., 8.3% yield). In some trials a third, high-melting, still-unidentified solid (about 0.2 g.) was obtained. The aziridine showed ir (nujol): 700, 890, 1190 and 1700 cm⁻¹; nmr δ 7.73 (s, 4H, aromatic H), 3.70 (s, 6H, methyl H), 3.37 (s, 2H, methine H adjacent to COOCH₃), 3.13 (broad s, 4H, bridgehead H) and 1.40 (AB, 2H, methylene H); mass spectrum: *m/e* 370 (M⁺).

Anal. Calcd. for C₁₉H₁₈N₂O₆: C, 61.62; H, 4.90; N, 7.56. Found: C, 61.48; H, 5.02; N, 7.52.

Synthesis of *endo, cis*-Dimethyl-3-aza-3-(2-methyl-4-quinazolyl)-tricyclo[3.2.1.0^{2,4}]octane-6,7-dicarboxylate (**2b**).

To a solution of 1.09 g. (6.2 mmoles) of 3-amino-2-methyl-4-quinazolone and 3.95 g. (18.8 mmoles) of *endo, cis*-dimethylbicyclo[2.2.1]hept-2-ene-5,6-dicarboxylate in dry dichloromethane (18 ml.) was added 2.79 g. (6.3 mmoles) of lead tetraacetate over a period of 12 minutes in the dark. After stirring for an additional 15 minutes, the reaction mixture was filtered and the solid washed with additional dichloromethane (20 ml.). The combined dichloromethane solutions were evaporated to dryness on a rotary evaporator and the residue treated with several portions of benzene to remove the acetic acid. The benzene was removed to leave an orange-brown solid, purified by column chromatography (basic alumina; chloroform) to give a compound **2b** (0.14 g., 6% yield) as off-white crystals, m.p. 165-167°. Continued elution with acetone provides a white solid. Recrystallization from chloroform gave 2-methyl-4-quinazolone (0.24 g., 24% yield) as white needles, m.p. 235-240°. The aziridine showed many peaks in the ir (nujol): *eg.*, 775, 1150, 1190, 1580, 1660, 1705, 1715 cm⁻¹; nmr: δ 7.49 (m, 4H, aromatic H), 3.62 (s, 6H, ester methyl H), 3.37 (s, 2H, methine H adjacent to COOCH₃), 3.10 (broad s, 4H, bridgehead H), 2.71 (s, 3H, olefinic methyl H) and 1.80 (AB, 2H, methylene H); mass spectrum: *m/e* 383 (M⁺).

Anal. Calcd. for C₂₀H₂₁N₃O₅: C, 62.65; H, 5.52; N, 10.96. Found: C, 62.52; H, 5.58; N, 11.12.

REFERENCES AND NOTES

- (1) Robert A. Welch Undergraduate Scholar, 1976.
- (2) D. J. Anderson, T. L. Gilchrist, D. C. Horwell and C. W. Rees, *J. Chem. Soc. (C)*, 576 (1970).
- (3) Hoesch and Dreiding have added *N*-aminophthalimide to bicyclo[2.2.1]heptadiene. They obtained the expected aziridine, but no experimental details are available. [L. Hoesch and A. S. Dreiding, *Chimia*, **23**, 405 (1969)].
- (4) L. Hoesch and A. S. Dreiding, *Chimia*, **23**, 405 (1969).
- (5) G. R. Meyer and P. Cipolla, unpublished observations.
- (6) J. E. Franz and C. Osuch, *Chem. Ind. (London)*, 2058 (1964).
- (7) A. C. Oehlschlager and L. H. Zalkow, *Chem. Commun.*, 70 (1965).
- (8) A. C. Oehlschlager and L. H. Zalkow, *J. Org. Chem.*, **30**, 4205 (1965).
- (9) L. F. Fieser, "Organic Experiments", 2nd Ed., D. C. Heath and Company, Lexington, Mass., 1968, p. 87.