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# ADDITION OF ETHYL DIAZOACETATE TO BICYCLIC OLEFINS

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**Abstract**—Several new derivatives of the tricyclo(3.2.1.0$^{2,4}$)octane system have been synthesized. The key reaction involved addition of ethyl diazoacetate to norbornenes and norbornadiene.

## INTRODUCTION

The main objective of the present research was to study the addition of ethyl diazoacetate to some bicycloheptenes. Of particular interest were the stereochemistry of addition and the possibility of homo-conjugate addition to bicycloheptadiene. It was also desirable to develop a simple synthesis of substituted tricyclo(3.2.1.0$^{2,4}$)octanes for use in some further experiments

## DISCUSSION AND RESULTS

Previous workers have established that the elements of carbalkoxy carbene, generated either photolytically[1] or catalytically with copper-bronze,[2,3] add to olefins in a *cis* fashion to produce the least hindered olefin. Cyclohexene, for example, leads to a 16:1 mixture of *exo*:*endo*-norcarane-7-carboxylates.[2] This kind of observation does not allow prediction about the mode of addition to a system like norbornene in which the two faces of the double bond are exposed to differing steric interactions. Since the exact role of the copper in these reactions is not well understood,[2,4] mechanistic considerations are not fruitful in this respect, either.

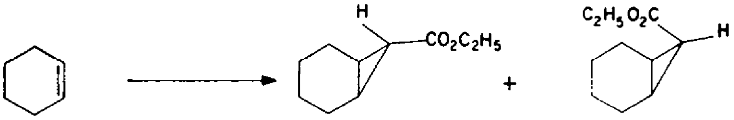

FIG. 1

In the present study, norbornene (I) was condensed with ethyl diazoacetate in the presence of cuprous cyanide. A 1:1 adduct was isolated which appeared to be homogeneous by gas chromatography on several columns. Structure II is assigned to this product on the basis of spectral evidence and chemical evidence to be presented. Thus, hydrolysis of the ester II gave a crystalline acid (III) which was converted to

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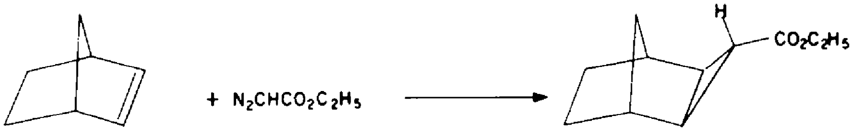
[1] W. von E. Doering and T. Mole, *Tetrahedron* **10**, 65 (1960).

[2] P. S. Skell and R. M. Etter, *Proc. Chem. Soc.* 443 (1961).

[3] P. S. Skell and R. C. Woodworth, *J. Amer. Chem. Soc.* **78**, 4496 (1956).

[4] P. Yates, *J. Amer. Chem. Soc.* **74**, 5376 (1952).

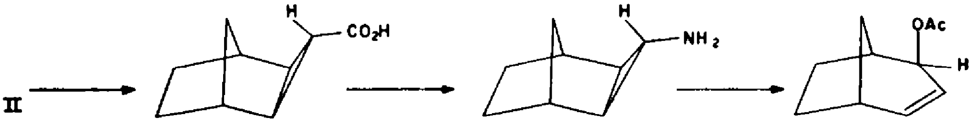


I

II

FIG. 2

the amine IV by a modified Curtius reaction.[5] Nitrous acid deamination led, *via* the expected rearrangement,[6] to the known[7] acetate V. This sequence assures the basic ring structure.



III

IV

V

FIG. 3

The *anti*-nature of the carbethoxy function is assigned by analogy,[1–3] and the *exo*-ring fusion of the cyclopropyl ring follows from the discussion below.

Attention was next turned to the reaction of norbornadiene (VII) with ethyl diazoacetate. The 1:1 adduct again appeared to be homogeneous by gas chromatography, but it was readily apparent from the NMR spectrum that a mixture was on hand. The most striking feature in this respect was the presence of two triplets at 3·6 and 4·2$\tau$ (relative area 2:1) which could only be due to the protons of two different olefinic systems. The presence of tetracyclic products formed by homo-conjugate addition could be ruled out by the finding that the mixture readily absorbs one mole of hydrogen on catalytic reduction and from a consideration of the integrated areas of the NMR spectrum.

Assignment of structures to these two components rests on the close analogies between these systems and the molecules VIa[8] and VIb.[9] The olefinic proton resonance absorptions of these two systems appear at 4·3 and 3·6$\tau$, respectively. Thus, the major and minor products from the ethyl diazoacetate:norbornadiene reaction can safely be assigned to structures VIII and IX, respectively.

VI a

VI b

FIG. 4

[5] J. Weinstock, *J. Org. Chem.* **26,** 3511 (1961).

[6] P. Lipp, J. Buchkremer and H. Seeles, *Liebig's Ann.* **499,** 1 (1932).

[7] W. C. Wildman and D. R. Saunders, *J. Amer. Chem. Soc.* **76,** 946 (1954).

[8] K. B. Wiberg and W. J. Bartley, *J. Amer. Chem. Soc.* **82,** 6375 (1960).

[9] H. E. Simmons and R. D. Smith, *J. Amer. Chem. Soc.* **81,** 4256 (1959).

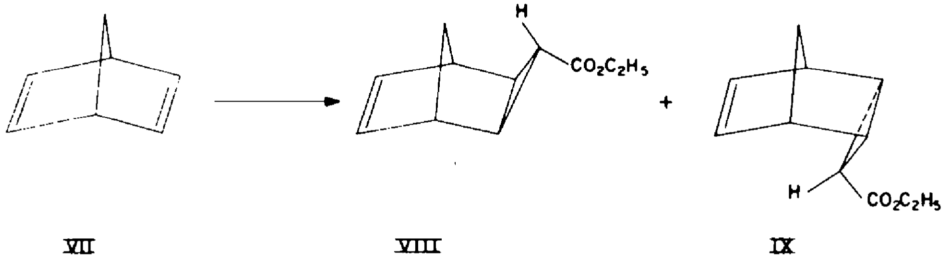


FIG. 5

The large diamagnetic shift of the olefinic protons of the *endo*-system is of considerable theoretical interest. Variations of ring strain between the two isomers appear to be minor, and, in any case, could hardly account for the magnitude of the observed shifts (0·6–0·7 ppm).[10]

As an alternate possible rationale we have considered the possibility of shielding by ring current effects of the cyclopropyl ring system. Molecular models show that the olefinic protons of the *endo*-system lie within the cone circumscribed by the protons of the cyclopropyl ring and perpendicular to this ring. Thus, the induced ring current of the cyclopropyl ring would effect shielding of these protons as well as the ring protons.[10,11]

Further evidence on the correctness of the interpretation of the spectrum of the mixture of VIII and IX was provided by an alternate synthesis of VIII in which the double bond was introduced after the cyclopropane ring. To this end, 5,6-dichloronorbornene (X) was prepared and condensed with ethyl diazoacetate. The adduct, XI, was dehalogenated with magnesium in ether to give an olefin which showed only the 3·6τ absorption in the NMR. This product can only be the pure *exo*-system, VIII. The structure assigned to II is further confirmed by the finding that catalytic reduction of the pure VIII also gave II. Thus, addition of ethyl diazoacetate to norbornenes appears to be mainly from the *exo*-side.

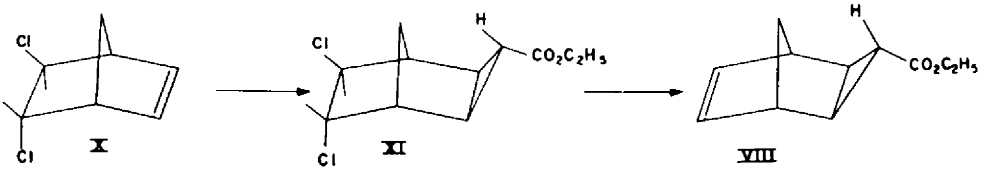


FIG. 6

Of incidental interest was the appearance in the NMR spectrum of VIII of a triplet (J = 2·5 c/s) at 7·5τ of relative area corresponding to one proton. This absorption must correspond to the proton adjacent to the carbethoxyl function on the cyclopropyl ring. The abnormally small value for the *trans* vicinal coupling

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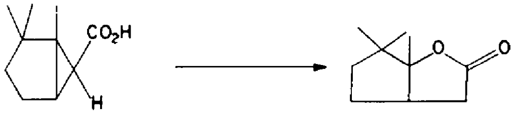
[10] K. Wiberg and B. J. Nist, *J. Amer. Chem. Soc.* **83**, 1226 (1961), have reported chemical shifts for the olefinic protons of various cycloalkenes. The difference between cyclobutene and cyclopentene, for example, is only 0·37 ppm, whereas the change in geometry is considerably greater than in the systems discussed here.

[11] For some other possible examples, see R. R. Sauers and P. E. Sonnet, *Chem. & Ind.* 786 (1963); R. S. Boikess and S. Winstein, *J. Amer. Chem. Soc.* **85**, 343 (1963); W. R. Moore, W. R. Moser and J. E. LaPrade, *J. Org. Chem.* **28**, 2200 (1963); and D. J. Patel, M. E. H. Howden and J. D. Roberts, *J. Amer. Chem. Soc.* **85**, 3218 (1963).

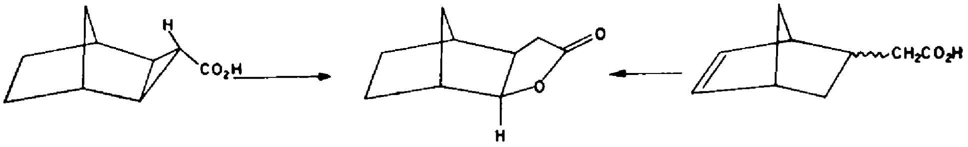
constant[12] may be caused by the distorted bond angles of the three-membered ring system. Both the dihedral H—C—C—H angle and the H—C—C angles would be expected to change on introduction of the fused norbornyl ring system to a cyclopropyl ring.[13]

Some lactonization experiments were carried out on acid III. The closely analogous system, XII, has been reported by Meinwald, Lewis and Gassman[14] to lead to lactone XIII on treatment with sulfuric acid. In our system, the major product was also a $\gamma$-lactone as evidenced by IR absorption at 5·63 $\mu$. The fact that *exo-* and *endo*-norbornenyl acetic acids (XV) lead to the same product strongly suggests that this product arises from cleavage of the $C_2$—$C_3$ bond. The NMR spectrum appears to be most consistent with XIV as the structure of this lactone. The proton on the ether-oxygen carbon appears at 5·6$\tau$ as a doublet (J = 5 c/s), much the same as the similar proton in *exo*-norbornanols.[15] Structure XVI seems unlikely since coupling to the bridgehead proton should complicate the spectrum of the $\alpha$-proton.[15b] Structure XVII seems unlikely in view of the relatively large number of low-field protons in the spectrum (ca. 5 protons between 7·3–8·0$\tau$).



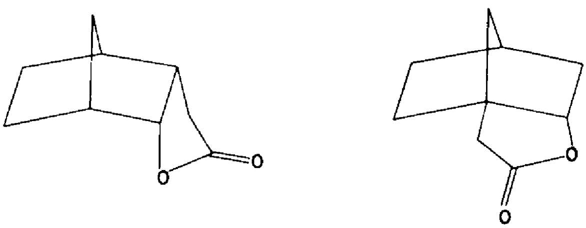
XII XIII

FIG. 7



XIV XV

FIG. 8



XVI XVII

FIG. 9

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[12] The corresponding value for cyclopropane carboxylic acid is 4·6 c/s as reported by K. B. Wiberg and B. J. Nist, *J. Amer. Chem. Soc.* **85**, 2788 (1963). Other values given by these authors range from 3·9 to 7·5 c/s for *trans* couplings.

[13] M. Karplus, *J. Amer. Chem. Soc.* **85**, 2870 (1963), has suggested variations of J with both of these parameters.

[14] J. Meinwald, A. Lewis and P. G. Gassman, *J. Amer. Chem. Soc.* **84**, 978 (1963).

[15] [a] S. J. Cristol, L. K. Gaston and D. W. Johnson, *Tetrahedron Letters* No. 4, 185 (1963); [b] F. A. L. Anet, *Canad. J. Chem.* **39**, 789 (1961).

## EXPERIMENTAL

Analyses were performed by G. Robertson, Florham Park, New Jersey and W. Manser, Herliberg, Switzerland. IR spectra were recorded with a Perkin–Elmer Model 21 IR spectrophotometer. NMR spectra were taken on a Varian Model A-60 spectrometer. All chemical shifts were measured relative to tetramethylsilane. Vapor-phase chromatograms were obtained on a Model A-90-P Aerograph Gas Chromatograph using helium as the carrier gas at a flow rate of 60 cc/min. Columns and temp are noted in context. The Carbowax column was 15% Carbowax 20M on 35/80 mesh firebrick. The Craig column was 15% butanediol succinate on 35/80 mesh firebrick. The Silicone column was 20% Silicone oil SE-30 on 60/80 mesh firebrick and the T.C.E.P. column was 20% tricyanoethoxypropane on 35/80 mesh firebrick.

*Ethyl* exo-*tricyclo*(3.2.1.$0^{2,4}$)*octane*-3-anti-*carboxylate* (II). A mixture of 19·8 g (0·211 mole) norbornene and 1·60 g (0·00895 mole) CuCN was heated to reflux in 50 ml hexane. To this mixture was added dropwise a solution of 20·0 g (0·175 mole) ethyl diazoacetate in 50 ml hexane at such a rate as to maintain vigorous $N_2$ evolution. After the addition had been completed, the deep red mixture was heated under reflux for 30 more min. The mixture was cooled to room temp and filtered. The residue was washed thoroughly with ether and then filtrate and washings were combined and concentrated on a steam bath. The material was distilled through a Holzman column to give 17·6 g (55·8%) of a colorless liquid, b.p. 80–90° at 1·5 mm. A molecular distillation of the residue from this distillation provided another 0·8 g (2·6%) of liquid having an IR spectrum identical with that of the original distillate. Gas chromatographic analysis was made with a Carbowax column at 190°. The two minor components had IR spectra which were virtually identical with the published spectra of diethyl maleate and diethyl fumarate. The NMR spectrum of the major component displayed a quartet centered at 5·9$\tau$ (2 protons) ascribed to the methylene of the ethyl group and a triplet centered at 8·8$\tau$ which was ascribed to the methyl group. (Found: C, 73·06; H, 9·06. $C_{11}H_{16}O_2$ requires: C, 73·30; H, 8·95%).

exo-*Tricyclo*(3.2.1.$0^{2,4}$)*octane*-3-anti-*carboxylic acid* (III). Ethyl *exo*-tricyclo(3.2.1.$0^{2,4}$)octane-3-*anti*-carboxylate (21 g; 0·117 mole) was heated under reflux in 20 ml ethanol and 30 ml water containing 16·8 g (0·30 mole) KOH for 6 hr. The reaction mixture was evaporated in a stream of air, diluted to 100 ml with water and acidified with conc. HCl aq., precipitating the crude product which was collected by filtration, yield 14·9 g (83·7%). Recrystallization from aqueous ethanol yielded colorless platelets, m.p. 115–116·5°. The NMR spectrum exhibited a singlet at $-1·7\tau$ (1 proton) and a broad singlet at 7·6$\tau$ (2 protons). The former absorption was ascribed to the carboxyl proton and the latter to the protons on carbons 1 and 5. (Found: C, 71·03; H, 8·01. $C_9H_{12}O_2$ requires: C, 71·02; H, 7·95%).

The p-*nitrobenzyl ester* was prepared in the usual manner,[16] and had m.p. 71–72°. (Found: C, 66·70; H, 6·24; N, 5·10. $C_{16}H_{17}NO_4$ requires: C, 66·88; H, 5·97; N, 4·88%).

exo-*Tricyclo*(3.2.1.$0^{2,4}$)*octane*-3-anti-*amine* (IV). The procedure employed was a modification of the Curtius reaction.[5] The tricyclic acid (8·75 g, 0·059 mole) was suspended in 10 ml water and brought into solution with a minimum of acetone. The solution was cooled to 0–5° and this temp was maintained while a solution of 9·1 g (0·09 mole) triethylamine in 90 ml acetone was slowly added. A solution of 9·9 g (0·091) ethyl chloroformate in 25 ml acetone was then slowly added. The mixture was stirred for 2 hr at 0–5° and then 7·9 g (0·12 mole) $NaN_3$ in 25 ml water was added. The mixture was stirred for another 2 hr at 0–5°. The mixture was then poured over 100 g cracked ice and extracted 4 times with 30-ml portions of ether. After the ethereal solution had been dried ($MgSO_4$) the ether was removed *in vacuo* leaving a fragrant oil. This material showed the typical strong IR bands for azides at 4·3, 4·7 and 5·9 $\mu$.

This oil was dissolved in 80 ml toluene containing 20 ml ethanol and heated on a steam bath for 16 hr. The solvents were distilled and the oily residue poured over 70 g $Ca(OH)_2$. After 35 hr of steam distillation, 3·55 g (48·9%) of the amine was obtained. This compound did not give a good analysis due to rapid absorption of $CO_2$ from the air.

The N-*phenylurea derivative* was prepared in the usual manner,[16] m.p. 216–217°. (Found: C, 74·13; H, 7·53; N, 11·39. $C_{15}H_{18}N_2O$ requires: C, 74·35; H, 7·49; N, 11·56%).

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[16] R. L. Shriner, R. C. Fuson and D. Y. Curtin, *The Systematic Identification of Organic Compounds*. John Wiley, New York (1960).

The N-*phenylthiourea derivative* was prepared in the usual manner,[16] m.p. 126·5–127°. (Found: C, 69·58; H, 7·14; N, 10·84. $C_{15}H_{18}N_2S$ requires: C, 69·73; H, 7·02; N, 10·85%).

*2-Bicyclo*(3.2.1)*octene-3-acetate* (V). A solution of 0·30 g (0·0025 mole) of the tricyclic amine in 20 ml glacial acetic acid containing 1 drop of conc. HCl aq. was prepared. The solution was stirred at room temp while 0·65 g (0·094 mole) $NaNO_2$ was added in small portions over a period of 30 min. The resulting solution was allowed to stand at ambient temp for 16 hr. It was then made alkaline with 20% NaOH aq. and extracted 4 times with 20-ml portions of ether. The ethereal layer was washed with dil. HCl aq. and then 3 times with 5-ml portions of water. After the organic layer had been dried ($CaCl_2$), the ether was removed leaving 0·20 g (54%) of the acetate. Gas chromatography using a Carbowax column at 185° revealed identity of retention time with a known sample.[17] The IR spectra were also identical.

*Ethyl 6-tricyclo*(3.2.1.$0^{2,4}$)*octene-*3-anti-*carboxylate* (exo *and* endo *mixture*) (VIII and IX). Norbornadiene (19·3 g, 0·213 mole) was dissolved in 50 ml hexane containing 1·60 g (0·00895 mole) CuCN. This mixture was heated under reflux on a steam bath while a solution of 20·2 g (0·178 mole) ethyl diazoacetate in 45 ml hexane was added at such a rate as to maintain a vigorous evolution of $N_2$. When the addition was complete the mixture was heated under reflux for another 30 min. The mixture was cooled to room temp, filtered, and concentrated on a steam bath. It was then distilled through a Holzman column to give 14·6 g (45·9%) of a colorless liquid, b.p. 67–73° at 0·35 mm. Gas chromatographic analysis was made on a Carbowax column at 195°. Two of the minor components were shown to be diethyl fumarate and maleate by a comparison of retention times with known samples. The peak of the major component had an area of ca. 85% of the total absorption. Its IR spectrum displayed bands at 5·8 and 14·2 μ ascribed to carbonyl and *cis* olefin structures.

The NMR spectrum of this ester exhibited an olefinic triplet centered at 3·6τ and another at 4·2τ. The total area was equivalent to 2 protons and the ratio of areas was 67:33, respectively. Two staggered quartets were present centered at ca. 6·0τ (total of 2 protons). Other assigned absorptions were a broad singlet at 7·1τ (2 protons) which was ascribed to the protons on carbons 1 and 5 in both isomers, and a triplet centered at 8·8τ which was attributed to the methyl group of both isomers. The lone cyclopropyl proton of the *exo* isomer appeared as a triplet centered at 7·5τ (J = 2·5 c/s). Other protons appeared as multiplets at 8·9τ and 8·2τ. (Found: C, 73·92; H, 7·76. $C_{11}H_{14}O_2$ requires: C, 74·13; H, 7·92%).

*6-Tricyclo*(3.2.1.$0^{2,4}$)*octene-*3-anti-*carboxylic acid* (exo *and* endo *mixture*). The unsaturated tricyclic ester was saponified to the acid as previously described for the saturated compound except that the resulting solution of the potassium salt of the unsaturated acid was evaporated in a stream of $N_2$. The tricyclic unsaturated ester (15 g; 0·082 mole) and 14 g (0·25 mole) KOH were allowed to react. The yield of acid once recrystallized from aqueous ethanol was 9·58 g (77·9%), m.p. 79–83·5°, analytical sample m.p. 85–85·5°. (Found: C, 71·91; H, 6·64. $C_9H_{10}O_2$ requires: C, 71·98; H, 6·71%).

The NMR spectrum of these acids displayed olefinic triplets at 3·6 and 4·2τ. The total areas were equivalent to 1 proton and the relative areas were 2:1. The carboxyl proton appeared at −2·1τ. A broad singlet at 7·1τ was assigned to the protons on $C_1$ and $C_5$. The lone cyclopropyl proton appeared at 7·5τ as a triplet with J = 2·5 c/s assuming that there is no difference between the ester and the acid.

*Ethyl tricyclo*(3.2.1.$0^{2,4}$)*octane-*3-anti-*carboxylic acid* (exo *and* endo *mixture*). The isomeric mixture of unsaturated esters obtained from norbornadiene was hydrogenerated. Unsaturated ester (206 mg, 1·16 moles) was dissolved in 15 ml 95% ethanol to which was then added 5 mg Pd-C. The stirred mixture was hydrogenated (atm. press.), the $H_2$ used being 94·6% of the theoretical amount for one double bond. The product was isolated by diluting the ethanol with 150 ml water and extracting 4 times with 25 ml ether. After the combined extracts had been dried ($Na_2SO_4$), the ether was removed leaving 162 mg (77·5%) of the saturated ester. Although gas chromatographic analysis showed only one peak, the IR and NMR spectra showed differences from the corresponding spectra of the ester prepared from norbornene and ethyl diazoacetate.

trans-*6,7-Dichloro-*exo-*tricyclo*(3.2.1.$0^{2,4}$)*octane-*3-anti-*carboxylic acid, ethyl ester* (XI). The *trans*-5,6-dichloronorbornene (16·9 g, 0·103 mole) which had been prepared by the method of

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[17] R. R. Sauers, *Tetrahedron Letters*, 146 (1961).

Schmerling and Luvisi[18] was dissolved in 50 ml hexane. To this solution was added 0·79 g (0·00448 mole) CuCN. This mixture was heated under reflux while a solution of 9·8 g (0·086 mole) ethyl diazoacetate in 50 ml hexane was added dropwise at such a rate as to maintain vigorous evolution of $N_2$. After the addition had been completed, the mixture was heated under reflux for another 30 min and then it was cooled to room temp and filtered. The solvent was boiled off (at atm. press.) and the residual oil distilled (red. press.) through a Claisen adapter, yielding a first fraction, 4·87 g, b.p. 31·5–34° at 0·50 mm; and the second fraction 2·64 g, b.p. 52–63° at 0·50 mm. The IR spectra of these fractions indicated that they were predominantly *trans*-5,6-dichloronorbornene (first fraction) and diethyl fumdrate and maleate (second fraction). A molecular distillation of the remaining material provided 5·32 g (24·8%) of an oil which was employed for the subsequent step.

*Ethyl* 6-exo-*tricyclo*(3.2.1.0$^{2,4}$)*octene*-3-anti-*carboxylate* (VIII). The crude mixture containing the dichlorotricyclic ester was dehalogenated with Mg turnings (0·9 g, 0·04 g atom) and 3·6 g (0·01 mole) $I_2$ under reflux in 60 ml anhydrous ether. The mixture was stirred at room temp while a solution of 4·0 g of the dichlorotricyclic ester in 10 ml ether was added. Stirring at room temp was continued for 16 hr. The mixture was then filtered and washed thoroughly with ether. The combined ether layers were washed 4 times with 10 ml water and dried ($Na_2SO_4$). The solvent was removed and the residual oil was distilled by molecular distillation to give 2·1 g of a colorless liquid. Gas chromatography with a Carbowax column at 180° showed a major peak with the retention time of the unsaturated tricyclic ester mixture obtained from norbornadiene and ethyl diazoacetate. The IR spectrum of the purified material coincided with that of the unsaturated ester mixture but was more clearly defined. The NMR spectrum showed olefinic proton absorption (area 2) at 3·6τ and the lone cyclopropyl proton as a triplet (J = 2·5 c/s) at 7·5τ. The NMR spectrum of the minor product (IX) of the norbornadiene–ethyl diazoacetate reaction could readily be obtained by subtraction of the spectrum of VIII from that of the mixture.

*Ethyl* exo-*tricyclo*(3.2.1.0$^{2,4}$)*octane*-3-anti-*carboxylic acid* (II). The *exo* unsaturated tricyclic ester was hydrogenated (atm. press.). 213 mg of the impure unsaturated ester was dissolved in 25 ml 95% ethanol to which had been added 6·5 mg $PtO_2$. The product was isolated as described in the previous hydrogenation procedure. The major peak was collected on a Craig gas chromatography column at 190°. The IR and NMR spectra were superimposable with those of the tricyclic ester obtained by reaction of norbornene and ethyl diazoacetate.

exo- *and* endo-5-*Norbornenyl acetic acids* (XV). A mixture of the two acids was prepared by carbonation of the Grignard reagent prepared from the commercially available mixture of *exo*- and *endo*-5-norbornenylmethyl chloride.[19]

*Lactonization of* exo- *and* endo-5-*norbornenyl acetic acids*. The norbornenyl acetic acids (1·00 g) were dissolved in 16 g 75% $H_2SO_4$ aq. which had been chilled in an ice bath. The solution was kept at ca. 0° for 22 hr. It was then quenched with 100 ml of ice-water and extracted 3 times with ether. The combined extracts were washed ($Na_2CO_3$ aq. and water) and dried ($MgSO_4$). Removal of the ether gave 0·87 g (87%) of neutral material. Gas chromatography on the Carbowax column at 190° indicated two peaks with relative areas 85:15. The major peak showed carbonyl absorption at 5·62 μ. The NMR spectrum showed a doublet (J = 5 c/s) of relative area 0·95 protons at 5·6τ. The remainder of the spectrum showed two main groups of multiplets centered at 2·4 ppm (ca. 5 protons) and 1·5 ppm (ca. 6 protons). (Found: C, 71·02; H, 7·90. $C_9H_{12}O_2$ requires: C, 71·02; H, 7·95%).

The minor peak showed carbonyl absorption at 5·62 μ. (Found: C, 70·91; H, 8·19%).

*Lactonization of acid* III. The tricyclic acid III (0·050 g) was allowed to stand in conc. $H_2SO_4$ at room temp for 18 days. The dark solution was poured over ice and extracted with ether. After washing ($NaHCO_3$ aq.), the dried extracts were evaporated to give 0·45 g of product. The retention time and IR spectrum of the major product were identical with those of the product prepared above. Two minor components were observed in the gas chromatogram whose total relative area was about 48%. These lactones were waxy materials with poorly defined m.ps.

*Acknowledgement*—We gratefully acknowledge the financial support of the National Institutes of Health (RG-8701).

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[18] L. Schmerling and J. P. Luvisi, *J. Amer. Chem. Soc.* **78**, 2819 (1956).

[19] This procedure was developed by Dr. R. Hawthorne.