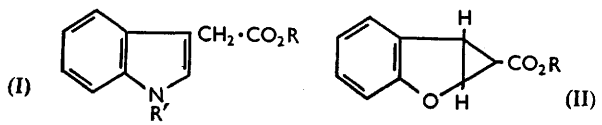
233. *Polynuclear Heterocyclic Systems. Part XIII.* The Reaction of Ethyl Diazoacetate with Naphthalene and its Heterocyclic Analogues.*

By G. M. Badger, B. J. Christie, H. J. Rodda, and Jenneth M. Pryke.

Thionaphthen and benzofuran with ethyl diazoacetate yield ethyl 2 : 3-dihydrothionaphthen-2 : 3-yleneacetate (III; R = Et) and 2 : 3-dihydrobenzofur-2 : 3-yleneacetate (II; R = Et) respectively. The structure of the former has been established by reductive desulphurisation to 2-*cyclo*hexyl-*cyclo*propanecarboxylic acid (IV). Under the same conditions, indole and 1-methylindole react with ethyl diazoacetate, by substitution, to give ethyl 3-indolylacetate and 1-methyl-3-indolylacetate (I; R = Et, R′ = H and Me respectively).

Reaction of ethyl diazoacetate with naphthalene yields ethyl 1 : 2 : 3 : 4-tetrahydronaphth-1 : 2-3 : 4-di(yleneacetate) (X; R = Et) as well as the monoadduct (IX; R = Et).

At elevated temperatures ethyl diazoacetate adds to carbon–carbon double bonds, with elimination of nitrogen, to form *cyclo*propane derivatives. The reaction is not confined to ethylenic compounds, and several aromatic hydrocarbons undergo this addition.[1] With polycyclic aromatic hydrocarbons, the addition occurs at the bond having the greatest bond order.[2,3] and ethyl diazoacetate has been classified as a "double-bond reagent."[4] Few attempts have so far been made to apply the reaction to heterocyclic systems, although reaction with thiophen is said to give a *cyclo*propane adduct.[5] On the other hand, pyrrole undergoes substitution to give (after hydrolysis) 2-pyrrylacetic acid.[6] The reaction of ethyl diazoacetate with naphthalene and its heterocyclic analogues has now been investigated.



Indole, 1-methylindole, thionaphthen, and benzofuran were heated with ethyl diazoacetate and the resulting esters distilled and hydrolysed. The acidic product from indole was identified as 3-indolylacetic acid (I; R = R′ = H), and no addition product was obtained. This is a surprising result, but it confirms the findings by previous workers [7,8] who obtained the same acid after hydrolysis of the product obtained by heating indole and ethyl diazoacetate in the presence of copper powder. It is clear that the presence of the copper does not affect the course of the reaction. The acidic hydrogen of indole is also without effect, for 1-methylindole gave 1-methyl-3-indolylacetic acid (I; R = H, R′ = Me), under the same conditions. Its structure was confirmed by direct comparison with a specimen prepared by *N*-methylation of 3-indolylacetic acid.

The acid obtained on reaction of benzofuran with ethyl diazoacetate was not identical with 2- or 3-benzofurylacetic acid. Addition to the 2 : 3-bond was therefore indicated, and the properties of the acid agree with its formulation as 2 : 3-dihydrobenzofur-2 : 3-yleneacetic acid (II; R = H). Its ultraviolet absorption spectrum is given in Fig. 1.

* Part XII, *J.*, 1958, 913.

[1] Badger, "Structures and Reactions of the Aromatic Compounds," Cambridge, 1954.
[2] Buchner and Hediger, *Ber.*, 1903, **36**, 3502.
[3] Badger, Cook, and Gibb, *J.*, 1951, 3456.
[4] Badger, *J.*, 1949, 456.
[5] Steinkopf and Augestad-Jensen, *Annalen*, 1922, **428**, 154.
[6] Piccinini, *Gazzetta*, 1899, **29**, 363.
[7] Jackson and Manske, *Canad. J. Chem.*, 1935, **13**, *B*, 170.
[8] Nametkin, Mel'nikov, and Bokarev, *Zhur. priklad. Khim.*, 1956, **29**, 459; *Chem. Abs.*, 1956, **50**, 13867.

The acid obtained from thionaphthen and ethyl diazoacetate likewise differed from the known 2- and 3-thionaphthenylacetic acid, and a *cyclo*propane addition structure (III) again appeared likely. This was supported by its stability to oxidation, for treatment with permanganate gave only 2 : 3-dihydrothionaphthen-2 : 3-yleneacetic acid 1 : 1-dioxide (VI). The ultraviolet absorption spectrum of the adduct (III; R = H) resembled that of the parent compound rather closely (Fig. 2).

The structure of the adduct (III; R = H) was proved by reductive desulphurisation with W-7 Raney nickel which not only removed the sulphur but simultaneously hydrogenated

FIG. 1. FIG. 2.

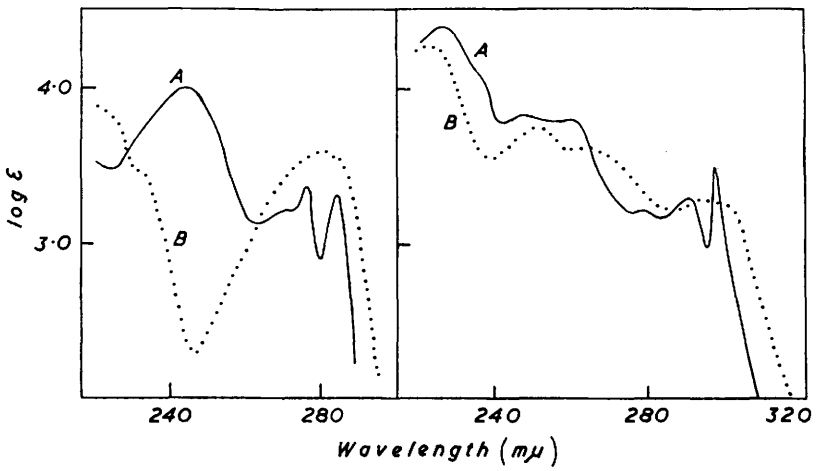
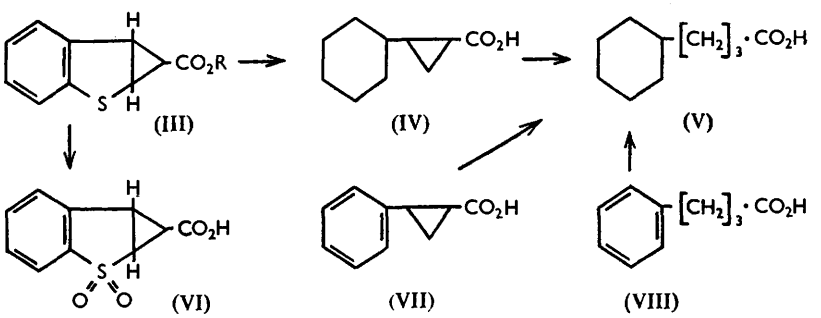


FIG. 1. *Ultraviolet absorption of* (*A*) *benzofuran and* (*B*) 2 : 3-*dihydrobenzofur*-2 : 3-*yleneacetic acid* (II) *in* 95% EtOH.

FIG. 2. *Ultraviolet absorption of* (*A*) *thionaphthen and* (*B*) 2 : 3-*dihydrothionaphthen*-2 : 3-*yleneacetic acid* (III) *in* 95% EtOH.

the benzene ring to give 2-*cyclo*hexyl*cyclo*propanecarboxylic acid (IV) (characterised as the amide). This result was surprising; for 2-phenyl*cyclo*propanecarboxylic acid (VII) was expected; but all attempts to bring about the desulphurisation with less active



catalysts were either unsuccessful or gave the same hydrogenated product. Moreover, both *cis*- and *trans*-2-phenyl*cyclo*propanecarboxylic acid (VII) were recovered unchanged after treatment with W-7 Raney nickel under " desulphurisation " conditions. It seems that the hydrogenation must proceed by addition of hydrogen to some other intermediate (possibly of a radical nature) formed after removal of the sulphur. In this reaction the *cyclo*propane ring must be important, for no hydrogenation of the benzene ring is observed in the desulphurisation of 3-thionaphthenylacetic acid.[9]

[9] Blicke and Sheets, *J. Amer. Chem. Soc.*, 1948, **70**, 3768.

With Adams catalyst, both *cis*- and *trans*-2-phenyl*cyclo*propanecarboxylic acid were hydrogenated to γ-*cyclo*hexylbutyric acid (V); this was also obtained by similar hydrogenation of 2-*cyclo*hexyl*cyclo*propanecarboxylic acid (IV) or γ-phenylbutyric acid (VIII). These examples of the reductive fission of *cyclo*propanes under relatively mild conditions, with Adams catalyst, parallel that recorded by Linstead and his co-workers,[10] who obtained ethyl *n*-butylmalonate from ethyl 2-vinyl*cyclo*propane-1 : 1-dicarboxylate. In all these cases rupture of the *cyclo*propane ring occurs at the bond linking the two substituents.

Buchner and Hediger [2] have shown that ethyl diazoacetate also reacts with naphthalene by addition. Hydrolysis of the adduct gave 1 : 2-dihydro-1 : 2-naphthyleneacetic acid (IX; R = H), the structure of which was firmly established. Conjugation of the *cyclo*propane ring with the 3 : 4-bond [1] would be expected to reduce the ethylenic nature of

FIG. 3. FIG. 4.

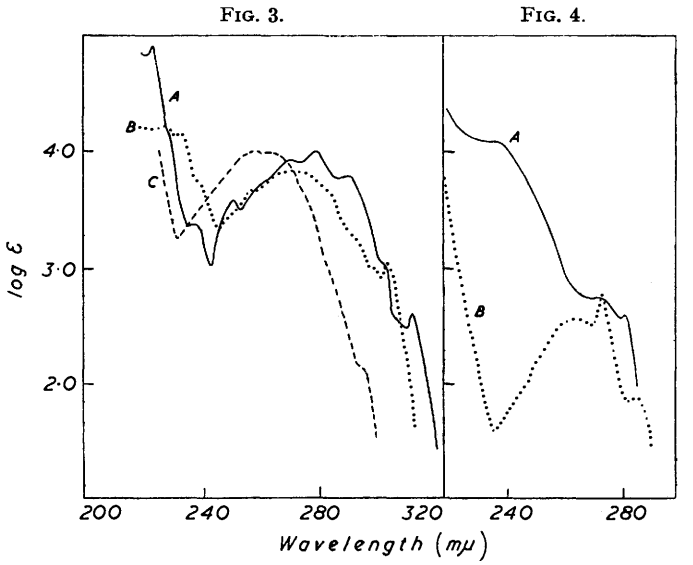
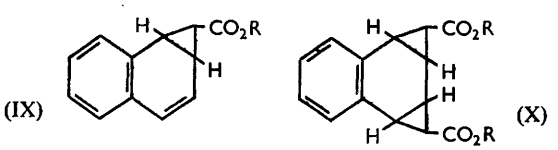


FIG. 3. *Ultraviolet absorption of* (*A*) *ethyl* 1-*naphthylacetate and* (*B*) *ethyl* 1 : 2-*dihydro*-1 : 2-*naphthyleneacetate, in* 95% EtOH, *and of* (*C*) 1 : 2-*dihydronaphthalene in* C_6H_6 (Hückel, Vevera, and Wörffel, *Chem. Ber.*, 1957, **90**, 901).

FIG. 4. *Ultraviolet absorption of* (*A*) *ethyl* 1 : 2-3 : 4-*tetrahydronaphth*-1 : 2-3 : 4-*di*(*yleneacetate*) *and* (*B*) *tetralin, in* 95% EtOH.

this bond; and its reactivity would also be affected by the electron-attracting effect of the ethoxycarbonyl group, and by steric hindrance. Nevertheless, the formation of a monoadduct as the sole product is unexpected, and the reaction of naphthalene with ethyl



diazoacetate has accordingly been re-investigated. On careful fractionation, the monoadduct (IX; R = Et) was obtained as the major product; but a little diadduct (X; R = Et) was also isolated. The same product was obtained when the monoadduct was heated with a further quantity of ethyl diazoacetate. Hydrolysis of this diadduct gave 1 : 2-3 : 4-tetrahydronaphth-1 : 2-3 : 4-di(yleneacetic acid) (X; R = H). This was not identical with 1 : 4- or 1 : 5-naphthylenediacetic acid, and its structure is supported by the ultraviolet absorption spectrum of the diester (X; R = Et) (Fig. 4).

[10] Kierstead, Linstead, and Weedon, *J.*, 1952, 3610.

Several authors [11] have pointed out that *cyclo*propane derivatives all show a moderately strong absorption infrared band between 1000 and 1050 cm.$^{-1}$. *cyclo*Propane itself [12] has a peak at 1028·7 cm.$^{-1}$, which has been assigned to a ring-bending vibration, and many substituted *cyclo*propanes absorb around 1021 ± 5 cm.$^{-1}$. All of our *cyclo*propanes examined had an absorption peak in this region (see Table) but its diagnostic value with heterocyclic derivatives must be accepted with great caution. 3-Indolylacetic acid (I; R = R′ = H), 1-methyl-3-indolylacetic acid (I; R = H, R′ = Me), and 3-thionaphthenylacetic acid all gave a similar peak in this region, although not containing a *cyclo*propane ring. Moreover, other simple indoles absorb in this region.[13]

3-Indolylacetic acid (I; R = H) is a potent plant hormone (auxin). So Dr. N. P. Kefford of the C.S.I.R.O., Canberra, very kindly tested our materials, using the *Avena* section test. 3-Indolylacetic, 1-methyl-3-indolylacetic, and 3-thionaphthenylacetic acid [14] all showed auxin activity; but 2 : 3-dihydrobenzofur-2 : 3-yleneacetic (II), 2 : 3-dihydrothionaphthen-2 : 3-yleneacetic acid (III), and 1 : 2-dihydro-1 : 2-naphthyleneacetic acid were active as auxin *antagonists*. 2 : 3-Dihydrothionaphthen-2 : 3-yleneacetic acid dioxide (VI) was inactive in both respects. It may be noted that *cis*-2-phenyl*cyclo*propanecarboxylic acid displays auxin activity,[15] but the *trans*-acid is inactive both as an auxin and as an auxin antagonist.

Infrared absorption (cm.$^{-1}$) *in the* 1000—1050 *cm.*$^{-1}$ *region.*[a]

Compound	Frequency
cis-2-Phenyl*cyclo*propanecarboxylic acid [b]	1025 w
trans-2-Phenyl*cyclo*propanecarboxylic acid [b]	1026 w
2-*cyclo*Hexyl*cyclo*propanecarboxylic acid [c]	1031 m
1 : 2-Dihydro-1 : 2-naphthyleneacetic acid [b]	1012 w
Ethyl 1 : 2-dihydro-1 : 2-naphthyleneacetate [d]	1025 m
Ethyl 1 : 2-3 : 4-tetrahydronaphth-1 : 2-3 : 4-di(yleneacetate)	1026 s
2 : 3-Dihydrothionaphthen-2 : 3-yleneacetic acid [b]	1018 m
Ethyl 2 : 3-dihydrothionaphthen-2 : 3-ylene acetate [d]	1031 m
2 : 3-Dihydrobenzofur-2 : 3-yleneacetic acid [b]	1015 w
Ethyl 2 : 3-dihydrobenzofur-2 : 3-ylene acetate [c]	1036 m
3-Indolylacetic acid [b]	1010 w
Ethyl 3-indolylacetate [c]	1026 s
1-Methyl-3-indolylacetic acid [b]	1012 m
3-Thionaphthenylacetic acid [b]	1019 w

[a] NaCl prism. [b] Nujol mull. [c] Liquid film. [d] In $CHCl_3$.

Experimental

2 : 3-*Dihydrothionaphthen*-2 : 3-*yleneacetic Acid*.—Ethyl diazoacetate (25 g.) was added with stirring during 7 hr. to thionaphthen (65 g.) at 145—150°. Evolution of nitrogen began after 15 min. and continued throughout the addition. After a further hour's stirring and heating, the product was distilled, to yield a pale yellow oil (5·5 g.), b. p. 113—120°/0·04 mm., which was hydrolysed by 4 hours' refluxing with sodium hydroxide (2 g.) in 95% ethanol (30 c.c.). 2 : 3-*Dihydrothionaphthen*-2 : 3-*yleneacetic acid* crystallised from hexane in needles, m. p. 150° (Found: C, 62·6; H, 4·2; S, 16·6. $C_{10}H_8O_2S$ requires C, 62·5; H, 4·2; S, 16·7%). Its 4-*phenylphenacyl ester* formed needles (from ethanol), m. p. 129—130° (Found: C, 74·3; H, 4·6; S, 8·1. $C_{24}H_{18}O_3S$ requires C, 74·55; H, 4·7; S, 8·3%). The *amide*, prepared *via* the acid chloride, separated from water in needles, m. p. 225° (Found: S, 16·5. $C_{10}H_9ONS$ requires S, 16·8%).

The acid (1 g.) in dilute sodium carbonate was treated with potassium permanganate. After 18 hr. at room temperature, and 4 hr. on the steam-bath the excess of permanganate was

[11] Slabey, *J. Amer. Chem. Soc.*, 1954, **76**, 3604; Mohrbacher and Cromwell, *ibid.*, 1957, **79**, 401.
[12] Baker and Lord, *J. Chem. Phys.*, 1955, **23**, 1636.
[13] Brown, Henbest, and Jones, *J.*, 1952, 3172.
[14] See also Kefford and Kelso, *Austral. J. Biol. Sci.*, 1957, **10**, 80.
[15] Veldstra and Van de Westeringh, *Rec. Trav. chim.*, 1951, **70**, 1127.

removed and the solution acidified. 2 : 3-*Dihydrothionaphthen*-2 : 3-*yleneacetic acid* 1 : 1-*dioxide* separated from water in needles, m. p. 240—241° (Found: C, 53·5; H, 3·8; S, 14·3. $C_{10}H_8O_4S$ requires C, 53·6; H, 3·6; S, 14·3%). It showed infrared (Nujol mull, NaCl prism) bands at 1136 and 1312 cm.$^{-1}$ characteristic of sulphones.

A solution of the acid (2 g.) in 10% aqueous sodium carbonate (20 c.c.) was added to a stirred suspension of W-7 Raney nickel (15 g.) in water (250 c.c.). The mixture was heated for 1 hr. on the steam-bath, filtered, and acidified. The oily product was extracted with ether, and the ether dried ($CaSO_4$), and evaporated, to yield 2-*cyclo*hexyl*cyclo*propanecarboxylic acid. Its amide, prepared *via* the acid chloride, crystallised from water in needles, m. p. 151° unchanged by further purification; but a completely satisfactory analysis could not be obtained (Found: C, 71·3; H, 10·9; N, 8·3. Calc. for $C_{10}H_{17}ON$: C, 71·8; H, 10·3; N, 8·4%).

γ-cyclo*Hexylbutyric Acid.*—(i) *trans*-2-Phenyl*cyclo*propanecarboxylic acid was hydrogenated in ethanol at 60° over Adams catalyst, at atmospheric pressure. The resulting oil was converted *via* its acid chloride into γ-*cyclo*hexylbutyramide, which crystallised from water in needles, m. p. 109—110° alone or admixed with a specimen prepared by similar hydrogenation of γ-phenylbutyric acid.

(ii) Similar hydrogenation of *cis*-2-phenyl*cyclo*propanecarboxylic acid likewise gave γ-*cyclo*hexylbutyramide.

(iii) Catalytic hydrogenation of 2-*cyclo*hexyl*cyclo*propanecarboxylic acid in 50% ethanol over Adams catalyst was also effected at 60°, and yielded γ-*cyclo*hexylbutyramide. The infrared spectra of these amides were identical.

2 : 3-*Dihydrobenzofur*-2 : 3-*yleneacetic Acid.*—Ethyl diazoacetate (23 g.) was added with stirring during 3 hr. to benzofuran (50 g.) at 150°. After being stirred at this temperature for a further 4 hr. the mixture was distilled, to give a yellow oil (7·5 g.), b. p. 93—100°/0·04 mm. Hydrolysis with alcoholic sodium hydroxide gave 2 : 3-*dihydrobenzofur*-2 : 3-*yleneacetic acid*, which crystallised from dilute ethanol in plates, m. p. 181—181·5° (Found: C, 68·1; H, 4·65; O, 26·9. $C_{10}H_8O_3$ requires C, 68·2; H, 4·6; O, 27·2%). The *amide* formed needles (from water), m. p. 198—199° (Found: C, 68·2; H, 5·2. $C_{10}H_9O_2N$ requires C, 68·5; H, 5·2%).

3-*Indolylacetic Acid.*—Ethyl diazoacetate (25 g.) was added with stirring during 4 hr. to indole (60 g.) at 140° (no catalyst was added; cf. refs. 7 and 8) and the temperature maintained for a further hr. Distillation gave indole (26 g.; b. p. 134°/18 mm.), and a crude product (23 g., b. p. 142—144°/0·1 mm.) which was hydrolysed with alcoholic sodium hydroxide. The resulting 3-indolylacetic acid recrystallised from water and from benzene–light petroleum and had m. p. and mixed m. p. 164—165°.

1-*Methyl*-3-*indolylacetic Acid.*—(i) Ethyl diazoacetate (13·1 g.) was treated with 1-methylindole (15 g.) as above.[6] After a fore-run of 1-methylindole (3 g.; b. p. 46°/0·05 mm.) the crude product (12·3 g., b. p. 116°/0·05 mm.) was obtained. The acid obtained by hydrolysis recrystallised from water and from benzene–light petroleum as needles, m. p. 128° alone or mixed with a specimen prepared as described below. The picrate formed red needles, m. p. 171° (decomp.) (lit., m. p. 174°, 161°).

(ii) 3-Indolylacetic acid (1 g.) was added to a solution of sodium (0·29 g.) in liquid ammonia (20 c.c.). Methyl sulphate (2 c.c.) was added dropwise to the stirred solution during 15 min., and stirring continued for 1 hr.[16] After evaporation of the ammonia, methanol and then water were added. Removal of the methanol and acidification gave the crude acid, which recrystallised from benzene–light petroleum, to give 1-methyl-3-indolylacetic acid as needles, m. p. 128° (lit., m. p. 127—129°).

Reaction of Ethyl Diazoacetate with Naphthalene.—(i) Ethyl diazoacetate (23 g.) was added dropwise during 6 hr. to naphthalene (50 g.) at 140° (bath-temperature) (cf. ref. 2). The mixture was distilled, and after a fore-run of naphthalene the fraction of b. p. 112—180°/0·15 mm. was collected. Re-distillation gave the crude monoadduct, b. p. 94—120°/0·05 mm. (7·5 g.), and a residue (6 g.) which was chromatographed in light petroleum on alumina. Trituration of the resulting yellow oil with light petroleum gave a solid product which was re-chromatographed and repeatedly recrystallised from light petroleum. *Ethyl* 1 : 2-3 : 4-*tetrahydronaphth*-1 : 2-3 : 4-*di*(*yleneacetate*) was obtained as prisms, m. p. 89° (Found: C, 72·2; H, 6·7; O, 21·1. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7; O, 21·3%). When tested with osmium tetroxide in pyridine the monoadduct showed the presence of a reactive double bond, but the diacetate remained unchanged. Hydrolysis of this diester was effected with alcoholic potassium

[16] Cf. Plieninger, *Chem. Ber.*, 1954, **87**, 127.

hydroxide. Recrystallisation from aqueous ethanol gave 1 : 2-3 : 4-*tetrahydronaphth*-1 : 2-3 : 4-*di*(*yleneacetic acid*) (X) as needles, m. p. 286° (Found: C, 68·9; H, 5·1; O, 26·0. $C_{14}H_{12}O_4$ requires C, 68·8; H, 4·95; O, 26·2%).

(ii) The same diester was obtained on addition of ethyl diazoacetate (8 g.) to the mono-adduct (9 g.) at 145° during ½ hr. and further heating for 1½ hr.

Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory, Melbourne. One of us (B. J. C.) has been working with an I.C.I.A.N.Z. Fellowship. We also thank Dr. N. P. Kefford for the biological tests.

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