

## Reactions of Cyclohexadienes. Part XIV.<sup>1</sup> Addition Reactions of Dienamines and Electrophilic Olefins

By Arthur J. Birch and Ewen G. Hutchinson, Research School of Chemistry, Australian National University, P.O. Box 4, Canberra, ACT 2600, Australia

Treatment of acrylonitrile and of methyl acrylate with the mixture of dienamines [(2) and (3)] obtained by metal-ammonia reduction of *N-m*-tolylmorpholine gave products corresponding to the presence of different dienes. From this and other evidence it appears that equilibration of isomeric dienamines is brought about by dienophiles. Unlike acrylonitrile and methyl acrylate, which give principally or solely Diels-Alder adducts in several cases investigated, but-1-en-3-one gives a Michael-type adduct.

REACTIONS of mixed dienamines prepared from cyclic ketones [usually 3-alkyl-5,5-dimethylcyclohex-2-enones (1)] with electrophilic olefins have been reported.<sup>2,3</sup> Some dienamines derived from octalones have also been similarly examined.<sup>4</sup> The metal-ammonia reduction of aromatic amines<sup>5</sup> now permits the ready preparation of a variety of cyclohexa-1,3-dienylamines, and the reactions of several of them with electrophilic olefins have been described. The products can be formally of Diels-Alder<sup>2,6</sup> or Michael<sup>2,7</sup> types. Problems have been raised by the results of reactions of the mixed dienamines from isophorone (1; R = Me) because the ratios of addition products do not necessarily correspond to the ratios of the corresponding dienes in the

initial mixture.<sup>3</sup> Similar evidence in favour of ready equilibration of isomeric dienamines is now presented in the reaction of the mixture<sup>5</sup> of dienamines (2) and (3), which gives with acrylonitrile only the Diels-Alder adduct (4) in an amount which indicates conversion of isomer (3) into isomer (2) in the process. Only one stereoisomer of (4) was detected (sharp m.p.; <sup>1</sup>H n.m.r. spectrum); this may have the *endo*-configuration by analogy with other examples<sup>8</sup> (see later however for the acrylic ester case).

The reaction of the mixed dienamines (2) and (3) with 2-acetoxyacrylonitrile gave the adduct (5) as a mixture of two epimers (<sup>1</sup>H n.m.r. spectrum), the more abundant being assigned<sup>9</sup> the *endo*-6-acetoxy-*exo*-6-cyano-structure, since the OAc and olefinic proton

<sup>1</sup> Part XIII, A. J. Birch and K. P. Dastur, *J.C.S. Perkin I*, 1973, 1650.

<sup>2</sup> H. Nozaki, T. Yamaguti, S. Ueda, and K. Kondo, *Tetrahedron*, 1968, **24**, 1445.

<sup>3</sup> N. F. Firrell and P. W. Hickmott, *J. Chem. Soc. (B)*, 1969, 243.

<sup>4</sup> N. F. Firrell and P. W. Hickmott, *J. Chem. Soc. (C)*, 1968, 2320.

<sup>5</sup> A. J. Birch, E. G. Hutchinson, and G. Subba Rao, *J. Chem. Soc. (C)*, 1971, 637.

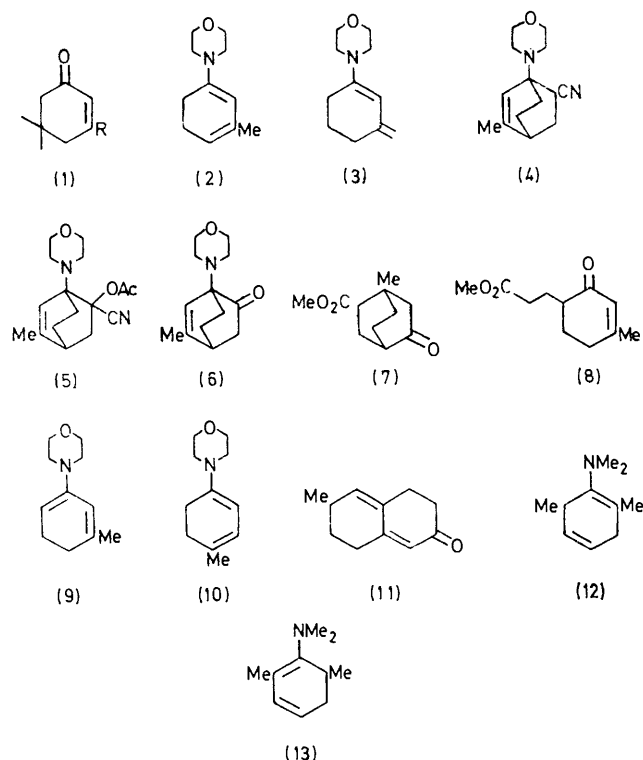
<sup>6</sup> J. O. Madsen and S. O. Lawesson, *Tetrahedron*, 1968, **24**, 3369.

<sup>7</sup> D. Bertin and J. Perronnet, *Bull. Soc. chim. France*, 1968, 1422.

<sup>8</sup> Y. Kobuke, T. Fueno, and J. Furukawa, *J. Amer. Chem. Soc.*, 1970, **92**, 6548.

<sup>9</sup> M. A. Qusseem, N. A. J. Rogers, and A. A. Othman, *Tetrahedron*, 1968, **24**, 4535.

signals are upfield of those for the other isomer, as expected because of shielding by carbonyl and carbon-carbon double bonds. Hydrolysis of the product mixture with base<sup>10</sup> to give the ketone (6) effectively



represents, for synthetic purposes, an addition of a keten residue to the dienamine (2).

The reaction of the mixture of compounds (2) and (3) with methyl acrylate took a different course, possibly because of the much lower reactivity, as shown by the longer reaction time required. We could not separate the initial mixed adduct, which was therefore submitted to alkaline hydrolysis. Two keto-acids which resulted were separated by preparative g.l.c. as the methyl esters, which were assigned the structures (7) and (8) on the bases of analyses and spectra. Structure (7) was supported by the nature of the bridgehead Me and H resonances at  $\delta$  0.99 and 2.62. Structure (8) was supported by evidence for the  $\alpha\beta$ -unsaturated ketone and ester groups and signals at  $\delta$  1.93 (Me) and 5.82 (=CH). These products are both derivable only from the dienamine (9), so far undetected in the mixture of dienamines, and may result from further equilibration through migrations due to charge-transfer complexes with the dienophile, such as appear to happen with methoxycyclohexadienes.<sup>11</sup> The ester (8) could result

from a Michael-type addition and (7) could be formed from a Diels-Alder reaction; there is no evidence that the skeletons are interconvertible under the alkaline hydrolysis conditions.

Reaction of the dienamine (10) with methyl acrylate proceeded normally, giving a mixture of the *endo*- and *exo*-adducts, identified on the basis of the agreement of the <sup>1</sup>H n.m.r. spectrum and analyses of the product with the expected gross structure, and the presence of two AB sets of resonances at  $\delta$  5.98 and 6.34, and 6.03 and 6.14. Several reported<sup>12</sup> spectra of bicyclo[2.2.2]-octenes indicate that the components of the AB system are closer for *exo*- than for the *endo*-isomers; on this basis the major component has the *exo*-configuration. This result contrasts with the reaction of the same diene with acrylonitrile, which gave an 80% yield of one crystalline isomer.

The reaction of but-1-en-3-one with 1-dimethylamino-4-methylcyclohexa-1,3-diene,<sup>5</sup> followed by treatment with acid, yielded the bicyclic ketone (11), the structure of which was supported by spectra, which were similar to those of the corresponding 5-methyl derivative.<sup>13</sup> This result is in accord with the reported Michael-type reaction of  $\alpha\beta$ -unsaturated ketones with enamines,<sup>14</sup> with subsequent cyclisation on hydrolysis. With 6-methylhept-2-en-4-one, a 2-substituted cyclohexenone resulted, identical with that obtained from the same ketone and 4-methyl-1-tetrahydropyran-2-yloxy-cyclohexa-1,4-diene.<sup>15</sup>

The non-conjugated dienamine (12)<sup>5</sup> on reaction with methyl acrylate gave the conjugated dienamine (13) and a mixture of adducts of the latter.

The results show that, although adducts are obtained corresponding to the starting, or expected, conjugated dienes in the 4-methyl and 2,6-dimethyl series, this is not so with the 3-methyl series, and caution must be exercised in deducing structures of products.

#### EXPERIMENTAL

*Reaction of N-(3-Methylcyclohexa-1,3-dienyl)morpholine (2) and N-(3-Methylenecyclohex-1-enyl)morpholine (3) with Acrylonitrile.*—A solution of the mixed dienamines<sup>5</sup> (5.0 g, 28 mmol) and acrylonitrile (1.5 g, 28 mmol) in dioxan (25 ml) was heated at reflux under nitrogen for 7 h. Solvent was removed under reduced pressure, aqueous methanol (100 ml) was added, and the mixture was heated for 1 h. The product was isolated by extraction with ether as an oil (5.3 g). Crystallisation from ether-light petroleum gave *endo*-6-cyano-3-methyl-1-morpholinobicyclo[2.2.2]oct-2-ene (4) (75% based on total dienamine), m.p. 124–125°,  $\nu_{\max}$  (CHCl<sub>3</sub>) 2250, 1670, and 1125 cm<sup>-1</sup>,  $\delta$  1.4–2.1 (m, 3 × CH<sub>2</sub>), 1.80 (d, *J* 2 Hz, =CMe), 2.35 (m, C=C·CH), 2.75 (5H, m, CH<sub>2</sub>·N·CH<sub>2</sub>, CH·CN), 3.73 (m, CH<sub>2</sub>·O·CH<sub>2</sub>), and 5.82 (s, =CH), *m/e* 232 (*M*<sup>+</sup>) (Found: C, 72.4; H, 8.5;

<sup>10</sup> P. D. Bartlett and B. E. Tate, *J. Amer. Chem. Soc.*, 1956, **78**, 2473.

<sup>11</sup> N. A. J. Rogers, Lancaster University, personal communication, 1969.

<sup>12</sup> R. J. Ouellette and G. E. Booth, *J. Org. Chem.*, 1965, **30**, 423.

<sup>13</sup> S. A. Julia and M. Julia, *Compt. rend.*, 1953, **237**, 1714.

<sup>14</sup> G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Amer. Chem. Soc.*, 1963, **85**, 207; I. Fleming and M. H. Karger, *J. Chem. Soc. (C)*, 1967, 26.

<sup>15</sup> A. J. Birch, J. Diekman, and P. L. Macdonald, *Chem. Comm.*, 1970, 52.

N, 11.8.  $C_{14}H_{20}N_2O$  requires C, 72.4; H, 8.7; N, 12.1%. The  $^1H$  n.m.r. spectrum of the crude material showed no splitting of Me or =CH resonances attributable to the presence of the other [*exo*- (?)] isomer.

A solution of the adduct (4) (500 mg) in ethanol was hydrogenated over Adams catalyst (40 mg) until uptake ceased. Crystallisation of the product from ether-light petroleum gave 6-cyano-3 $\xi$ -methyl-1-morpholinobicyclo[2.2.2]octane, m.p. 84–85°,  $\nu_{max}$  (CHCl<sub>3</sub>) 2245  $cm^{-1}$ ,  $\delta$  1.00 (d, *J* 6 Hz, CHMe), 1.2–2.2 (10H, m, CH<sub>2</sub> and CHR), 2.56 (m, CH<sub>2</sub>·N·CH<sub>2</sub>), 2.90 (m, bridgehead H), and 3.68 (m, CH<sub>2</sub>·O·CH<sub>2</sub>), *m/e* 234 (*M*<sup>+</sup>) (Found: C, 71.7; H, 9.3.  $C_{14}H_{22}N_2O$  requires C, 71.8; H, 9.5%).

**Reaction of the Dienamines (2) and (3) with Methyl Acrylate.**—The dienamines (3.0 g, 16.7 mmol) and methyl acrylate (1.5 g, 17.5 mmol) in dioxan (30 ml) were heated at reflux under nitrogen for 65 h. Solvent was removed under reduced pressure to give an oil which could not be separated by g.l.c. or t.l.c.;  $\nu_{max}$  1725  $cm^{-1}$ ,  $\delta$  0.99 (s, bridgehead Me), 1.78 and 1.85 (2d, *J* 2 Hz, =CMe), 2.68 (m, CH<sub>2</sub>·N·CH<sub>2</sub>), 3.64 (m, CO<sub>2</sub>Me and CH<sub>2</sub>·O·CH<sub>2</sub>), and 5.71br and 5.94br (2s, =CH). The product was heated with aqueous 10% potassium hydroxide, and gave a dark oil after extraction with ethyl acetate at pH 3;  $\nu_{max}$  1720, 1665, and 1640  $cm^{-1}$ . Methylation of the acid with ethereal diazomethane gave two compounds, separable by preparative g.l.c., in a 3 : 1 ratio: methyl 1-methyl-5-oxobicyclo[2.2.2]octan-2-carboxylate (7),  $\nu_{max}$  1735 and 1725  $cm^{-1}$ ,  $\delta$  0.99 (s, bridgehead Me), 1.4–2.2 (m, 4 × CH<sub>2</sub>), 2.33 (t, *J* 3 Hz, CH<sub>2</sub>·CHR), 2.62 (m, bridgehead H), and 3.68 (s, CO<sub>2</sub>Me), *m/e* 196 (*M*<sup>+</sup>) (Found: *m/e* 196.1095.  $C_{11}H_{16}O_3$  requires *M*, 196.1099) [2,4-dinitrophenylhydrazone, m.p. 154–155°,  $\lambda_{max}$  367 nm ( $\epsilon$  24,800) (Found: N, 14.6.  $C_{17}H_{20}N_4O_6$  requires N, 14.9%)]; and methyl 3-(4-methyl-2-oxocyclohex-3-enyl)propionate (8),  $\nu_{max}$  1730 and 1665  $cm^{-1}$ ,  $\lambda_{max}$  233 nm ( $\epsilon$  12,100),  $\delta$  1.93 (s, =CMe), 1.6–2.5 (9H, m, CH<sub>2</sub> and CHR), 3.66 (s, CO<sub>2</sub>Me), and 5.82br (s, =CH), *m/e* 196 (*M*<sup>+</sup>) [2,4-dinitrophenylhydrazone, m.p. 130–131°,  $\lambda_{max}$  382 nm ( $\epsilon$  26,500) (Found: C, 54.3; H, 5.2; N, 14.8.  $C_{17}H_{20}N_4O_6$  requires C, 54.3; H, 5.4; N, 14.9%)].

**Reaction of the Dienamines (2) and (3) with 2-Acetoxyacrylonitrile.**—The dienamines (3.0 g, 17 mmol) and 2-acetoxyacrylonitrile (1.9 g, 17 mmol) (kindly presented by Dr. J. E. T. Corrie) in dioxan (30 ml) were heated at reflux for 65 h under nitrogen. The solvent was removed to yield a crystalline solid, which on column chromatography gave a mixture of both stereoisomeric forms of 6-acetoxy-6-cyano-3-methyl-1-morpholinobicyclo[2.2.2]oct-2-ene (5) (90%), m.p. 120–150°,  $\nu_{max}$  (CHCl<sub>3</sub>) 2245, 1745, and 1660  $cm^{-1}$ ,  $\delta$  (first isomer) 1.2–2.6 (m, 3 × CH<sub>2</sub>), 1.83 (d, *J* 2 Hz, =CMe), 2.04 (s, OAc), 2.34 (m, bridgehead H), 3.07 (m, CH<sub>2</sub>·N·CH<sub>2</sub>), 3.68 (m, CH<sub>2</sub>·O·CH<sub>2</sub>), and 5.79br (s, =CH),  $\delta$  (second isomer) 1.2–2.6 (m, 3 × CH<sub>2</sub>), 1.86 (d, *J* 2 Hz, =CMe), 2.14 (s, OAc), 2.36br (s, bridgehead H), 3.07 (m, CH<sub>2</sub>·N·CH<sub>2</sub>), 3.68 (m, CH<sub>2</sub>·O·CH<sub>2</sub>), and 5.83br (s, =CH), *m/e* 290 (*M*<sup>+</sup>) (Found: C, 66.0; H, 7.5; N, 9.5.  $C_{16}H_{22}N_2O_3$  requires C, 66.2; H, 7.6; N, 9.5%).

**Basic Hydrolysis of the Mixed Acetoxy-nitriles (5).**—The mixed acetoxy-nitriles (3.8 g) dissolved in aqueous methanolic sodium hydroxide (2.8 g) were kept at 20° under nitrogen for 20 h, then poured into water. Extraction with ether gave 5-methyl-1-morpholinobicyclo[2.2.2]oct-5-en-2-one, m.p. 62–64°,  $\nu_{max}$  1718  $cm^{-1}$ ,  $\lambda_{max}$  292 nm ( $\epsilon$  235),  $\delta$  1.6–1.9 (m, 2 × CH<sub>2</sub>), 1.87 (d, *J* 2 Hz, =CMe),

2.08 (d, *J* 3 Hz, CH<sub>2</sub>·CO), 2.63 (m, bridgehead H), 2.84 (m, CH<sub>2</sub>·N·CH<sub>2</sub>), 3.76 (m, CH<sub>2</sub>·O·CH<sub>2</sub>), and 5.78 (d, *J* 2 Hz, =CH) (Found: *m/e* 221.1418.  $C_{13}H_{19}NO_2$  requires *M*, 221.1416).

**Reaction of N-(4-Methylcyclohexa-1,3-dienyl)morpholine (10) with Acrylonitrile.**—A solution of the dienamine<sup>6</sup> (5.0 g, 28 mmol) and acrylonitrile (1.60 g, 28 mmol) in dioxan (25 ml) was heated at reflux under nitrogen for 7 h. The solvent was removed, and the product was heated with 1 : 1 water-methanol for 8 h. Extraction with ether gave a semicrystalline solid. Crystallisation from ether-light petroleum gave endo(?) 6-cyano-4-methyl-1-morpholinobicyclo[2.2.2]oct-2-ene (80%), m.p. 96–97°,  $\nu_{max}$  (CHCl<sub>3</sub>) 2250, 1614, and 1140  $cm^{-1}$ ,  $\delta$  1.18 (s, bridgehead Me), 1.4–2.2 (m, 3 × CH<sub>2</sub>), 2.78 (5H, m, CH<sub>2</sub>·N·CH<sub>2</sub> and CH·CN), 3.76 (m, CH<sub>2</sub>·O·CH<sub>2</sub>), and 6.05 and 6.24 (2d, *J* 9.3 Hz, 2 × =CH), *m/e* 232 (*M*<sup>+</sup>) (Found: C, 72.2; H, 9.1; N, 12.2.  $C_{14}H_{20}N_2O$  requires C, 72.4; H, 8.7; N, 12.1%).

**Reaction of the Dienamine (10) with Methyl Acrylate.**—A solution of the dienamine<sup>6</sup> (2.0 g, 11 mmol) and methyl acrylate (1.0 g, 11 mmol) in dioxan (20 ml) was heated at reflux under nitrogen for 65 h. The solvent was removed, to give as an uncrystallisable oil the endo- and exo-isomers of methyl 4-methyl-1-morpholinobicyclo[2.2.2]oct-5-ene-2-carboxylate (90%),  $\nu_{max}$  1740, 1650, and 1250  $cm^{-1}$ ,  $\delta$  1.16 (s, bridgehead Me), 1.2–1.8 (m, 3 × CH<sub>2</sub>), 2.72 (m, CH<sub>2</sub>·N·CH<sub>2</sub>), 3.06 (1H, 2d, *J* 5.5 Hz, CH<sub>2</sub>·CH·CO<sub>2</sub>Me), 3.65 (m, CH<sub>2</sub>·O·CH<sub>2</sub>), 3.61 (s, CO<sub>2</sub>Me), 6.03 and 6.14 (1.3H, 2d, *J* 9 Hz, exo-? =CH), and 5.98 and 6.34 (0.7H, 2d, *J* 9 Hz, endo-? =CH) (Found: C, 67.8; H, 8.5; N, 4.9.  $C_{15}H_{22}NO_3$  requires C, 67.9; H, 8.7; N, 5.3%).

**Reaction of 1-Dimethylamino-4-methylcyclohexa-1,3-diene with But-1-en-3-one.**—A solution of the dienamine (2.0 g, 14 mmol) and but-1-en-3-one (1.12 g, 13 mmol) in dry benzene (5 ml) was heated at reflux under nitrogen for 3 h. Acetate buffer [from sodium acetate (1.0 g), acetic acid (1.5 ml), and water (1.5 ml)] was added, and the mixture was heated for 3 h. Extraction with ether gave an oil (3.0 g),  $\nu_{max}$  1710 and 1655  $cm^{-1}$ . Treatment of the oil with 5*N*-hydrochloric acid for 4 h gave 4,6,7,8-tetrahydro-6-methylnaphthalen-2(3H)-one, b.p. 101–103° at 0.5 mmHg,  $\nu_{max}$  1655, 1625, and 1586  $cm^{-1}$ ,  $\lambda_{max}$  287 nm ( $\epsilon$  11,300),  $\delta$  1.09 (d, *J* 7 Hz, CHMe), 1.5–2.6 (9H, m, CH<sub>2</sub> and CHMe), 5.26 (m, =CH·CO), and 5.88 (m, CHMe·CH=) (Found: *m/e* 162.1045.  $C_{11}H_{14}O$  requires *M*, 162.1047) [2,4-dinitrophenylhydrazone, m.p. 182–183°,  $\lambda_{max}$  397 nm ( $\epsilon$  32,200), *m/e* 342 (*M*<sup>+</sup>) (Found: C, 59.6; H, 5.6; N, 16.2.  $C_{17}H_{18}N_4O_4$  requires C, 59.5; H, 5.3; N, 16.4%)].

**Reaction of 1-Dimethylamino-4-methylcyclohexa-1,3-diene with 6-Methylhept-2-en-4-one.**—A solution of the dienamine (2.4 g, 18 mmol) and 6-methylhept-2-en-4-one (3.0 g, 24 mmol) in dioxan (10 ml) was heated at reflux under nitrogen for 24 h. Acetate buffer [from sodium acetate (1.5 g) as before] was added and the mixture was heated for 1 h. Extraction with ether gave an oil (6.0 g), which, apart from a small portion of unchanged ketone, was 6-methyl-2-(3-methyl-6-oxocyclohex-2-enyl)heptan-4-one,  $\nu_{max}$  1710  $cm^{-1}$ ,  $\lambda_{max}$  225 and 282 nm ( $\epsilon$  1200 and 212),  $\delta$  0.90–0.95 (9H, 3d, *J* 7 Hz, CHMe), 1.78 (s, =CMe), 1.8–2.6 (11H, m, CH<sub>2</sub> and CHR), and 5.36br (s, =CH), *m/e* 236 (*M*<sup>+</sup>), identical with an authentic specimen kindly presented by Dr. J. Diekman.

**Reaction of 1,3-Dimethyl-2-dimethylaminocyclohexa-1,4-diene (12) with Methyl Acrylate.**—Reaction of the dienamine (4.0 g, 26 mmol) with methyl acrylate (2.25 g, 26

mmol) in dioxan (20 ml) as before for 16 h gave, after preparative g.l.c., the conjugated dienamine (45%), identical with an authentic specimen, and endo- and exo-methyl 6,7-dimethyl-1-dimethylaminobicyclo[2.2.2]oct-5-ene-2-carboxylate (55%),  $\nu_{\max}$  1730 and 1165  $\text{cm}^{-1}$ ,  $\delta$  0.71 (d,  $J$  6.5 Hz, CHMe), 1.55—1.70 (2t,  $J$  1.5 Hz,  $\text{CH}_2$ ), 1.6—1.9 (3H, m,  $\text{CH}_2$  and CHR), 1.89 (2H, d,  $J$  1 Hz, endo- =CMe),

1.97 (1H, d,  $J$  1 Hz, exo- =CMe), 2.1 (m, CHMe), 2.40 (4H, s, endo-NMe<sub>2</sub>), 2.42 (2H, s, exo-NMe<sub>2</sub>), 3.58 (1H, s, exo-CO<sub>2</sub>Me), 3.66 (2H, s, endo-CO<sub>2</sub>Me), and 5.98 (1H, m, =CH),  $m/e$  237 ( $M^+$ ) (Found: C, 71.1; H, 10.1; N, 6.1. C<sub>14</sub>H<sub>23</sub>NO<sub>2</sub> requires C, 70.9; H, 9.8; N, 5.9%).

[3/632 Received, 26th March, 1973]

---