# Constitution of Hofmann's Dimethylconiine and Conylene

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Hofmann's 'dimethylconiine' is confirmed as a mixture of 5-N,N-dimethylamino-oct-1-ene (2), (E)-1-N,N-dimethylamino-oct-4-ene (3), and (E)-1-N,N-dimethylamino-oct-5-ene (4). 'Conylene' is a mixture of (2E,4E)-and (2Z,4E)-octa-2,4-dienes (11) and (12) respectively, (E)-octa-1,4-diene (13), and, probably, (E)-octa-1,5-diene (14).

In his classical work [1] on the exhaustive methylation of coniine (1), previously carried out by Wertheim,[2] Hofmann obtained successively 'dimethylconiine' (unsaturated amines) and 'conylene' (octadienes). The identity of the former was established by Hasiak [3] as a mixture of 5-N,N-dimethylamino-oct-1-ene (2), (E)-1-N,N-dimethylamino-oct-4-ene (3), (E)-1-N,N-dimethylamino-oct-5-ene (4), and its (Z)-isomer (5). We have repeated this work using (±)-coniine and generally confirm Hasiak's results but have found little evidence for the presence of (5) in the mixture of products obtained from the thermal decomposition of(±)-N-methylconiine methohydroxide (6; X = OH).

Column chromatography gave pure (±)-5-N,N-dimethylamino-oct-1-ene (2) but failed to separate (3) from (4). The i.r. spectrum of the mixture of (3) and (4) showed the presence of trans-olefins (cf. ref. 3). The 360 MHz ¹H n.m.r. spectrum (see Experimental section) of the methoiodides derived from the mixture of (3) and (4) confirmed the trans-configurations of their double bonds, and indicated that (E)-1-N,N-dimethylamino-oct-4-ene (3) comprised at least 80% of the mixture. A very small extra triplet signal, J 6 Hz, in the δ 0.9—1.0 region could tentatively be assigned to the C=C–CH₂Me group of the methoiodide of (5).
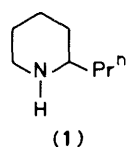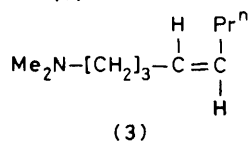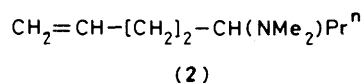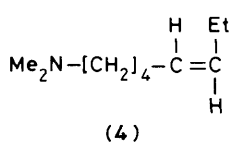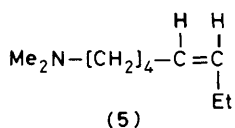
The formation of succinic acid can be attributed to the intermediacy of the hydroxyamine (7).[4]

The formation of (E)-1-N,N-dimethylamino-oct-4-ene (3) from the quaternary base (6; X = OH) is predictable from the antiperiplanar arrangement of the C-3 equatorial hydrogen atom and the C-2–N bond in the base (cf. ref. 3). The formation of (E)-1-N,N-dimethylamino-oct-5-ene (4) is preferred to its (Z)-isomer because of greater freedom from vicinal interaction of alkyl groups in conformer (8) than in conformer (9) of the quaternary base. The former is the precursor of the trans- and the latter of the cis-olefin.

(8)   (9)

$$CH_2=CH-[CH_2]_2-CH(\overset{+}{N}Me_3)Pr^n \; X^-$$

(10)
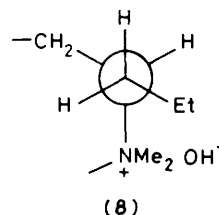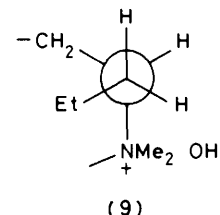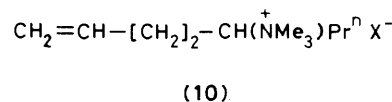
Thermal decomposition of (±)-N,N,N-trimethyl-N-oct-1-en-5-ylammonium hydroxide (10; X = OH), the methohydroxide of (2), gave a mixture of (2E,4E)-octa-2,4-diene (11), (2Z,4E)-octa-2,4-diene (12), (E)-octa-1,4-diene (13), and probably (E)-octa-1,5-diene (14). This mixture is Hofmann's 'conylene'. These compounds were separated on a silica column impregnated with silver nitrate, but (14) was not obtained in a pure state. Although relative yields varied a little with changes in experimental conditions, the diene (12) was always predominant. Surprisingly these hydrocarbons do not appear to have been previously isolated in a pure form.

(2E,4E)-Octa-2,4-diene (11) absorbed at 228 nm (log ε 4.5) and strongly at 986 cm⁻¹ (trans-CH=CH). Its isomer (12) absorbed at 231 nm (log ε 4.4), but its absorption at 980 cm⁻¹ was weak and a band at 712 cm⁻¹ indicated the presence of a cis-CH=CH group.

The reaction of the diene (11) with maleic anhydride afforded (±)-(3aS,4S,7R,7aR)-4-methyl-7-n-propyl-3a,4,7,7a-tetrahydrobenzo[c]furan-1,3-dione (15) whereas its isomer (12) was polymerised [5] under similar circumstances.

(E)-Octa-1,4-diene (13) showed only end group absorption in the u.v., but bands at 990 and 914 cm⁻¹ (CH₂=CH) and at 976 cm⁻¹ indicate its structure. Its diallylic methylene group was clearly shown as a multiplet at δ 2.75 in its ¹H n.m.r. spectrum.
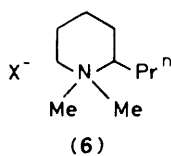

(1)

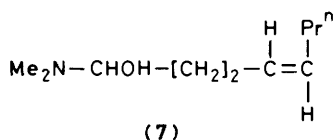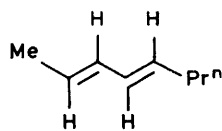$$CH_2=CH-[CH_2]_2-CH(NMe_2)Pr^n$$

(2)

(3)

(4)

(5)

(6)

(7)

Permanganate–periodate oxidation of the mixture of (3) and (4) gave butanoic and propanoic acids, the former predominating. Ozonolysis of the mixture followed by peroxide work-up gave a similar mixture of acids, and succinic acid but not glutaric acid; reductive work-up gave butanal and propanal.

(11)
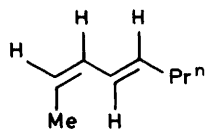
(12)
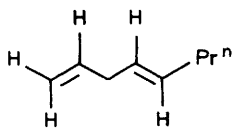
(13)

(14)

(15)

The assignment of the structure of the impure diene as (14) is based (a) on its g.l.c. retention time and (b) on its i.r. spectrum. It has been shown[6,7] that on silver nitrate in ethylene glycol impregnated columns, conjugated dienes have lower complex-forming capacity than their unconjugated isomers. In accordance with this, the conjugated dienes (11) and (12) were eluted well before (13) and (14). Moreover, (Z,E)-dienes have greater retention time than their (E,E)-isomers; we found that (2E,4E)-octa-2,4-diene (11) was eluted before (2Z,4E)-octa-2,4-diene (12). The impure diene cannot be the (Z)-isomer of (E)-octa-1,4-diene (13) since it is eluted before (13). Moreover it cannot be (Z)-octa-1,5-diene since it shows no cis-olefinic a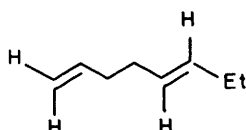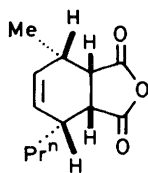bsorption in the i.r. region and also the stereochemical restriction which inhibits the formation of the (Z)-isomer of (4) operates here. It is therefore reasonable to suggest that the impure diene is (E)-octa-1,5-diene (14).

Thermal decomposition of the mixture of quaternary bases derived from amines (3) and (4) gave the dienes (11), (12), and (13), the first of these being the largest component of the mixture. This is in contrast to the result of the decomposition of the quaternary base (10; X = OH) where the octadiene (12) was the predominant product. We did not encounter any significant amount of (E)-octa-1,5-diene (14); [1]H n.m.r. measurements on the methoiodides derived from (3) and (4) indicated that (3) represented at least 80% of the mixture. It is possible that isomerisation of the 5-ene bond takes place during the course of the reaction. It is known[8] for example that hepta-1,5-diene affords hepta-2,4-diene with slight preference for the (E,E)-form on base catalysed isomerisation. The 360 MHz [1]H n.m.r. spectrum of the mixture of octadienes confirmed their structures. Spin decoupling experiments enabled an assignment of the olefinic signals (see Experimental section). In particular irradiations of the methyl doublet region at δ 1.72 led to the collapse of two multiplets at δ 5.37 and 5.55 each to two doublets, J 10.6 Hz and J 16.5 Hz respectively corresponding to the MeCH=C protons of (12) and (11) respectively. Irradiation of the diallylic methylene (C=CH-CH₂-CH=C) of (13) at δ 2.75 led

to the collapse of the multiplet at δ 5.83 to a double doublet, J 16.5 and 10.5 Hz of the 2 H proton ($CH_2=CH$) of (13).

Experimental
Ether refers to diethyl ether throughout.

(±)-Coniine (1).—2-n-Propylpyridine. A stirred solution of phenyl-lithium [bromobenzene (158 g), lithium (14 g)] in ether (1 l) was slowly treated with 2-methylpyridine (93 g). After 1 h, ethyl iodide (156 g) in ether (80 ml) was added over 2 h to the stirred, ice-cold solution. After a further 0.5 h, more ethyl iodide (31 g) was added and the mixture was warmed over 1 h to 15 °C. Water (200 ml) was added, the ether layer was separated, and the aqueous layer was extracted with ether (3 × 50 ml). The dried, combined extracts were fractionated on an adiabatic spinning band column giving 2-n-propylpyridine (72 g), b.p. 167—168 °C;[9] $v_{max.}$ (liq. film) 1 600, 1 580, and 780 cm⁻¹; δ($CDCl_3$) 0.92 (t, J 7 Hz, Me), 1.77 (m, CH_2Me), 2.72 (t, J 7 Hz, ArCH_2), 7.7—6.8 (3 H, m, 3-, 4-, 5-H), and 8.45 (m, 6-H).

2-n-Propylpyridine (72 g) in hydrochloric acid (75 ml) and water (250 ml) was hydrogenated over Adams's catalyst (1.55 g) at 1 atm hydrogen. After removal of the catalyst, the ice-cold solution was covered with ether (200 ml) stirred, and basified. The ether layer was separated and the aqueous solution, saturated with salt, was extracted several times with ether. The combined extract was fractionated giving (±)-coniine (66 g), b.p. 55 °C at 15 mmHg (cf. ref. 10); $v_{max.}$ (liq. film) 3 200 and 2 760 cm⁻¹ (NH); δ($CHCl_3$) 0.9 (t, J 7 Hz, Me), 1.52 (1 H removed by D_2O, NH), 1.1—2.0 (10 H, m, CH_2), 2.5 (2 H, m, 6-H), and 3.0 (1 H, m, 2-H).

(±)-N-Methylconiine Methoiodide (6; X = I).—A stirred solution of (±)-coniine (66 g) in ethanol (350 ml) containing anhydrous potassium carbonate (145 g) was treated over 4 h with methyl iodide (182 g) and stirring was continued for 24 h. After cooling, the solid was collected, washed several times with a mixture of ethanol and ethyl acetate (1 : 5 v/v), the combined filtrate and washings were evaporated to dryness, and the residue was crystallised from ethyl acetate containing a little ethanol. N-Methylconiine methoiodide (119 g) had m.p. 158—159 °C;* δ(D_2O) 2.93 (s, MeN), 3.14 (s, MeN), and 3.44 (3 H, m, 2-, 6-H) (Found: C, 42.4; H, 7.55; N, 5.2. Calc. for $C_{10}H_{22}IN$: C, 42.4; H, 7.8; N, 4.9%).

Thermal Decomposition of N-Methylconiine Methohydroxide (6; X = OH).—The corresponding methoiodide (6; X = I) (119 g) in water (280 ml) was stirred with freshly prepared silver oxide (69 g) until the aqueous solution was free from iodide. The solution of the base was evaporated to a syrup below 40 °C at 15 mmHg and then heated at 75—80 °C (bath temp.) giving an oil (59.6 g) b.p. 74—78 °C at 20 mmHg. This was fractionated on a spinning band column giving 5-N,N-dimethylamino-oct-1-ene (2) (17.6 g) and an unresolved mixture (33 g) of (E)-1-N,N-dimethylamino-oct-4-ene (3) and (E)-1-N,N-dimethylamino-oct-5-ene (4). 5-N,N-Dimethylamino-oct-1-ene (2) was eluted [hexane–ether (90:10)] from Woelm Brand, grade III, basic alumina (350 g) and distilled at 66—67 °C at 20 mmHg; $v_{max.}$ (liq. film) 2 820, 2 760 (MeN), 1 640, 1 002, and 917 cm⁻¹; δ($CDCl_3$) 0.89 (t, J 6 Hz, Me), 2.08 (m, CH_2-C=C), 2.2 (s, Me_2N), and 6.25—4.8 (3 H, m, CH_2=CH) (cf. ref. 3) (Found: C, 77.1; H, 13.3; N, 8.9. Calc. for $C_{10}H_{21}N$: C, 77.4; H, 13.6; N, 9.0%). The unresolved mixture of unsaturated amines (3) and (4) had b.p. 77 °C at 20 mmHg; $v_{max.}$ (liq. film) 2 821, 2 760, 1 675, 967, and 936 cm⁻¹; δ($CHCl_3$) 0.88 [t, J 7 Hz, Me (3)], 0.96 [t, J 7 Hz, Me (4)], 2.22 (s, Me_2N), 2.26 (t, J 7 Hz, CH_2CH_2N), and 5.42 (m, CH=CH).

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* Mugdan[11] describes an inactive quaternary iodide, m.p. 152 °C, prepared from N-methylconiine and methyl iodide.

Oxidation of the Mixture of Amines (3) *and* (4).—(*a*) *With permanganate–periodate.* A mixture of the amines (88 mg), potassium permanganate (13 mg), potassium periodate (0.6 g), methanol (30 ml), and water (225 ml) was adjusted to pH 8 with potassium carbonate and then stirred for 18 h. Usual work-up, extraction of the acidic products with ether, and esterification with diazomethane gave (g.l.c. on a 100 m squalane column) methyl propanoate and methyl butanoate.

(*b*) *With ozone.* A solution of the amines (1.01 g) in methyl acetate (10 ml) was ozonised at −20 °C. Solvent was removed under reduced pressure, and hydrogen peroxide (10 ml; 30%) and sodium hydroxide (10 ml; 25%) were carefully added to the residue. After 1.5 h the mixture was acidified and extracted with ether giving an oil from which succinic acid (0.14 g), m.p. and mixed m.p. 180 °C, separated with time. The mother liquor was treated with boron trifluoride in methanol (25 ml; 14%), neutralised with sodium hydrogen carbonate, and extracted with ether. G.l.c. of the extract on a SCOT-DEGS column revealed the presence of methyl propanoate (25%) and methyl butanoate (75%). In another experiment, the ozonide was reduced in methanol over palladised charcoal and the products converted into their 2,4-dinitrophenylhydrazones. Chromatography (t.l.c.) on silica with hexane–benzene (7:3 v/v) (*cf.* ref. 12) gave the 2,4-dinitrophenylhydrazones of propanal and butanal.

Thermal Decomposition of (±)-N,N,N-*Trimethyl*-N-*oct*-1-*en*-5-*ylammonium Hydroxide* (10; X = OH).—(±)-5-*N,N*-Dimethylamino-oct-1-ene (2) treated in methanol with methyl iodide gave (±)-N,N,N-*trimethyl*-N-*oct*-1-*en*-5-*ylammonium iodide* (10; X = I) as plates (ethyl acetate–ethanol), m.p. 218—219 °C; $v_{max.}$(Nujol) 1 640, 1 005, and 915 cm⁻¹; δ(D₂O) 1.05 (t, J 6 Hz, *Me*CH₂), 3.08 (s, Me₃N), and 4.34—6.33 (m, C*H₂*=C*H*) (Found: C, 44.0; H, 8.2; N, 4.95. C₁₁H₂₄IN requires C, 44.4; H, 8.1; N, 4.7%). Thermal decomposition, at 140—150 °C (bath temp.), of the quaternary base (10; X = OH), from quaternary iodide (2.5 g), gave hydrocarbons (0.72 g) and the recovered amine (2) (0.24 g). G.l.c. of the hydrocarbons on a silver nitrate–ethylene glycol column revealed the presence * of (2*E*,4*E*)-octa-2,4-diene (11) (13.5%), (2*Z*,4*E*)-octa-2,4-diene (12) (55%), probably (*E*)-octa-1,5-diene (14) (21.5%), and (*E*)-octa-1,4-diene (13) (10%) in this order of elution from the column. These compounds were separated on a silver nitrate (20%)–silica column with hexane as eluant, but (14) was not obtained in a pure state.

(2E,4E)-*Octa*-2,4-*diene* (11) was an oil, $\lambda_{max.}$(EtOH) 228 nm (log ε 4.5); $v_{max.}$(liq. film) 986 cm⁻¹ (*trans* CH=CH); δ(CHCl₃) 0.89 (t, J 6.1 Hz, *Me*CH₂), 1.34 (m, C*H₂*Me), 1.73 (d, J 5.6 Hz, *Me*CH=C), 1.93 (m, CH₂C=C), and 5.2—6.3 (4 H, m, olefinic H) (Found: C, 87.2; H, 12.8. C₈H₁₄ requires C, 87.3; H, 12.7%).

(2Z,4E)-*Octa*-2,4-*diene* (12) was an oil, $\lambda_{max.}$(EtOH) 231 nm (log ε 4.4); $v_{max.}$ (liq. film) 980 and 712 cm⁻¹; δ(CDCl₃) 0.91 (t, J 6 Hz, *Me*CH₂), 1.36 (m, C*H₂*Me), 1.78 (d, J 6.5 Hz, *Me*CH=C), 2.04 (m, CH₂C=C), and 5.1—6.7 (4 H, m, olefinic H) (Found: C, 87.0; H, 12.6. C₈H₁₄ requires C, 87.3; H, 12.7%).

(E)-*Octa*-1,4-*diene* (13) was an oil, log ε 3.5 at 205 nm; $v_{max.}$ (liq. film) 990, 967, and 914 cm⁻¹; δ(CHCl₃), 0.89 (t, J 5.9 Hz, *Me*CH₂), 1.33 (m, C*H₂*Me), 2.75 (m, C=C-C*H₂*-C=C), and 4.8—6.3 (5 H, m, olefinic H) (Found: C, 87.5; H, 13.2. C₈H₁₄ requires C, 87.3; H, 12.7%).

The Adduct of (2E,4E)-*Octa*-2,4-*diene* (11) *with Maleic Anhydride:* (±)-(3aS,4S,7R,7aR)-4-*Methyl*-7-*n-propyl*-3a,4,7,7a-*tetrahydrobenzo*[c]*furan*-1,3-*dione* (15).—A solution of the diene (11) (75 mg) and maleic anhydride (0.39 g) in benzene (5 ml) was kept at −80 °C for 4 h. The usual work-up gave a gum which, from pentane–benzene, gave the *dione* (15) (45 mg), m.p. 43 °C; $v_{max.}$(Nujol) 1 821 and 1 766 cm⁻¹; δ(CDCl₃) 0.99 (t, J 5.9 Hz, *Me*CH₂), 1.15 (d, J 7.1 Hz, *Me*CH), 3.33 (2 H, m, 3a-, 7a-H), and 5.81 (2 H, m, C*H*=C*H*) (Found: C, 69.5; H, 7.8. C₁₂H₁₆O₃ requires C, 69.2; H, 7.7%).

Mixture of Methoiodides from the Amines (3) *and* (4).—This consisted of needles, m.p. 125—129 °C; $v_{max.}$(Nujol) 975 cm⁻¹ (*trans* CH=CH); δ (360 MHz, D₂O) [signals for methoiodide of (3) unless stated otherwise] 0.90 (t, J 6 Hz, *Me*[CH₂]₂CH=C), 0.96 [2 t, J 6 Hz, *Me*CH₂CH=C of methoiodide of (4) and possibily (5)] (ratio of signal intensities at 0.90 and 0.96; 4:1), 1.38 (sextet, J 6 Hz, MeC*H₂*CH₂CH=C), 1.88 (m, Me₃N⁺-CH₂C*H₂*), 2.02 (q, J 6 Hz, CH=CHC*H₂*CH₂Me), 2.13 (q, J 6 Hz, Me₃N⁺[CH₂]₂C*H₂*CH=C), 3.13 (s, Me₃N⁺), 3.32 (m, Me₃N⁺C*H₂*CH₂), 5.52 (dt, J 14, 6 Hz, CH=C*H*), and 5.62 (dt, J 14, 6 Hz, C*H*=CH).

Thermal decomposition of the mixture of the corresponding hydroxides gave (g.l.c. on a 25 m OV1 quartz capillary column at 78 °C; i.r. and ¹H n.m.r. spectra) a mixture of the dienes (11), (12), and (13) in the approximate ratios 45:32:23 and possibly a small amount of (14). ¹H N.m.r. at 360 MHz (CHCl₃) gave the following signals, δ 0.9 [t, J 6.5 Hz, *Me*CH₂, (11), (12), and (13)], 1.39 [m, J 6.5 Hz, C*H₂*Me, (11), (12), and (13)], 1.72 [d, J 6 Hz, *Me*CH=CH, (11) and (12)], 2.02 [part obs. m, C*H₂*–CH=C, (11) and (13)], 2.1 [m, C*H₂*–CH=C, (12)], 2.75 [t, J 5.5 Hz, C=CH–C*H₂*–CH=C, (13)], 5.0 [d, J 10.5 Hz, CH=C(*H*)H, (13)], 5.03 [d, J 16.5 Hz, CH=C(H)*H*, (13)], 5.37 [dq, J 10.6 Hz, Me*C*H=C (12)], 5.44 [m, CH₂–C*H*=C*H*–CH₂, (13)], 5.55 [m, Me*C*H=C, (11); m, CH₂C*H*=C, (12)], 5.65 [dt, J 16.5, 6.5 Hz, CH₂–C*H*=C, (11)], 5.83 [doublet of double triplets, J 16.5, 10.5, 5.5 Hz, *H*C=C(H)H, (13)], and 6.0 and 6.34 [two m, C=C*H*–C*H*=C, (11) and (12)].

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* Average of two experiments.