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PROPELLANES—XXXIV

ELECTROPHILIC REACTIONS OF PROPELLANES: ATTACK BY CARBETHOXYCARBENE†‡

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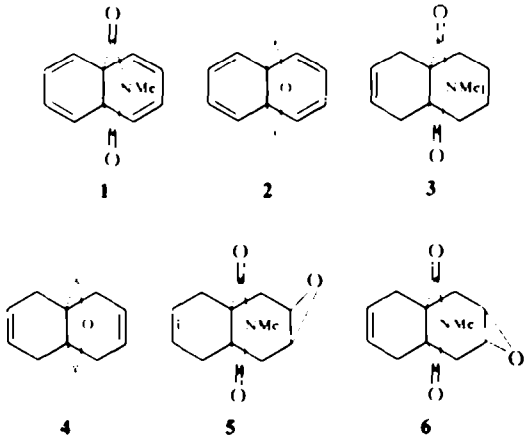
Abstract—The configurations of *mono*- and *bis*- adducts obtained on reaction of **3** and **20**, respectively, with ethyl diazoacetate in the presence of copper sulfate, were determined. Attack *anti*- to the imide ring is greater than that *syn*- to it.

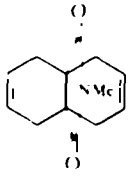
This work serves to probe whether, analogously to the apparent situation in the relative courses of reaction of tetraenic propellanes **1** and **2**,[1] the imide carbonyl groups in **3** also cause greater preference for reaction from the top side. In an electrophilic reaction of **3** and **4**, epoxidation of **3** is much preferred from the top leading to the epoxide **5** as the major product and **6** (attack from bottom).[2] In epoxidation a cationoid reagent is involved in the reaction.

In a recent series of papers Wulfman has reviewed the manifold reaction routes and mechanisms for attack by carbenoid species.[3] Although we appreciated this situation for what it is we used olefinic propellane substrates to probe whether **3** exhibits preference for attack from above also when a carbenoid reagent is employed.



Scheme 1 summarizes the structures of the various *mono*- and *bis*-adducts obtained when **3** was treated with ethyl diazoacetate in dichloroethane at 80° in the presence of copper sulfate.[4] The relative yields are listed in Table 1. The scheme also indicates results of epimerization experiments, showing how various epimers were correlated (in 3 steps indicated by B' in Scheme 1). Further, each of the pure *mono*-adducts isolated from the complex mixture of products obtained from **3** was subjected to separate reaction with the carbenoid reagent (indicated by A in Scheme 1). It should be noted in this connection that **12** was neither found in nor isolated from the original mixture. Here, too, yields of the separate reactions of the *mono*-adducts appear in Table 1.

Table 1.



recovered **3** (9%) + *mono*adducts (50%) [composed of **7**, m.p. 73–74° (16%) + **8**, m.p. 109–111° (65%) + **9** (0%) + **10**, m.p. 134–135° (19%) + *bis*adducts (39%) [composed of **11**, m.p. 94–96° (20%) + **13**, m.p. 195°(48%) + **14**, m.p. 151° (23%) + **15**, m.p. 177–178° (7%) + **16**, m.p. 137–138° (2%).]

7 $\xrightarrow{\Delta}$ **7** (recovered, 40%) + *bis*addadducts (50%) [composed of **11** (77%) + **12**, m.p. 115–116° (23%)]

8 $\xrightarrow{\Delta}$ **8** (recovered, 28%) + *bis*adducts (55%) [composed of **11** (14%) + **13** (71%) + **14** (15%)]

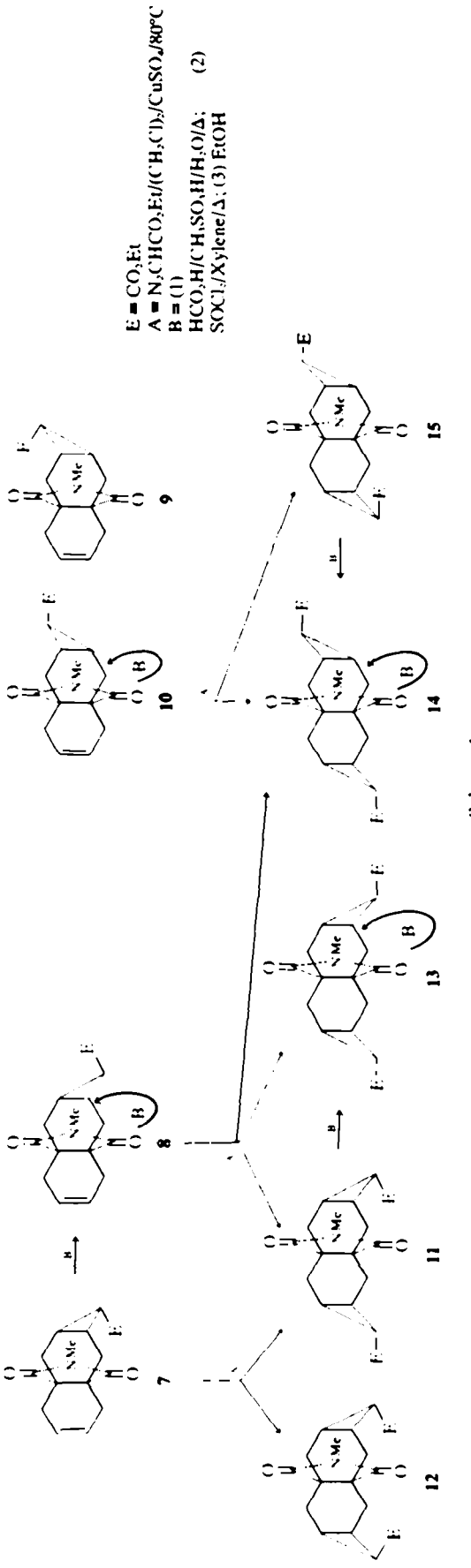
10 $\xrightarrow{\Delta}$ **10** (recovered, 16%) + *bis*adducts (67%) [composed of **14** (74%) + **15** (26%)]

We admit that we were prejudiced by the fact that **3** afforded much more of **5** than of **6** upon epoxidation and expected (and more than half-hoped) that attack by the carbenoid reaction from the top side of **3** would again far exceed that from below. Nevertheless it was clear that we needed an unequivocal frame of reference in order to be certain of the configurations of the compounds listed in Scheme 1. We first sent to Prof. J. D. Dunitz crystals of **11** and when it turned out that this would require measurement of some 8000 reflections[5] we agreed that since the compounds in Scheme 1 were all interconnected it would be unreasonable to require so much work of the X-ray crystallographer. We then submitted **13** which was rather disordered and had **4** molecules in the unit cell.[6] Finally, the acids **17** and **18** corresponding to the esters **8** and **10** were sent to Prof. Dunitz who informed us that **17**, m.p. 239°, corresponding to **8**, albeit twinned, unravelled the secret of its structure, as formulated.

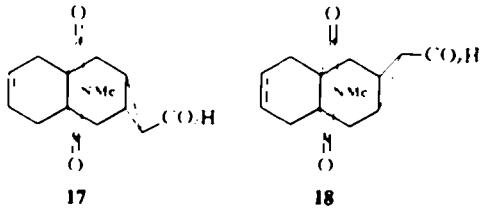
On this basis taken together with symmetry con-

†Propellanes—XXXIII. C. Amith, M. Hackmeyer and D. Ginsburg, *Tetrahedron* **32**, 1015 (1976).

‡Dedicated to Prof. R. B. Woodward on the occasion of his 60th birthday.



Scheme 1.



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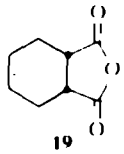
siderations as observed in NMR spectra, all of the compounds, whether *mono*-adducts or *bis*-adducts, have the configurations shown in Scheme 1. Thus attack in this case is preferred from below, *not* from above but the ester group prefers the *exo*- rather than the *endo*-configuration.

We are aware of calculations by Prof. R. Gleiter showing that $:CH_2$ attacks **19** from the direction *anti* with respect to the anhydride ring.[7] This corresponds, although the substrate and reagent are not strictly comparable, to



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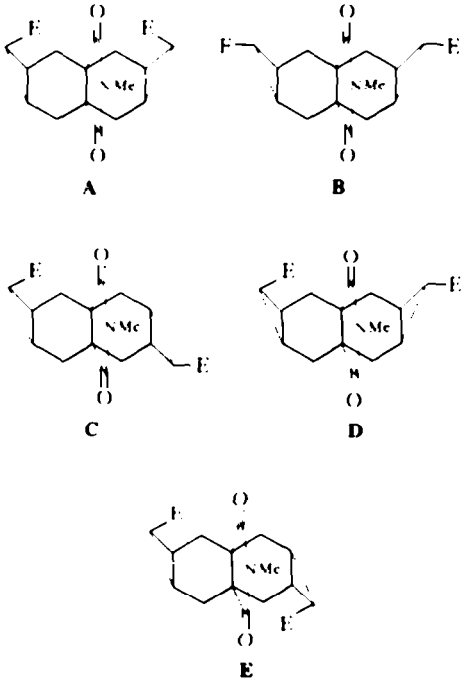
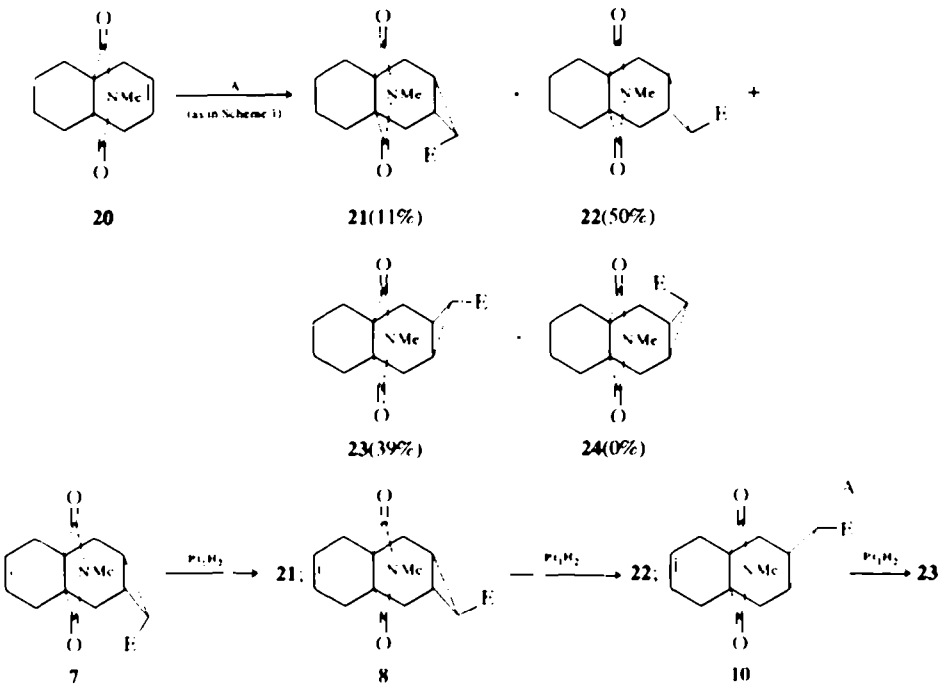
what is found for **3**, in which there is more attack *anti* to the imide ring as compared to *syn*.

Another *bis*-adduct **16** was isolated from the original reaction mixture in only 2% yield. It has an unsymmetrical NMR spectrum and this rules out structures **A** and **B**. The only other possibilities remaining for **16** are **C**, **D** or **E** but the assignment of the correct structure has not been made.



A B C D E

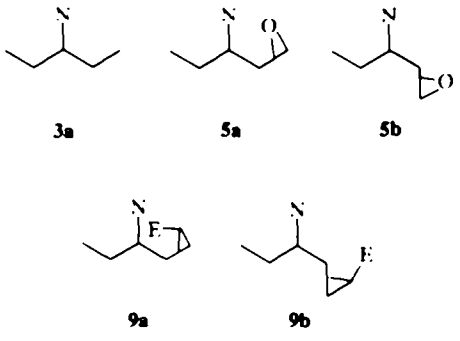
The methylimide-monoene **20** (dihydro-**3**) was incidentally subjected to reaction with ethyl diazoacetate under the same reaction conditions as its dienic homolog **3**. This affords a much simpler exercise in symmetry but probes whether here too the carbenoid reagent prefers to attack



Scheme 2.

the bottom face of the cyclohexene. Scheme 2 summarizes the results obtained. Here too, no **24**, the analog of **9** was obtained.

We have shown that **3** in solution prefers conformation **3a**.[8] This conformation (**5a**) is maintained in the crystal of



5.[9] Perhaps this type of *exo-exo*- configuration is so preferred in **3** and its derivatives that **9** is the only one of the four possible *mono*-adducts which cannot form. Dreiding models clearly show that conformation **9a** cannot exist because of the bulk of the ester group. The compound can exist in conformation **9b** but this is an *exo-endo* structure. It should be noted that **5** exists as **5a** even though unfavorable electrostatic interactions between electronegative atoms could be decreased in **5b**. It was in order to obtain information about this structural aspect that we first submitted the unsymmetrical **11** for X-ray crystallographic investigation. But as stated above the expenditure of work required did not appear justified to furnish an answer to this question in addition to the fundamental problem of above:below.

The structures of **21**, **22** and **23** were established through their preparation by catalytic reduction from **7**, **8** and **10**, respectively.

EXPERIMENTAL

IR spectra were measured on a Perkin-Elmer model 257 grating spectrophotometer. NMR spectra were measured on a Varian T-60 spectrometer. Mass spectra were measured either on an Atlas CH4 instrument using the heated inlet system at 200°, maintaining the ionization current at 20 μA and the electron energy at 70 eV or on a Varian 711 spectrometer using the heated inlet system at 200° and maintaining the electron energy at 100 eV. Only the major fragments are listed. All m.ps are uncorrected.

Reaction of **3** *with ethyl diazoacetate*

To a soln of **3**[10] (2.61 g) in 1,2-dichloroethane (filtered on Alox; 40 ml) was added anhyd $CuSO_4$ (Fluka puriss dried overnight at 160°; 3.5 g) under dry N_2 (P_2O_5). To this slurry was added with vigorous magnetic stirring during 4.5 hr a soln of ethyl diazoacetate[11] (6.0 g) in the same solvent (20 ml), at 80–82° (bath temp.). The brownish suspension was stirred for 30 min more at same temp. After cooling to room temp. removal of $CuSO_4$ by filtration and removal of solvent in a vacuum, a dark viscous oil (7.0 g) was obtained. This was chromatographed on a column of neutral Alox (Merck, deactivated with 6% water; 140 g) with mixtures of hexane–ether at 0°.[12]

Hexane–ether (9:1, 600 ml) eluted impure **3** (631 mg) which afforded pure **3** after crystallization at 0° (233 mg, 9%, m.p. 156–157°), identical in all respects to the starting material.

Hexane–ether (9:1; additional 100 ml) eluted **7** (205 mg, oily). The analytical sample had m.p. 73–74° (hexane).

Compound **7**. (Found: C, 67.40; H, 6.96; N, 4.69; M.W. 303. $C_{17}H_{21}NO_4$ requires: C, 67.31; H, 6.98; N, 4.62%; M.W. 303.35). NMR (CCl_4): τ 4.10 (t, J = 3 Hz, 2 vinylic H); 5.88 (q, J = 7 Hz, OCH_2CH_3); 7.08 (s, NCH_3); 7.30, 7.53 (2m, 2 H); 8.0 (m, 5 H); 8.1–8.9 (m, 4 H); 8.72 (t, J = 7 Hz, OCH_2CH_3).[13] IR($CHCl_3$): 1765, 1685, 1460, 1430, 1380, 1320, 1280, 1160 cm^{-1}. MS. (*m/e*): 303(M^+, 99), 256(70), 227(100), 175(51), 162(89), 143(55), 130(84).

Hexane–ether (8:2; 700 ml) eluted a mixture of three *mono*-adducts **7**, **8**, **10** (1.543 g). It contained according to integral of the NCH_3 singlets, **7** (85 mg), **8** (1.16 g), **10** (0.3 g). Crystallization at 0° gave **8** (717 mg); m.p. 108–109° (ether–hexane). Recrystallization from same solvent mixture gave the analytical sample; m.p. 109–111°.

Compound **8**. (Found: C, 67.06; H, 7.18; N, 4.66%; M.W. 303). NMR (CCl_4): τ 4.09 (t, J = 3 Hz, 2 vinylic H); 5.93 (q, J = 7 Hz,

OCH_2CH_3); 7.02 (s, NCH_3); 7.30, 7.54 (2m, 4 H); 8.13, 8.39 (2bs, 2 H); 8.5–9.0 (m, 3 H); 8.77 (t, J = 7 Hz, OCH_2CH_3); 9.0–9.4 (m, 2 cyclopropane H). IR ($CHCl_3$): 1770, 1690, 1430, 1325, 1282, 1160 cm^{-1}. MS. (*m/e*): 303(M^+, 100), 257(55), 229(28), 175(53), 162(67), 144(36), 130(33).

Evaporation of the mother liquor and crystallization from benzene–hexane gave **10** (150 mg), m.p. 132–133°. A second crystallization gave the analytical sample, m.p. 134–135° (ether–hexane).

Compound **10**. (Found: C, 67.32; H, 7.02; N, 4.59%; M.W. 303). NMR (CCl_4): τ 4.09 (t, J = 4 Hz, 2 vinylic H); 5.90 (q, J = 7 Hz, OCH_2CH_3); 7.13 (s, NCH_3); 7.3–8.1 (m, 5 H); 8.2–9.0 (m, 5 H); 8.73 (t, J = 7 Hz, OCH_2CH_3); 9.0–9.3 (m, 1 cyclopropane H). MS (*m/e*): 303(M^+, 100), 257(99), 229(63), 203(42), 172(53), 162(54), 144(42), 125(57), 95(90).

Further elution with ether–hexane (8:2; 400 ml) gave a mixture of 3 compounds (389 mg). According to chemical shift and integration of NCH_3 singlets this comprised of the *bis*-adduct **11** (325 mg) and more of the *mono*-adducts **8** (18 mg) and **10** (46 mg). Crystallization from benzene–hexane afforded pure **11** (267 mg), m.p. 94–96°.

Compound **11**. (Found: C, 65.01; H, 6.99; N, 3.62; M.W. 389. $C_{21}H_{27}NO_6$ requires: C, 64.76; H, 6.99; N, 3.60%; M.W. 389.43). NMR (CCl_4): τ 5.90, 5.93 (2q, J = 7 Hz, 4 OCH_2CH_3), 6.95 (s, NCH_3); 7.38 (m, 1 H); 7.58 (m, 1 H); 7.8–8.3 (m, 4 H); 8.3–9.4 (m) + 8.73 (t, J = 7 Hz) + 8.77 (t, J = 7 Hz; total 14 H). IR($CHCl_3$): 1765, 1690, 1460, 1430, 1380, 1325, 1160 cm^{-1}. M.S. (*m/e*): 389(M^+, 4), 343(42), 302(100), 241(25).

Further elution with ether–hexane (8:2; 100 ml) gave a mixture of 4 *bis*-adducts (176 mg). According to chemical shift and integration of NCH_3 singlets this was a mixture of **15** (85 mg), **11** (42 mg), **13** (10 mg) and **16** (39 mg, 2%). Crystallization from ether–hexane gave **15** (58 mg), m.p. 172–173°. A second crystallization gave the analytical sample, m.p. 177–178° (ether–hexane).

The mother liquor was chromatographed on a prep Alox plate with cyclohexane–ether (8:2), rerun 3 times. Elution with CH_2Cl_2–10% MeOH and crystallization at −10° gave **16** (15 mg), m.p. 128–131° (ether–hexane). The analytical sample had m.p. 137–138° (ether–hexane).

Compound **16**. (Found: High resolution M.W. 389.1808. $C_{21}H_{27}NO_6$ requires: M.W. 389.1839). NMR (CCl_4): τ 5.91, 5.93 (2q, J = 7 Hz, 4 OCH_2CH_3); 6.98 (s, NCH_3); 7.4, 7.6 (2m, 2 H); 7.8–9.2 (complex m) + 8.75 (t, total 18 H). IR ($CHCl_3$): 1765, 1690, 1430, 1385, 1320, 1160 cm^{-1}. MS. (*m/e*): 389(M^+, 41), 344(47), 343(100), 315(28), 287(17), 269(37), 175(21).

Compound **15**. (Found: C, 64.94; H, 6.95; N, 3.74%; M.W. 389). NMR (CCl_4): τ 5.83, 5.90 (2q, J = 7 Hz, 4 OCH_2CH_3); 7.07 (s, NCH_3); 7.4–8.1 (m, 6 H); 8.2–9.1 (m) + 8.70 (t, J = 7 Hz) + 8.73 (t, J = 7 Hz, OCH_2CH_3, total 14 H). IR ($CHCl_3$): 1760, 1685, 1425, 1380, 1285, 1140 cm^{-1}. MS. (*m/e*): 389(M^+, 58), 343(100), 315(25), 269(41), 203(33).

Further elution with ether–hexane (7:3; 1500 ml) afforded a mixture of 3 *bis*-adducts. Judging from NMR as above this contained **13** (873 mg), **14** (410 mg) and **15** (52 mg). Crystallization from ether–hexane gave **13** (902 mg), m.p. 175–180°. Two recrystallizations gave pure **13** (354 mg), m.p. 193–194° but the analytical sample had m.p. 195° (ether–hexane).

Compound **13**. (Found: C, 65.00; H, 7.09; N, 3.67%; M.W. 389). NMR (CCl_4): τ 5.95 (q, J = 7 Hz, 4 OCH_2CH_3); 6.90 (s, NCH_3); 7.27–7.50 (m, 2 H); 7.50–7.77 (m, 2 H); 8.4–9.0 (m) + 8.77 (t, J = 7 Hz, OCH_2CH_3; total 12 H); 9.32 (dd, J_{AB} = 14 Hz, J_{BC} = 8 Hz, 4 cyclopropane H). IR ($CHCl_3$): 1765, 1690, 1455, 1425, 1365, 1320, 1275, 1155 cm^{-1}. MS. (*m/e*): 389 (M^+, 17), 343(100), 315(31), 302(13), 269(36), 241(27).

Evaporation of the mother liquor and crystallization from ether–hexane gave **14** (211 mg), m.p. 140–145°. Recrystallization at 0° afforded analytically pure **14**, m.p. 151° (ether–hexane).

Compound **14**. (Found: C, 64.78; H, 6.95; N, 3.60%; M.W. 389). NMR (CCl_4): τ 5.91, 5.93 (2q, J = 7 Hz, 4 OCH_2CH_3); 6.98 (s, NCH_3); 7.3–8.1 (m, 4 H); 8.2–9.3 (m) + 8.72 (t, J = 7 Hz) + 8.75 (t, J = 7 Hz, total 16 H). IR ($CHCl_3$): 1765, 1690, 1425, 1380, 1365, 1325, 1290, 1170 cm^{-1}. MS (*m/e*): 389(M^+, 100), 343(98), 315(29), 269(39).

Reaction of **7** *with ethyl diazoacetate*

From **7** (57 mg) reacted and worked up as above was obtained after recovery of **7** (23 mg) by using hexane–ether (3:1), a mixture of *bis*-adducts (36 mg; 54%) consisting of **11** (29 mg) and a heretofore unisolated *bis*-adduct **12** (7 mg).

Crystallization at 0° afforded **11** (20 mg) identical with an authentic specimen. Chromatography of the mother liquor (obtained from several runs) on an Alox plate with cyclohexane–ether (8:2) rerun 5 times and elution with CH_2Cl_2–MeOH (9:1) followed by crystallization gave the analytical sample of **12** (10 mg), m.p. 115–116° (hexane).

Compound **12**. (Found: High resolution M.W. 389.1871, $C_{21}H_{27}NO_6$ requires: 389.1839). NMR (CCl_4): τ 5.88 (q, J = 7 Hz, 4 OCH_2CH_3); 7.02 (s, NCH_3); 7.7–8.9 (complex m) + 8.72 (t, J = 7 Hz, total 20 H). IR ($CHCl_3$): 1765, 1690, 1465, 1430, 1380, 1285, 1160, 975 cm^{-1}. MS. (*m/e*): 389(M^+, 5), 344(25), 343(18), 315(14), 303(19), 302(100), 269(16), 241(24), 228(16), 184(13), 156(21).

Reaction of **8** *with ethyl diazoacetate*

From **8** (510 mg) as above was obtained from a column of neutral Alox (65 g) at 0° with hexane–ether (9:1; 1 liter) a mixture (112 mg) of **8** (38 mg) and **11** (74 mg). Separation using 44 mg on an Alox plate with hexane–ether (2:1) and elution with CH_2Cl_2–MeOH (9:1) gave **8** (14 mg); pure **8** (12 mg), m.p. 110–111° (ether–hexane) and **11** (18 mg); pure **11**, m.p. 97–98° identical with an authentic specimen, m.p. 94–96°; m.m.p. 97°.

Ether–hexane (1:1; 800 ml) eluted a mixture (398 mg) of **13** (335 mg) and **14** (63 mg) as judged by NMR. Recrystallization several times gave **13** (214 mg) m.p. 194–195° identical with authentic **13**. More ether–hexane (1:1; 400 ml) eluted impure **13** + **14** (106 mg) which was rechromatographed on neutral Alox (15 g) with hexane–ether. (1:1) gave a purer mixture of **13** + **14**. Crystallization again gave **13** (21 mg), m.p. 192–193° (ether–hexane) whilst combining all of the mother liquors from **13** afforded **14** after crystallization (11 mg), m.p. 151–152° (ether–hexane) identical with authentic **14**.

Reaction of **10** *with ethyl diazoacetate*

From **10** (118 mg) reacted and worked up as above, **10** was recovered (46 mg) after elution from neutral Alox (35 g) with hexane–ether (9:1). Hexane–ether (8:2) gave a mixture of **14** and **15** (76 mg). Separation on a preparative Alox plate using cyclohexane–ether and rerun five times, gave after elution with CH_2Cl_2–MeOH (9:1); **15** (10 mg; less polar zone). Crystallization at 0° gave **15** (4 mg, m.p. 176–177°) identical with an authentic specimen. Elution of the more polar zone with the same solvent mixure gave **14** (40 mg) which on crystallization gave pure **14**, m.p. 149–150° identical with an authentic sample.

Epimerization of **7**

(a) A soln of **7** (87 mg) in a stock soln made up of 90% aq formic acid containing 0.1 mole $MeSO_3H$ per 100 ml of 90% acid, (4 ml) was heated under refluxing during 4.5 hr at a bath temp. of 110°. The resulting clear colorless soln was poured into water (30 ml) and the whole was extracted with ether–CH_2Cl_2 (9:1; 3 × 50 ml). The organic layer was dried ($MgSO_4$) and the solvent removed in a vacuum affording a colorless solid (79 mg). This *acid* was crystallized giving the pure acid (62 mg; 79%), m.p. 209–211° ($CHCl_3$–hexane). (Found: N, 5.12, M.W. 275. $C_{15}H_{17}NO_4$ requires: N, 5.09%; M. W. 275.29). NMR ($CDCl_3$): τ 1.20 (bm, CO_2H); 4.07 (t, J = 3 Hz, 2 vinylic H); 7.00 (s, NCH_3); 7.24–7.50 (2m, 2 H); 7.7–8.8 (m, 9 H). IR ($CHCl_3$): 1760, 1680, 1430, 1380, 1320, 1115 cm^{-1}. (KBr): 1760, 1710, 1660, 1430, 1380, 1320, 1160, 690 cm^{-1}. MS. (*m/e*): 275(M^+, 100), 257(20), 229(30), 175(45), 162(74), 144(32), 130(57).

(b) To a suspension of the acid (49 mg; 0.178 mmol) in dry *p*-xylene (filtered through Alox, 5 ml) under dry N_2 (P_2O_5) was added $SOCl_2$ (450 μl; 6.2 mmol) at room temp. with magnetic stirring and the whole was then heated 80° for 2 hr [IR($CHCl_3$): 1760 cm^{-1} (COCl)]. The clear soln was then heated under reflux for 1.5 hr (bath temp. 150°) under a slow stream of dry N_2. After cooling to room temp. abs EtOH (1 ml) was added. After

standing overnight the yellow soln was poured into saturated salt soln and the whole was extracted with ether (2 × 50 ml). After drying ($MgSO_4$) the solvent was removed in a vacuum. The NMR spectrum of the crude product showed the presence of **7** and **8** (1:3; NCH_3 singlets at τ 7.08 and 7.00, respectively). Chromatography on a column of neutral Alox (Merck, deactivated with 6% water, 10 g) with hexane–ether (1:1), starting with pure hexane, gave the pure mixture of **7** + **8** (28 mg; 52%; 1:3). Crystallization at 0° gave pure **8** (9 mg), m.p. 103–104° (ether–hexane) whose NMR (CCl_4) and IR ($CHCl_3$) were identical with those of the analytical sample of **8**, m.p. 109–111°.

Attempted epimerization of **8**

(a) Compound **8** (100 mg) in stock soln (5.5 ml) as for **7** 4.5 hr. Identical workup gave the corresponding *acid* (96 mg); pure acid (83 mg; 91%) by recrystallization had m.p. 239° ($CHCl_3$–hexane). (Found: C, 65.14; H, 6.21; N, 5.09%; M.W. 275). NMR ($CDCl_3$): τ 1.30 (bm, CO_2H); 4.05 (t, J = 3 Hz, 2 vinylic H); 6.98 (s, NCH_3); 7.07–7.34, 7.34–7.60 (2m, 4 H); 8.06, 8.26 (2m, 2 H); 8.37–9.40 (m, 5 H). IR ($CHCl_3$): 1760, 1678, 1430, 1380, 1320 cm⁻¹. MS (*m/e*): 275(M⁺, 100), 257(35), 162(85), 144(35).

(b) Acid (70 mg; 0.255 mmol), $SOCl_2$ (700 μl; 9.7 mmol) as above, including workup. NMR spectrum showed that only **8** was present. Chromatograpy (12 g Alox) as above gave **8** (61 mg; 79%), then pure **8** (43 mg), m.p. 105–107° (ether–hexane) identical with starting material.

Attempted epimerization of **10**

(a) Compound **10** (102 mg) in stock soln (5.5 ml) as above. Same workup gave the corresponding crude *acid* (90 mg); pure acid (66 mg; 72%), m.p. 229–230° ($CHCl_3$–hexane). (Found: C, 65.35; H, 6.39; N, 4.95%; M.W. 275). NMR ($CDCl_3$): τ 1.40 (bm, CO_2H); 4.07 (m, 2 vinylic H); 7.07 (s, NCH_3); 7.2–8.4 (m, 7 H); 8.5–9.3 (m, 5 H). IR ($CHCl_3$): 1765, 1685, 1430, 1380, 1290 cm⁻¹. (KBr): 1760, 1680, 1440, 1375, 1290, 1210, 690 cm⁻¹. MS (*m/e*): 275 (M⁺, 100); 257 (61), 229(41), 162(72), 144(41), 105(55), 91(65).

(b) Acid (20 mg; 0.073 mmol), dry *p*-xylene (3 ml), $SOCl_2$ (450 μl; (6.2 mmol) as above. After same workup NMR spectrum showed only **10** to be present. Chromatography (14 g Alox) as above gave **10** (10 mg, 45%), m.p. 128°; pure **10** (8 mg, m.p. 130–131°) identical with starting material.

Epimerization of **11**

(a) A soln of **11** (102 mg) in stock soln (6 ml) was heated under reflux for 4 hr (bath temp. 110°). After cooling to room temp., ether (4 ml) was added to the clear colorless soln. Standing overnight at 0° afforded colorless crystals which were removed, washed with ether (2 × 4 ml) and dried (64 mg; 72%). The diacid had m.p. > 310°. NMR(py): τ 6.90 (s, NCH_3); 7.1–8.0 (m, 6 H); 8.1–9.2 (m, 8 H). IR (KBr): 1750, 1715, 1665, 1430, 1280, 1160, 1055, 695 cm⁻¹.

(b) The diacid (50 mg; 0.15 mmol) in dry *p*-xylene (6 ml) under dry N_2 was treated with 400 μl (5.5 mmol) $SOCl_2$ at room temp. and heated to 80°. After 90 min more $SOCl_2$ (400 μl) was added and heating continued at 80° for 90 min more, then heated under reflux (bath temp. 150°) under slow stream of N_2 during 6 hr. After cooling to room temp., abs EtOH (1 ml) was added. After standing 4 hr the whole was poured into water (30 ml), extracted with ether (2 × 50 ml), the organic layer was dried ($MgSO_4$) and solvent removed. Chromatography of the oily brown residue (97 mg) on neutral Alox (15 g) as above gave a mixture of **11** and **13** (1:1; 39 mg; 67%) according to NCH_3 singlets at τ 6.95 and 6.89. Crystallization gave pure **13** (18 mg, m.p. 188–190°) identical spectroscopically with analytical **13**.

Attempted epimerization of **13**

(a) Compound **13** (300 mg) in stock soln (15 ml) and workup as above for **11**. The diacid (225 mg; 87%), m.p. >310°. NMR (py): 6.96 (s, NCH_3); 7.30, 7.50 (2m, 4 H); 8.0–8.6 (m, 6 H); 8.7–9.4 (m, 4H). IR (KBr): 1755, 1730, 1665, 1435, 1325, 1280, 1230, 1160, 1040 cm⁻¹.

(b) Diacid (100 mg; 0.3 mmol), dry *p*-xylene (5 ml), $SOCl_2$ (1 ml; 14 mmol); then $SOCl_2$ as for **11** (300 μl) and pyridine (25 μl) for total of 2 hr at 80° and 2 hr at 150°. After addition of EtOH (3 ml) similar workup gave brown oil (150 mg) whose NMR spectrum showed presence of **13** only. Chromatography as above (14 g neutral Alox) gave pure **13** (50 mg; 43%), m.p. 192°; pure **13** (38 mg), m.p. 193° (ether–hexane) identical to analytical specimen.

Attempted epimerization of **14**

(a) Compound **14** (210 mg) in stock soln (12 ml) as for **13**; diacid (144 mg; 80%), m.p. > 310°. NMR (py): τ 7.05 (s, NCH_3); 7.2–7.9 (m, 4 H); 8.0–9.0 (m, 10 H). IR (KBr): 1755, 1710, 1660, 1430, 1380, 1320, 1290, 1230, 1180 cm⁻¹.

(b) Diacid (100 mg), other reagents as for **13**, same workup, gave brown oil (125 mg) whose NMR spectrum showed that only **14** was present (only 1 singlet at τ 7.03). Chromatography (15 g neutral Alox) as above gave **14** (45 mg; 38%), pure **14** (33 mg), m.p. 150–151° identical in all respects with analytical sample.

Epimerization of **15**

(a) Compound **15** (71 mg) in stock soln (6 ml) as for **11**, same workup, gave diacid (52 mg; 86%) m.p. 257–260°. NMR (py): τ 6.95 (s, NCH_3); 7.1–9.0 (bm, 14 H). IR (KBr): 1760, 1670, 1430, 1380, 1285, 1230, 1020, 970 cm⁻¹.

(b) The diacid (41 mg, 0.12 mmol), dry *p*-xylene (6 ml), $SOCl_2$ (400 μl, 5.7 mmol) at 80° for 90 min. $SOCl_2$ (400 μl; added, 90 more min at 80°, then 6 hr at 150°. Workup as for **11** gave brown oil (64 mg) whose NMR spectrum showed NCH_3 singlets at 7.03 and 7.07 (1:3) corresponding to **14** and **15**. Preparative separation on an Alox plate with cyclohexane–ether (8:2), rerun 5 times, and elution with CH_2Cl_2–MeOH (9:1) gave **15** (24 mg) m.p. 172–173° then pure **15** (20 mg) m.p. 176–177°, identical to analytical **15**. Elution of the second zone with CH_2Cl_2:MeOH (9:1) gave **14** (5 mg), then pure **14** (3 mg), m.p. 150–151° ether–hexane, identical in all respects with analytical **14**.

Reaction of **20** *with ethyl diazoacetate*

To a soln of **20** (285 mg) in dichloroethane (10 ml) was added $CuSO_4$ (0.65 g) and a soln of ethyl diazoacetate (1.5 g) in $(CH_2Cl)_2$ (5 ml) was added with vigorous stirring at 80–82° during 90 min. Stirring was continued at this temp. 30 more min. After cooling to room temp. and removing the solid and then the solvent in a vacuum, a dark viscous oil (1.18 g) was obtained. It was chromatographed on a column of neutral Alox (55 g) at 0° with hexane–ether (9:1; 250 ml). Impure **20** (32 mg) was recovered. Further elution (60 ml) gave nearly pure **21** (42 mg). Separation on a preparative Alox plate with hexane–ether (8:2) gave after crystallization at −10°, **21** (18 mg), m.p. 67°, identical with product prepared by reduction of **7**. More hexane–ether (9:1; 300 ml) eluted a mixture (267 mg) judged from N–CH_3 singlets in NMR to consist of **19** (154 mg) and **21** (123 mg).

Crystallization gave **22** (37 mg, m.p. 120–121°) identical with product of reduction of **8**. Crystallization and recrystallization of the product in the mother liquor gave pure **23** (63 mg), m.p. 125–126° (ether–hexane) identical with the reduction product of **10** (see below for data on **21**, **22**, **23**).

Reductions

(a) A soln of **7** (27 mg) in EtOH (10 ml) and PtO_2 (24 mg) was subjected to reduction for 1 hr. H_2 uptake (8.5 ml) ceased after 20 min. Removal of catalyst and solvent gave a colorless oil (30 mg). Crystallization at −10° gave the analytical sample of **21** (19 mg; 70%), m.p. 69° (hexane). (Found: C, 66.95; H, 7.50; N, 4.74; M.W. 305. $C_{17}H_{23}NO_4$ requires: C, 66.86; H, 7.59; N, 4.59%; M.W. 305.36). NMR (CCl_4): τ 5.88 (q, J = 7 Hz, OCH_2CH_3); 7.02 (s, NCH_3); 7.9–8.9 (m) + 8.72 (t, J = 7 Hz, OCH_2CH_3, total 18 H). IR ($CHCl_3$): 2940, 1765, 1690, 1430, 1380, 1280, 1160, 1060, 980 cm⁻¹. MS. (*m/e*): 305 (M⁺, 63), 259(16), 231(100), 174(12), 166(15), 146(68), 125(11), 91(27).

(b) Reduction of **8** (50 mg) in EtOH (20 ml) with Adams' catalyst (30 mg) during 1 hr (12 ml H_2 taken up within 20 min) gave after similar workup **22** (49 mg), m.p. 118–119°. Crystallization afforded purer **22** (32 mg; 63%), m.p. 121° (ether–hexane). (Found C, 66.65; H, 7.45; N, 4.63%. M.W. 305). NMR (CCl_4): τ 5.95 (q, J = 7 Hz, OCH_2CH_3)); 6.96 (s,, NCH_3); 7.4 (m, 1 H); (7.6 (m, 1 H), 8.0–9.4 (m) + 8.77 (t, J = 7 Hz, OCH_2CH_3,, total 16 H). IR

($CHCl_3$): 2930, 1760, 1685, 1460, 1430, 1380, 1320, 1280, 1155, 1040 cm^{-1}. MS. (*m/e*): 305(M^+, 72), 259(100), 231(49), 174(28), 166(28), 146(35), 125(36), 91(24).

(c) Reduction of **10** (30 mg) in EtOH (20 ml) with PtO_2 (25 mg) during 1 hr (H_2 uptake 10 ml within 20 min) gave after same workup, **23** (32 mg) m.p. 120–122°. The analytical sample (17 mg; 56%), had m.p. 125–126° (ether–hexane). (Found: C, 67.11; H, 7.34; N, 4.80%; M.W. 305). NMR (CCl_4): τ 5.88 (q, J = 7 Hz, OCH_2CH_3); 7.07 (s, NCH_3); 7.63 (m, 1 H); 7.86 (m, 1 H); 8.0–9.1 (m) + 8.72 (t, J = 7 Hz, OCH_2CH_3, total 16 H). IR($CHCl_3$): 2940, 1765, 1690, 1430, 1385, 1330, 1310, 1285, 1170 cm^{-1}. MS. (*m/e*): 305(M^+, 37), 259(100), 231(28), 174(22), 166(19), 146(20), 125(37), 91(18).

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