Tetrahedron Letters No. 2, pp 211 - 214, 1977. Pergamon Press. Printed in Great Britain.

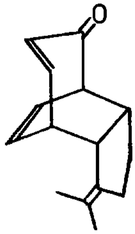
A NEW SYNTHETIC ROUTE TO FUNCTIONALISED TRICYCLO [5.3.2.0^{2,6}] DODECADIENES

A.M. Chalmers[1] and A.J. Baker
Department of Organic Chemistry, The University, Glasgow G12 8QQ

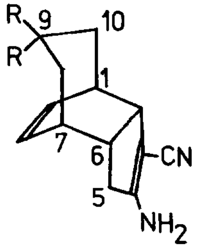
(Received in UK 18 November 1976; accepted for publication 29 November 1976)

Interest in recent years[2] in tricyclo adducts of type 1 has prompted us to report our findings in synthesising molecules of this type.

Literature to date has been confined to reactions of tropones[2a,b,c,d,e,f], cycloheptatriene[2g] and, more recently, the tropylium ion[2h] with various cyclopentadienes, the resulting adducts being formed by an *endo* [2+4]cyclo addition. In this paper we wish to report an alternative synthesis of substituted tricyclo [5.3.2.0^{2,6}]dodecadienes which we investigated in the course of work on bicyclo [3.2.2]nonanes[3]. This synthesis has been achieved for both the substituted and unsubstituted structures, 2b and 2a respectively.

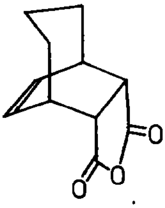


1

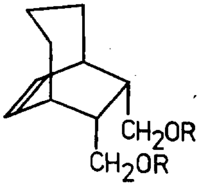


2a R = H
2b R,R = OCH_2CH_2O

The synthesis of 2a makes use of the known adduct 3 which has been shown[4] chemically to have the *endo* configuration. Reductions using lithium aluminium hydride in ether are known[5] to proceed without epimerisation of the adjacent asymmetric centres. Thus the adduct 3 afforded diol 4a (97%, m.p. 72-72.5°) which, when slowly added to excess methane sulphonyl chloride in pyridine at 0°, yielded the bis-mesylate 4b (96%, m.p. 96-97°). Ring closure was then effected using the method of Bloomfield and Fennessey[6] by *in situ* replacement of the mesylate groups with cyanide followed, on addition of NaH, by a Thorpe cyclisation to yield the β-cyanoamine 2a [68%, m.p. 188°; IR ν^{NUJ}_{N-H} 3460, 3390, 1645 cm^{-1}, $\nu^{NUJ}_{C\equiv N}$ 2210 cm^{-1}; UV λ^{EtOH}_{max} 263.5 nm (ε 15,000), HCl addition, hypsochromic shift to 238 nm (ε 10,700); NMR δ 1.44 (s, 6H, H_8, H_9, H_{10}), *ca* 2.2 (m, 1H, H_6), *ca* 2.7(m,4H, H_1, H_5,H_7) 3.20 (d, J=8Hz, 1H, H_2), 4.24 (s(broad), 2H, D_2O exchange, NH_2) 7.03 ppm (m, 2H, H_{11}, H_{12}); analysis $C_{13}H_{16}N_2$].



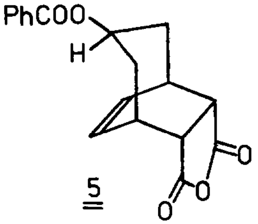
3



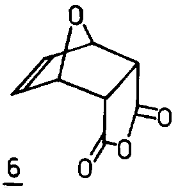
4a R=H

4b R=SO_2CH_3

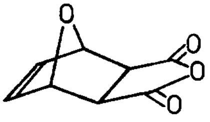
For the synthesis of the substituted compound 2b we used the benzoate 5 which we reported [3a] in an earlier paper as having the endo configuration as shown. We assigned this by NMR (δ 3.66 ppm, s, 2H, H_8, H_9) being aware that the dihedral angle (ϕ) between the exo proton and the bridgehead proton is ca 75° and by the Karplus theory[7] there should be little or no coupling. Anet[8] in 1962 identified endo and exo adducts 6 (ϕ = ca 45°, coupling) and 7 (ϕ = ca 80°, no coupling) by correlation of dihedral angles. Subsequent X-ray analysis[3b] of the p-bromo benzoate derivative of 5 confirmed the endo structure.



5



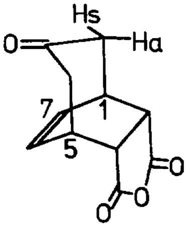
6



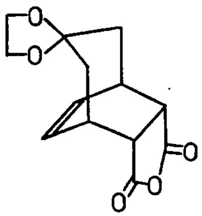
7

To avoid complications of comcomitant reduction of the benzoate when the anhydride is reduced, 5 was converted to the corresponding ketal derivative which would be stable to reductive conditions. Thus hydrolysis of 5 with sodium carbonate solution and Jones oxidation of the crude product afforded the keto anhydride 8 [42% (from 5), m.p. 199.5-200.5°; analysis $C_{11}H_{10}O_4$; IR $\nu^{KBr}_{(CO)_2O}$ 1867, 1834, 1768 cm^{-1}, ν^{KBr}_{CO} 1697 cm^{-1}; NMR δ 2.57 (q, J=18, 4 Hz, 2H, $H_{2a,\ 4a}$), 2.86 (q, J=18,4 Hz, 2H, $H_{2s,\ 4s}$), 3.24 (m, 2H, $H_{1,5}$), 3.96 (s, 2H, $H_{8,9}$), 6.31 ppm (q, J=5.5, 3.5 Hz, 2H, $H_{6,7}$)]. As in the case of benzoate 5 the singlet for protons H_8 and H_9 indicated that the anhydride was in the endo configuration. Using ethylene glycol/pTSA, ketone 8 readily gave the ketal derivative 9 (55%, m.p. 225-226.5°; analysis $C_{13}H_{14}O_5$; IR $\nu^{KBr}_{(CO)_2O}$ 1860, 1829, 1778 cm^{-1}; NMR δ 1.67 (d, J=14 Hz, 2H, $H_{2a,4a}$), 1.99 (q, J=14, 7 Hz, 2H, $H_{2s,4s}$), 2.02 (s(broad), 2H, $H_{1,5}$), 3.80 (q, 4H, methylene), 3.98 (s, 2H, $H_{8,9}$), 6.15 ppm (q, J=5,4 Hz, 2H, $H_{6,7}$).

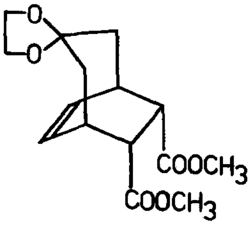
8



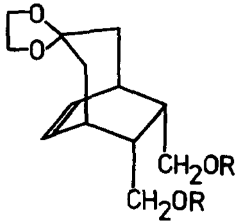
9



Before reduction of 9, it was first converted to the diester 10 [49%, m.p. 89.5–91.5°; analysis $C_{15}H_{20}O_6$; IR $\nu^{CHCl_3}_{COOCH_3}$ 1745 cm^{-1}; NMR δ 1.71 (q, J=14,2 Hz, 2H, $H_{2a,4a}$), 1.97 (q, J=14,6 Hz, 2H, $H_{2s,4s}$) 2.86 (s(broad), 2H, $H_{1,5}$), 3.55 (s, 6H, methyl), 3.76 (s, 2H, $H_{8,9}$), 3.86 (q, 4H, methyl) 3.76 (s, 2H, $H_{8,9}$), 3.86 (q, 4H, ethylene), 6.28 ppm (q, J=5.5, 3.5 Hz, 2H, $H_{6,7}$)] by hydrolysis followed by diazomethane treatment. NMR confirmed the *endo* configuration of the two ester groups and these were reduced with lithium aluminium hydride to yield 11a (76%, m.p. 137.5–138.5°; analysis $C_{13}H_{20}O_4$; IR ν^{NUJ}_{OH} 3350 cm^{-1}). The bis-mesylate 11b [77%, m.p. 106–107.5°; NMR δ 2.98 ppm (s, 6H, CH_3SO_2)] and the desired β-cyanoamine 2b [19%, m.p. 149–151°; IR ν^{NUJ}_{NH} 3460, 3345, 1646 cm^{-1}, $\nu^{NUJ}_{C\equiv N}$ 2175 cm^{-1}; UV λ^{EtOH}_{max} 263.5 nm (ϵ 12,700) HCl addition, hypsochromic shift to 238 nm (ϵ 8,870); mass analysis[9] m/e 258.13762 ($C_{15}H_{18}O_2N_2$ requires 258.13682)] were prepared under the conditions described above.



10



11a R=H

11b R=SO_2CH_3

The financial support of the Science Research Council is gratefully acknowledged.

REFERENCES AND FOOTNOTES

1 Present address: Ciba-Geigy Plastics and Additives Company, Manchester M17 1WT

2 a) K.N. Houk and R.B. Woodward, J. Amer. Chem. Soc., 92 4145 (1970)
  b) K.N. Houk, L.J. Luskus and N.S. Bhacca, J. Amer. Chem. Soc., 92 6392 (1970)
  c) T. Uyehara and Y. Kitahara, Chem. and Ind., 354 (1971)
  d) H. Tanida, T. Yano and M. Veyama, Bull. Chem. Soc. Japan, 45 946 (1972)
  e) T. Sasaki, K. Kanematsu and T. Kataoka, Chemistry Letters, 1183 (1973)
  f) K.N. Houk and L.J. Luskus, J. Org. Chem., 38 3836 (1973)
  g) K.N. Houk and R.B. Woodward, J. Amer. Chem. Soc., 92 4143 (1970)
  h) S. Ito, I. Itoh, I. Saito and A. Mori, Tetrahedron Letters, 44 3887 (1974)

3 a) A.J. Baker, A.M. Chalmers, W.W. Flood, D.D. MacNicol, A.B. Penrose and R.A. Raphael, Chem. Comm. 166 (1970)
  b) A.F. Cameron and G. Ferguson, J. Chem. Soc. (B), 943 (1970)

4 K. Alder and H-H. Mölls, Chem. Ber. 89 1960 (1956); K. Alder and G. Jacobs, Chem. Ber 86 1528 (1953)

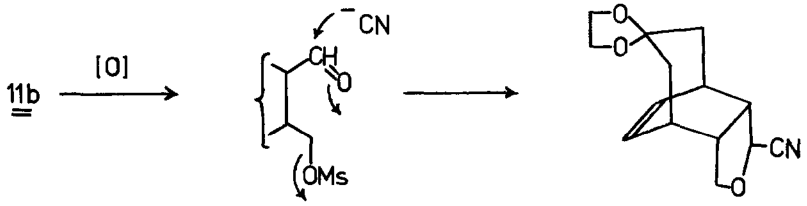
5 V.M. Micovic and M.L. Mihailovic. "Lithium Aluminium Hydride in Organic Chemistry", Serbian Academy of Sciences Monograph, Vol. 237, No. 9 (1955)

6 J.J. Bloomfield and P.V. Fennessey, Tetrahedron Letters, 33 2273 (1964)

7 M. Karplus, J. Chem. Phys. 30 11 (1959); J. Amer. Chem. Soc., 85 2870 (1963)

8 F.A.L. Anet, Tetrahedron Letters, 25 1219 (1962)

9 A minor contaminant was present formed by the mechanism:



12

(m/e 12 requires 247.12083; found 247.12024)