A Convenient Synthesis of 7-Substituted Norbornadienes

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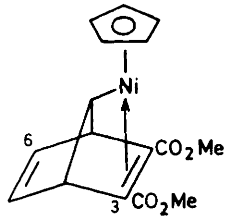
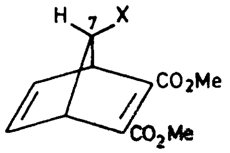
Contrary to an earlier claim, reactions of (**1**) with *m*-chloroperbenzoic acid, *N*-bromosuccinimide, and *N*-chlorosuccinimide give the diester (**15**) and the *syn*-norbornadienes (**2**), (**4**), and (**6**), respectively; reactions of (**1**) with lead tetra-acetate and iodine also proceed with retention of C-7 stereochemistry but with bromine and chlorine inversion at C-7 is increasingly dominant.

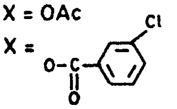
The complex (**1**), readily prepared by addition of dimethyl acetylenedicarboxylate to nickelocene,[1] was recently claimed to be a useful source of 7-substituted norbornadienes.[2] The *syn* and *anti* norbornadienols (**2**) and (**3**) were said to be formed



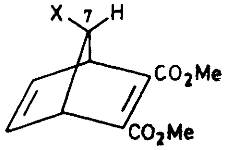
(1)



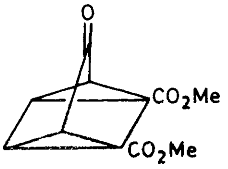
(2) X = OH
(4) X = Br
(6) X = Cl
(11) X = OAc
(14) X =



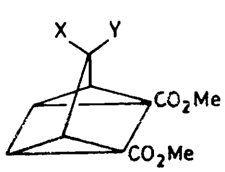
(16) X = I



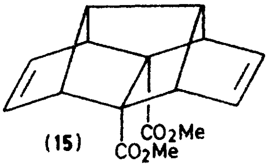
(3) X = OH
(5) X = Br
(7) X = Cl
(12) X = OAc



(8)



(9) X = H, Y = OH
(10) X = OH, Y = H
(13) X = OAc, Y = H



(15)

(68% yield, 1 : 1 ratio) upon reaction of (1) with *m*-chloroperbenzoic acid, and reaction of (1) with *N*-bromosuccinimide was claimed to give a 1 : 4 mixture of the bromides (4) and (5) (61% yield); with *N*-chlorosuccinimide (1) apparently gave a 47% yield of (6) and (7) (ratio 1 : 1).[1] We describe a reinvestigation of these reactions with conclusions that differ from those previously reported. We also describe the reactions of (1) with lead tetra-acetate, iodine, bromine, and chlorine which reaffirm the utility of (1) as a precursor of 7-substituted norbornadienes; an increasing degree of inversion accompanies cleavage of the carbon–nickel bond as the electronegativity of the halogen increases.

The alleged *syn* and *anti* isomers (2) and (3) were said to show olefinic resonance at very different shifts (δ 6.00 and 6.90, respectively). Similarly different shifts were reported for the olefinic protons in (4) and (5) (Δδ 0.7) and (6) and (7) (Δδ 0.7).[2] Since the olefinic protons in *syn* and *anti* norbornenes show Δδ values of only *ca.* 0.1 p.p.m.[3] and the olefinic protons in norbornadienes usually[3] resonate at δ > 6.5 the assignment of resonances at *ca.* δ 6.0 to the *syn* norbornadienes (2), (4), and (6) was surprising. Accordingly we attempted preparation of the norbornadienols (2) and (3) by an alternative route. Reduction of the known[4] quadricyclanone (8) ($NaBH_4$, EtOH) gave a *ca.* 1 : 1 mixture of the quadricyclanols (9) and (10) from which the individual epimers were obtained by a combination of crystallization from ether and silica chromatography. Ring opening of the quadricyclanol (9) with a trace of $Pd(OAc)_2$ in $CDCl_3$ led to a clean conversion into the norbornadienol (2), δ ($CDCl_3$) 6.73 (2H, t, *J* 2 Hz, olefinic), 4.02 (1H, m, 7-H), 3.85 (2H, m, obscured), 3.80 (6H, s, 2 × OMe), which however decomposed upon attempted chromatography over both silica and alumina (*cf.* ref. 2); isomer (2) was therefore further characterised as its acetate (11) formed by acetylation (Ac_2O/pyridine) of the crude product of quadricyclane ring-opening, δ ($CDCl_3$) 6.84 (2H, dd, *J* 2 and 2.5 Hz, olefinic), 4.68 (1H, t, *J* 1.75 Hz, 7-H), 3.98 (2H, ddd, *J* 2, 2.5, and 1.75 Hz, bridgehead), 3.81 (6H, s, 2 × OMe), and 2.01 (3H, s, OCOMe). Ring-opening of the quadricyclanol (10) proceeded less cleanly and was best carried out by stirring (10) with palladised charcoal in ethyl acetate[5] at 20 °C. This gave a mixture of starting material, unidentified products, and (3); the ^1H n.m.r. spectrum of the crude product showed a well defined resonance at δ 6.78 (2H, m) assigned to the olefinic protons of (3). Acetylation of this product (Ac_2O/pyridine) followed by silica chromatography gave the *anti*-norbornadienyl acetate (12) (38%), δ ($CDCl_3$) 6.72 (2H, td, *J* 2 and *ca.* 0.6 Hz, olefinic), 4.81 (1H, m, 7-H), 4.02 (2H, td, *J* 2 and 1.85 Hz, bridgehead), 3.80 (6H, s, 2 × OMe), and 1.99 (3H, s, OCOMe). The acetate (12) was more efficiently prepared (85%) by ring-opening (Pd–C/$MeCO_2Et$, reflux) of the acetate (13). The olefinic resonance in (11) is a well defined double doublet unaffected upon irradiation of the C-7 proton whereas the olefinic protons in (12) appear as a triplet of doublets owing to coupling to the C-7 proton (*J ca.* 0.6 Hz). The well established stereospecificity of this long-range coupling[6] allows firm assignment of stereochemistry to the epimeric norbornadienes.† The norbornadienols (2) and (3) prepared as above differ from the oxidation products of (1) in being unstable to chromatography, and in the chemical shifts of their olefinic protons. Repetition of the reaction of (1) with *m*-chloroperbenzoic acid gave a complex product mixture the ^1H n.m.r. spectrum of which showed olefinic triplets at δ 6.73, 6.90, and 6.05 (ratio *ca.* 4 : 4 : 1). Extraction of the crude product with sodium hydrogen carbonate solution removed the signal at δ 6.73,‡ and acetylation of the crude product (Ac_2O/pyridine) left the signals at δ 6.90 and 6.05 unchanged but shifted that at 6.73 to 6.84. Chromatography of the acetylated product gave the acetate (11) (9%) (δ 6.84), the *m*-chlorobenzoate (14), m.p. 68—71 °C (14%) (δ 6.90), and the known[7] compound (15) (3%) (δ 6.05). Compound (15) was also obtained (10%) together with (4) (16%) from the reaction of (1) with *N*-bromosuccinimide as well as from several other reactions of (1) (see below); it had properties identical with those reported[7] and gave a satisfactory mass spectrum. Thus the allegedly different products obtained from (1) and assigned structures (2), (4), and (6) are in fact the same diester (15) presumably derived from (1) by oxidative removal of nickel with coupling of the cyclopentadienyl and norbornadienyl moieties followed by an intramolecular Diels–Alder reaction. Moreover the products claimed to be (3), (5), and (7) are in fact their epimers (2), (4), and (6). The reactions of (1) with *m*-chloroperbenzoic acid, *N*-bromosuccinimide, and *N*-chlorosuccinimide are, contrary to the earlier claim, quite stereoselective but proceed in poor yield.

We have found that reaction of (1) with lead tetra-acetate (CH_2Cl_2, 20 °C) also proceeds with retention of C-7 stereo-

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† All assignments of *syn*–*anti*-stereochemistry made herein are based on this long range coupling which was clearly observed using a Jeol FX90Q spectrometer and 8-fold enhanced digital resolution; the highly resolved multiplets observed in expanded spectra were appropriately simplified in double irradiation experiments.

‡ The decomposition of this norbornadienol with sodium hydrogen carbonate may explain the failure of the original authors to observe this product.

chemistry giving the *syn*-acetate (**11**) (37%) and (**15**) (6%). Likewise with iodine in dichloromethane (−78 °C to 20 °C) (**1**) gives the *syn*-iodide (**16**) (51%) and (**15**) (28%). With bromine (CH_2Cl_2, −78 °C), however, the carbon–nickel bond is cleaved with predominant inversion of stereochemistry, a 1 : 2.3 mixture of the epimers (**4**) and (**5**) being formed (53% yield) together with (**15**) (18%). This trend continues in the reaction of (**1**) with chlorine (CH_2Cl_2, −78 °C) which gave (**6**) and (**7**) (62% yield; ratio *ca.* 1 : 10). An increasingly important oxidation-induced S_N2 reaction,[8] competing with an oxidative addition–reductive elimination process at the metal[9] may explain these results. Alternatively, the product of apparent inversion at C-7 may arise by electrophilic attack at C-6 followed by migration of C-3 to C-5 and loss of the metal.

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