Novel Synthesis of Benzotropolones

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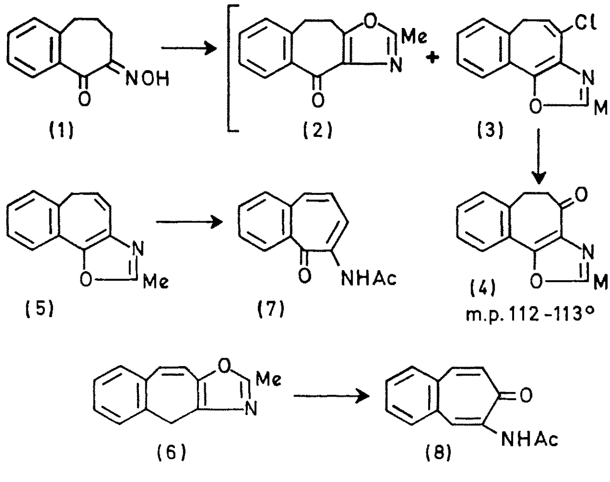
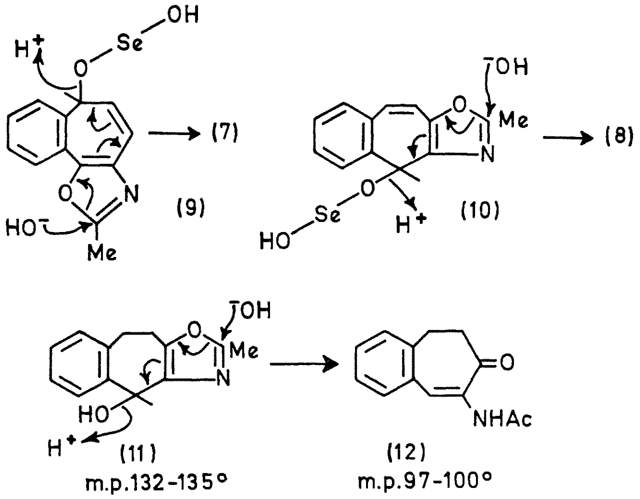
Summary The oxazolo-benzocycloheptenes (**5**) and (**6**), easily available through earlier work,[1] are smoothly converted by SeO_2 into the acetamido-benzotropones (**7**) and (**8**) respectively, which in turn can be hydrolysed to the corresponding benzotropolones.

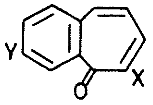
THE existing syntheses of a $\alpha\beta$-benzotropolone have the limitations of either giving poor yields[2a,c] or, since hydrogenolysis[2b] or reduction[3] is the last step, of not being adaptable to the synthesis of $\alpha\beta$-benzotropolones bearing reducible substituents (*e.g.* a nitro-group) on the benzene ring. An *a posteriori* introduction of such groups by electrophilic substitution on $\alpha\beta$-benzotropolone itself does not appear to be possible.[4]



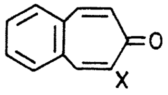
As we reported earlier,[1] the reaction of α-oximino-benzosuberone (**1**) with Ac_2O–AcOH–HCl (misleadingly still called "Beckmann's Mixture") leads smoothly to a 5 : 2 mixture of oxazoles (**2**) and (**3**).

Treatment of this mixture with conc. H_2SO_4 at room temperature gives as the sole product the ketone (**4**), which after reduction with $NaBH_4$ and dehydration of this alcohol (Me_2SO–H_2SO_4; 200°) affords the olefin (**5**).† The facility of this sequence is such that (**5**) may be produced from benzosuberone in an overall yield of 65%. An isomeric olefin (**6**) can be obtained from (**2**) (i, $NaBH_4$; ii, $SOCl_2$; iii, 160°).





X	Y	m.p.
NHAc	H	75-76°
NH2		88-89°
OH		81·5-84°
NHAc	Cl	177-179°
NH2		140-144°
OH		150-152°
NHAc	NO_2	205-206°
NH2		200-205°
OH		228-230°



X	m.p.
NHAc	132°
NH2	105-109°
OH	156-159°

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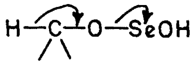
† Complete elemental analyses, i.r., u.v., n.m.r., and low resolution mass spectra were accumulated on all new compounds discussed. The structures were deduced by considering these data as well as data obtained on analogues and subsequent transformation products.

We have discovered recently that with one mole of SeO_2 in refluxing dioxan or xylene, olefins (**5**) and (**6**) are quantitatively converted into the corresponding acetamidobenzotropones (**7**) and (**8**). These reactions are surprising when one considers the normal tendency of SeO_2 to convert suitably activated methylene groups to ketones, a pathway followed by the dibenzocycloheptatriene analogues of (**5**) and (**6**).[5]

We suggest that in our cases, the Se^{II}-intermediates usually postulated for the ketone-forming reactions are also formed [(**9**), (**10**)] but rather than undergoing Se–O fission to the respective ketones, they decay *via* replacement reactions involving C–O fission, as shown.



We have found a reasonable analogy for this type of oxazole ring opening in the acid-catalysed (H_2SO_4–Me_2SO; 180°; 5 mins) rearrangement of (**11**) to (**12**), the dihydroderivative of (**8**).

Hydrolysis (2N-HCl; 100°; 4 hr) of the acetamidobenzotropones (**7**) and (**8**) gave (again quantitatively) the corresponding benzotropolones, the physical properties of which (m.p., u.v.,) were identical to those respectively reported[1,6] for $\alpha\beta$- and $\beta\gamma$-benzotropolone. Use of milder hydrolytic conditions (HOAc–conc. HCl, 4 : 1; 100°; 10 min) enabled the intermediate amino-benzotropones[‡] to be obtained.

Our synthetic scheme could easily be adapted to the new 3-nitro- and 3-chloro-$\alpha\beta$-benzotropolones.[7] In these cases the transformations from the oximino-ketones to the mixed oxazoles were effectively quantitative [*cf.* 70% for (**1**) → (**2**) + (**3**)].

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[‡] An alternative way of obtaining amino-benzotropolones consisted in the fusing of benzotropolones with ammonium acetate (120—150°).

[1] Eugene Galantay, Clarence Hoffman, and Nicholas Paolella, *Chem. Comm.*, 1970, 274.

[2] (a) J. W. Cook and A. R. Somerville, Nature, 1949, **163**, 410; (b) J. W. Cook, A. R. M. Gibbs, R. A. Raphael, and A. R. Somerville, *J. Chem. Soc.*, 1952, 603; (c) T. Nozoe, Y. Kitahara, and T. Ando, *Proc. Japan Acad.*, 1952, **27**, 107; (*Chem. Abs.*, 1952, **46**, 5034).

[3] G. Read and V. M. Ruiz, *Chem. Comm.*, 1969, 735.

[4] M. Hoshiro and S. Ebine, *Bull. Chem. Soc. Japan*, 1968, **41**, 2949, and literature cited therein.

[5] *E.g.* J. W. Cook, G. Dickson, and J. D. Loudon, *J. Chem. Soc.* 1947, 746.

[6] D. S Tarbell, G. P. Scott, and A. D. Kemp, *J. Amer. Chem. Soc.*, 1950, **72**, 379.

[7] The 3-nitrobenzosuberone starting material was obtained as described by P. A. Smith and W. L. Berry, *J. Org. Chem.*, 1961, **26**, 27. 3-Chlorobenzosuberone could be obtained from the former *via* a Sandmeyer sequence or through direct chlorination of benzosuberone in the presence of large amounts of $AlCl_3$ (E. Galantay, U.S. Pat. 3,458,522).