Generation and inter- and intra-molecular trapping of isoindenones (inden-2-ones)

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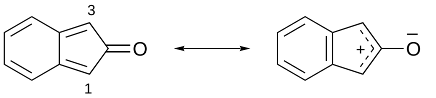
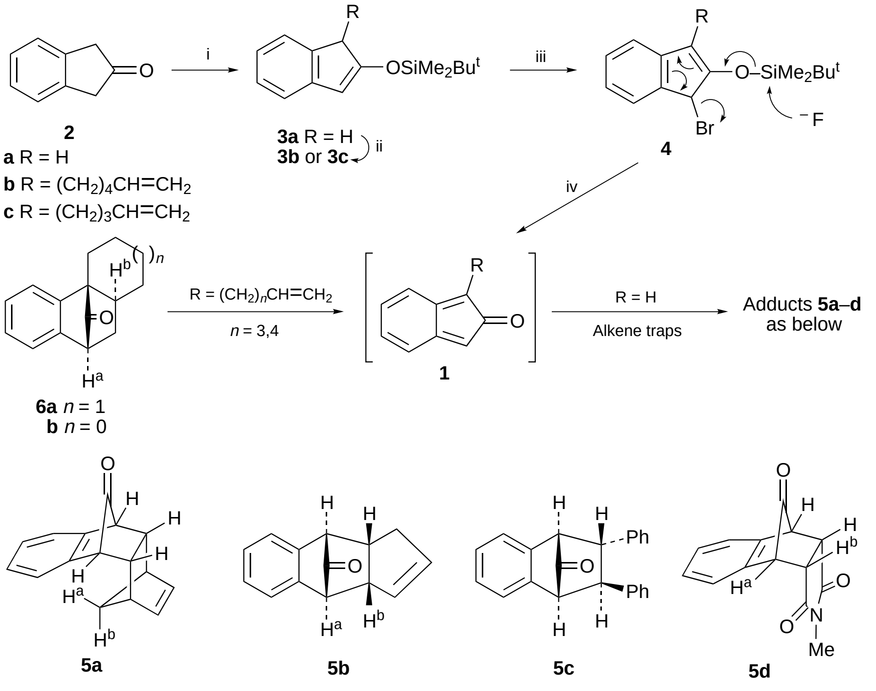
Inden-2-one and some simple derivatives are smoothly generated by reaction of caesium fluoride with 1-bromo-2-*tert*-butyldimethylsilyloxyindenes and they can be efficiently trapped in both intra- and inter-molecular additions; the intramolecular additions proceed with *exo*-addition of the tether, in contrast to the intermolecular additions and intramolecular additions to 2-benzopyran-3-ones.

Isoindenones (inden-2-ones) are of interest as derivatives of two very reactive dienes, *o*-quinodimethane and cyclopentadienone; resonance involving the oxyallyl structure is also a possibility (Scheme 1).

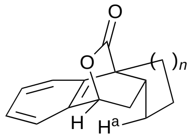


Scheme 1

From the MO point of view the HOMO–LUMO energy gap is expected to be particularly small for isoindenones as it is for cyclobutadienes and other antiaromatic species.[1] We have shown that 1,3-diphenylinden-2-one is readily generated by dissociation of its dimer,[2] and that it is efficiently trapped by a range of alkenes in Diels–Alder reactions.[2,3] We further showed that the potentially more synthetically useful parent system (Scheme 1) could be generated from 1,3-dibromoindan-2-one by reaction with copper powder or sodium iodide, but generation/trapping was inefficient (8% yield of adduct with cyclopentadiene using copper powder in boiling benzene).[4] We now describe an efficient method of generating and trapping simple inden-2-ones **1** (Scheme 2). Commercially available indan-2-one **2** was converted into enol silyl ether **3a** (64%). This could be alkylated to give either **3b** or **3c** in 61 and 75% yield, respectively. With *N*-bromosuccinimide in refluxing CCl_4 and irradiation with a sun lamp (500 W), **3b** and **3c** gave **4b** (75%) and **4c** (71%) respectively. Slow addition of **4b** (syringe pump) to a refluxing mixture of MeCN and CsF gave the adduct **6a** in good yield (66%).† The adduct showed a characteristic high frequency carbonyl stretch at 1778 cm^{-1}. In the ^1H NMR spectrum a shielded resonance such as that found for related *endo*-2-benzopyran-3-one adducts like **7** (n = 1 or 2) was absent.[5] A similar adduct **6b** was obtained in 73% yield† from **4c** but again the NMR spectrum showed the absence of a shielded proton. Since modelling[6] suggested a very similar location of the proton H^a with respect to the aromatic ring in the (hypothetical) *endo*-chain adducts from the isoindenones and the known *endo*-chain adducts of the 2-benzopyran-3-ones,[5] an *exo*-chain addition to the isoindenones seemed likely. The assignment was reinforced by Baeyer–Villiger oxidation of **6b** to **8** (79% yield) which also failed to show a shielded proton, although if **8** were an *endo*-chain adduct the location of H^a with respect to the aromatic ring would be very similar to that in **7** (n = 1). Finally the stereochemistry of **6a** was confirmed by



Scheme 2 *Reagents and conditions*: i, LDA (1.4 equiv.), THF, −78 °C, 10 min; then Bu^tMe_2SiCl (1 equiv.), −78 °C, 10 min, then HMPA, −78 °C, 15 min, allowed to warm to 20 °C; ii, BuLi (1 equiv.), THF, 0 °C, 10 min, then iodo-alkene (1.7 equiv.), HMPA (1 ml g^{-1} of base) added, allowed to warm to 20 °C and stirred for 10 min; iii, NBS, CCl_4, AIBN, reflux, sun lamp (500 W), 2 h; iv, CsF (2 equiv.), MeCN, reflux, bromo compound added in MeCN (10 ml mg) *via* syringe pump, 4 h



$n = 2$, $\delta H^a = 0.68$
$n = 1$, $\delta H^a = 0.74$

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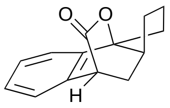

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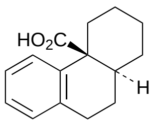

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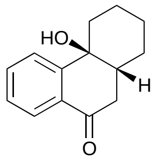

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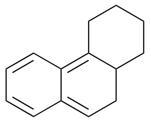

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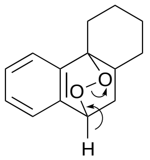

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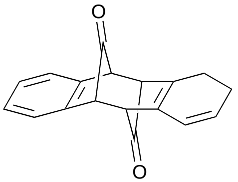

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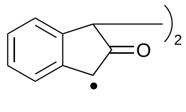

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modified Haller–Bauer cleavage[7] to give the *trans* acid **9** (62%), mp 164.5–167 °C (lit.,[8] mp 162 °C: the *cis* acid has mp 143 °C). Accordingly, and in contrast to the IMDA additions to 2-benzopyran-3-ones, the inden-2-one additions proceed with clean *exo*-selectivity.

The synthetic utility of products of type **6a** is illustrated by the foregoing cleavage of **6a** to **9** and photodecarbonylation of **6a** in the presence of oxygen; **6a** in benzene saturated with oxygen was irradiated through silica with a MP 125 W mercury lamp with slow passage of oxygen through the solution to give the hydroxy ketone **10** (70% yield). This probably arises *via* the expected *o*-quinodimethane **11** and the *endo* peroxide **12** in the manner indicated by the arrows in **12**. An alternative mechanism for the decomposition of related peroxides involves homolytic cleavage of the O–O bond.[9] Such a route is also possible for our example.

This route to inden-2-ones appears general as it can be applied to the parent compound **1a** (Scheme 2). Allylic bromination of **3a** gave **4a** (62%) which, upon reaction with CsF in the presence of norbornadiene (10 equiv.), gave the *endo* norbornadiene adduct **5a** (68% yield). The related norbornene adduct was obtained in a similar way (43% yield), as was the cyclopentadiene adduct **5b** (49% yield). Trapping with *trans*-stilbene was less satisfactory, giving **5c** in 8% yield. Trapping with *N*-methylmaleimide gave only 22% yield of **5d**, although here there is a problem isolating the adduct from a considerable amount of polymeric material derived from the dienophile, which streaked extensively upon chromatography.

In view of the *exo*-chain addition observed for the intramolecular reactions, the exclusive *endo*-addition† in the intermolecular reactions is noteworthy. Evidence for the *endo* configuration of the intermolecular adducts includes the value of the vicinal coupling constant J_{HaHb} (see structures **5b** and **5d**, Scheme 2). This is *ca*. 4 Hz, as expected for an *endo*-adduct (ϕ_{ab} *ca*. 40°) rather than < 0.5 Hz expected for an *exo*-adduct (ϕ_{ab} *ca*. 80°). Additional evidence is provided by the strong shielding of *endo*-disposed groups, *e.g.* H^a in the norbornadiene adduct **5a** resonates at $\delta -0.64$ and H^b at $\delta +0.47$. In the corresponding norbornene adduct, H^a and H^b appear at $\delta -0.72$ and $+0.34$, respectively. In the *N*-methylmaleimide adduct **5d** the NMe resonance is shielded (δ 2.2) in comparison with the methyl in *N*-methylmaleimide (δ 3.07). The contrasting stereochemistry of the intra- and inter-molecular additions is presumably due to conformational factors in the connecting chain. Work on this question is continuing.

In the absence of a trap, **1** (R = H) gives the dimer **13**† of a formal $\pi^4s{+}\pi^4s$ addition. The parent isoindenone therefore dimerises in the same way as its diphenyl derivative. As in that case[2] a biradical intermediate like **14** is likely to be involved in forming this orbital symmetry forbidden product.

In summary, we have provided an efficient way of generating simple inden-2-ones and trapping them both intra- and intermolecularly. In addition to their theoretical interest, these molecules are useful intermediates in making benzonorbornenones and hence products like **9** and **10**. Regioselective Haller–Bauer-like cleavage,[7] in combination with the clean *exo*-selective addition of the tether observed in the IMDA additions, is clearly of potential use in the synthesis of diterpenoids like pisiferic acid which have the *trans*-BC ring junction.[10]

Footnotes

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† For the intramolecular additions the TLC and 300 MHz ^{1}H NMR spectra of the crude reaction products failed to reveal any *endo* addition product. Similarly, the adduct fraction obtained by chromatography indicated a single adduct in both cases. The intermolecular additions proceeded somewhat less cleanly and the presence of some 5–10% of *exo*-adduct cannot be excluded. In the preparation of **5a** without the use of slow addition (syringe pump), the spectra of the crude product clearly showed the presence of the dimer **13**.

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