Tetrahedron Letters,Vol.27,No.43,pp 5253-5254,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

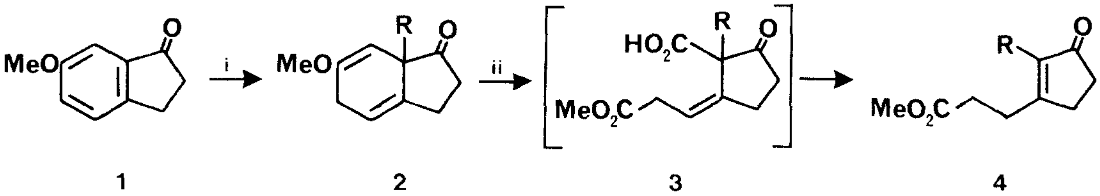
A NEW USE OF THE BIRCH REDUCTION.
SYNTHESIS OF 2,3-DISUBSTITUTED CYCLOPENT-2-EN-1-ONES FROM 6-METHOXYINDANONE

Christopher J. Moody* and Judy Toczek
Department of Chemistry, Imperial College of Science and Technology,
London SW7 2AY, U.K.

Summary: Reductive alkylation of 6-methoxyindanone (**1**) gives the dihydroindanones (**2**), ozonolysis and oxidation of which leads directly to 2,3-disubstituted cyclopent-2-en-1-ones (**4**).

The metal-liquid ammonia reduction (Birch reduction) of aromatic compounds such as alkyl- and alkoxy-benzenes has found wide application in organic synthesis over many years, and more recently it has been shown that the reduction of the aromatic ring of aromatic esters and ketones, traditionally regarded as unsuitable substrates, is also possible.[1] Optimum conditions for the reduction and reductive alkylation of aromatic ketones were first established for acetophenone and its methoxy-derivatives,[2] and we have made use of similar reductive alkylations of indan-1-ones in the synthesis of novel tricyclic [10]annulenes.[3] We now report a new use of the Birch reduction as a key step in the conversion of the readily available aromatic ketone, 6-methoxyindanone (1), into 2,3-disubstituted cyclopent-2-en-1-ones.

This totally new approach to cyclopentenones[4] is based on selective ozonolysis of the dihydroindanones (2) obtained by reductive alkylation of the ketone (1) (Scheme). Thus addition of 6-methoxyindanone (1)[5] and tert-butanol in tetrahydrofuran (THF) to a preformed solution of potassium in liquid ammonia at -78°C, followed by addition of lithium bromide and quenching with an alkyl halide in the usual way,[3] gave the dihydroindanones (**2**), which without purification were immediately ozonised. As expected, the vinyl ether double bond in (**2**) was selectively cleaved; direct oxidative work up was unsatisfactory, but addition of zinc and acetic acid gave an aldehyde which was immediately oxidised further with Jones' reagent. The resulting β-keto acids (**3**) underwent spontaneous decarboxylation with concomitant movement of the exocyclic double bond into conjugation with the carbonyl to give the desired cyclopentenones (**4**). Low overall yields were obtained with MeI and EtI as alkylating agents, and this presumably reflects their lower reactivity in the alkylation step.



Scheme. Reagents: i, K, NH_3, ^tBuOH, THF, -78°C; LiBr, RX; ii, O_3, MeOH; Zn, AcOH, then Jones' reagent.

Alkylating agent, RX	Overall isolated yield of (4) (%)
MeI	11
EtI	9
$H_2C=CHCH_2I$	30
$EtC\equiv CCH_2Br$	23
$EtC\equiv CCH_2I$	29
$Me(CH_2)_4C\equiv CCH_2Br$	25
$PhCH_2Br$	44
EtO_2CCH_2Br	21

Thus the 2,3-disubstituted cyclopent-2-en-1-ones (**4**) are available in just two operations (reduction/alkylation and ozonolysis/oxidation) comprising 6 reaction steps from 6-methoxyindanone in, with reactive alkylating agents, moderate overall yield. The application of this new route to cyclopentenones to the synthesis of the naturally occurring cyclopentenoid fatty acid, tetrahydrodicranenone B, will be reported elsewhere.[6]

We thank Glaxo Group Research, Greenford for their generous support (fellowship to J.T.), and Drs. S.M. Roberts and H.C. Gibbard for helpful discussions.

References

1. For an excellent up to date review see J.M. Hook and L.N. Mander, Nat. Prod. Rep., 1986, **3**, 35.
2. M. Narisada and F. Watanabe, J.Org.Chem., 1973, **38**, 3887.
3. R. McCague, C.J. Moody, and C.W. Rees, J. Chem. Soc., Perkin Trans. **1**, 1983, 2399; Z. Lidert, R. McCague, C.J. Moody, and C.W. Rees, ibid., 1985, 383; H.C. Gibbard, C.J. Moody, and C.W. Rees, ibid., 1985, 735.
4. B.M. Trost, Chem. Soc. Rev., 1982, **11**, 141; L.A. Paquette, Top. Curr. Chem., 1984, **119**, 1; S.C. Welch, J.-M. Assercq, and J.-P. Loh, Tetrahedron Lett., 1986, **27**, 1115, and references therein.
5. H.O. House and C.B. Hudson, J. Org. Chem., 1970, **35**, 647.
6. C.J. Moody, S.M. Roberts, and J. Toczek, J. Chem. Soc., Chem. Commun., in press.

(Received in UK 22 August 1986)