

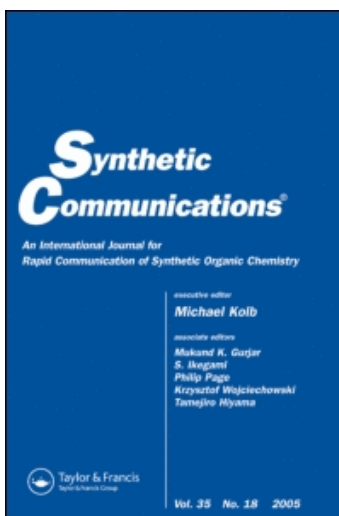
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STEREOSPECIFIC SYNTHESIS OF  
ENDO-6-ARYL-2-OXOBICYCLO [3.3.1] NONANES

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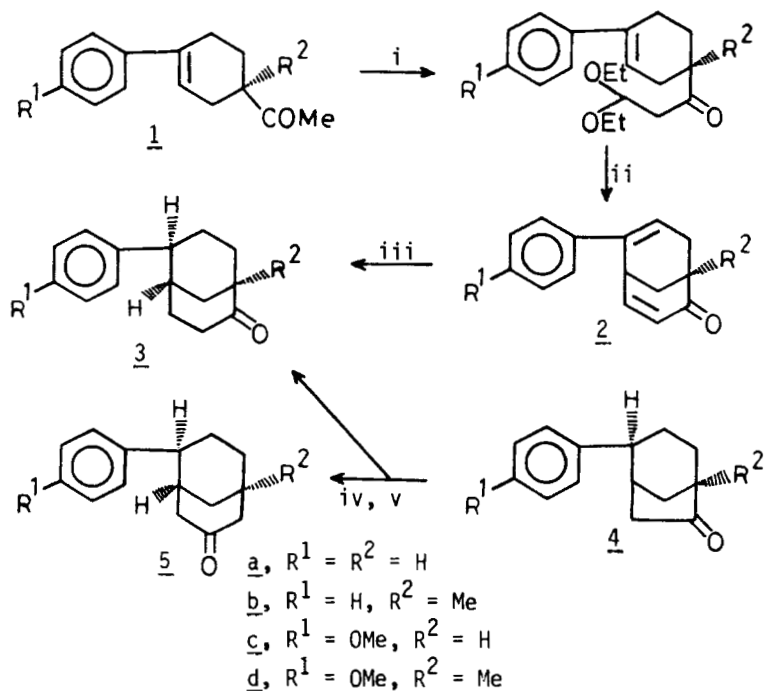
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*ABSTRACT: Two alternate synthetic routes to endo-6-aryl-2-oxobicyclo[3.3.1]nonanes (3a-d) by stereospecific catalytic hydrogenation of the easily accessible 6-arylbicyclo[3.3.1]nona-3,6-dien-2-ones (2a-d), and regioselective homologation of endo-2-aryl-6-oxobicyclo[3.2.1]octanes (4a-d) are described.*

The bicyclo[3.3.1]nonane ring system<sup>1</sup> has attracted considerable interest<sup>2-7</sup>. Recently, we have described<sup>8,9</sup> a simple general synthesis of 6-aryl substituted bicyclo[3.3.1]nonadienones (2a-d) from the corresponding  $\gamma,\delta$ -unsaturated methyl ketones (1a-d) through an efficient diethoxymethylation and cyclization route. In this communication, we report two alternate routes to the endo-6-aryl substituted bicyclo[3.3.1]nonanes (3a-d) by stereospecific catalytic hydrogenation of the dienones (2a-d), and regioselective homologation of the easily accessible 2-endo-aryl substituted bicyclo[3.2.1]octanones (4a-d)<sup>10</sup>.

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i,  $CH(OEt)_3, BF_3 \cdot OEt_2, (iPr)_2NEt, CH_2Cl_2$ ; ii,  $HClO_4-C_6H_6$ ; iii,  $H_2/Pd-C(10\%), EtOH$ ; iv,  $N_2CHCO_2Et, Et_3O^+BF_4^-$ ; v,  $HOAc, HCl, H_2O, \Delta$ .

Catalytic hydrogenation (Method A) of the dienones (2a-d) over palladium charcoal (10%) in ethanol produced the endo-6-aryl ketones (3a-d) in high yields as the only isolable products. The stereochemistry of these ketones was assigned by their direct synthesis from the known bicyclo[3.2.1]octanes (4a-d). Thus, reactions of (4a-d) with ethyl diazoacetate in the presence of triethyloxonium fluoborate<sup>11,12</sup> followed by hydrolytic decarboxylations of the resulting crude  $\beta$ -keto esters with aqueous acetic acid-hydrochloric acid (Method B) produced the regioisomeric mixtures of the ketones (3a-d) and (5a-d) in  $\sim 75-80 : 25-20$  as indicated by G.L.C. and  $^1H$  N.M.R. The pure major regioisomers (3a-d) were separated by column chromatography or by crystallization and were found to be identical with the samples prepared from the dienones (2a-d).

### Experimental

Melting points were recorded on a Mettler FP-16 instrument. Melting Points are not corrected. IR spectra of solids (KBr) and liquids (neat) were recorded on a Perkin-Elmer model PE298.  $^1\text{H}$  N.M.R spectra were recorded at 60 MHz on Varian Associates T-60A for solutions in  $\text{CCl}_4$  or  $\text{CDCl}_3$ , with  $\text{SiMe}_4$  as internal standard. Analytical GLC was performed on a Hewlett-Packard Model 5730A chromatograph using UCW-982 (20ft x  $\frac{1}{8}$ in) column. Solid compounds were recrystallized from light petroleum (b.p. 40-60°C). Column chromatography was performed on neutral alumina using aluminium oxide 'standardised for chromatographic analysis acc. to Brockmann' (B.D.H., India). Elemental analysis was performed in this laboratory by Mr. P.P. Bhattacharya, and the differences with the calculated values are within C  $\pm$  0.25, H  $\pm$  0.19.

### endo-6-Phenyl-2-oxobicyclo[3.3.1]nonane 3a; Method A :

#### General Procedure :

A solution of the dienone (2a) (100 mg, 0.47 mmol) in ethanol (5 ml) was hydrogenated at room temperature and pressure in presence of 10% Pd-C (30 mg). After 2 h the hydrogenation was complete and the solution was filtered off and evaporated in vacuo to furnish (3a) (90 mg, 88%).

#### Method B : General Procedure :

To a cooled (5-10°C) solution of the bicyclooctanone (4a) (650 mg, 3.25 mmol) in dry methylene chloride (20 ml) was added a solution of triethyloxonium fluoborate (2 g, 9.17 mmol) [prepared from freshly distilled borontrifluoride ether (10 ml) and epichlorohydrin (5ml) in ether (20 ml)] in methylene chloride (10 ml) with continuous stirring under nitrogen. Immediately after, rapid dropwise addition of ethyl diazoacetate (1.0 g, 8.77 mmol) was commenced. Addition was regulated such that the solution temperature was maintained in the range of 15-25°C. After stirring for an additional 3 h, the reaction mixture was added

Table : Physical and spectral data of endo-6-Aryl-2-oxobicyclo-  
[3.3.1]nonanes (3a-d).

Com- pound	Yield (%)	m.p. (0°C)	I.R. ( $\text{cm}^{-1}$ )	$^1\text{H N.M.R. } (\delta)$	Elemental analysis
<u>3a</u>	88 <sup>a</sup> 40 <sup>b</sup>	oil	1720	1.06-3.00(m, 13H); 7.00-7.33(m, 5H);	C, 83.82 H, 8.54%
<u>3b</u>	93 <sup>a</sup> 50 <sup>b</sup>	52-53	1690	1.0(s, 3H); 1.23- 3.03(m, 11H); 7.0-7.26(m, 5H)	C, 84.34 H, 8.9%
<u>3c</u>	90 <sup>a</sup> 45 <sup>b</sup>	106	1710	1.1-3.03(m, 12H); 3.75(s, 3H); 6.57-7.20(m, 4H)	C, 78.53 H, 8.44%
<u>3d</u>	92 <sup>a</sup> 56 <sup>b</sup>	65	1705	1.03(s, 3H); 1.2- 3.03 (m, 11H); 3.73(s, 3H); 6.6-7.13(m, 4H)	C, 79.03 H, 8.66%

a : Method A,

b : Method B.

cautiously to a solution of sodium bicarbonate (10%, 40ml) and stirred until the evolution of  $\text{CO}_2$  ceases. The organic layer was separated and the aqueous layer was washed with methylene chloride (2 x 20 ml). The combined methylene chloride solution was washed with water, dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to leave a yellow residue which was distilled to yield a pale yellow oil, b.p.  $120-130^\circ\text{C}$  at 0.5 mm of Hg. This oil was then refluxed with a mixture of acetic acid (5 ml), hydrochloric acid (3 ml) and water (3 ml) at  $140^\circ\text{C}$  (oil bath) for 2 h under nitrogen. The reaction mixture was cooled, and poured into ice-water and extracted with ether (3 x 25 ml). The ether extract was washed with water, 5% sodium bicarbonate solution, water, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated to leave a yellow residue which was purified by column chromatography (neutral alumina, light petroleum) to afford (3a).

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