

SYNTHESIS OF CARBAZOLES VIA 2-VINYLIINDOLES.

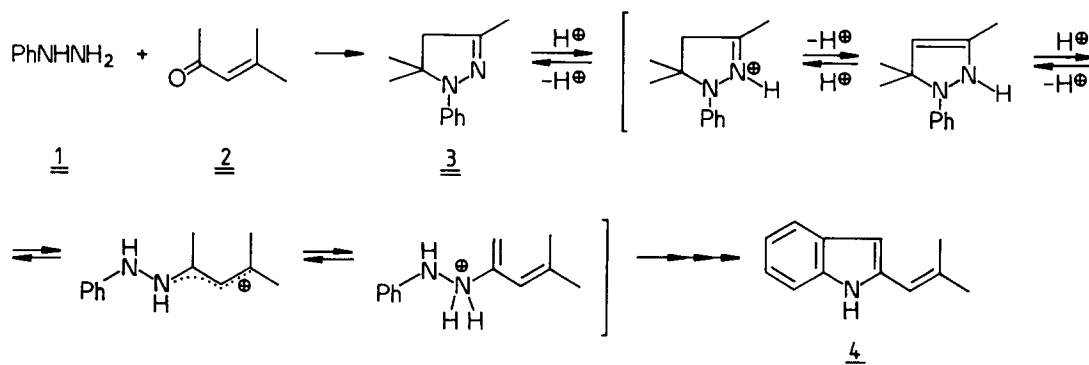
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ABSTRACT: 2-Vinyliindoles are obtained from the Fischer indolization of  $\alpha,\beta$ -unsaturated ketones. Heating 2-(2-methylpropenyl)indole (4) with the Vilsmeier reagent (DMF/ $\text{POCl}_3$ ) gave 2-methylcarbazole in good yield, presumably via an electrocyclic ring closure of a hexatrienic intermediate.

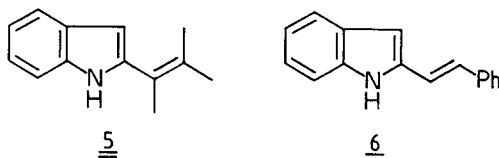
3-Vinyliindoles have been extensively used in the synthesis of carbazoles and related systems.<sup>1-4</sup> Certain 2-vinyliindoles have also been used for such purposes,<sup>3-8</sup> particularly in connection with the synthesis of *Aspidosperma* alkaloids.<sup>9-11</sup> 2-Vinyliindoles without electronwithdrawing groups on the vinylic moiety or N-unsubstituted 2-vinyliindoles have only rarely been utilized<sup>11-13</sup> due to their relative inaccessibility.

In spite of the fact that  $\alpha,\beta$ -unsaturated ketones repeatedly have been reported to be unsuccessful partners in attempted Fischer indolizations,<sup>14-16</sup> we decided to make further trials since we felt that at least some of the intermediate 2-pyrazolines might undergo acid induced rearrangement under suitable reaction conditions. This was indeed found to be the case. A representative example (Scheme 1) is the synthesis<sup>17</sup> of 2-(2-methylpropenyl)indole (4) from phenylhydrazine (1) and mesityl oxide (2). The 2-vinyliindole 4 is thus quickly

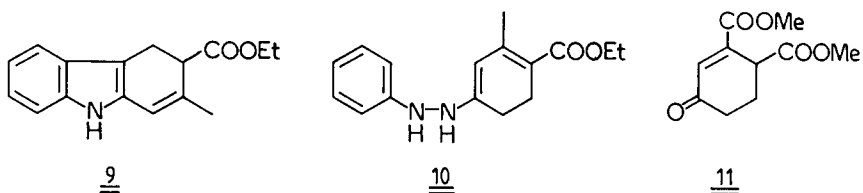
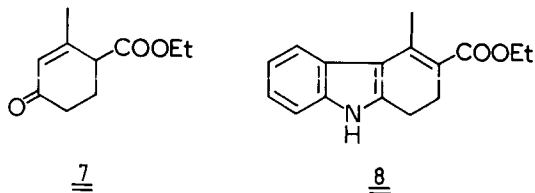


Scheme 1

obtained in a reasonable yield from cheap starting materials without the need of isolation or purification of the intermediate 2-pyrazoline 3. Related compounds such as 2-(1,2-dimethylpropenyl)indole (5) and 2-styrylindole (6)<sup>18</sup> could be prepared in similar yields. Compound 4 has previously been prepared by several routes which are lengthy or involve more sophisticated and/or expensive reagents.<sup>19-21</sup>



In some related experiments it was found that ethyl 2-methyl-4-oxo-2-cyclohexene-1-carboxylate (7, Hagemann's ester),<sup>22</sup> readily yielded the carbazole derivative 8 when heated with phenylhydrazine (1) in acetic acid. The 1,2-dihydrocarbazole 8 has previously been prepared by a lengthy route<sup>23</sup> (which we could not reproduce) involving the alkylation of ethyl acetoacetate with 2-(2-tosyloxyethyl)indole. The reported PMR data are however in good agreement with those of our compound. The structure of 8 was finally corroborated by conversion to 4-methylcarbazole.<sup>24</sup>



Theoretically the phenylhydrazone of 7 could cyclize at position 3 (as observed) or at position 5, which would have given rise to a 2-methyl-3-carbethoxydihydrocarbazole such as 9. The regioselectivity observed can be explained in terms of conjugation with the ester carbonyl group in the crucial intermediate<sup>25</sup> 10 in the Fischer indolization. Interestingly no regioselectivity was observed<sup>7</sup> in the indolization of the phenylhydrazone of 11. In this case the intermediates on both reaction pathways will benefit from conjugation with ester groups.

Treatment of the 2-vinylindole 4 with the Vilsmeier reagent,<sup>26</sup> DMF/ $\text{POCl}_3$ , gave the indolenine 12, which was readily hydrolyzed (Scheme 2) to the 3-formylindole 13. Heating of the DMF solution of 12 gave, presumably via 14, rise to 2-methylcarbazole<sup>27</sup> 15 in high



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17. A mixture of 1, 43.3 g (0.4 mol), 2, 39.3 g (0.4 mol) and HOAc (25 drops) was heated on a water-bath for 1 h. The water formed was separated and the residue mixed with PPA (150 ml). After heating (125 °C, 20 min), the mixture was poured into NH<sub>3</sub> (aq, 10%), and extracted with ether. The ethereal extracts were washed with H<sub>2</sub>O, dried (MgSO<sub>4</sub>) and concentrated. Treatment of the residue with hexane induced crystallization. The crystals were collected and washed with cyclohexane to give 4, 18.2 g (26%). Mp 104-105 °C (lit. 103-105 °C).<sup>20</sup> IR (KBr): 3390 cm<sup>-1</sup>. PMR (DMSO-d<sub>6</sub>) δ 1.8 (3H, s), 1.9 (3H, s), 6.2 (1H, s), 6.3 (1H, s), 7.1 (4H, broad m), 10.7 (1H, broad s). MS: 171(M<sup>+</sup>).
18. (a) This well-known<sup>18b</sup> compound has been prepared by a similar<sup>18c</sup> procedure (see also refs 18d and 18e for papers of related interest).  
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