REISSERT COMPOUND STUDIES. XXXVIII. PRELIMINARY OBSERVATIONS ON 3,4-DIHYDRO-β-CARBOLINE+

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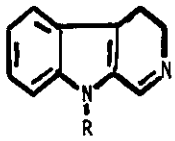
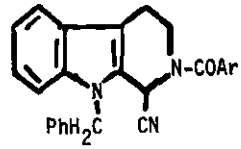
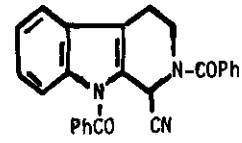
Abstract - 3,4-Dihydro-β-carboline and its 9-benzyl derivative have been converted to Reissert compounds. The anion of these Reissert compounds has been alkylated with methyl iodide. A compound with great potential as an intermediate in the synthesis of indole alkaloid systems has been prepared by treatment of the Reissert compound formed from 9-benzyl-3,4-dihydro-β-carboline and 2-chloromethylbenzoyl chloride with sodium hydride.

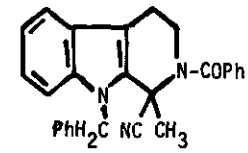
Throughout the years the major volume of work in the area of Reissert compound chemistry[1] has centered on isoquinoline and quinoline. In recent years, however, systems with more than one nitrogen[2] have been receiving increasing attention. We now wish to report our preliminary observations on the Reissert compounds derived from the 3,4-dihydro-β-carboline system. Reaction of the 9-benzyl derivative (1) of 3,4-dihydro-β-carboline (2) with benzoyl chloride or 2-chloromethylbenzoyl chloride and trimethylsilyl cyanide[3] in methylene chloride gave the Reissert compound 3[4], m.p. 209-210°; ir (KBr) 1640 cm^{-1}; m/e 391.1683 ($C_{26}H_{21}N_3O$, 100%), in 31% yield; and the Reissert compound 4[4], m.p. 190-191°; ir (KBr) 1640 $cm.^{-1}$, in 23% yield respectively. In a similar manner 2 reacted with benzoyl chloride in the trimethylsilyl cyanide method[3] to give 5[4], m.p. 257-260°; ir (KBr) 1670, 1625 $cm.^{-1}$; m/e 405.1476 ($C_{26}H_{19}N_3O_2$, 12.4%), 105 (100%). Reaction of 3 with methyl iodide and sodium hydride in dimethylformamide at room temperature gave rise to the alkylation product 6[4], m.p. 213-214°; ir (KBr) 1645 $cm.^{-1}$; m/e 405.1828 ($C_{27}H_{23}N_3O$, 42.0%), 105 (100%), in 60% yield. A similar alkylation of 5 with an excess of methyl iodide gave a product $C_{21}H_{19}N_3O$ which resulted from alkylation at the 1-position and displacement of a benzoyl group by a methyl group. This novel product[4], m.p. 250-251°; ir (KBr) 1645 $cm.^{-1}$; m/e 329.1536 ($C_{21}H_{19}N_3O$, 10.4%), 105 (100%), which was obtained in quantitative yield is being further

+ Dedicated to Professor Tetsuji Kametani on the occasion of his retirement from the Chair of Organic Chemistry at the Pharmaceutical Institute of Tohoku University.







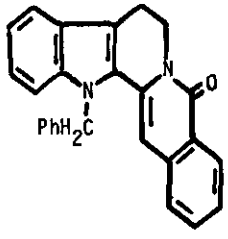


1 R = CH_2Ph 3 Ar = C_6H_5 5 6

2 R = H 4 Ar = 2-$ClCH_2C_6H_4$

investigated. This alkylation product has structure 8.

The Reissert compound 4 when stirred at room temperature with 50% sodium hydride/oil in dimethylformamide underwent intramolecular alkylation accompanied by loss of hydrogen cyanide[5]. The product (7)[4], ir (KBr) 1640, 1600 $cm.^{-1}$; m.p. 213-215°; m/e 376.1576 ($C_{26}H_{20}N_2O$, 100%), was obtained in 92% yield. The value of this specific compound (7) and this type of reaction sequence as a potential route to indole alkaloid systems is obvious and is being investigated further.



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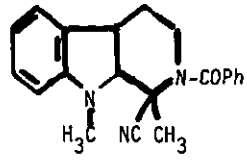

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Acknowledgements - We thank Susan Chapman for her assistance in the preparation of 2.

References and Notes -

1. F. D. Popp, Adv. Heterocyclic Chem., 1979, 24, 187.
2. F. D. Popp, Heterocycles, 1980, in press.
3. S. Ruchirawat, N. Phadungkul, M. Chuankamnerdkarn, and C. Thebtaranonth, Heterocycles, 1977, 6, 43.
4. Satisfactory elemental analyses have been obtained.
5. This type of reaction has been used as a route to the berbine and azaberbine systems, S. Veeraraghavan and F. D. Popp, unpublished results.

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