

STUDIES IN TERPENOIDS - VIII (1): SOME OBSERVATIONS ON
(-)-3, 3a, 4, 5, 6, 7-HEXAHYDRO-3, 3, 6-TRIMETHYL-
2H-INDAZOLE AND ITS CONVERSION TO (+)-trans-CARANE

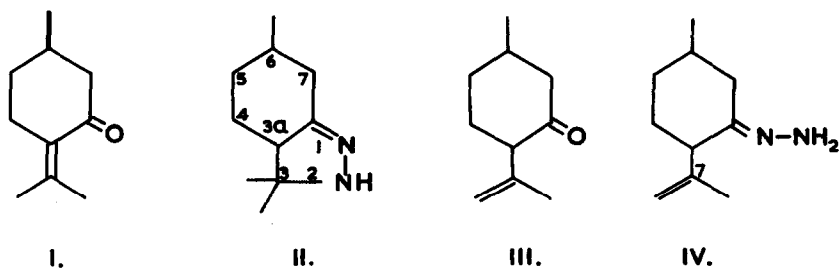
B. RAMAMOORTHY and G.S. KRISHNA RAO

Department of Organic Chemistry, Indian Institute of Science,
Bangalore-12 (India)

(Received in UK 4 September 1967)

The synthesis, physical properties and reactions of 1- and 2-pyrazolines have attracted much interest in recent times in view of their practical applications (2) and also in connection with their conformational and mechanistic studies of their pyrolytic and photolytic decomposition (3,4). Such studies however, appear to have been carried out to a limited extent on the bicyclic 3,3a,4,5,6,7-hexahydro-2H-indazole system in which the 2-pyrazoline moiety is incorporated (5-7).

Kischner and Zavadowsky (8) were the earliest to react (+)-pulegone (I) with hydrazine and study the properties of the cyclic base. From the mechanism of addition of a base to an α,β -unsaturated ketone to give initially by Michael addition (vide infra), a substituted β -aminoketone (9,10) which in the present case further cyclises, the cyclic base from pulegone was assumed to be 3,3a,4,5,6,7-hexahydro-3,3,6-trimethyl-2H-indazole (II) (11).



Using (+)-pulegone (12) and following the procedure of Andrews and Harvey (5), we reinvestigated this reaction in order to carry out further studies on the indazole (II). In Table 1 are summarised its properties. On exposure to bromine vapour it gave immediate red colouration changing to green, characteristic of pyrazolines (13).

TABLE 1: PROPERTIES OF THE INDAZOLE (II)

Physical data	Present work	Russian work (8)
B.P.	140-45°/20 mm	143-44°/35 mm
Yield	79%	-
n_D	1.4921 (26°)	1.4943
d	0.9756 (26°)	0.9602
α_D	-7.52° (26°, neat)	-5.55°
λ ethanol max	230 $m\mu$ ($\log \epsilon$ 2.35) (4a, 5)	-
IR (neat)	3448(N-H), 1639 cm^{-1} (C=N) (4a, 5)	-
Derivatives	Perchlorate, m.p. 160-62° Picrate, m.p. 145-46°.	-

The regeneration of the parent indazole was attempted by filtration of its picrate through basic alumina by elution with chloroform. The IR spectrum of the recovered base revealed bands due to C=C-C=O and saturated C=O besides the N-H band. The lability of pyrazolines is well known (14). In view of the report that the pyrazoline from pulegone regenerates pulegone on exposure to air (8), the appearance of a saturated carbonyl band (1710 cm^{-1}) is of interest. The likely formation of the saturated keto-base (XIII) (vide infra) by the action of basic alumina on II is suggested.

We have found that a mixture of pulegone (I) and isopulegone (III) (15) in which the latter predominated (83%) also gave the indazole (II) in 65% yield, the hydrazine apparently isomerising in situ the α,β - to the γ,δ -unsaturated ketone. The formation of the indazole from isopulegone hydrazone (IV), if it were the initial product, to the extent of 65% (by the attack of NH_2 on C-7 under basic conditions) appears unlikely. This serves to emphasise the initial Michael addition aspect of the base (9,10) to the α,β -unsaturated ketone which is predominantly produced by the in situ base equilibration.

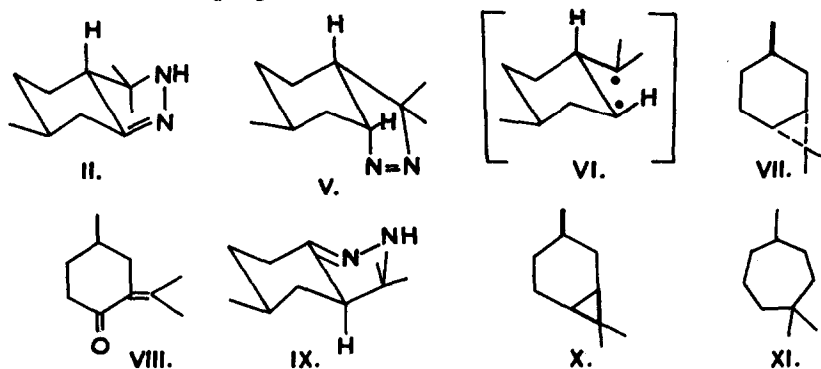
Alkali pyrolysis (5) of the levorotatory base (II) gave (+)-trans-carane (VII) in 72% yield. Its properties summarised in Table 2 establish the identity of (+)-trans-carane and confirm the reliability of this procedure for obtaining it in excellent purity and in high yield.

TABLE 2: PROPERTIES OF (+)-trans-CARANE (VII)

Physical data	Present work	Russian work (8,11)	From (-)-carvone (16)	From (+)- <u>trans</u> -caran- <u>cis</u> -5-ol (17)
B.P.	78-86°/40-45mm	169.5°/759mm	-	-
Yield	72.5%	-	-	-
n_D	1.4570(26°)	1.4567(20°)	1.4565(20°)	1.4575(20°)
d	0.8397(26°)	0.8409(20°)	-	0.852(20°)
α_D	+56.9°(26°, neat) +41.2°(26°, c = 2.4 benzene)	+57.64°	+63.5°(20°, c = 1.8 ethanol)	+40.0°(20°, c = 2.4 benzene)
IR	Identical with the IR of authentic sample (18,19).	-	(16)	(17)
NMR	Identical with the NMR of authentic sample (18,20)	-	(16)	
VPC	Single peak (21)			

The high stereoselectivity (4c) of this reaction suggests that the pyrolysis of the indazole (II) (22) involves (consequent on its isomerisation to 4,5-hexahydrobenzo-1-pyrasoline V, followed by the extrusion of nitrogen) a diradical transition state (VI)(4) with 1,4-trans-dialkyl groups, which collapses to give (+)-trans-carane (VII). From this it follows that the isomeric 3,3a,4,5,6,7-hexahydro-3,3,5-trimethyl-2H-indazole (IX) prepared from 2-isopropylidene-4-methylcyclohexanone (VIII) should under these conditions of pyrolysis collapse to give stereoselectively cis-carane (X).

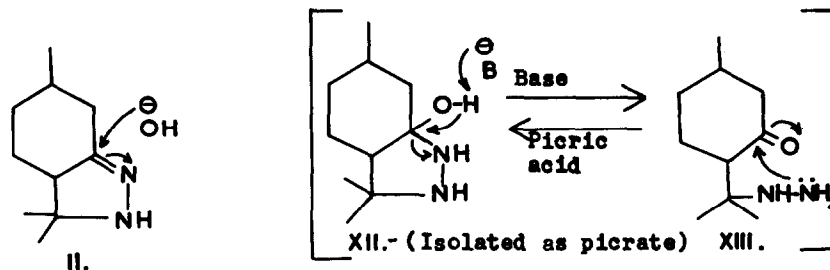
This work is in progress in our laboratories.



Car-3-ene under appropriate conditions of hydrogenation was shown by Cocker *et al.*, (23) to give exclusively 1,1,4-trimethylcycloheptane (XI)(24,25). Its formation was explained on the basis of the isomerisation of car-3-ene to car-2-ene followed by 1,4-addition of hydrogen and subsequent reduction. Failure of (-)-cis-carane (23) and of (+)-trans-carane obtained in the present study to furnish XI under identical conditions (26) supports and supplements Cocker's findings.

Treatment of the indazole (II) with LAH (one mole equivalent), expected to furnish the corresponding dihydro compound (27) gave interesting results. The IR spectrum of the resulting base ν_{3450} (N-H), ν_{1715} (saturated $>C=O$), no absorption due to $C=C$ is consistent with the 2-hydrazinoisopropyl-5-methylcyclohexanone structure (XIII). It gave a picrate (m.p. $157-58^\circ$), the IR spectrum of which differed from that of the picrate of the indazole II and did not show any saturated carbonyl absorption. The spectrum and

the analytical data are consistent with the picrate of the carbinolamine XII. The possibility that II under the conditions



of aqueous alkaline work up (after the LAH treatment) might have given the keto base XIII (vide supra for its behaviour on basic alumina) with its further ring closure as shown to XIII on treatment with picric acid is under examination. Addition of hydroxide ion at the C-N bond in a related system to give a carbinolamine of the type XII and its further base catalysed cleavage to a β -amino-ketone have been recently discussed (28).

Acknowledgements. We thank Prof. D.K. Banerjee of this department for his interest in this work. One of us (B.R.) thanks the authorities of the Indian Institute of Science for a research scholarship.

References and Footnotes

1. Part VII - L.R. Subramanian and G.S. Krishna Rao, Tetrahedron Letters, In press.
2. A. Wagner, C.W. Schellhammer and S. Petersen, Angew. Chemie (Internat. Edn.), **5**, 699 (1966).
3. D.E. McGreer and W.S. Wa, Can. J. Chem., **45**, 461 (1967).

4. (a) R.J. Crawford, A. Mishra and R.J. Dummel, J. Am. Chem. Soc., **88**, 3959 (1966); (b) R.J. Crawford and A. Mishra, J. Am. Chem. Soc., **88**, 3963 (1966); (c) W.M. Jones, P.O. Sanderfer and D.G. Baarda, J. Org. Chem., **32**, 1367 (1967).
5. E.D. Andrews and W.E. Harvey, J. Chem. Soc., 4636 (1964).
6. S. Olsen and E. Aalrust, Ann., **648**, 29 (1961).
7. A. Hassner and M.J. Michelson, J. Org. Chem., **27**, 298 (1962).
8. N. Kischner and A. Zavadowsky, J. Russ. Phys. Chem. Soc., **43**, 1132, 1554 (1911); Am. Chem. Abst., **6**, 854 (1912).
9. M.E. Smith and H. Adkins, J. Am. Chem. Soc., **60**, 407 (1938).
10. H.F. Curtis and R.W. Hay, Chem. Comm., 524 (1966).
11. J.L. Simonsen, The Terpenes, Vol.I, p.384, 2nd Edn., Cambridge University Press (1947).
12. The pulegone, supplied by Keith Harris & Co., Ltd., Australia, had b.p. 82-85°/6mm, n_D^{20} 1.4820 (26°), d_4^{20} 0.9311 (26°), α_D^{20} +24.60° (26°, neat) and $\lambda_{\text{max}}^{\text{EtOH}}$ 252 m μ (log ϵ 3.86).
13. L.C. Raiford and W.J. Petersen, J. Org. Chem., **1**, 544 (1937).
14. D.E. McGreer, R.S. McDaniel and M.C. Vinje, Can. J. Chem., **43**, 1389 (1965).
15. The isopulegone was obtained from isopulegol (supplied by M/s. S.H. Kelkar & Co., Bombay) by Jones oxidation and its percentage in the mixture was estimated spectrophotometrically.
16. W. Cocker, P.V.R. Shannon and P.A. Staniland, J. Chem. Soc. (C), 946 (1966).
17. K. Gollnick and G. Schade, Tetrahedron Letters, 2335 (1966).
18. We are grateful to Prof. W. Cocker for the IR and the NMR spectra of authentic (+)-trans-carane.
19. We thank Prof. K. Gollnick for the IR spectrum of authentic (+)-trans-carane.
20. We thank Dr. R. Ranganathan for taking the NMR spectrum of our sample.
21. The VPC was run on Perkin-Elmer Vapor Fractometer, Model No. 154-C at 150° using silicone oil DC-200 column (2m) with hydrogen as carrier gas (80 ml/min). The retention time was 3min.36sec.
22. The geometry of the 1- and 2-pyrasoline rings in II, V and IX is assumed to have folded arrangement as depicted (4a and 4b).
23. W. Cocker, P.V.R. Shannon and P.A. Staniland, J. Chem. Soc. (C), 41 (1966).

24. Dr. Sukh Dev informed us that similar results were independently obtained by him on hydrogenation of car-3-ene.
25. Our thanks are due to Dr. Sukh Dev and Prof. W. Cocker for the IR spectrum of XI.
26. The hydrogenation of VII in propionic acid [in contrast to that of I (23)] appears to have led to cleavage products of the cyclopropane ring. [IR(neat): 1745 (satd. ester >C=O), 1185 (O=C-OR), 1647 and 807 cm^{-1} (C=C)].
27. N.G. Gaylord, Reduction with Complex Metal Hydrides, p. 797, Interscience, New York (1956).
28. J.A. Moore, H. Kwart, G. Wheeler and H. Bruner, J. Org. Chem., 32, 1342 (1967); J.A. Moore et al., J. Org. Chem., 32, 1355 (1967).