ACKNOWLEDGEMENTS

The authors are thankful to Prof. R. Vijayaraghavan of T.I.F.R., Bombay, and Prof. B. G. Gokhale, Head of Physics Department, University of Lucknow, Lucknow, for providing necessary facilities. One of the authors (Miss) Ratna Sircar is thankful to C.S.I.R. for providing financial help in the form of fellowship.

1. Vicles, P., Donniol, A. and Lissorgues, B., *C.R. Acad. Sci. (Paris), Ser. C*, 1968, **266**, 1482.
2. Pirkle, W. H. and Beare, S. D., *Tetrahedron Letter*, 1960, **21**, 2579.
3. Frendenberg, K., Brauns, F. and Segel, H., *Berlin*, 1923, **86B**, 193.
4. Roger, R., *J. Chem. Soc.*, 1932, p. 2168.
5. Van Vleck, J. H., *Phys. Rev.*, 1948, **74**, 1168.
6. Andrew, E. R. and Eades, R. G., *Proc. Phys. Soc.*, 1953, **A66**, 415.
7. Gutowsky, H. S. and Pake, C. E., *J. Chem. Phys.*, 1950, **18**, 162.
8. Smith, G. W., *Ibid.*, 1965, **42**, 4299.
9. Mori, N., Asano, Y., Iril, T. and Tsuzuky, Y., *Bull. Chem. Soc. (Japan)*, 1966, **39**, 1490.
10. Schmid, H., *Mohatsch Chem.*, 1968, **99**, 1932.
11. Lehman, F., Pedro, A. and Shlz, P. E., *Rev. Soc. Quim. Mex.*, 1969, **13**, 215 A.
12. Lawrence, V., *J. Am. chem. Soc.*, 1965, **87**, 1617.
13. Bloembergen, N., Purcell, E. M. and Pound., R. V., *Phys. Rev.*, 1948, **73**, 679.
14. Waugh, J. S. and Fedin, F. J., *Sov. Phys. Solid State*, 1963, **4**, 1633.
15. Evans, B. W., Fenn, D. J. and Tighe, B. J., *J. Chem. Soc.*, 1970, **B6**, 1049.
16. Verbit, L. and Hetteon, P. J., *Tetrahedron*, 1968.

STUDIES ON KAWA-PYRONES : SYNTHESIS OF 5,6-DEHYDROKAWAIN

AVIJIT BANERJI* AND ARUP KUMAR SIDDHANTA

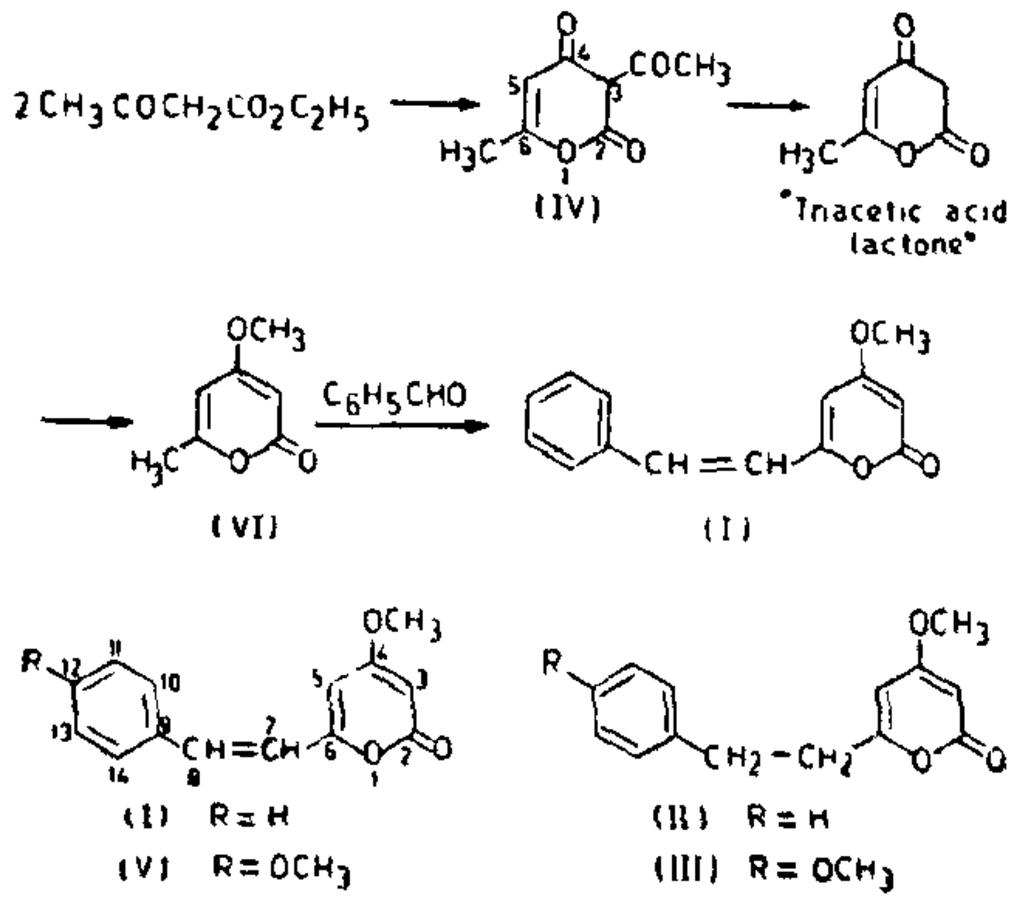
Department of Pure Chemistry, University College of Science, 92, Acharya Prafulla Ch. Road, Calcutta 700 009

ABSTRACT

A convenient synthesis of 5,6-dehydrokawain(I) is reported. The ^{13}C–NMR study of the key intermediate(IV) was also carried out. The preparation of 7,8-dihydroyangonin and its spectroscopical properties are also described.

DURING the course of our studies on the ^{13}C-NMR of kawa-pyrones[1] we needed the compounds 5,6-dehydrokawain (I), 7,8-dihydro-5,6-dehydrokawain (II) and 7,8-dihydroyangonin (III). A convenient synthesis of 5,6-dehydrokawain (I) was achieved by adopting the process Bu'Lock *et al.*[2] used for yangonin(V). The ^{13}C–NMR spectrum of the key synthetic intermediate 3-acetyl-4-hydroxy-6-methyl-2-pyrone (enol form of IV, Scheme I) was also investigated. Compounds(II) and (III) were obtained by the catalytic hydrogenation of (I) and yangonin(V) respectively and characterised by their spectroscopic properties.

5,6-dehydrokawain(I) was synthesised from ethylacetoacetate according to Scheme I. The yields in the final condensation step utilising magnesium methoxide, the base that Bu'Lock used, are fairly low (19%). In an attempt to improve the yield the condensation was carried out in benzene in the presence of sodium hydride but with no significant improvement. (I) was characterised from its spectral properties which are similar to those reported earlier[3] as a constituent of *Aniba firmula*.



SCHEME I. Synthesis of 5,6-dehydrokawain

Catalytic hydrogenation of (I) gave 7,8-dihydro-5,6 dehydrokawain(II). The IR and ^1H-NMR spectra of the dihydro derivative(II) were similar to those described earlier[1]. Similarly, 7,8-dihydroyangonin(III) which was obtained by the catalytic hydrogenation

of yangonin(V) exhibited the expected IR bands for the pyrone ring and 1,4-disubstituted phenyl nucleus. Its structure was confirmed by an examination of its 80 MHz ^{1}H-NMR spectrum ($CDCl_3$).

A detailed ^{13}C–NMR study of the kawapyrones has been carried out by us[1]. In IV, the ^{13}C–NMR assignments of C–3 (δ 99·5, s in SFORD), C–4 (δ 180·8, s), C–5 (δ 101·1, d), C–6–$\underline{C}H_3$ (δ 20·3, q), –$\underline{C}OCH_3$ (δ 204·9, s) and –$COCH_3$ (δ 29·6, q) could be made from a comparison of the chemical shifts with those of 4-methoxy-6-methyl-2-pyrone[1](VI) [C-2, δ 164·5; C–3, δ 86·9; C–4, δ 171·0; C–5, δ 100·0; C–6, δ 161·7; C–6–$\underline{C}H_3$, δ 19·3; –O$\underline{C}H_3$, δ 55·4] and from SFORD multiplicities.

Of the remaining two quaternary carbons of (IV) appearing at δ 160·8 and 168·8, the former was of much lower intensity. Under the usual operating conditions for recording ^{13}C–NMR spectra, the spin-lattice relaxation process is not complete for most of the carbons. Hence this observation indicated that the relaxation time for the carbon at δ 160·8 would be much longer than for the other. The most important contribution to the relaxation proces comes from the dipole-dipole relaxation mechanism[5]. The effectiveness of this will be greater for a carbon bearing a larger number of protons attached to it or to neighbouring carbons. Thus C–6 is expected to have a smaller relaxation time than C–2. Hence the signal at δ 160·8 was assigned to the latter.

Experimental

Dehydroacetic acid(IV) (Scheme I) was obtained from ethylacetoacetate by the method described by Arndt[6], as shining yellow crystals, m.p. 100–108° (yield 27%). This was then triturated with a little ethanol when a colourless solid, m.p. 100–105° [lit.[6] m.p. 104–110°] was obtained. IR (ν_{max}^{KBr}, cm^{-1}) : 1715–40 (br) (carbonyl); 1650, 1635, 1560 (>C = C< in pyrone ring); 1260 (–C(|)–O–C(|)– of pyrone ring).

(IV) was converted to the "triacetic acid lactone" (Scheme I) which was methylated to give 4-methoxy-6-methyl-2-pyrone(VI) (Scheme I) by Me_2SO_4 according to the method described by Bu'Lock *et al.*[2]

Condensation of (VI) with Benzaldehyde

Method 1 : The methyl ether(VI) (300 mg) was added to magnesium methoxide (from 200 mg of Mg and 10 ml of anhydrous MeOH), and freshly distilled benzaldehyde (300 mg) in anhydrous MeOH (10 ml) was added. After refluxing for 4 hr, the solvent was evaporated under reduced pressure, the residue was acidified with dil. HCl, and then extracted with EtOAc (3 × 20 ml). The extract was washed with water (3 × 15 ml), dried (Na_2SO_4) and evaporated to give a yellow gummy residue. The latter on PTLC (silica gel adsorbent; C_6H_6 : EtOAc (4 : 1) developing system) gave 5,6-dehydrokawain(I) [yield: 100 mg; 19% on the baxis of (VI)].

Method 2 : The methyl ether (VI) (300 mg) was taken in dry C_6H_6 (20 ml). 70 mg of a 55% NaH dispersion in oil and freshly distilled benzaldehyde (300 mg) were added to the solution and stirred magnetically for 4 hr. The mixture was filtered, the filtrate was evaporated and the product was worked up by the procedure described in Method 1 above [yield: 105 mg; 20% on the basis of (VI)].

In both the cases 5,6-dehydrokawain (I) was obtained as yellow needles; m.p. 135° (MeOH) [lit.[3] m.p. 138–139°]. IR (ν_{max}^{KBr}, cm^{-1}) : 1710 (pyrone carbonyl); 1625, 1535 (>C = C< in pyrone ring); 1245, 1135 (–C(|)–O–C(|)– stretching in pyrone ring); 1600, 740, 675 (monosubstituted benzene ring); 990, 945 (trans-double bond). 80 MHz ^{1}H–NMR ($CDCl_3$, δ) : 3·81 (3H, s; –O$\underline{C}H_3$); 5·47 (1H, d, J = 1·7 Hz; C–3–$\underline{H}$); 5·91 (1H, d, J = 1·7 Hz; C–5–$\underline{H}$) ; 6·45 (1H, d, J = 16·0 Hz; C–7–$\underline{H}$); 7·35–7·57 (6H, m, aromatic protons and C–8–$\underline{H}$). MS : M^+ 228.

Catalytic hydrogenation of 5,6-dehydrokawain(I)

5,6-Dehydrokawain (100 mg) was dissolved in 30% MeOH in $CHCl_3$ (50 ml), and 10% Pd–C (15 mg) was added to it. The solution was magnetically stirred under hydrogen atmosphere for 2 hr at room temperature. The reaction mixture was filtered. The residue, on evaporation of the filtrate, was crystallised from methanol when colourless needles of 7,8-dihydro-5,6-dehydrokawain(II) (90 mg, 90% yield), m.p. 94° [lit.[4] m.p. 96°], was obtained. IR (ν_{max}^{KBr}, cm^{-1}) : 1710 (pyrone carbonyl); 1645, 1560 (>C=C< in pyrone ring); 1495 (aromatic >C=C<); 1265, 1230, 1130 (aromatic ether or pyrone ring); 1605, 740, 675 (monosubstituted phenyl nucleus). 80 MHz ^{1}H–NMR ($CDCl_3$, δ) : 2·57–3·01 (4H, m ; C–7·$\underline{H}_2$ and C–8·$\underline{H}_2$); 3·66 (3H, s; 4–O$\underline{C}H_3$); 5·32 (1H, d, J = 2·3 Hz; C–3–$\underline{H}$); 5·62 (1H, d; J = 2·3 Hz; C–5–$\underline{H}$); 7·04–7·20 (5H, m; five aromatic protons). MS : M^+ 230.

Catalytic hydrogenation of yangonin(V)

The procedure described above for hydrogenation of (I) was followed for the hydrogenation of yangonin(V), when 7,8-dihydroyangonin was obtained (yield 90%) as shining white platelets after recrystallisation from methanol, m.p. 99–100° [lit.[8] m.p. 102–103°). IR (ν_{max}^{KBr}, cm^{-1}) : 1710 (pyrone carbonyl) 1650, 1550 (>C=C< in pyrone ring), 1500 (aromatic

>C=C<); 1235, 1130, 1030, (aromatic ether and pyrone ring); 1000, 825, 810, 800 (1,4-disubstituted phenyl nucleus). 80 MHz ^{1}H NMR ($CDCl_3$, δ): 2·61–2·97 (4H, m; C–7–H$_2$ and C–8–H$_2$), 3·75 (6H, s; 4 OCH$_3$ and 12–OCH$_3$); 5·37 (1H, d, J = 1·8 Hz; C–3–H); 5·66 (1H, d, J = 1·8 Hz; C–5–H); 6·78 (2H, d, J_o = 8·8 Hz; C–11–H and C–13–H); 7·05 (2H, d, J_o = 8·8 Hz; C–10–H, C–14–H). MS M$^+$ 260.

ACKNOWLEDGEMENT

One of the authors (A. K. S.) thanks the University Grants Commission and the Council of Scientific and Industrial Research, New Delhi, for financial assistance.

1. Banerji, A., Siddhanta, A. K., Acharya, A. K. and Dutta, C. P., *Org. Magn. Reson.*, 1979 (in Press).
2. Bu'Lock, J. D. and Smith, H.-G., *J. Chem. Soc. (London)*, 1960, p. 502.
3. Gottlieb, O. R. and Mors, W. B., *J. Org. Chem.*, 1959, **24**, 17 and 1614.
4. Kimura, Y., Takido, N., Nakano, K. and Takishita, N., *Yakugaku Zasshi*, 1966, **86**, 1184.
5. Wehrli, F. W. and Wirthlin, T., "*Interpretation of Carbon-13 NMR Spectra*, Heyden and Son Ltd., 1976, p. 129.
6. Arndt, F., *Org. Synth. Coll. Vol. III*, p. 231.
7. Collie, N., *J. Chem. Soc.*, 1891, **59**, 612.
8. Chmielewska, J., Cieślak, J., Gorozyńska, K., Kontnik, B. and Pitakowska, J., *Tetrahedron*, 1958, **4**, 36.

SOME NEWER PIPERAZINO SILANES AS CARDIOVASCULAR AGENTS

JAGDISH C. AGARWAL, A. K. MATHUR, J. N. SINHA, K. SHANKER* AND K. P. BHARGAVA
Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow 226 003, India

AND

V. S. MISRA
Department of Chemistry, Lucknow University, Lucknow 226 003, India

ABSTRACT

Some new N^1-aryl-N^4-(Trimethylsilyl) piperazines have been prepared by the condensation of appropriate piperazines with trimethyl chlorosilane in presence of sodium methoxide and these have been evaluated for their cardiovascular activity. Some of these compounds are found to have marked cardiovascular activity. Compound N^1-(*m*-tolyl)-N^4-(trimethylsilyl) piperazine showed potent and sustained hypotensive activity of long duration.

INTRODUCTION

SILYL group incorporated compounds have got high permeability and affect the surface of biological membranes. They have also been reported to possess diverse types of biological properties[1]. It is reported that phenethylamines containing silyl groups at various positions in the aromatic nucleus have a blood pressure lowering activity, the extent of which depends on the type of substituents attached to the silicon atom[2]. Substituted piperazines have been reported to possess potent anti-hypertensive activity[3–6]. It was, therefore, thought worthwhile to synthesize some newer N^1-aryl-N^4-(trimethylsilyl) piperazines and to evaluate them for their cardiovascular activity.

* Address for correspondence.

EXPERIMENTAL

The structures of all the compounds were checked by I.R. spectra recorded on Perkin Elmer 337 infracord or Perkin Elmer 337 grating spectrophotometer. NMR was recorded on Varian A–60 D instrument and chemical shifts were expressed in τ scale. Melting points were determined in a capillary tube on an electrically heated block and are uncorrected. The compounds were checked for their homogeneity by TLC on Silica gel G.

Substituted Piperazines

Various substituted piperazines were prepared by the method already reported in literature[7–8].

N^1-Aryl-N^4-(Trimethylsilyl Piperazine)

0·05 mole of phenyl piperazine, 0·05 mole sodium methoxide and 50 ml of dry benzene were taken in a