trihydrate, 1.69 g (9.61 mmol) of 50% aqueous pyruvic acid, 8 mL of acetic acid, and 4 mL of water was heated for 45 min on the steam bath. A 100-mL portion of water was then added, and the heating was continued for an additional 15–20 min. The mixture was cooled, basified with $NaHCO_3$, and extracted with chloroform. Evaporation of the dried chloroform solution gave 1.39 g of residue which was recrystallized from benzene–ligroin (bp 66–75 °C) to afford 0.61 g (46%) of ketone: mp 89–90 °C; IR (KBr) 1623, 1597 cm^{-1} (C=O); NMR (CF_3COOH) δ 2.45 (s, 3, CH_3C=O), 3.83 (s, 3, NCH_3), 4.02 (s, 2, CH_2C=O), 7.72 (s, 5, ArH).

Anal. Calcd for $C_{11}H_{14}N_2O_2$: C, 64.06; H, 6.84; N, 13.58. Found: C, 63.96; H, 6.75; N, 13.51.

α-Methyl-β-[(1,2-dimethyl-3-indole)carbonyl]phenylhydrazine (3). A solution of 0.93 g (3.0 mmol) of **1a** in 10 mL of 2 N ethanolic hydrogen chloride was heated at reflux for 80 min. The alcohol was evaporated at reduced pressure, and the residue was suspended in 10 mL of water. The mixture was basified with solid $NaHCO_3$ and extracted with chloroform. After the extract was dried, evaporation of solvent left an oily brown residue which solidified when triturated with petroleum ether and hexane. The resulting solid (0.5 g, 57%) was recrystallized from ethanol and afforded colorless crystals: mp 181.5–182 °C; NMR ($CDCl_3$) δ 2.73 (s, 3, CCH_3), 3.33 (s, 3, $NNCH_3$), 3.65 (s, 3, NCH_3), 6.53–8.10 (m, 10, NH and ArH); mass spectrum (70 eV) *m/e* 293.

Anal. Calcd for $C_{18}H_{19}N_3O$: C, 73.70; H, 6.53; N, 14.32. Found: C, 73.69; H, 6.47; N, 14.25.

4,5-Dimethyl-8-(methylamino)naphth[3,2,1-*cd*]indol-6-(4*H*)-one (5). Method A. From Ketone Hydrazide 1b. A mixture of 2.06 g (0.01 mol) of **1b** and 78 g of polyphosphoric acid was manually stirred and heated on the steam bath for 50 min. After slight cooling the mixture was poured into 350 mL of ice–water with stirring and then basified to pH 6–7 (pHydrion paper) with 50% aqueous NaOH. The precipitated solid was filtered, washed with water, and dried. Trituration with benzene resulted in 0.76 g (28%) of a yellow solid, mp 274–280 °C dec. Two recrystallizations from aqueous dimethylformamide afforded analytically pure golden crystals: mp 283–286 °C dec; IR (KBr) 1648 (C=O), 3367 cm^{-1} (NH); mass spectrum (70 eV) *m/e* 276; NMR (Me_2SO-d_6) δ 2.81 (d, 3 H, J = 1.9 Hz, NCH_3), 2.89 (s, 3 H, 2-indole CH_3), 3.86 (s, 3 H, 1-indole CH_3), 6.11 (q, J = 4.7 Hz, NH), 6.95 (dd, 1 H, J = 8.5, 2.5 Hz, Ar), 7.32–7.56 (m, 3 H, Ar), 7.82 (d, 1 H, J = 6.8 Hz, Ar), 8.12 (d, 1 H, J = 8.6 Hz, Ar); NMR (CF_3CO_2H) δ 3.34 (s, 3 H, CH_3), 3.56 (s, 3 H, CH_3), 4.26 (s, 3 H, CH_3), 7.87–8.45 (m, 4 H, Ar), 8.75 (dd, 1 H, J = 6, 2.5 Hz, Ar), 9.08, (s, 1 H, J = 7 Hz, Ar), 9.18 (br s, 1 H, Ar).

Anal. Calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84; N, 10.14. Found: C, 78.29; H, 5.76; N, 10.07.

The corresponding picrate was prepared in acetone–methanol and recrystallized from DMF–acetone; mp 228–229 °C dec.

Anal. Calcd for $C_{24}H_{19}N_5O_8$: C, 57.03; H, 3.79; N, 13.86. Found: C, 57.28; H, 3.88; N, 13.81.

Method B. From Hydrazone Hydrazide 1a. A mixture of 3.0 g (9.66 mmol) of **1a** and 100 g of polyphosphoric acid was stirred and heated at 95–105 °C on an oil bath for 75 min. Workup as described under method A gave 1.2 g of crude golden solid. Recrystallization from aqueous DMF afforded crystals, mp 275–280 °C dec. IR and NMR spectra are identical with those of the product obtained from the ketone hydrazide **1b**.

Method C. From Indole Ester 6 and α-Methylphenylhydrazine. A mixture of 1.1 g (5.0 mmol) of ethyl 1,2-dimethyl-3-indolecarboxylate (**6**), 0.61 g (5.0 mmol) of α-methylphenylhydrazine, and 45 g of polyphosphoric acid was heated at 110 °C with stirring for 40 min. Workup as described under method A yielded 0.66 g of crude solid. Two recrystallizations from aqueous DMF gave golden crystals, mp 273–278 °C. A mixture melting point with the product obtained from **1b** was not depressed, and the IR and NMR spectra for the two compounds are identical.

Method D. From Indole Hydrazide 3. Polyphosphoric acid (100 g) and 2.91 g (9.93 mmol) of **3** were heated to 140 °C over a period of 90 min with manual stirring. Workup as described under method A afforded 2.63 g of crude product. Trituration with chloroform followed by recrystallization from DMF–dioxane gave pure crystals, mp 278–281 °C dec. IR and NMR spectra for this compound are identical with those obtained from the product of ketone hydrazide **1b**.

Registry No. **1a**, 72036-43-2; **1b**, 72036-44-3; **3**, 72036-45-4; **5**, 72036-46-5; **5** picrate, 72060-04-9; **6**, 20357-14-6; ethyl acetoacetate *N*-methyl-*N*-phenylhydrazone, 72036-47-6; 4-methylene-2-oxetanone, 674-82-8; α-methylphenylhydrazone, 618-40-6.

Synthesis and Reduction of Pentacyclic Immonium Salts. Application to the Synthesis of (±)-(*E*)-Norvincamone[1]

André Buzas,*[2a] Jean-Pierre Jacquet,[2b] and Gilbert Lavielle[2b]

Laboratoire de Synthèse Organique, UER Sciences, Université d' Orleans, 45045 Orleans, France, and Centre de Recherches SAUBA, 93104 Montreuil, France

Received July 24, 1979

The immonium perchlorates **7** and **10**, prepared by one-step double cyclization of the corresponding amide acids **6** and **9**, were reduced by $Zn/AcOH/H_2O$ to (±)-(*E*)-norvincamone (**8**) and (±)-vincamone (**11**), correspondingly.

We have recently reported the stereoselective reduction of the pentacyclic immonium salts of type **1**[3,4] (see Scheme I). The chemical ($NaBH_4$) or catalytic reduction of this quasi-planar molecule led exclusively the "trans isomer" **2**.[5] This result can be explained by the interaction of the reagent with the immonium carbon atom controlled by the neighboring angular ethyl group, perpendicular to the plane of the molecule. On the other hand, the dissolving-metal reduction ($Zn/CH_3COOH/H_2O$) led mainly to the formation of the "cis isomer" **3**.

We have attempted to apply this specific reduction to the synthesis of vincamine derivatives. This alkaloid family has recently been intensively investigated, as some

(1) Nomenclature and numeration are according to J. Le Men and W. I. Taylor, *Experientia*, **21**, 508 (1965).

(2) (a) Laboratoire de Synthèse Organique, UER Sciences, Université d'Orleans, 45045 Orleans, France; (b) Centre de Recherches SAUBA, 93104 Montreuil, France.

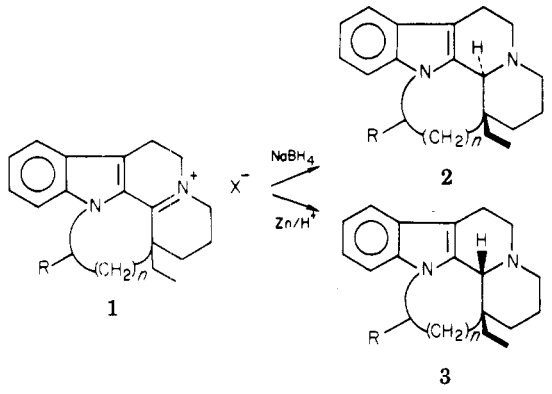
(3) A. Buzas, C. Herisson, and G. Lavielle, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **283**, 763 (1976).

(4) A. Buzas, C. Retourne, J.-P. Jacquet, and G. Lavielle, *Tetrahedron*, **34**, 3001 (1978).

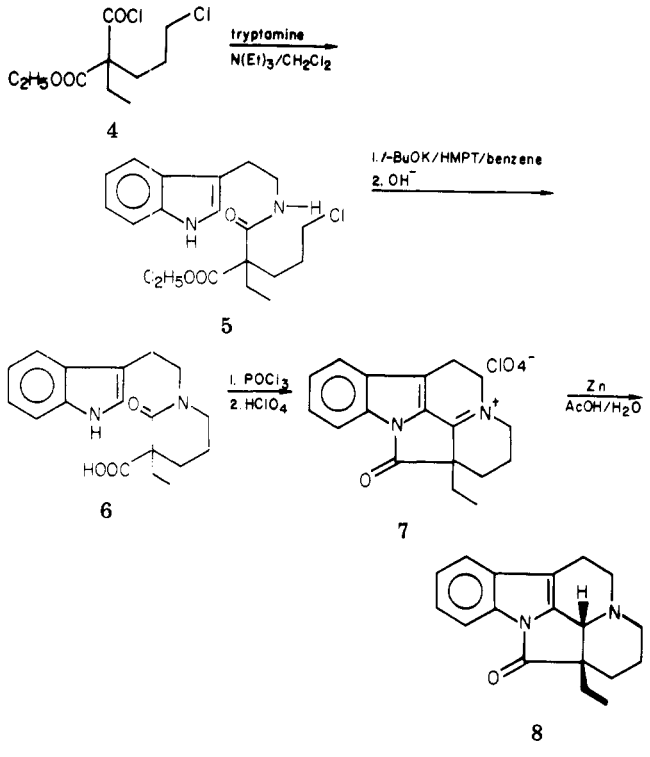
(5) (a) E. Wenkert and B. Wickberg, *J. Am. Chem. Soc.*, **87**, 1580 (1965); (b) W. I. Taylor, "The Vinca Alkaloids", Marcel Dekker, New York, 1973, p 199.

0022-3263/80/1945-0032$01.00/0

Scheme I



Scheme II



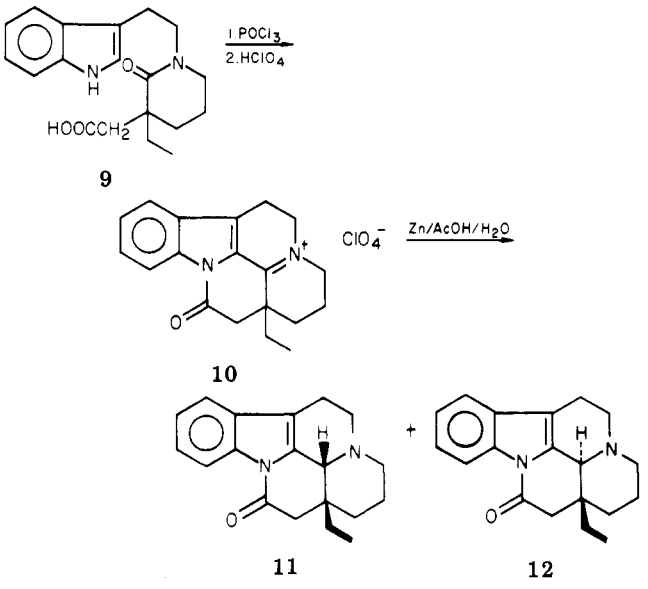
of its members show important cerebrovascular activity.[6]

Amidification of tryptamine with the acid chloride **4** afforded **5**, which was subsequently cyclized and hydrolyzed to the acid amide **6** (Scheme II). The immonium salt **7** was obtained in one step by double cyclization of **6**, by means of $POCl_3$. The dissolving-metal reduction led exclusively to (±)-(*E*)-norvincamone (**8**).

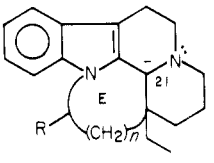
The structure was clearly established by spectral examination. The "cis" configuration is confirmed by the absence of the Bohlmann bands in the infrared spectrum[7] and by the position of the ^1H NMR signal of the C_{21} hydrogen at δ 4.3.[8] The carbonyl group of the pentacyclic system is evident from its ^{13}C NMR singlet at δ 175.

The acid **9**, obtained from the corresponding ethyl ester,[9] was submitted to the double cyclization by means of $POCl_3$ to yield the immonium perchlorate **10**[10] (see Scheme III).

Scheme III



The dissolving-metal reduction led in this case to a mixture of (±)-vincamone (**11**) and its "trans" isomer **12** (1:4). This behavior of the six-membered ketone salt **10** is unexpected when compared to our previous findings. The mechanism of this reduction is assumed to be identical with the one given for the reduction of ketones.[11] The stereochemistry of the final product is determined by the stability of the intermediate anion **13**, which depends on the size of the ring E and on the nature and the position of its substituents.



Experimental Section

Infrared spectra were recorded on a Perkin-Elmer 257 spectrometer. The ^1H NMR spectra were determined in $CDCl_3$ on a Perkin-Elmer R-24B instrument using Me_4Si as internal standard.

***N*-(2-Carbethoxy-2-ethyl-5-chloropentanoyl)tryptamine (5).** To a suspension of 2.5 g (18.4 mmol) of tryptamine in 50 mL of dry chloroform, containing 2 g (20 mmol) of triethylamine, was added at 0 °C dropwise 4.7 g (18.4 mmol) of the acid chloride **4**.[12] The mixture was stirred for 2 h at room temperature, washed with dilute HCl and water, dried, and evaporated to give 6.6 g of **5** (95%): mp 76 °C (petroleum ether–isopropyl ether); IR (KBr) 3350, 3300, 1735, 1640 cm^{-1}. Anal. Calcd for $C_{20}H_{27}ClN_2O_3$: C, 63.40; H, 7.18; N, 7.40. Found: C, 63.39; H, 7.05; N, 7.51.

Preparation of the Amide Acid 6. To a solution of 4.6 g (12.1 mmol) of **5** in 20 mL of a 1:1 mixture of benzene–HMPT at 0 °C under N_2 was added 1.41 g (12.6 mmol) of *t*-BuOK in small portions. The mixture was stirred for 8 h at room temperature and poured into a cold dilute HCl solution. The organic layer was washed with water, dried, and evaporated to give 4 g (96%)

(6) J. L. Herrmann, R. J. Cregge, J. E. Richman, G. R. Kieczykowski, S. E. Normandin, M. J. Quesada, C. L. Semmelhack, A. J. Poss, and R. H. Schlessinger, *J. Am. Chem. Soc.*, **101**, 1540 (1979), and references cited therein.

(7) F. Bohlmann, *Chem. Ber.*, **91**, 2157 (1958); *ibid.*, **92**, 1798 (1959).

(8) M. Uskokovic, H. Bruderer, C. von Planta, T. Williams, and A. Brossi, *J. Am. Chem. Soc.*, **86**, 3364 (1964).

(9) J. L. Herrmann, G. R. Kieczykowski, S. E. Normandin, and R. H. Schlessinger, *Tetrahedron Lett.*, 801 (1976).

(10) This salt was previously prepared in low yield by a several-step reaction.[5a] This simultaneous double cyclization is facilitated by the proximity of the reacting centers and the planarity of the final immonium salt.

(11) (a) H. O. House, "Modern Synthetic Reactions", 2nd ed., W. A. Benjamin, Menlo Park, CA, 1972, Chapter 3; (b) J. W. Huffman and W. W. McWhorter, *J. Org. Chem.*, **44**, 594 (1979).

(12) The corresponding diester [C. Szantay, L. Szabo, and G. Kalaus, *Tetrahedron*, **33**, 1803 (1977)] was hydrolyzed with 1 equiv of KOH in 2-propanol at room temperature. This free acid was transformed to **4** by treatment with $SOCl_2$ at 30 °C overnight.

of the intermediate ester: mp 84 °C (isopropyl ether); IR (KBr) 3250, 1730, 1620 cm^{-1}. Anal. Calcd for $C_{20}H_{26}N_2O_3$: C, 70.15; H, 7.65; N, 8.13. Found: C, 69.97; H, 7.65; N, 8.20.

A solution of 4 g of this ester and 1.6 g of KOH in 100 mL of ethanol was refluxed for 6 h. The residue left after the evaporation of the solvent was dissolved in water and washed with CH_2Cl_2. The aqueous solution was acidified with dilute HCl to liberate the acid, which was subsequently isolated by extraction with benzene. Recrystallization from a mixture of 2-propanol and isopropyl ether afforded 3.0 g (80%) of **6**: mp 132 °C; IR (KBr) 3340, 2800–2300, 1700, 1590 cm^{-1}; ^1H NMR δ 11.4 (s, 1 H, OH), 8.35 (s, 1 H, NH), 7.60–6.90 (m, 5 H, aromatic), 0.9 (t, 3 H, CH_3). Anal. Calcd for $C_{18}H_{22}N_2O_3$: C, 68.77; H, 7.05; N, 8.91. Found: C, 68.41; H, 7.00; N, 8.71.

(±)-(*E*)-Norvincamone. A mixture of 1.5 g of **6** and 8 mL of $POCl_3$ in 15 mL of toluene was refluxed under N_2 for 6 h. The solid[13] left after the evaporation in vacuo of the solvent and excess chloride was suspended in 120 mL of 65% aqueous acetic acid, treated slowly with 7 g of zinc powder, and stirred for 6 h. The filtered solution was extracted with CH_2Cl_2. The organic layer was stirred with 10% NaOH solution, separated, washed with water, and evaporated to give 0.78 g of **8** (58%): mp 64 °C (isopropyl ether); IR (KBr) 1795, 1665 cm^{-1}; ^1H NMR δ 7.7–7.85 (m, 1 H, aromatic), 7.1–7.5 (m, 3 H, aromatic), 4.3 (m, 1 H, C_{21}), 1.15 (t, 3 H, CH_3); MS *m/e* (relative intensity) 280 (M^+, 100), 265 (4), 252 (11), 251 (16), 224 (12), 223 (26), 222 (14), 212 (43), 210 (19), 208 (16), 195 (4), 167 (26); UV λ_{max} (EtOH) 295 nm, 260, 238, 200; ^{13}C NMR (performed on the hydrochloride in D_2O with Me_4Si as standard) δ 175 (CO), 135.2, 134.3, 133.3, 116.4, 121.4, 115.5, 111.8, 60.2, 53.9, 52.5, 45.1, 30.6, 27.3, 19.9, 17.7, 10.1. Anal. Calcd for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99. Found: C, 77.07; H, 7.16; N, 9.99.

Amide Acid 9. This acid was prepared in 80% yield by hydrolysis of the corresponding ester,[9] as described for the preparation of **6**. For **9**: IR (KBr) 3400, 3600–2300, 1715, 1600 cm^{-1}; ^1H NMR δ 10.3 (s, 1 H, OH), 8.1 (s, 1 H, NH), 7.6–6.85 (m, 5 H, aromatic), 0.8 (t, 3 H, CH_3).

Immonium Salt 10. A suspension of 0.7 g of the amide acid **9** in 10 mL of toluene and 6 mL of $POCl_3$ was refluxed for 8 h under N_2. The solid left after evaporation in vacuo of the solvent and excess $POCl_3$ was dissolved in CH_2Cl_2 and stirred with 20 mL of an aqueous 1 M $LiClO_4$ solution. The separated organic layer was dried and evaporated to give 0.7 g (80%) of **10**, mp 220 °C (lit.[5a] mp 215–220 °C).

Reduction of 10. The salt **10** was reduced as described for the preparation of **8**. The products obtained (86% yield) were separated by chromatography on neutral alumina (eluant CH_2Cl_2) and identified as (±)-vincamone (**11**; 20%), mp 200 °C (lit.[5a] mp 200–202 °C), and *trans*-(±)-vincamone (**12**; 80%), mp 135 °C (lit.[5a] mp 135–136.5 °C).

Acknowledgment. We are indebted to Dr. M. Avramoff, Weizmann Institute of Science, Rehovot, Israel, for his helpful discussions in the preparation of the manuscript.

Registry No. (±)-**4**, 70672-14-9; (±)-**5**, 70672-15-0; (±)-**6**, 72036-10-3; (±)-**6** ethyl ester, 70672-16-1; (±)-**8**, 70672-25-2; (±)-**8**·HCl, 70672-26-3; (±)-**9**, 72036-11-4; (±)-**10**, 72074-19-2; (±)-**11**, 2580-88-3; (±)-**12**, 60384-17-0; tryptamine, 61-54-1.

(13) The instability of the intermediate immonium salt prevents its purification. The reduction must be performed with the crude product.

Benzo- and Naphthoquinone Adducts of Hexamethyl-2,4-cyclohexadienone. Synthesis, Enolization, and Rearrangements

Harold Hart* and Katsuhiko Takagi

Department of Chemistry, Michigan State University, East Lansing, Michigan 48824

Received June 12, 1979

The benzoquinone adduct **2** of hexamethyl-2,4-cyclohexadienone is readily converted to its dienolic form **4** by sodium methoxide and base. In contrast, the analogous 1,4-naphthoquinone adduct **3** cannot be similarly converted to its dienolic form **7**. However, **3** can be aromatized under nonequilibrating conditions (sodium hydride followed by methyl iodide) to give the dimethyl ether **8**. Reflux of **2** in HBr–HOAc gives rearrangement product **9** as a consequence of enolization and 1,2-aryl migration. Only one isomer is formed, whereas acid-catalyzed rearrangement of the dimethyl ether **5** gives products corresponding to both aryl and vinyl migration (**11** and **12**). In contrast, in the naphthalene series **3** does not rearrange in acid, and its dimethyl ether **8** gives only **23**, the product of aryl migration. Adduct **2** on irradiation gives the product of intramolecular cycloaddition **25** and the oxa-di-π-methane rearrangement product **26** in a ratio which depends on solvent. Adduct **3** on irradiation gives only the latter type of product (**27**). Adduct **3** is readily oxidized in base and air to the novel epoxy trione **30**.

2,4-Cyclohexadienones react as dienes toward a variety of dienophiles[1,2] to provide a useful entry to bicyclic systems. Their reaction with quinones as dienophiles, however, has not been studied. We describe here adducts formed by reaction of benzoquinone and 1,4-naphthoquinone with hexamethyl-2,4-cyclohexadienone, their different enolization behavior, a novel acid-catalyzed rearrangement which they undergo, their photoisomerization, and several other of their transformations.

Results and Discussion

Treatment of hexamethyl-2,4-cyclohexadienone (**1**)[3] with benzoquinone or 1,4-naphthoquinone in refluxing toluene gave a good yield of crystalline adducts **2** and **3**, respectively. In each case a single stereoisomer was isolated, and

(1) Waring, A. J. *Adv. Alicyclic Chem.* **1966**, *1*, 223–8.
(2) Hart, H.; Collins, P. M.; Waring, A. J. *J. Am. Chem. Soc.* **1966**, *88*, 1005. Oku, A.; Kakihana, T.; Hart, H. *Ibid.* **1967**, *89*, 4554. Hart, H.; Ramaswami, S. K.; Willer, R. *J. Org. Chem.* **1979**, *44*, 1.

(3) Hart, H.; Lange, R. M.; Collins, P. M. "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. V, p 598.

0022-3263/80/1945-0034$01.00/0