and crystallized from petroleum ether in colorless flakes: mp 72–73°; R_f 0.68 (light orange); ir (Nujol) 2212 cm^{-1}.

Anal. Calcd for $C_8H_8N_2$: C, 72.79; H, 6.1; N, 21.2. Found: C, 72.55; H, 5.90; N, 21.5.

Condensation of Anthranilamide with Anthranilic Acid.—Thionyl chloride (3 ml) was added to a pyridine (3 ml) solution of anthranilamide (1 g) and anthranilic acid (1 g) and kept for 24 hr (i) at room temperature and (ii) at 0° in separate experiments. Crushed ice was then added; the reaction mixture was left for 2 hr and extracted with chloroform. The aqueous layer was filtered, an insoluble residue (0.4 g), not yet characterized, was kept aside, and the filtrate was mixed with the 2 *N* hydrochloric acid extract of the chloroform layer. The latter yielded a mixture of solid substances (1 g).

The combined acid aqueous solution was basified and extracted with chloroform, and the crude product (0.26 g) was chromatographed. Benzene–chloroform (9:1) eluted first an uncharacterized yellow crystalline compound (0.04 g), mp 208–212°, giving a positive test for alkaloid, and then 2-(*o*-aminophenyl)-4-quinazolinone (0.04 g), mp 240–241°. Further increase in the chloroform percentage (20%) eluted uncoverted anthranilamide (0.15 g) along with VI, mp 94°.

The reaction at 0° afforded the insoluble residue (0.8 g), solid substance (0.6 g) from the original chloroform layer, and a mixture of bases liberated from the acid aqueous part. The base on chromatography resolved into IV (0.09 g), mp 241°, anthranilamide (0.26 g), an uncharacterized compound (0.07 g), mp 210–212°, and trace amount of VI.

Tricycloquinazoline (III) from IV.—A mixture of 2-(*o*-aminophenyl)-4-quinazolinone (0.06 g) and an equal amount of anthranilic acid dissolved in xylene (25 ml) was refluxed in the presence of phosphorus pentoxide for 3 hr. The insoluble residue (0.01 g) left after being treated with crushed ice was filtered and chromatographed over acid-washed alumina. The benzene eluate (30 ml) afforded tricycloquinazoline, mp 316° (benzene–chloroform).

Preparation of VII from IV.—2-(*o*-Aminophenyl)-4-quinazolinone (25 mg) and N^4-phenylacetylanthranilamide (50 mg) in xylene were refluxed in the presence of phosphorus pentoxide for 3 hr. The acid layer, after usual work-up and chromatography with benzene–chloroform (8:2) as eluents, yielded VII (3 mg), mp 280–281°, identical in all repects with compound E, besides IV (8 mg) and I (6 mg).

On the other hand, equal proportions (40 mg) of IV and 2-benzyl-4-quinazolinone (I) on similar treatment led only to the recovery of the starting materials and not even a trace of VII could be detected.

Registry No.—*o*-Aminobenzonitrile (compound A), 1885-29-6; III (compound B), 195-84-6; IV (compound C), 27259-73-0; VI (compound D), 27259-74-1; VI 2HCl, 27259-75-2; VII (compound E), 27259-76-3; anthranilamide, 88-68-6; *o*-(*N*-methylamino)benzonitrile, 17583-40-3.

Acknowledgments.—The author is indebted to Mr. P. P. Ghosh-Dastidar, Senior Laboratory Assistant, for expert technical assistance, to Dr. K. G. Das for the mass spectra, and to Dr. A. Bernhardt, W. Germany, and Dr. K. W. Zimmermann, C.S.I.R.O., Melbourne, Australia, for microanalyses.

Reaction of 1-Acetyl-3-piperidinoindole with Acetylenic Esters

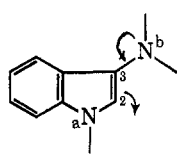
MEI-SIE LIN AND VICTOR SNIECKUS*

Department of Chemistry, University of Waterloo, Waterloo, Canada

Received July 23, 1970

The reaction of 1-acetyl-3-piperidinoindole (**2**) with dimethyl acetylenedicarboxylate and methyl propiolate gave the benzazepine derivatives **3a** and **3b**, respectively. These products were subjected to a degradation sequence (**3** → **5** → **7** → **8**), each step of which was supported by spectral evidence; in the case of **8b**, direct correlation with authentic material was made. An alternative structure (**9**) for the product of the transformations **7** → **8** was ruled out by synthesis. Compound **11** was obtained and shown to be an intermediate for the formation of **3b**. Compounds **3a** and **3b** as well as a number of their degradation products exhibited geometrical isomerism due to restricted rotation about the *N*-acetyl function. In the case of **3b**, temperature-variable 100-Mc nmr spectra have been recorded and discussed.

Even a cursory reading of the literature of indole compounds reveals that the chemistry of simple 2- and 3-aminoindole derivatives has received scant attention.[1] The lack of activity in this area is undoubtedly related to the absence of versatile methods for the preparation of these compounds[2] and to their pronounced inherent instability.[1,3] Recent work dealing with new aspects of aminoindole chemistry[4,5] further emphasizes the latter point. The above survey gave impetus to devise new synthetic routes to ammoindoles[6] and to investigate some of their reactions. In particular, our intention was to put to experimental test the hypothesis that the system **1** may behave



1

to some extent like an enamine (arrows). This proposal had potentially important synthetic implications since enamine behavior of the N^b-enamine system would allow acylation and alkylation reactions to occur at

(1) A. Albert, "Heterocyclic Chemistry," 2nd ed, Oxford University Press, New York, N. Y., 1968, pp 205–206, and references to reviews therein.

(2) There are recent scattered investigations which may have a bearing on any new developments in aminoindole syntheses: (a) M. Colonna, P. Bruni, and G. Guerra, *Gazz. Chim. Ital.*, **99**, 3 (1969); (b) A. S. Bailey, M. C. Chum, and J. J. Wedgwood, *Tetrahedron Lett.*, 5953 (1968); (c) T. Hino, M. Nakagawa, and S. Akoboshi, *Chem. Commun.*, 656 (1967); (d) F. Yoneda, T. Miyamae, and Y. Nitta, *Chem. Pharm. Bull.*, **15**, 8 (1967); (e) D. Raileanu, V. Daniel, E. Mosanu, and C. D. Nenitzescu, *Rev. Roum. Chim.*, **12**, 1367 (1967). For an obvious but apparently unexplored approach, see E. Coxworth, *Alkaloids*, **8**, 40 (1965).

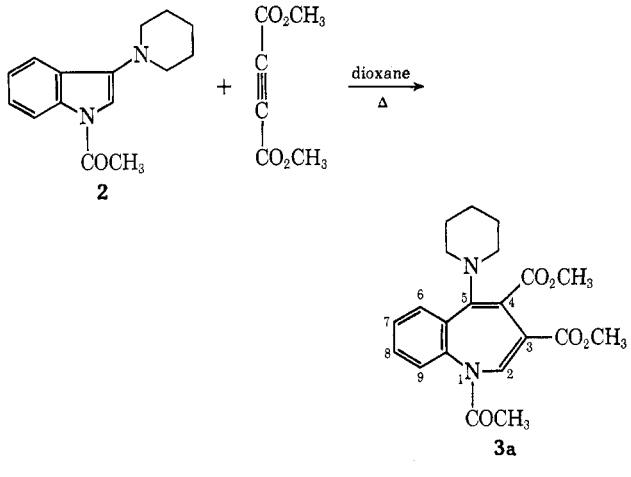
(3) J. Kebrle and K. Hoffmann, *Helv. Chim. Acta*, **39**, 116 (1956).

(4) J. Schmitt, M. Langlois, G. Callet, and C. Perrin, *Bull. Soc. Chim. Fr.*, 2008 (1969), and previous papers in this series.

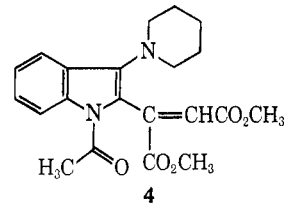
(5) M. Colonna and L. Greci, *Gazz. Chim. Ital.*, **99**, 1264 (1969), and references cited therein.

(6) For an unsuccessful attempt, see V. Snieckus and M.-S. Lin, *J. Org. Chem.*, **35**, 3994 (1970).

the indole 2 position.[7] Our investigations with the reasonably accessible 1-acetyl-3-piperidinoindole (**2**)[2e] have failed to uncover this desired enamine behavior notwithstanding the fact that the presence of the *N*-acetyl function may have been predicted to impart favorable effect on such reactions.[2e,11] On the other hand, in agreement with a generalized reaction in enamine chemistry,[12] we have found that **2** undergoes smooth cycloaddition–ring expansion with dimethyl acetylenedicarboxylate and methyl propiolate to yield the benzazepine derivatives **3a** and **3b**, respectively. Although the reactions of indole with acetylenic esters have been extensively studied,[13] our results constitute only the second example of this type of ring expansion reaction in the indole series.[14] When a mixture of **2** and dimethyl acetylenedicarboxylate was refluxed in dioxane solution for 1 day, a 96% yield of a 1:1 crystalline adduct was obtained. The ir spectrum of the adduct **3a** showed absorptions at 1725 and 1665 cm^{-1} while the 60-Mc nmr spectrum exhibited the following peaks: τ 2.0–2.38 and 2.40–2.76 (m, 4, aromatic), 2.97 (br s, 1, vinyl H), 6.28 (s, 6, $2CO_2CH_3$), 6.82 (br s, 4, α-CH_2 of piperidine ring), 7.77 (br d, 3, $COCH_3$), 8.25 (br s, 6, β- and γ-CH_2 of piperidine ring). It was suspected that the broad doublet at τ 7.77 was caused by hindered rotation about the acetyl function. This observation foreshadowed the more well-defined result of the same phenomenon obtained with compound **3b** (*vide infra*). The uv spectrum is tabulated in Table I. The spectral evidence was in agreement with two formulations **3a** and **4** as reasonable structures for the adduct.



In order to distinguish between structures **3a** and **4**, the chemical degradation outlined in Scheme I (series **a**) was undertaken. When the adduct from the reaction

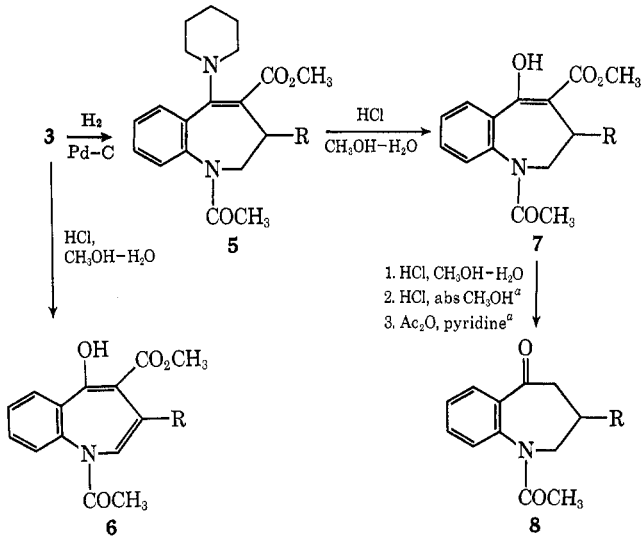


4

of **2** with dimethyl acetylenedicarboxylate was carefully hydrogenated over palladium on carbon, a dihydro derivative was obtained whose spectral properties [ir absorption at 1725 (saturated ester C=O), 1700 (unsaturated ester C=O), and 1665 (amide C=O) cm^{-1}; uv, see Table I; nmr absorption at τ 2.51–3.08 (m, 4, aromatic), 4.94–5.38 (m, 1), 6.02 (m, 1), 6.32 (s, 3, unsaturated CO_2CH_3), 6.40 (m, 1), 6.82 (s, 3, saturated CO_2CH_3), 7.03 (m, 4, α-CH_2 of piperidine ring), 8.19 (s, 3, $COCH_3$), 8.32 (br s, 6, β- and γ-CH_2 of piperidine ring)] were clearly consistent with structure **5a** and eliminated the alternate dihydro compound (**4**, reduced side-chain double bond). The nmr spectral evidence also ruled out any of the other possible dihydro tautomers corresponding to **5a**. Parenthetically, the readily accessible enol **6a** did not prove useful in attempts to develop an alternate degradation plan for compound **3a**.

Further evidence for structure **5a** was obtained by hydrolysis to **7a** which was then converted to **8a** according to Scheme I. At this point, however, literature

SCHEME I



a, R = CO_2CH_3
b, R = H

[a] Only in the case of **7a**.

precedent[15] led us to seriously consider the alternate structure **9** for the product of the above three-step sequence (**7a** → **8a**). Clearly, ir and uv data could not

(7) There are only two known methods by which such substitution can be safely introduced: (a) *via* the 2-lithio derivative, the formation of which requires prior N^a alkylation[8] which decreases the overall synthetic utility of the method; and (b) *via* a 3-substituted indole in which intermolecular alkylation usually leads mainly to 2-substituted product.[9] There are many examples of intramolecular 2 substitution which lead to 2,3-bridged systems.[10]

(8) J. Kebrle, A. Rossi, and K. Hoffmann, *Helv. Chim. Acta*, **42**, 907 (1959); F. E. Ziegler and E. B. Spitzner, *J. Amer. Chem. Soc.*, **92**, 3492 (1970).

(9) See G. Casnati, M. Francioni, A. Guareschi, and A. Pochini, *Tetrahedron Lett.*, 2485 (1969); M. Wakselman, G. Decodts, and M. Vilkas, *C. R. Acad. Sci., Ser. C.*, **266**, 1089 (1969).

(10) See, for example, F. E. Ziegler, J. A. Kloek, and P. A. Zoretic, *J. Amer. Chem. Soc.*, **91**, 2342 (1969).

(11) Recent work shows that 2-carbethoxy-3-hydroxyindole undergoes facile alkylation at the 2 position: H. Plieninger and H. Herzog, *Monatsh. Chem.*, **98**, 807 (1967). In this case, the ester function obviously enhances the observed reactivity.

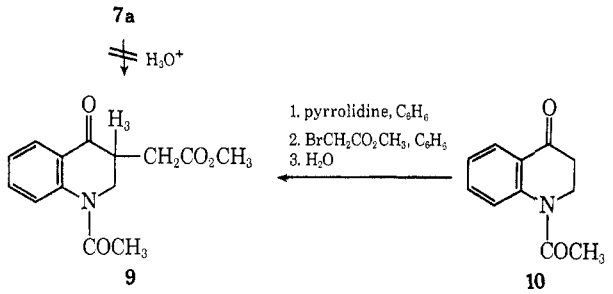
(12) For reviews, see (a) A. G. Cook, "Enamines," A. G. Cook, Ed., Marcel Dekker, New York, N. Y., 1969, pp 230–232; (b) R. Fuks and H. G. Viehe, "Chemistry of Acetylenes," H. G. Viehe, Ed., Marcel Dekker, New York, N. Y., 1969, pp 435–439.

(13) R. M. Acheson, *Advan. Heterocycl. Chem.*, **1**, 138 (1963).

(14) H. Plieninger and D. Wild, *Chem. Ber.*, **99**, 3070 (1966).

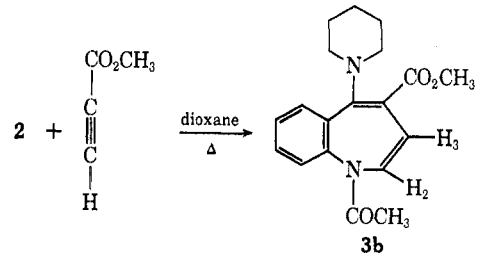
(15) J. A. Moore and E. Mitchell, *Heterocycl. Compounds*, **9**, 271, 284, (1967). See also E. D. Hannah, W. C. Pearson, and G. R. Proctor, *J. Chem. Soc. C*, 1280 (1968), and A. H. Rees and K. Simon, *Can. J. Chem.*, **47**, 1227 (1969).

distinguish between **8a** and **9** and the complicated nmr spectrum of the product added a final element of uncertainty. Independent synthesis of **9** from the known 1-acetyl-1,2,3,4-tetrahydro-4-quinolone (**10**)[16] ruled out the potential rearrangement and supported the structural assignment **8a**.



Our original plan was to convert **8a** into the known 1-acetyl-1*H*-2,3,4,5-tetrahydrobenzazepin-5-one (**8b**).[17] However, several attempts to achieve this goal proved unsuccessful and we turned to the reaction between **2** and methyl propiolate in the expectation[12] that the adduct **3b** would be formed, thus allowing for an unambiguous proof of ring structure by a similar degradative sequence to that carried out for adduct **3a**.

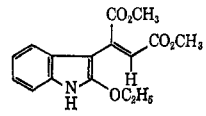
Indeed the reaction between **2** and methyl propiolate in refluxing dioxane gave 1-acetyl-4-carbomethoxy-5-piperidino-1(1*H*)-benzazepine (**3b**) in 68% yield. The structure was fully supported by spectral and chemical data. The ir spectrum again showed unsaturated ester (1700 cm^{-1}) and *N*-acetyl (1665 cm^{-1}) carbonyl absorptions while the uv spectrum was similar to that of compound **3a**. The 60-Mc nmr spectrum showed, in addition to absorptions due to the protons of the piperidine ring (7.07, br s, 4, α protons and 8.39, br s, 6, β and γ protons), peaks at τ 8.01 and 7.85 (2 s, 3, $COCH_3$), 6.26 (s, 3), 3.82 (m, 2) and 2.07–3.11 (m, 4). The multiplet at τ 3.82 assignable to the vinyl protons H_2 and H_3 in **3b** was in good agreement with observed vinyl proton chemical shifts in a similar 4,5-disubstituted benzazepine system.[18] Moreover, on the basis of the nmr data, the alternate 3-carbomethoxybenzazepine structure arising from the less likely opposite mode of cycloaddition[12a] could be dismissed from further consideration.



Monitoring the formation of compound **3b** by thin layer chromatography led to the isolation of an intermediate in the reaction which was assigned structure **11** on the basis of the following spectral and chemical data. The uv spectrum showed lack of extensive conjugation and similarity to that of acetanilide (see Table I) while the salient features of the nmr spectrum

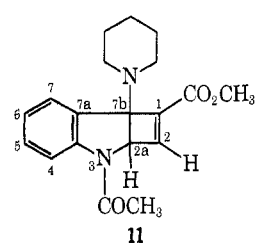
(16) R. F. Collins, *J. Chem. Soc.*, 2053 (1960).
(17) W. H. Bell, E. D. Hannah, and G. R. Proctor, *ibid.*, 4926 (1964).
(18) A. Cromarty and G. R. Proctor, *Chem. Commun.*, 842 (1968).

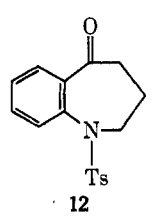
TABLE I
ULTRAVIOLET SPECTRA OF BENZAZEPINE DERIVATIVES AND RELATED MODEL SYSTEMS

Compd	λ_{max}^{MeOH}, mμ (ε)[a]
2[b]	222 (22,000), 248 (sh, 9900), 307 (8730)
3a	234 (18,000), 350 (8400)
 **i**[c]	225 (36,300), 267 (12,000), 356 (18,600)
6a	236 (19,200), 295 (9500)
5a	255 (12,000), 351 (8200)
$PhNHCOCH_3$[d]	242 (12,000)
7a	232.5 (15,600), 257 (7500), 306 (3600)
8a	227 (11,600), 250 (sh, 6750), 298 (1600)
9	237 (23,400), 261 (10,800), 322 (3000)
10	237 (22,600), 261 (10,600) 321 (3150)
3b	234 (19,600), 267 (6900), 350 (6900)
11	248.5 (12,700), 255 (11,700), 280 (3700)
6b	233 (19,300), 255 (sh, 10,200), 321 (6500)
5b	254 (15,000), 348 (9400)
7b	220 (sh, 18,800), 290 (15,700)
8b	226 (13,300), 250 (sh, 6750), 295 (1600)

[a] sh = shoulder. [b] Reference 2e; determined in ethanol. [c] Reference 14. [d] A. I. Scott, "Interpretation of the Ultra-violet Spectra of Natural Products," Pergamon Press Ltd., Oxford, 1964, p 130.

were two slightly broadened one-proton singlets at τ 5.00 and 3.52 which may be assigned to the H_{2a} and H_2 protons, respectively, in **11**.[19] Chemical confirmation of this structure was obtained by its conversion into the benzazepine derivative **3b** using longer reaction times.





Final structure proof of the ring expansion product **3b** and, by implication, that of the analogous compound **3a**, was obtained by the degradation sequence outlined in Scheme I (series **b**). Mild acid hydrolysis of the adduct **3b** gave compound **6b** which was not amenable to further degradation due to the same reason as already mentioned for compound **6a**. Like **3a**, however, adduct **3b** was transformed to the analogous saturated keto ester **7b** by successive hydrogenation and hydrolysis reactions. The latter compound was easily converted to the known 1-acetyl-1(1*H*)-2,3,4,5-tetrahydrobenz-

(19) For assignments in analogous adducts, see (a) D. C. Neckers, J. H. Dopper, and H. Wynberg, *Tetrahedron Lett.*, 2913 (1969); (b) K. C. Brannock, R. D. Burpitt, V. W. Goodett, and J. G. Thweatt, *J. Org. Chem.*, **29**, 818 (1964).

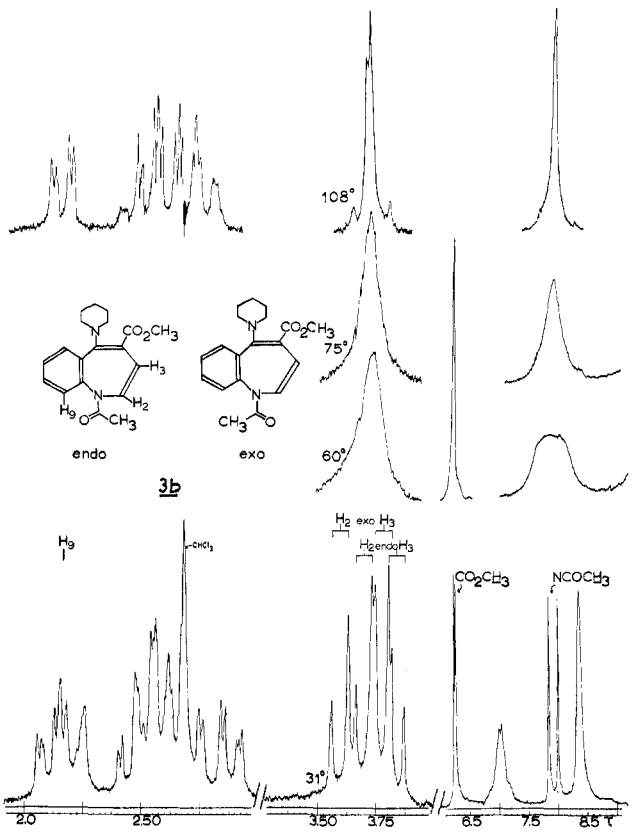


Figure 1.—Variable-temperature 100-Mc nmr spectrum of 1-acetyl-4-carbomethoxy-5-piperidino-1(1*H*)-benzazepine (**3b**). Determined at 250-Hz sweep width except for τ 6.0–9.0 portion at 31° which was run at 500 Hz.

azepin-5-one (**8b**).[17] An authentic sample of **8b** was prepared from the corresponding 1-tosyl derivative **12** according to the published procedure[17] and identity of the two substances was established.[20]

The mechanism of cycloaddition and ring opening of the resulting adducts has been previously discussed.[19b,21]

Temperature-Variable Nmr Spectra of 3b.—The well-known phenomenon[22] of restricted rotation about formal single bonds in amides has received substantial attention recently in connection with studies of heterocyclic systems.[23] Among the large number of benzazepine systems at various levels of oxidation in the heterocyclic ring which have been studied,[15,17,18] only Plieninger has briefly referred to observing such an effect.[14] The temperature-variable nmr spectrum of **3b** (Figure 1) at 31° shows approximately equal intensity spikes at τ 7.85 and 8.01 separated by 8 Hz which may be assigned to the *N*-acetyl methyl function in the exo and endo isomers, respectively, on the basis of the expected deshielding effect by the aromatic ring on the methyl group of the exo isomer. Analogous effect has been observed in the *N*-acetyl-1,2,3,4-tetrahydroquinoline and *N*-acetylindoline series.[23b,e] The multiplet centered at τ 2.14 (1 H) is attributed to overlapping signals of C_9 H for both exo and endo isomers.[24] At 108° this multiplet collapses to four lines as a result of rapid interconversion of the two conformers. This pattern now appears to be a deceptively simple X portion of an ABX system which cannot be further analyzed owing to the inability to extract the AB part from the other complex aromatic multiplet.[25] The vinyl proton region displays two overlapping AB quartets at τ 3.59 and 3.79 (J = 7 Hz) and at 3.69 and 3.84 (J = 7 Hz), the former pair corresponding to H_2 and H_3 of the exo isomer and the latter to H_2 and H_3 of the endo isomer.

At 60° the *N*-acetyl signals coalesce ($\Delta G^{\ddagger} \approx 14$ kcal) indicating an averaging of signals from the separate conformers. As the temperature is raised further, this peak begins to sharpen (75°) and becomes a singlet at 108°. Likewise, the two overlapping AB quartets due to H_2 and H_3 collapse to a broad peak at 60°, and then this in turn resolves into a quartet (J = 7 Hz) at 108°. The averaging effect is probably due to a combination of two rapid processes: (a) that of exo–endo rotational interconversion and (b) that due to conformational inversion of the seven-membered ring.[26] Finally, it is noted that at 31° the methyl ester resonance at τ 6.26 appears as two lines separated by 1.5 Hz and that these signals collapse to a single peak at 60°. We attribute this observation to the presence of two conformational isomers which result from restricted rotation about the carbomethoxy group.

Experimental Section

Microanalyses were performed by A. B. Gygli Toronto, and Microtech Laboratories, Skokie, Ill. Melting points were measured on a Fisher-Johns apparatus and are uncorrected. Infrared spectra were determined with Beckman IR-5A and -10 instruments in chloroform solution unless otherwise indicated; in recording the spectra, abbreviations used are w = weak and sh = shoulder. Ultraviolet spectra were recorded on a Hitachi EPS-3T spectrophotometer in methanol solution. Nuclear magnetic resonance spectra were obtained with JEOL C-60, Varian T-60, A-60, and HA-100 spectrometers in deuteriochloroform solution using tetramethylsilane as internal standard and are tabulated in the order: chemical shift (τ value), multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet, br = broad), number, coupling constant in hertz, and assignment of protons. Column, thin layer, and thick layer chromatography was carried out with silica gel obtained from Brinkmann (Canada) Ltd. Solvents were reagent grade and distilled before use.

The Preparation of 1-Acetyl-3,4-dicarbomethoxy-5-piperidino-1(1*H*)-benzazepine (3a).—A mixture of 1.21 g (5 mmol) of 1-acetyl-3-piperidinoindole (**2**) and 1.14 g (8 mmol) of dimethyl acetylenedicarboxylate in 10 ml of dioxane was refluxed for 24 hr. Evaporation of solvent and trituration of the residue with ether gave 1.86 g (96%) of yellow crystals, mp 171–172°. Three recrystallizations from methanol–ether gave an analytical sample, mp 171–174°; see text for spectral data.

Anal. Calcd for $C_{21}H_{24}N_2O_5$: C, 65.60; H, 6.25; N, 7.29. Found: C, 65.64; H, 6.32; N, 7.40.

(20) We are indebted to Professor Proctor for a sample of **12** and for helpful correspondence.

(21) G. A. Berchtold and G. F. Uhlig, *J. Org. Chem.*, **28**, 1459 (1963); L. A. Paquette and R. W. Begland, *J. Amer. Chem. Soc.*, **88**, 4685 (1966); A. Risaliti, E. Valentin, and M. Forchiassin, *Chem. Commun.*, 233 (1969); T. W. Doyle, *Can. J. Chem.*, **48**, 1629, 1633 (1970).

(22) G. Binsch, *Topics Stereochem.*, **3**, 97 (1968).

(23) Systems investigated include (a) pyrroles: T. Matsuo and H. Shosenji, *Chem. Commun.*, 501 (1969); (b) indolines: H. Wyler and J. Chiovini, *Helv. Chim. Acta*, **51**, 1476 (1968); (c) isoindolines: K. Fang and J. T. Gerig, *J. Amer. Chem. Soc.*, **91**, 3045 (1969); (d) 1,2,3,4-tetrahydroisoquinolines: D. R. Dalton, K. C. Ramey, H. J. Gisler, Jr., L. J. Lendvay, and A. Abraham, *ibid.*, **91**, 6367 (1969); (e) 1,2,3,4-tetrahydroquinolines: A. M. Monro and M. J. Sewell, *Tetrahedron Lett.*, 595 (1969).

(24) This may be contrasted to the situation in the tetrahydroquinoline and indoline series in which only the similarly disposed peri proton in the endo isomers is shifted substantially downfield from the rest of the aromatic resonances.[23b,e]

(25) F. A. Bovey, "Nuclear Magnetic Resonance Spectroscopy," Academic Press, New York, N. Y., 1969, p 105 ff.

(26) For an analysis of this effect in dibenzoazepine derivatives, see M. Nogradi, W. D. Ollis, and I. O. Sutherland, *Chem. Commun.*, 158 (1970).

1-Acetyl-3,4-dicarbomethoxy-5-hydroxy-1(1*H*)-benzazepine (6a).—A mixture of 100 mg (0.26 mmol) of **3a** in 5 ml of methanol containing 2 drops of concentrated hydrochloric acid was heated to boiling and then treated with 1 ml of water. After a reflux period of 10 min, the solution was concentrated to a small volume and the resulting crystalline material was collected and dried yielding 74 mg (88%) of colorless crystals, mp 160–162°. Three recrystallizations from methanol furnished the analytical sample: mp 163–165°; ir 3400–3100 (OH), 1720 (ester C=O), 1655 (enolic C=C and amide C=O) cm^{-1}; nmr τ −2.35 (s, 1, OH, exchanged with D_2O), 2.07–2.30 and 2.46–3.09 (m, 4, aromatic), 6.27 (s, 3, CO_2CH_3), 6.33 (s, 3, CO_2CH_3), 7.9 (br s, 3, $COCH_3$).

Anal. Calcd for $C_{16}H_{15}NO_6$: C, 60.57; H, 4.77; N, 4.41. Found: C, 60.42; H, 4.65; N, 4.56.

1-Acetyl-3,4-dicarbomethoxy-5-piperidino-1(1*H*)-2,3-dihydrobenzazepine (5a).—A solution of 1.54 g (4 mmol) of **3a** in 25 ml of alcohol was hydrogenated over 0.5 g of 10% palladium on charcoal and the reaction was stopped after 1 equiv of hydrogen (100 ml) was consumed. Normal isolation procedure and trituration with ether gave 1.06 g of crystals, mp 145°. Consecutive recrystallizations from ether and acetone–ether gave an analytical sample, mp 150–152°; see text for spectral data.

Anal. Calcd for $C_{21}H_{26}N_2O_5$: C, 65.27; H, 6.78; N, 7.25. Found: C, 65.50; H, 7.04; N, 7.25.

1-Acetyl-3,4-dicarbomethoxy-1(1*H*)-2,3,4,5-tetrahydrobenzazepin-5-one (7a).—The procedure described for the preparation of **6a** was followed except that the reflux time was extended to 1 hr. The mixture was concentrated, diluted with water, and extracted with chloroform. From 664 mg (1.71 mmol) of **5a** there was obtained 540 mg (98%) of crude **7a**. Four recrystallizations from acetone–ether gave an analytical sample: mp 116–119°; ir 3400–3050 (OH), 1740 (ester C=O), 1670 (br, enolic C=C, ketone and amide C=O) cm^{-1}; nmr τ 2.02 and 2.35–2.87 (m, 4, aromatic), 5.68 and 6.12–6.77 (m, 4, aliphatic), 6.25 (d, 6, $2CO_2CH_3$), 7.87 (s, 3, $COCH_3$). The spectrum was strongly concentration and solvent dependent.

Anal. Calcd for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.37; N, 4.39. Found: C, 60.40; H, 5.40; N, 4.32.

1-Acetyl-3-carbomethoxy-1(1*H*)-2,3,4,5-tetrahydrobenzazepin-5-one (8a).—A suspension of 540 mg (1.7 mmol) of **7a** in 5 ml of 4 *N* hydrochloric acid was refluxed for 2 hr. The mixture was evaporated to dryness *in vacuo* and the residue was dissolved in 10 ml of absolute methanol. This solution was saturated with gaseous hydrochloric acid and refluxed for 14 hr. The reaction mixture was evaporated to dryness and the residue was treated with aqueous sodium bicarbonate solution. Extraction of the basic solution with methylene chloride followed by evaporation to dryness of the organic extract yielded 380 mg of solid which, upon acetylation with acetic anhydride and pyridine gave 430 mg (94%) of **8a**. Three recrystallizations from methanol–ether gave an analytical sample: mp 96–97°; ir 1735 (ester C=O), 1685 (C=O), 1665 (amide C=O) cm^{-1}; nmr τ 2.06 and 2.28–2.79 (m, 4, aromatic), 5.74 (br s, 1, C_3H), 6.40–6.79 (m, 4, C_2 and C_4 H), 6.33 (s, 3, CO_2CH_3), 8.0 (s, 3, $COCH_3$).

Anal. Calcd for $C_{14}H_{15}NO_6$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.40; H, 5.76; N, 5.36.

The Preparation of 1-Acetyl-3-carbomethoxymethyl-1,2,3,4-tetrahydro-4-quinolone (9).—In an adaption of the conventional Stork procedure,[27] a solution of 386 mg (2 mmol) of **1-acetyl-1,2,3,4-tetrahydro-4-quinolone (10)**, 2 ml of pyrrolidine, and a trace of *p*-toluenesulfonic acid in 50 ml of dry benzene was refluxed under a Dean–Stark trap for 18 hr. An additional 2 ml of pyrrolidine was added and reflux was continued for 72 hr. The pale yellow solution was evaporated to dryness *in vacuo*, treated with 25 ml of benzene, and again evaporated to dryness. This process was repeated. The residue was dissolved in 25 ml of benzene; the resulting solution was flushed with dry nitrogen and then treated with 1.22 g (8 mmol) of methyl bromoacetate. The mixture was refluxed for 21.5 hr and treated with 15 ml of water. Following a further reflux period of 1.5 hr, the solution was cooled, diluted with 5 ml of water, and extracted with ether. The ether extracts were dried (Na_2SO_4), filtered, and taken to dryness *in vacuo*. The resulting mobile oil was chromatographed (25 g). Elution with ether–benzene (1:3) gave 422 mg of an oil from which 247 mg of starting material could be recovered by crystallization from ether. The filtrate was subjected to preparative tlc (ether) to yield 50 mg (25% based on recovered starting material) of a pale yellow oil which crystallized on standing. Recrystallization from petroleum ether (bp 30–60°)–ether yielded an analytical sample: mp 100–101.5°; ir (CCl_4) 1735 (ester C=O), 1680 (amide and ketone C=O) cm^{-1}; nmr τ 2.15 and 2.47–3.30 (m, 4, aromatic), 5.60 (m, 1, H_3), 6.38 (s, 3, CO_2CH_3), 6.20–6.49 and 7.08–7.64 (m, 4, CH_2N– and CH_2CO_2–CH_3), 7.78 (s, 3, $COCH_3$).

Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.20; H, 5.92; N, 5.16.

1-Acetyl-4-carbomethoxy-5-piperidino-1(1*H*)-benzazepine (3b).—A mixture of 2.8 g (11.5 mmol) of **2** and 1.7 g (20 mmol) of methyl propiolate[28] in 25 ml of dioxane was refluxed for 11 days. Evaporation of solvent *in vacuo* and trituration of the residue with ether gave 2.5 g (68%) of yellow crystals, mp 149–151°. Three recrystallizations from acetone–ether gave an analytical sample, mp 150–151°; see text for spectral data.

Anal. Calcd for $C_{19}H_{22}N_2O_3$: C, 69.92; H, 6.79; N, 8.58. Found: C, 70.16; H, 7.03; N, 8.48.

3-Acetyl-2a,7b-dihydro-7b-piperidino-3*H*-cyclobut[*b*]indole-1-carboxylic Acid Methyl Ester (11).—When a mixture of 484 mg (2 mmol) of **2** and 336 mg (4 mmol) of methyl propiolate in 10 ml of dioxane was refluxed for 2 days and the crude reaction product treated as above, there was obtained 168 mg (26%) of **11**, mp 172–174°. Two recrystallizations from acetone–ether furnished an analytical sample: mp 172–174°; ir 1725 (C=O), 1665 (amide C=O) cm^{-1}; nmr τ 1.82 and 2.34–3.21 (m, 4, aromatic), 3.52 (s, 1, H_2), 5.00 (s, 1, H_{2a}), 6.28 (s, 3, CO_2CH_3), 7.57 (br s, 4, α-piperidine protons), 7.67 (s, 3, $COCH_3$), 8.44 (br s, 6, β- and γ-piperidine protons).

Anal. Calcd for $C_{19}H_{22}N_2O_3$: C, 69.92; H, 6.79; N, 8.58. Found: C, 69.82; H, 6.89; N, 8.51.

When **11** was refluxed in dioxane solution for 44 hr, it rearranged completely to **3b** as shown by tlc, ir, and uv comparison with an authentic sample.

1-Acetyl-4-carbomethoxy-5-hydroxy-1(1*H*)-benzazepine (6b).—The procedure was essentially that used for the preparation of **6a** except that the reflux time was extended to 2 hr. From 417 mg of **3b** there was obtained 145 mg (43%) of yellow crystals of **6b**, mp 133–135°. Two recrystallizations from methanol–ether and then one from ether gave an analytical sample: mp 137–139°; ir 3200 (br, OH), 1735 (w sh, $>CHCO_2CH_3$), 1655 (br, C=C, $C=CCO_2CH_3$, and amide C=O) cm^{-1}; nmr τ −3.36 (s, 1, OH, exchanged with D_2O), 2.02 and 2.38–3.14 (m, 4, aromatic), 3.67 (m, 2, H_2, H_3), 6.10 (s, 3, CO_2CH_3), 7.78 and 8.00 (2 s, 3, $COCH_3$, conformational isomers in ratio 1:2).

Anal. Calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 65.04; H, 5.13; N, 5.45.

1-Acetyl-4-carbomethoxy-5-piperidino-1(1*H*)-2,3-dihydrobenzazepine (5b).—Following the procedure described for the preparation of **5a**, 1.06 g of **3b** was hydrogenated to yield 1.0 g (95%) of yellow crystals of **5b**. Three recrystallizations from methanol–ether gave an analytical sample: mp 165–166°; ir 1680 (C=O), 1655 (amide C=O) cm^{-1}; nmr τ 1.85–2.61 (m, 4, aromatic), 4.78–5.42 (m, 1, C_2 or C_3 H), 6.1 (s, 3, CO_2CH_3), 6.36–7.34 (m, 7, remaining C_2 and C_3 H and α-piperidine protons), 8.15 (s, 3, $COCH_3$), 8.29 (br s, 6, β- and γ-piperidine protons).

Anal. Calcd for $C_{19}H_{24}N_2O_3$: C, 69.49; H, 7.37; N, 8.53. Found: C, 69.33; H, 7.27; N, 8.56.

1-Acetyl-4-carbomethoxy-1(1*H*)-2,3,4,5-tetrahydrobenzazepin-5-one (7b).—Compound **7b** was obtained from **5b** (1.57 g, 98% yield) according to the procedure used for the preparation of **7a**. Three recrystallizations from acetone–ether gave an analytical sample: mp 93–97°; ir 3200 (br, OH), 1745 ($>CHCO_2CH_3$), 1650 (br, C=C, $C=CCO_2CH_3$, and ketone C=O) cm^{-1}; nmr τ −2.53 (s, 0.67, OH, exchanged with D_2O), 1.94–2.92 (m, 4, aromatic), 4.91–5.48 (m, 0.33, C_4 H of keto form), 5.7 (d, 0.67, J = 4, C_2 or C_3 H of enol form), 6.16 and 6.23 (2 s, 3, CO_2CH_3 of enol and keto forms, respectively), 6.32–6.77 and 6.93–7.82 (m, 3, remaining C_2 and C_3 H), 8.00 and 8.21 (2 s, 3, $COCH_3$, conformational isomers in ratio 1:2).

Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.31; H, 5.88; N, 5.54.

1-Acetyl-1(1*H*)-2,3,4,5-tetrahydrobenzazepin-5-one (8b).—A suspension of 480 mg (1.8 mmol) of **7a** in 4 ml of 4 *N* hydrochloric acid was heated until carbon dioxide evolution ceased (45 min). Water was added and the solution was extracted with methylene chloride. Evaporation to dryness of the organic extract yielded

(27) L. H. Hellberg, R. J. Milligan, and R. N. Wilke, *J. Chem. Soc. C*, 35 (1970).

(28) H. O. House, W. L. Roelofs, and B. M. Trost, *J. Org. Chem.*, **31**, 646 (1966).

350 mg (94%) of crude product. Trituration with ether gave crystals of **8b** which were recrystallized consecutively from acetone–ether, methanol–ether, and petroleum ether (bp 60–80°)–acetone to yield colorless crystals: mp 115–117° (lit.[17] 122°); ir 1680 (w, C=O), 1655 (amide C=O) cm^{-1}; nmr τ 1.97–3.0 (m, 4, aromatic), 5.97, 7.33, and 7.7–8.42 (m, 6, aliphatic), 8.08 (s, 3, $COCH_3$). This sample was characterized by identical ir, uv, and nmr spectra, melting point, and mixture melting point with those of authentic material prepared from the corresponding 1-*p*-toluenesulfonyl derivative **12** according to the method of Proctor.[17]

Registry No.—**2**, 19501-93-0; **3a**, 27150-46-5; **3b**, 27150-47-6; **5a**, 27150-48-7; **5b**, 27150-49-8; **6a**, 27150-50-1; **6b**, 27150-51-2; **7a**, 27150-52-3; **7b**, 27150-53-4; **8a**, 27150-54-5; **9**, 27150-55-6; **11**, 27150-56-7; dimethyl acetylenedicarboxylate, 762-42-5; methyl propiolate, 922-67-8.

Acknowledgments.—The support of this work by the Department of University Affairs, Province of Ontario, and the National Research Council of Canada is gratefully acknowledged. Thanks are also due to the Chemistry Departments of Guelph and McMaster Universities, in particular to Professor G. L. Lange and Mr. B. Sayer, for making their 60-Mc nmr facilities available to us. We are deeply indebted to Dr. K. N. Shaw and Professor L. W. Reeves for the 100-Mc temperature-variable nmr spectra. Dr. G. F. Grail kindly assisted in naming compound **11**.

Novel Cyclizations and Ring-Opening Reactions of 3-Phenylindene Derivatives

W. L. MATIER* AND S. J. DYKSTRA

Department of Chemical Research, Mead Johnson and Company, Evansville, Indiana 47721

Received July 13, 1970

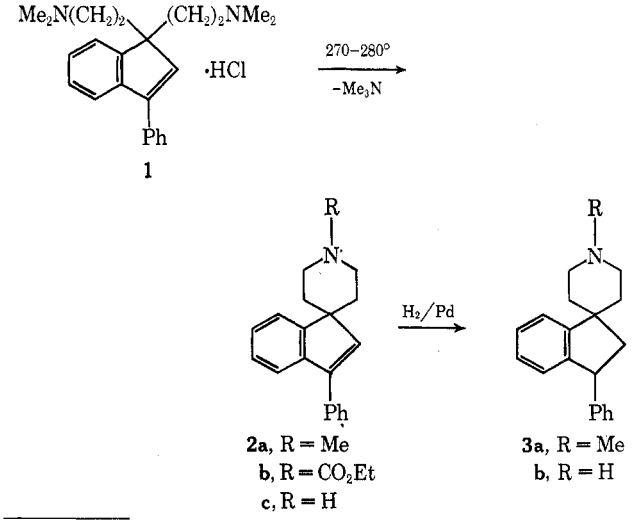
A spiroindenopiperidine **2a** is obtained by pyrolysis of the 1,1-dialkylated 3-phenylindene **1**. However, similar treatment of the 1,3-substituted isomer **4** yields a fused indenopyrrole **5**. Attempted N-demethylation of **5** with ethyl chloroformate causes ring opening to **10**. On refluxing **10** with alcoholic potassium hydroxide, competing intramolecular cyclization to **5** and bimolecular displacement of halogen by ethoxide ion to **12** occurs. Mechanisms of these transformations are discussed.

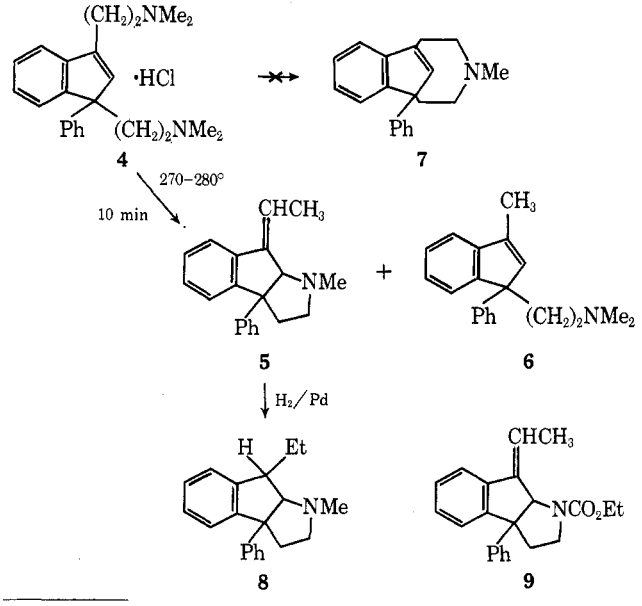
Our interest in alkylamino-3-phenylindene derivatives as CNS agents[1] led us to investigate the synthesis of some phenylindeno- and phenylindano heterocycles. Publications by Dykstra, *et al.*,[1] and by Ganellin, Loynes, and Ansell,[2] established the structure of the products of alkylation of 3-phenylindene with sodium amide and 2-dimethylaminoethyl chloride. They identified three monoalkylated materials as well as the 1,1- and 1,3-dialkylated materials. The present paper discusses some interesting transformations of these dialkylated compounds **1** and **4**.

The dialkylated indenes were obtained by a modification of the previously used method.[2] On pyrolysis of the diamine **1** monohydrochloride, according to the method of Blicke, *et al.*,[3] compound **2a** was isolated in high yield along with trimethylamine.

Treatment of the indene derivative **2a** with ethyl chloroformate[4] yielded the carbamate **2b**, which hydrolyzed to the secondary amine **2c** with ethanolic potassium hydroxide. The spiroindenes **2a** and **2c** were converted to the corresponding indans by hydrogenation over a palladium-on-carbon catalyst.

Pyrolysis of the 1,3-substituted compound **4**, however, did not give the bridged indene **7** but yielded a mixture of products from which **5** (42%) and **6** (9.5%) were separated by column chromatography.





(1) S. J. Dykstra, J. M. Berdahl, K. N. Campbell, C. M. Combs, and D. G. Lankin, *J. Med. Chem.*, **10**, 418 (1967).

(2) G. Ganellin, J. Loynes, and M. Ansell, *Chem. Ind. (London)*, 1256 (1965).

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(4) J. D. Hobson and J. G. McCluskey, *J. Chem. Soc. C*, 2015 (1967), and references therein.