(n-$C_{16}H_{34}$), the yields of alkylated products obtained after various reaction times (see Table I) at 2–7° were determined. The reaction solutions contained the enolate **8** (from 1.030 g or 4.12 mmol of enol acetate **12** and 8.3 mmol of MeLi), and 2.676 g (18.8 mmol) of MeI in 7.8 ml of 1,2-dimethoxyethane.

Registry No.—**7**, 28435-46-3; **8**, 35096-20-9; **12**, 35096-21-0; **13**, 35096-22-1; **14**, 35096-23-2; **15**, 35096-24-3; **16**, 2530-19-0; **17**, 35096-26-5; **18**, 35096-27-6; **19**, 35096-28-7; **20**, 35096-29-8.

Stereoselective Syntheses of Isoquinuclidones. I[1,2]

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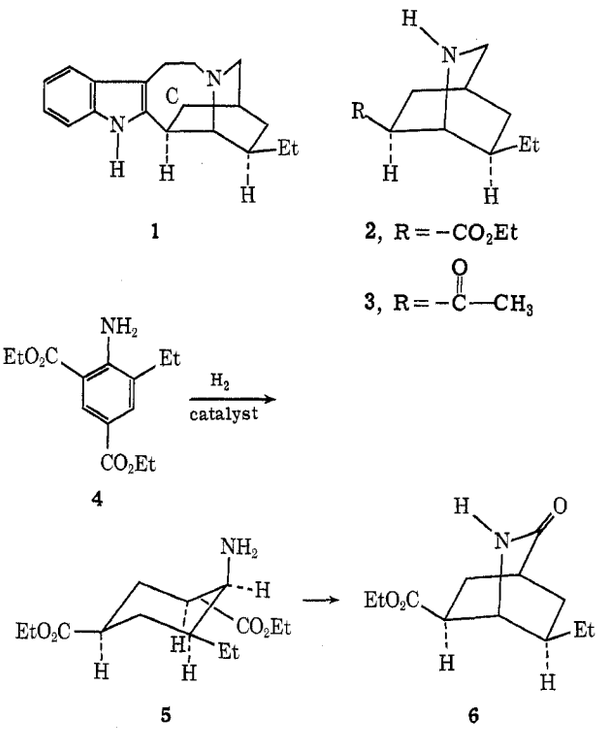
Catalytic hydrogenation of 2,4,6-trisubstituted anilines over a ruthenium catalyst occurs in all cis fashion with concomitant lactam formation to give the corresponding isoquinuclidone derivatives. The 6-acetyl-7-ethyl derivative **23** and the 6-carbethoxy-7-ethyl derivative **6**, prepared in this way, have interest as precursors for the synthesis of iboga and related alkaloids.

The first synthesis of ibogamine (**1**) was reported by Büchi, *et al.*, in 1965.[3] Since then, alternate and stereoselective syntheses of ibogamine have been reported by a number of different groups,[4] as well as partial syntheses[5,6] and alternate approaches.[7] Prior to the synthesis by Büchi, *et al.*,[3] we had undertaken an approach to the synthesis of ibogamine involving a stereoselective synthesis of the isoquinuclidine moiety of the molecule.[2] Since our work has not been duplicated in the intervening period[7] and since the methods employed may be useful to others, the present report and its companion paper[8] are presented to summarize our findings.

Through chemical studies and X-ray crystallographic analysis[9] the configuration of ibogamine has been shown to be as given by structure **1**. Thus, the isoquinuclidine moiety has both substituents cis to the nitrogen bridge. For an eventual synthesis of **1** it appeared desirable to synthesize an isoquinculidine moiety where R is carbethoxy (**2**) or acetyl (**3**). The key to our approach was the expectation that catalytic hydrogenation of a 2,4,6-trisubstituted aniline such as **4** could be accomplished in an all cis fashion to give **5** which, either spontaneously or on heating, would cyclize to the corresponding isoquinuclidone **6**. To test this idea, then, it was necessary to develop convenient syntheses of 2,4,6-trisubstituted anilines.

As starting material, *o*-ethylaniline was converted to 7-ethylisatin (**7**) in good yield following the general procedure of Marvel and Hiers.[10] This was readily brominated in high yield to the 5-bromo derivative **8** which, on treatment with hydrogen peroxide and base, gave the anthranilic acid derivative **9** in quantitative yield. A von Braun reaction between cuprous cyanide and the corresponding ester **10** proceeded in 83% yield to the cyano derivative **11**. Treatment of **11** with ethanolic hydrogen chloride then gave the desired diester **4** in 83% yield. Although, as summarized in Scheme I, five steps are involved in the formation of **4**, they all proceed in high yield and are convenient to carry out.

Although a number of catalysts and different procedures were investigated for the reduction of **4**, the best conditions found were those using ruthenium oxide as catalyst in absolute ethanol under 2200 psi of hydrogen at 125.° Under these circumstances spontaneous cyclization occurred and the desired isoquinuclidone **6** was isolated in 41% yield, accompanied by the cor-



(1) We thank the Public Health Service, National Heart Institute Grant No. 5-ROI-HE 09813, for financial support of this investigation.

(2) Abstracted from the doctoral dissertation of V. A. Snieckus, University of Oregon, 1965.

(3) G. Büchi, D. L. Coffen, K. Kocsis, P. E. Sonnet, and F. E. Ziegler, *J. Amer. Chem. Soc.*, **87**, 2073 (1965); *ibid.*, **88**, 3099 (1966).

(4) (a) Y. Ban, T. Wakamatsu, Y. Fujimoto, and T. Oishi, *Tetrahedron Lett.*, 3383 (1968); (b) W. Nagata, S. Hirai, T. Okumura, and K. Kawata, *J. Amer. Chem. Soc.* **90**, 1650 (1968); (C) S. Hirai, K. Kawata, and W. Nagata, *Chem. Commun.*, 1016 (1968); (d) S. Sallay, *J. Amer. Chem. Soc.*, **89**, 6762 (1967); (e) J. P. Kutney, W. J. Cretney, P. LeQueane, B. McKague, and E. Piers, *ibid.*, **88**, 4756 (1966); (f) J. Harley-Mason, Altaur-Rahman, and J. A. Beisler, *Chem. Commun.*, 743 (1966); *ibid.*, 208 (1967); (g) D. Khac Manh Duc and M. Fetizon, *Bull. Soc. Chim. Fr.*, 771 (1966); (h) *ibid.*, 4154 (1969).

(5) J. W. Huffman, C. B. S. Rao, and T. Kamiya, *J. Org. Chem.*, **32**, 697 (1967).

(6) R. L. Augustine and W. G. Pierson, *ibid.*, **34**, 1070 (1969).

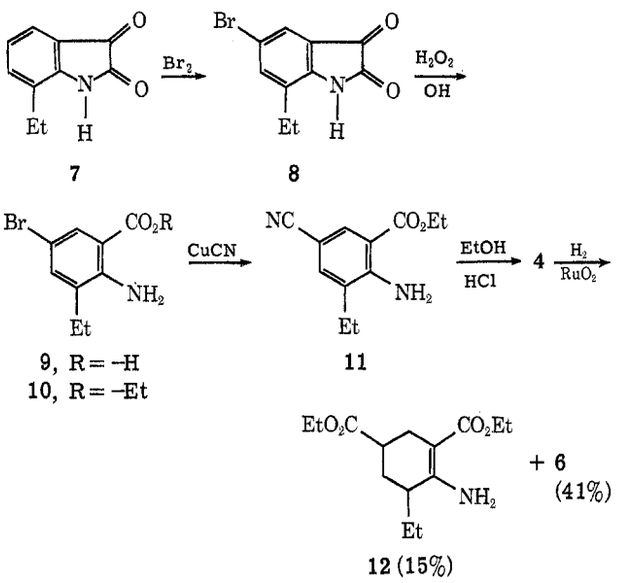
(7) R. L. Augustine and R. F. Bellina, *ibid.*, **34**, 2141 (1969). Although these authors have reported the synthesis of the methyl ester of **6**, their synthetic route is rather different from ours and apparently yielded a mixture of isomers.

(8) J. Witte, and V. Boekelheide, *J. Org. Chem.*, **37**, 2849 (1972).

(9) G. A. Jeffrey, G. Arai, and J. Coppola, *Acta Crystallogr.*, **13**, 553 (1960); J. P. Kutney, R. T. Brown, and E. Piers, *Can. J. Chem.*, **44**, 637 (1966).

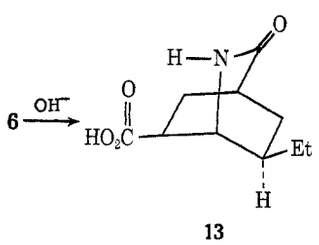
(10) C. S. Marvel and G. S. Hiers, "Organic Syntheses, Collect. Vol. I, Wiley, New York, N. Y., 1951, p 357.

SCHEME I



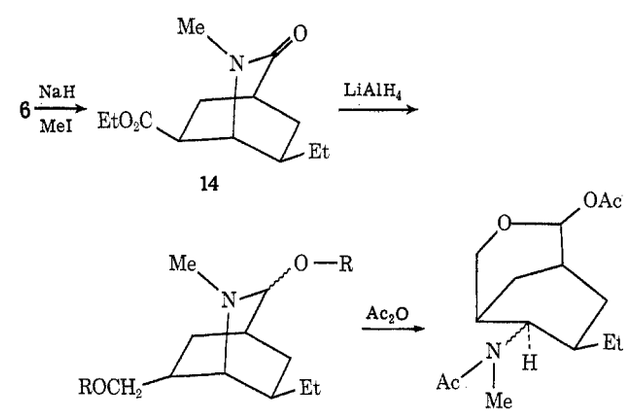
responding tetrahydroanthranilic ester derivative **12** in 15% yield.

Although **6** is a colorless oil, it gives a single spot on tlc and appears in all respects to be homogeneous as would be expected from formation of a single isomer through all cis addition of hydrogen to **4**. Furthermore, careful hydrolysis of **6** gave the corresponding acid **13**



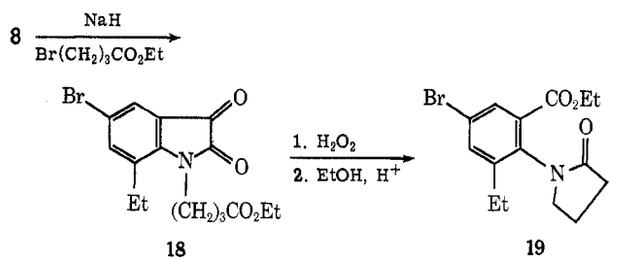
in high yield as a sharp-melting, crystalline compound. The nmr spectrum of **13** showed a single methyl triplet at τ 9.09, providing additional evidence for the absence of other stereoisomers.

Further evidence regarding the cis relationship of the carbethoxyl group and the nitrogen bridge was obtained in the following way. Methylation of **6** gave the *N*-methyl quinuclidone **14** and reduction of this with lithium aluminium hydride led to the carbinol



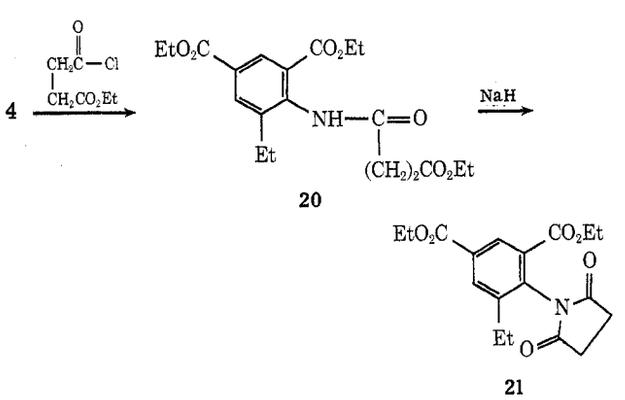
amine **15**. Interestingly enough, the carbinol amine, on acetylation, did not give the expected diacetate **16**, but rather the rearranged diacetate **17**, thus establishing the cis relationship of the carbethoxyl group and the nitrogen bridge in **6**.

With this evidence at hand attempts were then made to elaborate the synthesis to provide the seven-membered C ring of ibogamine. Although methylation of **6** had occurred smoothly, all attempts at its alkylation with ethyl γ-bromobutyrate were without success. We then attempted to introduce the carbethoxypropyl group at an earlier stage in the synthesis. However, alkylation of **10** with ethyl γ-bromobutyrate was also unsuccessful.[11] Alkylation of the isatin derivative **8** did occur in good yield to give **18**, but treatment of



18 with hydrogen peroxide and base, in the usual fashion for cleaving isatin derivatives, gave directly the pyrrolidone derivative **19**, a product not amenable to further elaboration.

Treatment of **4** with β-carbethoxypropionyl chloride did give the acyl derivative **20**. However, again an

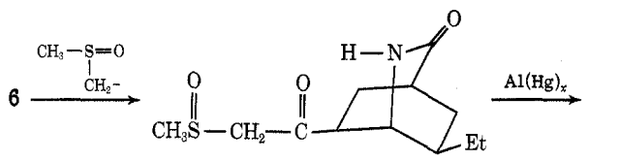


attempted Dieckmann cyclization led only to the corresponding succinimide derivative **21**. At this stage modifications of this synthesis to introduce the seven-membered ring were abandoned and a completely new approach, as described in the accompanying paper, was undertaken.[8]

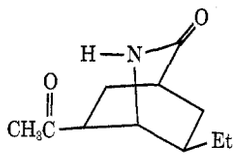
The conversion of the carbethoxy group to acetyl, as an entree for introducing the indole moiety, was also explored, though. Treatment of **6** with dimsyl anion, as described by Cory and Chaykovsky,[12] gave the corresponding β-keto sulfoxide **22** which, on reduction with aluminum amalgam, gave the acetyl derivative **23** as a colorless oil in 40% overall yield. The structure of the acetyl derivative **23** was further estab-

(11) H. B. MacPhillamy, R. L. Dziemian, R. A. Lueas, and M. E. Kuehne, *J. Amer. Chem. Soc.*, **80**, 2172 (1958), have likewise been unsuccessful in introducing the γ-carbethoxypropyl group by alkylation of anthranilate esters.

(12) E. J. Corey and M. Chaykovsky, *ibid.*, **87**, 1345 (1965).



22



23

lished by showing that its properties were completely identical in all respects with those of a sample of **23** prepared *via* an independent synthesis.[8]

Experimental Section[13]

5-Bromo-7-ethylisatin (**8**).—The conversion of *o*-ethylaniline to 7-ethylisatin occurred in 63% yield, following the procedure of Marvel and Hiers,[10] and gave orange needles: mp 194–195° (lit.[14] mp 193°). To a solution of 37.0 g of 7-ethylisatin in 1.0 l. of chloroform there was added dropwise with stirring over a period of 4.5 hr a solution of 13 ml of bromine in 350 ml of chloroform. The solution was then boiled under reflux for 11 hr, filtered hot to remove tarry impurities, and concentrated to one-quarter of its volume. From the cold solution there separated 41.9 g (78%) of orange crystals: mp 208–210°. An analytical sample, prepared by recrystallization from a methanol–water mixture, was obtained as orange-red needles: mp 209–210°; uv maxima (EtOH) 217 nm (log ϵ 3.72), 250 (3.73), 256 (sh, 3.69), 303 (2.98), and 443 (2.03); ir (KBr) 1745 cm^{-1} (C=O); nmr (F_3CCO_2H) τ 0.32 (broad s, 1 H, -N-*H*-), 2.20 (q, 2 H, Ar*H*), 7.33 (q, 2 H, ArCH_2-), and 8.67 (t, 3 H, -CH_2CH_3).

Anal. Calcd for $C_{10}H_8NO_2Br$: C, 47.26; H, 3.17; N, 5.51; Br, 31.45. Found: C, 47.25; H, 3.25; N, 5.66; Br, 31.48.

3-Ethyl-5-bromoanthranilic Acid (**9**).—To a solution of 53.1 g of 5-bromo-7-ethylisatin (**8**) in 1.0 l. of water containing 52 g of sodium hydroxide there was added dropwise with stirring a solution of 52 ml of 30% hydrogen peroxide in 450 ml of water. The temperature was maintained at 25–30° during the addition and, afterward, the mixture was stirred at room temperature overnight. The precipitate, which separated on acidification, was collected and dried to give 50.5 g (99%) of a crystalline solid of satisfactory purity for use in the next step. A sample recrystallized from an ethanol–water mixture gave fine white needles: mp 198–200°; ir (KBr), 3510 and 3400 cm^{-1} (-NH_2), 3000–2500 (-CO_2H, broad), and 1670 (C=O).

Anal. Calcd for $C_9H_{10}NO_2Br$: C, 44.28; H, 4.42; N, 5.74; Br, 32.73. Found: C, 44.26; H, 4.10; N, 5.98; Br, 33.00.

Ethyl 3-Ethyl-5-bromoanthranilate (**10**).—A stream of hydrogen chloride was bubbled through a boiling solution of 57.0 g of 3-ethyl-5-bromoanthranilic acid (**9**) in 1.5 l. of ethanol over a 48-hr period. Then the solution was poured into 8.0 l. of water containing 150 g of sodium carbonate. The precipitate, which separated, was collected, washed with water, and dried. On recrystallization from an ethanol–water mixture it gave 46.5 g (76%) of yellow needle: mp 37.5–38.0°; ir (CCl_4) 3509 and 3367 cm^{-1} (-NH_2), 1686 (C=O); nmr (CCl_4) 2.20 (d, 1 H, Ar*H*), 2.83 (d, 1 H, Ar*H*), 4.10 (broad s, 2 H, -NH_2), 5.72 (q, 2 H, -CH_2CH_3), 7.63 (q, 2 H, -CH_2CH_3), 8.72 (m, 6 H, -CH_2CH_3).

Anal. Calcd for $C_{11}H_{14}NO_2Br$: C, 48.53; H, 5.18; N, 5.15; Br, 29.36. Found: C, 48.38; H, 5.33; N, 5.33; Br, 28.95.

The *N*-**acetyl derivative** of **10** was prepared by treating **10** with acetic anhydride in pyridine and was obtained, after recrystallization from petroleum ether, as colorless needles: mp 97.0–97.5°; ir (KBr) 3260 cm^{-1} (-NH), 1720 (-C(O)-O-), and 1660 (-C(O)-NH).

Anal. Calcd for $C_{13}H_{16}NO_3Br$: C, 49.68; H, 5.13; N, 4.46; Br, 25.72. Found: C, 49.67; H, 5.09; N, 4.47; Br, 25.97.

5-Cyano-7-ethylisatin.—A mixture of 5.1 g of 5-bromo-7-ethylisatin (**8**) and 1.8 g of curpous cyanide in 15 ml of *N*-methyl-2-pyrrolidone was heated at 165° for 15 hr, cooled, and poured into 200 ml of ice water. The resulting precipitate was collected and washed with water. A clean suction flask was substituted and the precipitate was washed thoroughly with acetone. Concentration of the acetone filtrate gave orange crystals which, after recrystallization from chloroform, were obtained as thin orange needles: mp 246.0–247.5°; uv maxima (EtOH) 219 nm (log ϵ 4.19), 250 (4.30), 256 (4.03), 275 (3.85), 301 (3.53), and 4.06 (2.48); ir (KBr) 2245 cm^{-1} (CN) and 1750 (C=O).

Anal. Calcd for $C_{11}H_8N_2O_2$: C, 65.99; H, 4.03; N, 13.99. Found: C, 65.52; H, 4.25; N, 13.36.

Ethyl 3-Ethyl-5-cyanoanthranilate (**11**).—The procedure employed followed the general directions of Friedman and Schechter.[15] Boiling a mixture of 29.0 g of ethyl 3-ethyl-5-bromoanthranilate (**10**) and 11.4 g of cuprous cyanide in 145 ml of *N*-methyl-2-pyrrolidone under reflux for 3 hr, followed by work-up as described,[15] gave, after recrystallization from petroleum ether (60–90°), 18.5 g (83%) of fine white needles: mp 97.5–98.0°; ir ($CHCl_3$) 3472 and 3333 cm^{-1} (NH_2), 2222 (CN), and 1689 (C=O).

Anal. Calcd for $C_{12}H_{14}N_2O_2$: C, 66.03; N, 6.47. Found: C, 65.96; H, 6.48.

3-Ethyl-5-cyanoanthranilic Acid.—The reaction of 3-ethyl-5-bromoanthranilic acid (**9**) with cuprous cyanide in *N*-methyl-2-pyrrolidone following the procedure of Friedman and Schechter gave 3-ethyl-5-cyanoanthranilic acid as white needles, mp 222–225°, in 62% yield after recrystallization from an ethanol–water mixture. The same product was obtained by basic hydrolysis of **11**.

Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30. Found: C, 63.18; H, 5.41.

Ethyl 3-Ethyl-5-carbethoxyanthranilate (**4**).—A solution of 18.5 g of ethyl 3-ethyl-5-cyanoanthranilate (**11**) in 500 ml of absolute ethanol saturated with dry hydrogen chloride was boiled under reflux for 3 hr. After concentration, 500 ml of water was added to the residual solid and the mixture was made basic. The resulting solid imino ester was collected and recrystallized from an ethanol–water mixture to give 21.5 g (100%) of tiny, colorless needles: mp 174.5–175.5°; ir (Nujol) 3497, 3401, and 3344 cm^{-1} (NH, NH_2), 1667 (C=O), and 1634 (C=N). The amino ester was suspended in water and the mixture was shaken at room temperature for 60 hr. The resulting solid was collected and recrystallized from an ethanol–water mixture to give 18.0 g (83%) of white needles: mp 65–66°; ir (CCl_4) 3571 and 3401 cm^{-1} (NH_2) and 1709 and 1689 (C=O); nmr (CCl_4) τ 1.60 (d, 1 H, Ar*H*), 2.21 (d, 1 H, Ar*H*), 3.60 (broad s, 1 H, N-H), 5.67 (q, 4 H, -CH_2CH_3), 7.48 (q, 2 H, -CH_2CH_3), and 8.63 (m, 9 H, -CH_2CH_3).

Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.54; H, 7.18; N, 5.42.

The *N*-**acetyl derivative** of **4** was prepared by reaction of **4** with acetic anhydride and pyridine and obtained, after recrystallization from petroleum ether (30–60°), as colorless needles: mp 85.5–86.5°; ir (Nujol) 3279 cm^{-1} (NH), 1727 (C=O), and 1658 (-C(O)-NH); nmr (CCl_4) τ 0.75 (s, 1 H, N-*H*), 1.75 (d, 1 H, Ar*H*), 2.04 (d, 1 H, Ar*H*), 5.67 (q, 4 H, -OCH_2-), 7.47 (q, 2 H, -CH_2CH_3), 7.91 (s, 3 H, -C(O)-CH_3), and 8.67 (m, 9 H, -CH_3).

Anal. Calcd for $C_{16}H_{21}NO_5$: C, 62.52; H, 6.88. Found: C, 62.46; H, 6.93.

Reduction of Ethyl 3-Ethyl-5-carbethoxyanthranilate (**4**) **to give 6 and 12.**—A mixture of 10.7 g of ethyl 3-ethyl-5-carbethoxyanthranilate (**4**) and 25 of ruthenium oxide in 85 ml of ethanol was subjected to hydrogenation at 125° and 2200 psi of hydrogen. After 27 hr, the catalyst was removed and the filtrate concentrated. The resulting pale yellow oil was chromatographed over Florisil using chloroform for elution. The first main eluate fraction gave 1.37 g (15%) of a colorless oil whose spectral properties (uv maxima (EtOH) 294 nm (ϵ 20,000) and 331 (1250); ir (CCl_4) 3460 and 3375 cm^{-1} (NH_2), 1735 (C=O), 1690 (C=O), and 1630 (C=C); nmr ($CDCl_3$) τ 3.50 (broad t,

(13) Elemental analyses reported were determined by Micro-Tech Laboratories. Ultraviolet and visible spectra were taken using a Cary 15 spectrometer, infrared spectra using a Beckman IR-7 spectrometer, and nmr spectra using a Varian A-60. The mass spectral data are by courtesy of Professor D. F. Swinehart.

(14) N. P. Buu-Hoi and P. Jacquignon, *J. Chem. Soc.*, 3095 (1959).

(15) L. Friedman and H. Schechter, *J. Org. Chem.*, **26**, 2525 (1961).

6 H, $-CH_2CH_3$), and 9.07 (t, 3 H, $-CH_2CH_3$)) and elemental analysis (*Anal.* Calcd for $C_{14}H_{23}NO_4$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.54; H, 8.57; N, 5.25.) are in agreement with structure **12**.

The second main eluate fraction gave 3.65 g (41%) of a colorless oil: uv (EtOH) only end absorption; ir (CCl_4) 3205 cm^{-1} (N–H), 1740 (–C(O)–O–) and 1690 (–C(O)–NH); nmr (CCl_4) τ 2.68 (broad s, 1 H, N–*H*), 5.88 (q, 2 H, $-O-CH_2-$), 6.29 (m, 1 H), 8.75–9.05 (broad, multiplet with two overlapping triplets, 15 H). These properties and the elemental analysis are in agreement with structure **6**.

Anal. Calcd for $C_{12}H_{19}NO_3$: C, 63.97; H, 8.50; N, 6.22. Found: C, 63.87; H, 8.75; N, 6.22.

6-Carboxy-7-ethyl-2-azabicyclo[2.2.2]octan-3-one (13).—A solution of 300 mg of **6** in 10 ml of a 5% methanolic potassium hydroxide solution was allowed to stand at room temperature for 3 hr. After concentration, the residue was dissolved in water and carefully neutralized. The precipitate was collected and recrystallized to give 240 mg (90%) of colorless plates: mp 206.5–207.5°; ir (KBr) 3279 cm^{-1} (NH), 3000–2500 (broad, –OH), 1709 (–C(O)–OH), and 1634 (–C(O)–NH–). These crystals sublimed nicely under high vacuum.

Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.89; H, 7.67; N, 7.10. Found: C, 60.79; H, 7.75; N, 6.98.

6-Hydroxymethyl-7-ethyl-2-methyl-2-azabicyclo[2.2.2]octan-3-ol (15).—A solution of 850 mg of **6** and 197 mg of sodium hydride in 20 ml of toluene was boiled under reflux until gas evolution ceased and then a solution of 1.0 g of methyl iodide in 5 ml of toluene was added dropwise with stirring. The mixture was boiled under reflux for 11 hr, cooled, and poured into 50 ml of ice water. The organic layer was extracted with two 30-ml portions of benzene, dried, and concentrated. This gave **14** as 734 mg of a crude yellow oil: ir (CCl_4) 1730 cm^{-1} (–C(O)–O–) and 1670 (–C(O)–N<). This was dissolved in 20 ml of tetrahydrofuran and added dropwise with stirring to a suspension of 925 mg of lithium aluminum hydride in 18 ml of tetrahydrofuran. The mixture was boiled under reflux for 12 hr and cooled, and a saturated aqueous solution of sodium sulfate was added dropwise until the metallic hydroxides separated as a granular precipitate. The organic layer was decanted and the reside extracted with ether. After the combined organic extracts had been dried and concentrated, the residual oil was subjected to molecular distillation at 100° and 19 mm to give 500 mg (66%) of a colorless oil: ir (CCl_4) 3333 cm^{-1} (–OH) and 1100–1000 (–OH stretching); nmr (CCl_4) τ 6.42 (broad s, 2 H, O–*H*, lost on addition of D_2O), 7.47 (m, 1 H, –C*H*–N<), 7.70 (s, 3 H, N–CH_3), and 9.02 (t, 3 H, $-CH_2-CH_3$); mass spectrum (70 eV) *m/e* 181 ($m^+ - 18$), 167, 152, 124, 110, and 96.

Anal. Calcd for $C_{11}H_{21}NO_2$: C, 66.29; H, 10.62. Found: C, 66.32; H, 10.44.

Treatment of 100 mg of **15** with 500 mg of acetic anhydride in 3 ml of pyridine followed by addition of 10 ml of ice water caused separation of an oil which was extracted with ether. After the ether extract was dried and concentrated, the residual oil was taken up in chloroform and chromatographed over Florisil. The main eluate fraction gave 100 mg (70%) of a colorless oil (ir (CCl_4) 1750 cm^{-1} ($-O-C(O)-CH_3$) and 1640 (>N–C(O)–CH_3)), whose spectral properties and elemental analysis are in accord with structure **17**.

Anal. Calcd for $C_{15}H_{25}NO_4$: C, 63.58; H, 8.89; N, 4.94. Found: C, 63.65; H, 8.98; N, 5.01.

***N*-(γ-Carbethoxypropyl)-5-bromo-7-ethylisatin (18).**—A mixture of 4.0 g of 5-bromo-7-ethylisatin and 830 mg of sodium hydride in a solution of 55 ml of benzene and 15 ml of dimethyl sulfoxide was boiled under reflux for 30 min before adding 3.40 g of ethyl γ-bromobutyrate. After the resulting mixture had been boiled under reflux for 12 hr, it was cooled and diluted to four times its volume with water. After acidification, the benzene layer was separated and the aqueous layer was extracted twice more with benzene. The combined benzene extracts were concentrated and the red residual oil was chromatographed over silica gel using a 5% ether–benzene mixture for elution. The main fraction of eluate gave red crystals which, after recrystallization from petroleum ether (60–90°), yielded 1.5 g (25%) of fine red needles; mp 83.5–84.5°; uv maxima (EtOH) 219 nm (log ε 4.11), 252 (3.80), 259 (sh, 3.78), 306 (3.20), 4.35 (2.36); ir (KBr), 1740 cm^{-1} (C=O).

Anal. Calcd for $C_{16}H_{18}NO_4Br$: C, 52.20; H, 4.93; N, 3.81; Br, 21.71. Found: C, 52.40; H, 4.94; N, 4.05; Br, 21.75.

Reaction of 18 with Hydrogen Peroxide and Base. Formation of 19.—To a mixture of 1.30 g of **18** and 1.0 g of sodium hydroxide in 20 ml of water there was added 10 ml of a 3% aqueous hydrogen peroxide solution. After the mixture had stirred overnight at room temperature, it was brought to neutral pH and evaporated. The residue was taken up in 45 ml of absolute ethanol and saturated with dry hydrogen chloride. After the solution had been boiled under reflux for 2 hr, it was concentrated to dryness. The residue was taken up in chloroform and chromatographed over Florisil. The main eluate fraction was a yellow oil which, after molecular distillation at 155° and 0.1 mm, gave 541 mg of a pale yellow oil: ir (film) 1730 cm^{-1} (C=O) and 1690 (>N–C(O)–); nmr (CCl_4) τ 2.45 (d, 1 H, Ar*H*), 2.62 (d, 1 H, Ar*H*), 5.75 (q, 2 H, $-OCH_2-$), 6.40 (m, 2 H, $-CH_2-N-C=O$), 7.62 (m, 6 H), and 8.72 (t, 3 H, $-CH_2CH_3$).

Anal. Calcd for $C_{15}H_{18}NO_3Br$: C, 52.93; H, 5.29; N, 4.10. Found: C, 53.03; H, 5.33; N, 4.13.

Ethyl *N*-(β-Carbethoxypropionyl)-3-ethyl-5-carbethoxyanthranilate (20).—A mixture of 530 mg of ethyl 3-ethyl-5-carbethoxyanthranilate (**4**), 360 mg of β-carbethoxypropionyl chloride, and 280 mg of anhydrous potassium carbonate in 10 ml of tetrahydrofuran was boiled under reflux for 10 hr. The mixture was then concentrated and the organic residue was taken up in 50 ml of benzene. The benzene extract was then washed with water, dried, and concentrated. The resulting yellow solid was recrystallized from petroleum ether (60–90°) to give 587 mg (75%) of colorless needles: mp 70–71°; ir (CCl_4) 3390 cm^{-1} (N–H) and 1720 (broad, C=O); nmr (CCl_4) τ 0.75 (s, 1 H, NH), 1.71 (d, 1 H, Ar*H*), 1.98 (d, 1 H, Ar*H*), 5.73 (m, 6 H, $-OCH_2-$), 7.39 (m, 6 H, Ar–CH_2- and –C(O)–CH_2-), and 8.68 (m, 12 H, $-CH_3$).

Anal. Calcd for $C_{20}H_{27}NO_7$: C, 61.05; H, 6.92; N, 3.56. Found: C, 61.12; H, 7.06; N, 3.47.

***N*-(2′,4′-Dicarbethoxy-6′-ethyl)phenylsuccinimide (21).**—To a vigorously stirred and boiling suspension of 28 mg of sodium hydride in 50 ml of toluene there was added dropwise over a period of 2 hr a solution of 200 mg of **20** in 40 ml of toluene. The mixture was then boiled under reflux for an additional 10 hr before being cooled and then washed successively with water, dilute aqueous acid, and water. Concentration of the organic layer gave a yellow solid which, on recrystallization from petroleum ether (60–90°), yielded 106 mg (61%) of shiny, colorless needles: mp 104.0–104.5°; ir (CCl_4) 1789 cm^{-1} (imide C=O) and 1724 (imide and ester C=O); nmr (CCl_4) τ 1.45 (d, 1 H, Ar*H*), 1.82 (d, 1 H, Ar*H*), 5.68 (m, 4 H, $-O-CH_2-$), 7.22 (s, 4 H, –C(O)–CH_2), 7.47 (q, 2 H, Ar–CH_2-), and 8.71 (m, 9 H, $-CH_3$); uv maxima (EtOH) 213 nm (log ε 4.17), 230 (sh, 4.17), 287 (3.58), and 296 (3.59).

Anal. Calcd for $C_{18}H_{21}NO_6$: C, 62.24; H, 6.10. Found: C, 62.46; H, 6.26.

6-Acetyl-7-ethyl-2-azabicyclo[2.2.2]octan-3-one (23).—Following the procedure of Corey and Chaykovsky,[12] 225 mg of 6-carbethoxy-7-ethyl-2-azabicyclo[2.2.2]octan-3-one in 10 ml of tetrahydrofuran was added to dimethyl sulfoxide containing 1 molar equiv of dimsyl anion. From the work-up there was obtained 128 mg of **22** as a colorless oil. This was treated directly with aluminum amalgam, again following the procedure of Corey and Chaykovsky.[12] On work-up there was isolated, after chromatography over alumina (Woelm, neutral, activity I) using chloroform for elution, 78 mg of a colorless oil: ir ($CHCl_3$) 1720 (ketone C=O) and 1680 (amide C=O); nmr ($CDCl_3$) τ 7.82 (s, 3 H, $-C(O)-CH_3$) and 9.09 (t, 3 H, $-CH_2CH_3$). The behavior of this oil on tlc and its spectral properties were completely identical in all respects with those of a sample of **23** prepared independently as described elsewhere.[8]

Registry No.—**4**, 34921-57-8; **4** *N*-acetyl derivative, 34921-58-9; **6**, 34921-59-0; **8**, 34921-60-3; **9**, 34921-61-4; **10**, 34921-62-5; **10** *N*-acetyl derivative, 34921-63-6; **11**, 34921-64-7; **12**, 34921-65-8; **13**, 34921-66-9; **15**, 34921-67-0; **17**, 34921-68-1; **18**, 34921-69-2; **19**, 34934-80-0; **20**, 34921-70-5; **21**, 34921-71-6; **23**, 34921-72-7; 5-cyano-7-ethylisatin, 34921-73-8; 3-ethyl-5-cyanoanthracetic acid, 34921-74-9.