750 ml of distilled water, and digested overnight. The tan precipitate was filtered, washed with water, dried (vacuum oven), and weighed 48.1 g (96% pure by vpc), mp 64–66°. A 15-g portion of this material was dissolved and eluted from an alumina column with petroleum ether (30–60°). Two recrystallizations from methanol yielded 13.1 g of white needles, mp 67–68°.

9. 1,3-Bis(4-Carboxy-2,3,5,6-tetrafluorophenoxy)tetrafluorobenzene (IX).—VIII (4.0 g, 6.6 mmoles) was added to 20 ml of 60% fuming H_2SO_4. The reaction mixture was heated and stirred at SO_3 reflux for 19 hr. The dark mixture was then added to crushed ice and the white solid that settled was filtered, washed with water and dried yielding 3.4 g (92%) of crude diacid, mp 253–256°. Recrystallization from aqueous methanol afforded an analytical sample, mp 257–259°.

10. Reaction of Dilithium Salt of Tetrafluororesorcinol (VI) with Decafluorocyclohexene.—In an atmosphere of dry nitrogen, decafluorocyclohexene (10.0 g, 0.0380 mole), VI (from 3.44 g (0.0185 mole) of tetrafluororesorcinol and 23 ml of *n*-butyllithium (0.0370 mole)), and 70 ml of DMAC were stirred and heated at 65° for 2 days. After the reaction cooled, it was added to 300 ml of distilled water. The aqueous DMAC layer (top) was decanted and the bottom layer was taken up in 100 ml of benzene. This benzene solution was filtered (removing the inorganic salt), extracted with water, and concentrated, leaving 3.5 g of a dark liquid. This material was dissolved in petroleum ether (30–60°) and eluted from an alumina column with the same solvent, affording 2.9 g of a colorless liquid. Distillation of this liquid gave 1.4 g (12%) of 2:1 isomeric mixture (vpc) of X and XI, bp 80–82° (0.1 mm).

Registry No.—Perfluorocyclohexene, 355-75-9; II, 15053-71-1; III, 15077-30-2; IV, 14796-02-2; V, 14796-03-3; VII, 14796-04-4; VIII, 15038-90-1; IX, 14901-49-6; X, 14796-05-5; XI, 14901-50-9.

Aza Steroids. IV. Reaction of Arylamines with Ethyl 2-Ketocyclopentanecarboxylate[1,2]

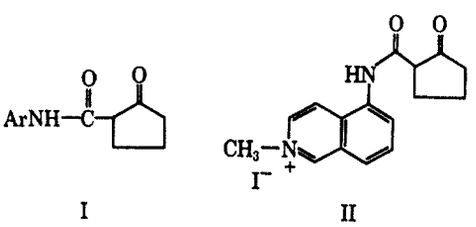
FRANK D. POPP, WILLIAM R. SCHLEIGH,[3] PETER M. FROEHLICH, RONALD J. DUBOIS, AND ADRIA CATALA CASEY

Department of Chemistry, Clarkson College of Technology, Potsdam, New York 13676

Received August 14, 1967

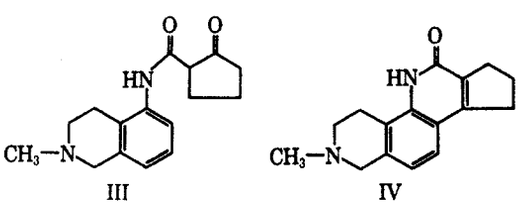
A possible approach to diaza steroids has been investigated by Bew and Clemo.[4] They prepared amides of the type I by heating ethyl 2-ketocyclopentanecarboxylate with various aminoquinolines and aminoisoquinolines. Attempts to cyclize the amides Ia and Ib failed. In the case of Ic, reduction of the heterocyclic ring before ring closure was attempted, but all attempts led to recovery of starting material or cleavage of the amide linkage. Bew and Clemo[4] also attempted to form the amide III by heating ethyl 2-ketocyclopentanecarboxylate with 5-amino-1,2,3,4-tetrahydro-2-methylisoquinoline but failed.

Since this still appeared to be an attractive route to a number of diaza steroidal systems, the general path of Bew and Clemo was reinvestigated, using the amide obtained from ethyl 2-ketocyclopentanecarboxylate and 5-aminoisoquinoline. The methiodide II was obtained in 90% yield by refluxing the amide Ib in methanol containing methyl iodide. A sample of the methiodide II, which contained carbonyl bands at 1750 and 1665 cm^{-1}, was reduced catalytically in an aqueous ethanol solvent to give a 60% yield of III (which still contained carbonyl bands at 1750 and 1650 cm^{-1}) as a light brown oil. Cyclization of III was attempted without further purification, giving 12-keto-1,2,3,4,11,12,15,16-octahydro-3-methyl-3,11-diazacyclopenta[*a*]phenanthrene (IV) as a light yellow solid. The infrared spectrum contained a single carbonyl band at 1650 cm^{-1} typical of a quinolin-2-one. Elemental analysis of IV indicated that a hydrate with formula $C_{16}H_{18}N_2O \cdot 0.5H_2O$ had been isolated. The same sample was dried *in vacuo* at 100° and analysis of the dried sample confirmed the formula $C_{16}H_{18}N_2O$.

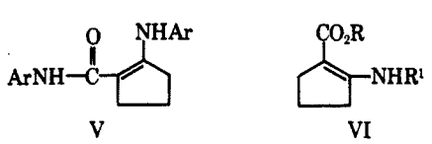


I II

a, Ar = 8-quinolyl
b, Ar = 5-isoquinolyl
c, Ar = 1-isoquinolyl
d, Ar = 5-quinolyl



III IV



V VI

Reaction of 5-aminoquinoline with ethyl 2-ketocyclopentanecarboxylate gave Id. Repetition of Bew and Clemo's preparation[4] of Ia gave a small amount of product from reaction at the keto group in addition to reaction at the ester. Nmr evidence indicates the structure V for this product.

Several model experiments were carried out with ethyl 2-ketocyclopentanecarboxylate and simple aromatic amines. In this manner ten aniline derivatives were converted to the bis adduct. Four of these were new compounds and are included in Table I while the

TABLE I

DERIVATIVES OF ETHYL 2-CYCLOPENTANEONECARBOXYLATE

Ar	Type	Mp, °C	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
o-FC_6H_4–	V	122–124[a]	68.78	5.13	8.91	69.18	5.17	8.82
p-FC_6H_4–	V	135–137[a]	68.78	5.13	8.91	68.61	5.15	8.96
p-FC_6H_4–	I	101–102[a]	65.12	5.47	6.33	64.90	5.35	6.17
2,3-$(CH_3)_2C_6H_3$–	V	164–166[b]	79.00	7.84	8.38	78.89	7.76	8.36
2-CH_3-4-FC_6H_3–	V	168–170[a]	70.16	5.89	8.18	70.06	5.91	8.08
3-CH_3-4-FC_6H_3–	I	132–133[a]	66.37	6.00	5.96	66.40	6.35	5.92

[a] Recrystallized from ethanol. [b] Recrystallized from methanol.

(1) Part III: W. R. Schleigh and F. D. Popp, *J. Chem. Soc., Sect. C*, 760 (1966).

(2) This work was supported in part by a research grant (T-239) from the American Cancer Society.

(3) U. S. Public Health Service Predoctoral Fellow (F1-GM-20,097).

(4) D. G. Bew and G. R. Clemo, *J. Chem. Soc.*, 1775 (1955).

melting points of the others agreed with that previously reported.[5] These ten compounds exhibited similar infrareds with characteristic peaks (KBr) at 3210–3250, 1610–1630, 1585–1608, and 1560–1575 cm^{-1} which are consistent with structure V. Examination of the nmr of several of these compounds indicated that these were indeed in the enamine form rather than the ketimine form as reported by earlier workers.[5,6] The enamine N–H and only six protons on the five-membered ring were observed. This assignment of the enamine structure V to these amides is consistent with the recent enamine assignment made to the related esters VI.[7]

Hydrolysis of seven of these compounds gave near quantitative yields of the keto amides I only one of which (Table I) had not been previously reported.[5] In addition, use of 3-methyl-4-fluoroaniline led only to the formation of I with no bis adduct being obtained. These eight keto amides exhibited consistent infrared spectra (KBr): 3025–3100, 1700–1720, 1600–1648 (two peaks or peak and shoulder), and 1563–1592 cm^{-1}.

This route to aza steroids is not being pursued further.

Experimental Section[8]

2-Keto-N-(5′-isoquinolyl)cyclopentanecarboxyamide Methiodide (II).—A mixture of 2.54 g (0.01 mole) of 2-keto-N-(5′-isoquinolyl)cyclopentanecarboxyamide[4] (Ib) in 30 ml of methanol containing 10 ml of methyl iodide was refluxed for 2 hr. The solutions was concentrated to a volume of 10 ml and cooled. The light orange plates that separated were filtered, washed with ether, and dried to give 3.56 g (90%) of the crude product. A small portion was recrystallized from water, mp 206–207.5°.

Anal. Calcd for $C_{16}H_{17}N_2O_2I$: C, 48.50; H, 4.33; N, 7.07; I, 32.03. Found: C, 48.24; H, 4.31; N, 6.98; I, 32.11.

12-Keto-1,2,3,4,11,12,15,16-octahydro-3-methyl-3,11-diazacyclopenta[*a*]phenanthrene (IV).—A solution of 3.96 g (0.01 mole) of 2-keto-N-(5′-isoquinolyl)cyclopentanecarboxyamide methiodide (II) in 30 ml of ethanol and 20 ml of water was shaken under 3 to 4 atm of hydrogen in the presence of 0.1 g of platinum oxide. After the uptake of hydrogen had ceased, the solution was filtered and the filtrate concentrated. The residue was taken up in water and treated with a concentrated potassium carbonate solution. The aqueous alkaline solution was extracted thoroughly with benzene. The benzene extracts were dried over anhydrous sodium sulfate and concentrated to give 1.63 g (60%) of the intermediate reduced amide as a light brown oil.

The intermediate reduced amide was added to 15 g of polyphosphoric acid at 100°. After 15 min, the reaction mixture was poured onto ice. The aqueous acidic solution was treated with dilute sodium hydroxide until alkaline and extracted with benzene. The benzene extracts were dried over anhydrous sodium sulfate and concentrated to give 0.29 g (19.7%) of the desired product as a light yellow solid. A portion was recrystallized from a mixture of ethanol–water, mp 197–200°.

Anal. Calcd for $C_{16}H_{18}N_2O \cdot 0.5H_2O$: C, 72.97; H, 7.27; N, 10.64. Found: C, 73.20; H, 7.42; N, 10.78.

A portion of the same analytical sample was dried *in vacuo* at 100°.

Anal. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13. Found: C, 75.66; H, 7.09.

2-Keto-N-(5′-quinolyl)cyclopentanecarboxyamide (Id).—To 11.0 g (0.07 mole) of ethyl 2-ketocyclopentanecarboxylate heated to 150° was added 10.0 g (0.069 mole) of 5-aminoquinoline over a 5-min period. After the addition was complete, the temperature was increased to 170–180° for 4 min. The mixture was cooled and triturated with ether; the solid that separated was filtered, giving 5.46 g (31%) of the desired product which gave a semicarbazone mp 204.5–206°.

Anal. Calcd for $C_{16}H_{17}N_5O_2$: C, 61.72; H, 5.50; N, 22.50. Found: C, 61.56; H, 5.61; N, 22.30.

Reaction of 8-Aminoquinoline and Ethyl 2-Ketocyclopentanecarboxylate.—In a similar manner these two compounds gave 2-keto-N-(8′-quinolyl)cyclopentanecarboxyamide (Ia), mp 100–102° (lit.[4] mp 100–102°), and a small amount of bis condensation product[9] (V): mp 218–219° from ethanol; nmr ($CDCl_3$) τ −2.20 (enamine NH), 0.22 (amide NH), 7.93 (splitting 6.5 cps, cyclopentene 4-CH_2).

Anal. Calcd for $C_{24}H_{20}N_4O$: C, 75.80; H, 5.28; N, 14.72. Found: C, 75.55; H, 5.38; N, 14.85.

Reaction of Simple Aromatic Amines with Ethyl 2-Ketocyclopentanecarboxylate.—Ethyl 2-ketocyclopentanecarboxylate (6 g) was heated to 150° and 3 g of the aniline was added. The temperature was raised to 180° and kept there for 24 hr. After cooling the product crystallized in 20–70% yield. New compounds are included in Table I. The infrared data is included in the discussion. The nmr ($CDCl_3$) data follow: *p*-chloroaniline product, τ −0.45 (enamine NH), 8.07 (cyclopentene 4-CH_2); 2-methyl-4-fluoroaniline product, 0.08 (enamine NH), 2.22 (amide NH), 7.97 (cyclopentene 4-CH_2) (in DMSO-d_6 the NH were at −0.13 and 1.83); *p*-fluoroaniline product, −0.28 (enamine NH), 2.03 (amide NH).

A mixture of 2 g of the above products (V), 250 ml of 80% methanol, and 10 ml of 5% hydrochloric acid was stirred at room temperature for 48 hr to give a near quantitative yield of I. The infrared data is included in the discussion. The nmr ($CDCl_3$) data follow: *p*-chloroaniline product, τ 1.27 (amide NH), 6.87 (t) (CH on cyclopentane ring attached to carbonyl); *p*-fluoroaniline product, 1.18 (amide NH), 6.83 (t) (CH on cyclopentane ring attached to carbonyl).

Registry No.—Ethyl 2-ketocyclopentanecarboxylate, 611-10-9; Id, 14901-52-1; I (Ar = *p*-FC_6H_4–), 14796-10-2; I (Ar = 3-CH_3-4-FC_6H_3–), 14796-15-7; II, 14796-16-8; IV, 14796-17-9; V (Ar = *o*-FC_6H_4–), 14796-18-0; V (Ar = *p*-FC_6H_4–), 14901-53-2; V (Ar = 2,3-$(CH_3)_2C_6H_3$–), 14789-52-7; V (Ar = 2-CH_3-4-FC_6H_3–), 14789-53-8.

(5) R. J. Brown, F. W. S. Carver, and B. L. Hollingsworth, *J. Chem. Soc.*, 4295 (1961).

(6) R. Mayer, "Newer Methods of Preparative Organic Chemistry," Vol. II, W. Forst, Ed., Academic Press Inc., New York, N. Y., 1963.

(7) F. C. Pennington and W. D. Kehret, *J. Org. Chem.*, **32**, 2034 (1967).

(8) Analyses were by Spang Microanalytical Laboratories, Ann Arbor, Mich. Melting points are corrected.

(9) This compound was first prepared at the University of Miami by S. Roth and F. D. Popp.

Nor Steroids. VII. Ring Contraction of 2α-Bromo-5α-cholestan-3β-ol

HAROLD R. NACE AND GUY A. CROSBY

Metcalf Chemical Laboratory, Brown University, Providence, Rhode Island 02912

Received June 28, 1967

Although halohydrins are known to undergo rearrangement in the presence of metal ions[1,2] including ring contraction in the case of cyclic compounds,[3] the reaction has not been used for the preparation of ring nor steroids. Steroidal α-halo ketones, particularly bromo ketones, are readily available and can be reduced to the halohydrins. In addition, the point of carbonium ion generation can be controlled by using, for example, silver salts, which then will determine the course of the subsequent rearrangement. In this manner

(1) M. Tiffeneau, *Ann. Chim.*, [8] **10**, 322 (1907).

(2) V. Pocker, *Chem. Ind.* (London), 322 (1959).

(3) P. D. Bartlett and R. H. Rosenweld, *J. Am. Chem. Soc.*, **56**, 1990 (1934); D. Y. Curtin and S. Schmukler, *ibid.*, **77**, 1105 (1955); D. Y. Curtin and R. J. Harder, *ibid.*, **82**, 2357 (1960); J. G. Traynham and J. Schneller, *ibid.*, **87**, 2398 (1965).