[CONTRIBUTION FROM LINWOOD LABORATORIES, REMINGTON RAND DIVISION OF SPERRY RAND CORPORATION]

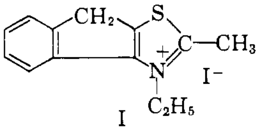
Cyanine Dyes. II.[1] Absorption of Cyanines Derived from 2-Methyl-8H-indeno[1,2-d]-thiazole

BY ROBERT H. SPRAGUE[1a] AND GEORGE DE STEVENS[2]

RECEIVED SEPTEMBER 10, 1958

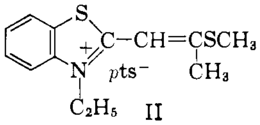
A new thiazole base has been prepared by condensing 2-bromo-1-indanone with thioacetamide. A quaternary salt of the product was condensed with cyanine dye intermediates to give a series of di- and trinuclear dyes with unusual absorption characteristics. The resonance theory is employed to explain the observed absorption and to elucidate the structure of the dyes.

Thioacetamide was condensed with 2-bromo-1-indanone[3] to give 2-methyl-8H-indeno[1,2-d] thiazole which forms a crystalline quaternary salt (I) with ethyl iodide. A number of dyes of varying complexity and absorption characteristics were prepared by condensation of I with benzoxazole, benzothiazole and quinoline derivatives. Ethyl orthoformate failed to react with I under any of the usual alkaline conditions. It was found that condensation occurs at the 2-methyl group of I to give a cyanine dye, and/or at the methylene group of the indenothiazole ring.

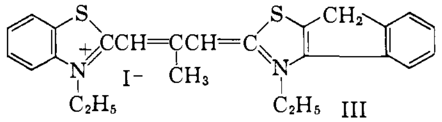


I

2 - (2 - Methylmercaptopropenyl) - benzothiazole etho-*p*-toluenesulfonate[4] (II) condensed readily with I to give a stable dye (III) with an absorption maximum at 540 mμ.

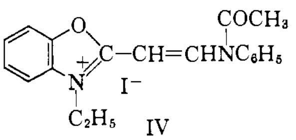


II



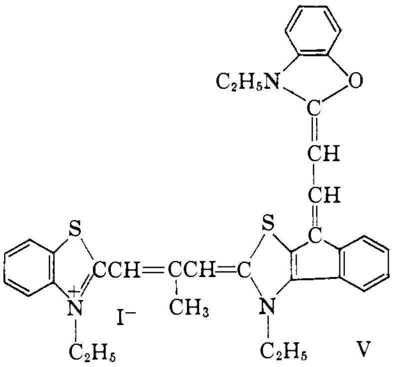
III

Compound III, in turn, reacted with the intermediate, 2-β-acetanilidovinylbenzoxazole ethiodide (IV), to give a green dye (V) with absorption maxima at 474 and 650 mμ, and a minimum at 540 mμ. As the methylene group adjacent to the sulfur atom in the indenothiazole moiety of III is activated by two double bonds, it is probable that condensation occurred at that point, giving structure V for the green dye.

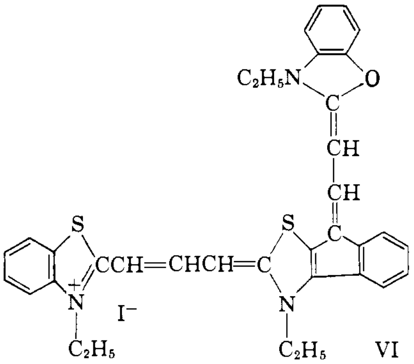


IV

Although the dye V was recrystallized repeatedly, analytical results agreeing with this formula were not obtained. However, the condensation of I and IV yielded a similar green dye (VI) with absorption maxima at 458 and 640 mμ; analysis agreed with the structure below. Absorption curves for dyes III, V and VI are given in Fig. 1.

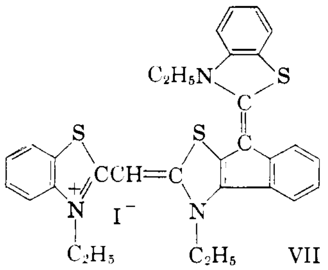


V



VI

The work which follows was undertaken in an attempt to confirm the structures assigned to V and VI and to explain their absorption characteristics. In both V and VI the absorption maximum in the green, characteristic of the normal carbocyanines, is absent. However, a similar dye of shorter chain length (VII), prepared by condensing I with 2-methylmercaptobenzothiazole etho-*p*-toluenesulfonate, showed an absorption maximum characteristic of the monomethine cyanines (430 mμ) as well as a new maximum at longer wave length (524 mμ).



VII

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(1) Part I of this series, THIS JOURNAL, **79**, 2275 (1957).

(1a) Horizons Ave., Cleveland, Ohio.

(2) Ciba Pharmaceutical Products, Inc., Summit, N. J.

(3) W. S. Johnson and E. Shelberg, THIS JOURNAL, **70**, 1745 (1948).

(4) L. G. S. Brooker and G. H. Keyes, U. S. Patent 2,369,657.

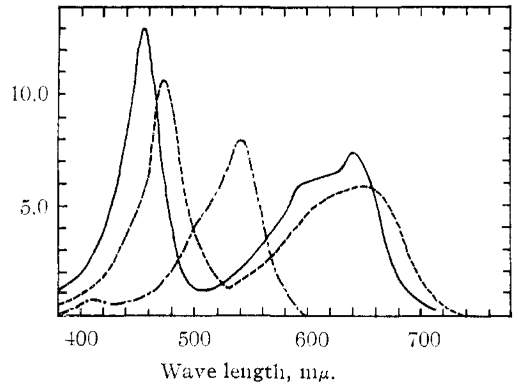
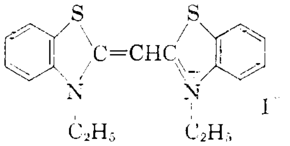


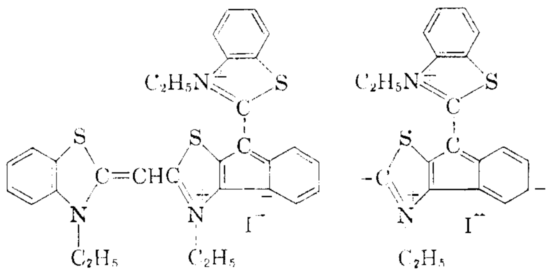
Fig. 1.—Absorption spectra in methanol: dye III, — - —; dye V, --------; dye VI, ———.

It seems probable that there are two modes of resonance operating in this molecule to produce the observed absorption. The first is the normal cyanine-type resonating system joining the two thiazole nitrogen atoms.[5] Since in 3,3′-diethylthiacyanine iodide (VIII) this system produces a strong absorption maximum at 430 mμ, the 430 mμ band of VII in all probability is due to this chromophore.



VIII

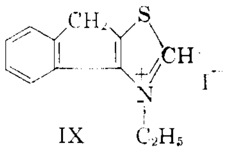
In addition, a dipolar chromophore may be present in VII in which the positive charge appears on the nitrogen of the benzothiazole ring linked to the methylene group of the indenothiazole, and the negative charge may be located on one of several carbon atoms of the ring, as



It is possible to write eleven structures which can contribute in this way to the resonance of the charged form; this results in a high degree of stabilization and, consequently, absorption at relatively long wave length.

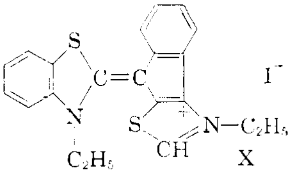
Therefore, the absorption maximum of VII at 524 mμ is probably due to this dipolar chromophore. The characteristic plus charge of the thiacyanine resonance will be attracted to the indenothiazole nitrogen by the minus charge induced in the near-by indene residue by the polarization of the "dipolar" chromophore. The dipolar contributing structure of this latter will, in turn, be stabilized by the presence of the thiacyanine plus charge close to its negative pole.

Accordingly, a similar dye containing only the dipolar chromophore should absorb at a shorter wave length than 524 mμ. Such a dye (X) was



IX

prepared by the condensation of 8H-indeno-[1,2-d]thiazole ethiodide (IX) with 2-methylmercaptobenzothiazole etho-*p*-toluenesulfonate. Since IX has only one reactive center (the methylene group), the dye necessarily has structure X.



X

The absorption maximum of X at 442 mμ is in the predicted range, although at somewhat shorter wave length than might have been expected. A comparison of X and VII shows that the introduction of the thiacyanine-type resonating chain causes a bathochromic shift in the absorption of the polar chromophore—in this case, a shift of 82 mμ. Absorption curves for dyes VII and X are given in Fig. 2.

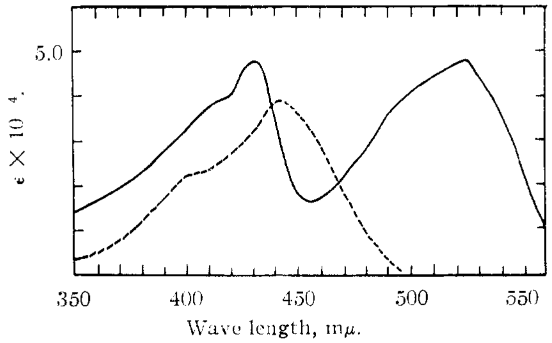
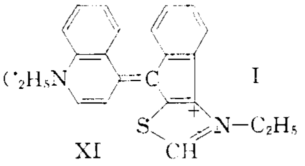


Fig. 2.—Absorption spectra in methanol: dye VII, ———; dye X, --------.

A second dye, containing only the dipolar chromophore, was prepared from IX by condensation with 4-phenylmercaptoquinoline etho-*p*-toluenesulfonate. This dye (XI) has its maximum absorption at 564 mμ, most of the shift toward longer wave length being attributable to the longer conjugated chain due to attachment of the quinoline ring in its 4-position.



XI

By analogy to VII then, the absorption of V and VI at shorter wave length is attributable to the carbocyanine chain, that at longer wave length to the dipolar chromophore. Thus, the maximum of VI at 458 mμ is due to the oxathiazolocarbo-

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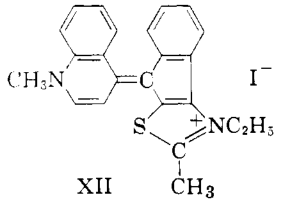
[5] L. G. S. Brooker, R. H. Sprague, C. P. Smyth and G. L. Lewis, THIS JOURNAL, **62**, 1116 (1940).

cyanine chain[1] (shifted 54 mμ to shorter wave length due to the imbalance introduced by the dipolar chromophore). In the case of V the first maximum (474 mμ) occurs at a longer wave length than that of VI, a shift which is attributable to the difference between a benzoxazole and a benzothiazole derivative.

The maxima of VI and V (640 and 650 mμ, respectively), which are attributable to the dipolar chromophore, occur at longer wave lengths than that of VII because of the longer conjugated chain of the former.

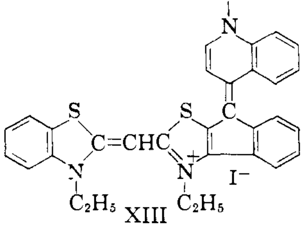
4-Phenylmercaptoquinoline metho-*p*-toluenesulfonate was condensed with I to give a dye (XII) which showed absorption characteristics strikingly similar to XI; in fact, the curves are almost identical. It is therefore probable that XII has the structure shown; if condensation had occurred at the 2-methyl group of I to give a thia-4-cyanine, the absorption maximum should be about 500 mμ—60 mμ shorter than that observed. The behavior of this quinoline intermediate is the reverse of that shown by II, which condensed preferentially with the 2-methyl group of I to give III.



XII

If XII has the structure shown, it should react with another highly reactive intermediate (2-methylmercaptobenzothiazole etho-*p*-toluene-sulfonate) to give a product, containing a thiacyanine chain, similar in structure to VII. If the interpretation of the absorption of VII is correct, this dye (XIII) should have two absorption maxima; one near 430 mμ due to the thiacyanine chain, and a second at a longer wave length. The second maximum should occur at a longer wave length than that of XII due to the effect of the thiacyanine chain on the dipolar chromophore; the shift should be about 80 mμ toward the red, *i.e.*, the absorption maximum of XIII should be about 640 mμ.

The condensation took place readily, and the new dye (XIII) was found to have absorption maxima quite close to those predicted—448 and 625 mμ. Absorption curves for XI, XII and XIII are given in Fig. 3.



XIII

Experimental[6]

2-Methyl-8H-indeno[1,2-d]thiazole.—2-Bromo-1-indanone[3] (106 g., 0.5 mole), thioacetamide (37.5 g., 0.5 mole) and absolute ethanol (250 ml.) were refluxed for 90 minutes.

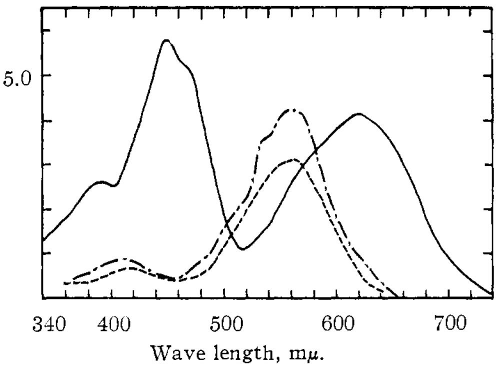


Fig. 3.—Absorption spectra in methanol: dye XIII, ———; dye XI, ---------; dye XII, — - —.

The solvent was evaporated under reduced pressure and 200 ml. of 5% HCl was added to the residue. The mixture was extracted with 200 ml. of ether, the aqueous layer made alkaline with ammonia, and the oil which separated was taken up in ether. The ether solution was dried with K_2CO_3, evaporated, and the residue was distilled under reduced pressure. The product was obtained as a strong-smelling oil which solidified on chilling; b.p. 147–150° at 12.8 mm., yield 25%.

3-Ethyl-2-methyl-8H-indeno[1,2-d]thiazolium Iodide (I).—2-Methyl-8H-indeno[1,2-d]thiazole (10.0 g., 0.05 mole) and ethyl iodide (9.5 g., 0.05 mole plus 10% excess) were refluxed for 8 hours. The mixture was chilled and crushed under 50 ml. of dry ether. The filtered product was washed with ether and acetone, and recrystallized from acetone; m.p. 233–235°, yield 70%.

For analysis, the ethiodide (0.1 g.), dissolved in 15 ml. of methanol, was converted to the less soluble perchlorate by the addition of 0.2 g. of sodium perchlorate; m.p. 218°.

Anal. Calcd. for $C_{13}H_{14}ClNO_4S$: N, 4.44; S, 10.16. Found: N, 4.43; S, 10.13.

3-Ethyl-8H-indeno[1,2-d]thiazolium Iodide (IX).—8H-Indeno[1,2-d] thiazole was prepared from thioformamide and 2-bromo-1-indanone as described for the 2-methyl derivative; b.p. 180–184° (24 mm.), yield 23%. The base was converted to the ethiodide by essentially the procedure given above; m.p. 210–211°, yield 67%.

Anal. Calcd. for $C_{12}H_{12}INS$: S, 9.74. Found: S, 9.68.

3,3'-Diethyl-9-methyl-8H-indeno[1,2-d]thiazolothiacarbocyanine Iodide (III).—Compound I (3.4 g., 1 mol), 2-(2-methylmercaptopropenyl)-benzothiazole etho-*p*-toluenesulfonate[4] (II) (4.4 g., 1 mol), 2.0 g. of triethylamine and 25 ml. of absolute ethanol were refluxed for 30 minutes, and the mixture cooled overnight. The precipitate was washed with water and acetone, dried and recrystallized from methanol (300 ml. per gram of dye) to give dark red crystals, m.p. 265–266°, yield 28%.

Anal. Calcd. for $C_{25}H_{25}IN_2S_2$: I, 23.32; S, 11.79. Found: I, 23.54; S, 11.77.

3,3'-Diethyl-8'-[(3-ethyl-2(3)-benzoxazolylidene)-ethylidene]-oxa-8H-indeno[1,2-d]thiazolocarbocyanine Iodide (VI).—Compound I (3.4 g., 1 mol), 2-β-acetanilidovinylbenzoxazole ethiodide (IV) (8.7 g., 2 mols), 6 ml. of triethylamine and 50 ml. of absolute ethanol were refluxed for 3 minutes. The product was filtered from the chilled mixture and washed with ethanol and water. Recrystallization from methanol (100 ml. per gram of dye) yielded tiny green crystals with a golden reflex, m.p. 280–281°, yield 58%.

Anal. Calcd. for $C_{35}H_{32}IN_3O_2S$: C, 61.30; H, 4.70; N, 6.13; I, 18.52. Found: C, 61.22; H, 4.74; N, 6.20; I, 18.34.

3,3'-Diethyl-8'-[(3-ethyl-2(3)-benzoxazolylidene)-ethylidene]-9-methyl-8H-indeno[1,2-d]thiazolothiacarbocyanine iodide (V) was similarly prepared by the condensation of IV (0.2 g., 1 mol) with the dye III (0.2 g., 1 mol) in 20 ml. of pyridine plus 0.2 g. of triethylamine. The purified dye melted at 236–238°, yield 30%.

3,3'-Diethyl-8'-(3-ethyl-2(3)-benzothiazolylidene)-8H-indeno[1,2-d]thiazolothiacyanine iodide (VII) was prepared

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[6] Melting points are uncorrected. Microanalyses are by Schwarzkopf Microanalytical Laboratory, New York, N. Y.

from 1 mole of I and 2 moles of 2-methylmercaptobenzothiazole etho-*p*-toluenesulfonate as described for III. The orange dye was recrystallized from methanol (1200 ml. per gram of dye); yield 35%, m.p. 280–282° dec.

Anal. Calcd. for $C_{29}H_{28}IN_3S_3$: N, 6.55; S, 15.00. Found: N, 6.49; S, 14.92.

3-Ethyl-8-(3-ethyl-2(3)-benzothiazolylidene)-8H-indeno[1,2-d]thiazolium Iodide (X).—The condensation of IX (1.0 g., 1 mol) with 2-methylmercaptobenzothiazole etho-*p*-toluenesulfonate (1.10 g., 1 mol), as described for III, yielded X as orange crystals; 200 ml. of methanol per gram of dye was used for recrystallization: m.p. 261–262°, yield 22%.

Anal. Calcd. for $C_{21}H_{19}IN_2S_2$: N, 5.71; S, 13.08. Found: N, 5.46; S, 12.92.

3-Ethyl-8-(1-ethyl-4(1)-quinolylidene)-8H-indeno[1,2-d]-thiazolium Iodide (XI).—Compound IX (1.5 g., 1 mol), 4-phenylmercaptoquinoline etho-*p*-toluenesulfonate (2.3 g., 1 mol), triethylamine (0.5 g.) and 15 ml. of absolute ethanol were refluxed for 20 minutes. The dye was recrystallized from methanol (50 ml. per gram of dye) as tiny black needles; yield 10%, m.p. 218–220°.

Anal. Calcd. for $C_{23}H_{21}IN_2S$: I, 26.21; N, 5.79. Found: I, 26.20; N, 5.59.

3-Ethyl-2-methyl-8-(1-methyl-4(1)-quinolylidene)-8H-indeno[1,2-d]thiazolium Iodide (XII).—Compound I (1.0 g., 1 mol) was condensed with 4-phenylmercaptoquinoline metho-*p*-toluenesulfonate (1.2 g., 1 mol) as above; the reflux time was 5 minutes. After recrystallization from methanol (150 ml. per gram of dye), the dye was obtained as black crystals, m.p. 235°, yield 50%.

Anal. Calcd. for $C_{23}H_{21}IN_2S$: I, 26.21; N, 5.79. Found: I, 26.15; N, 5.53.

3,3′-Diethyl-8′-(1-methyl-4(1)-quinolylidene)-8H-indeno-[1,2-d]-thiazolothiacyanine Iodide (XIII).—Dye XII (0.26 g., 1 mol) was condensed with 2-methylmercaptobenzothiazole etho-*p*-toluenesulfonate (0.19 g., 1 mol) as described for III; the mixture was refluxed for 10 minutes. The dye was washed with water followed by cold ethanol and recrystallized from methanol (200 ml. per gram of dye) as felted black needles, m.p. 240–243°, yield 25%.

Anal. Calcd. for $C_{32}H_{28}IN_3S_2$: I, 19.66; N, 6.51. Found: I, 19.42; N, 6.55.

MIDDLETOWN, CONN.

[CONTRIBUTION FROM THE WM. H. NICHOLS CHEMICAL LABORATORY, NEW YORK UNIVERSITY]

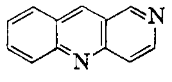
Synthesis of Pyrido[4,3-b]quinoline (2,10-Diazaanthracene) and Related Compounds

BY ANTHONY T. COSCIA AND S. CARLTON DICKERMAN

RECEIVED NOVEMBER 5, 1958

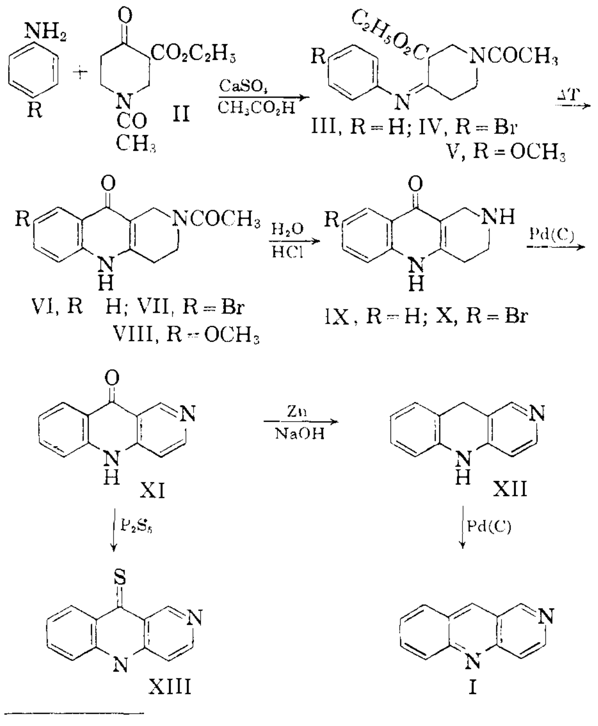
Pyrido[4,3-b]quinoline, previously unknown, has been synthesized from 1-acetyl-3-ethoxycarbonyl-4-piperidone and aniline. Various methods of removing oxygen from a pyridoquinolone have been investigated.

Although several derivatives of pyrido [4,3-b] quinoline (I) have been prepared[1-3], the parent heterocyclic compound has remained inaccessible. The failures of classical syntheses involving cyclization of acids derived from N-pyridylanilines[3-5] prompted us to investigate an approach which obviated such steps.[6]



I

1-Acetyl-3-ethoxycarbonyl-4-piperidone (II) was treated with aniline, *p*-bromoaniline and *p*-anisidine to yield the corresponding anils III, IV and V. The anil prepared from aniline was isolated as an intractable oil and the bromo and methoxy analogs were used to investigate experimental conditions for subsequent steps. The three anils were converted by heating to the corresponding tetrahydropyridoquinolones VI, VII and VIII. The possibility that the impure anil prepared from aniline contained an appreciable amount of anilide was excluded by quantitative estimation of the ethanol liberated during the cyclization reaction.[7] These precautions proved to be unnecessary since both the solid anil from *p*-bromoaniline and that prepared from aniline were converted eventually to pyrido[4,3-b]quinoline (I).



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[1] St. von Niementowski and E. Sucharda, *J. prakt. Chem.*, **94**, 193 (1916); *Ber.*, **52B**, 484 (1919).

[2] B. Bobranski and E. Sucharda, *Rocz. Chem.*, **7**, 192 (1927); *C. A.*, **24**, 1381 (1930).

[3] G. B. Bachman and R. S. Barker, *J. Org. Chem.*, **14**, 97 (1949).

[4] W. O. Kermack and A. P. Weatherhead, *J. Chem. Soc.*, 726 (1942).

[5] V. A. Petrow, *ibid.*, 927 (1945).

[6] B. M. Ferrier and N. Campbell [*Chemistry & Industry*, 1089 (1958)] have recently reported the synthesis of pyrido[4,3-b]quinolin-10(5H)-one (XI) from N-4-pyridylanthranilic acid.

[7] We have been unable to prepare an anilide from the keto ester II and aniline although B. K. Blount, Wm. H. Perkin, Jr., and S. G. P. Plant [*J. Chem. Soc.*, 1975 (1929)] reported the syntheses of both anil and anilide from aniline and 2-ethoxycarbonylcyclohexanone. The anilide would be expected to cyclize to the non-linear isomer in a strongly acidic reaction medium.