of 3-methyl-2-methylthiobenzoxazolium methylsulfate, and 3 ml of acetonitrile was heated to the boiling point, and 0.1 g (1 mmole) of triethylamine was added. The precipitated dye was removed by filtration and crystallized. The yield was 0.15 g.

2-R^1-3-R^2-4-R^3-8-Phenyl-6-[3-(3-ethyl-2(3H)-benzothiazolylidene)-1-propenyl]thiazolo[3,4-a]pyrimidinium Perchlorates (IXa-e). A mixture of 1 mmole of the corresponding perchlorate IVa-e, 0.43 g (1 mmole) of 3-ethyl-2-(2-acetanilidovinyl)benzothiazolium perchlorate, 5 ml of acetic anhydride, and 2 ml of alcohol was heated until the components dissolved, and 0.1 g (1 mmole) of triethylamine was added. The precipitated dye was removed by filtration and crystallized.

LITERATURE CITED

1. A. D. Kachkovskii, E. K. Mikitenko, and N. N. Romanov, Khim. Geterotsikl. Soedin., No. 5, 639 (1982).
2. E. K. Mikitenko, A. D. Kachkovskii, and N. N. Romanov, Khim. Geterotsikl. Soedin., No. 5, 634 (1982).
3. S. I. Shul'ga and V. A. Chuiguk, Ukr. Khim., Zh., 38, No. 5, 475 (1972).
4. E. Taylor, V. Anderson, and Y. Berchtold, J. Am. Chem. Soc., 77, 5444 (1955).

NEW SYNTHESES OF 3-INDOLYLGLYOXAL

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In a study of the possibilities of a simple method for the preparation of 3-indolylglyoxals two new methods for the synthesis of indolylglyoxal structures were proposed. The first method consists in oxidation of 3-hydroxyacetylindole with the dimethyl sulfoxide–oxalyl chloride complex, but for a number of reasons it is virtually inapplicable to the preparation of substituted indolylglyoxals. In the second case the readily synthesized 3-indolylglyoxyl chlorides are reduced to the corresponding aldehydes in good yields by means of trialkyltin hydrides.

The preparation of 3-indolylglyoxal (I) has already been reported [1-3]; however, the described methods for its synthesis are inconvenient and cannot always be reproduced [4]. It has therefore become necessary to develop a convenient and reliable method for the preparation of glyoxal I and its derivatives.

In the first variant we started from indole. It was converted by known methods [5] to hydroxyacetylindole (II), which we were able to oxidize under mild conditions by the method in [6] by means of the dimethyl sulfoxide (DMSO)–oxalyl chloride complex to glyoxal I, which is produced in the hydrate form. The spectral characteristics of the bisulfite and quinoxaline (VII) derivatives of aldehyde I were found to be identical to those previously obtained [1, 2]. A disadvantage of this method is the fact that many steps are involved in the preparation of hydroxyacetylindole (II). We made an attempt to simplify the process by synthesis of acetoxyacetylindole (IX) through an indolylmagnesium halide and acetylglyoxyl chloride. Unfortunately, the yields obtained in this case cannot be offset by the simplicity of the scheme.

The method set forth above is unsuitable for the synthesis of analogs of indolylglyoxal that are substituted in the indole ring because of the difficulty involved in obtaining the starting compounds and the sensitivity of many substituted indoles to oxidation.

The second method, which consists in acylation of 3-unsubstituted indoles with oxalyl chloride and subsequent reduction of the resulting acid chloride, makes it possible to

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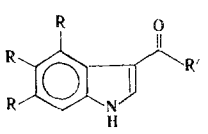
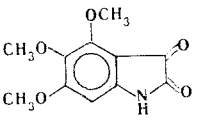
overcome these difficulties and to obtain the corresponding glyoxal in excellent yield in only two steps. For example, 4,5,6-trimethoxyindole was converted to acid chloride IV by the action of oxalyl chloride by the method in [8]. In searching for the best method for its reduction we carried out experiments with a simpler model (III) using various reducing agents [$Cu(PPh_3)_2BH_4$, $Li(tert\text{-}BuO)_3AlH_4$, $NaBH_4$, and $LiAlH_4$]. Success was achieved only with tributyltin and triethyltin hydrides.

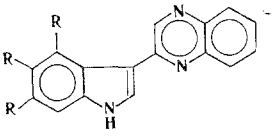
Because of the instability of aldehyde I, it was investigated in the form of bisulfate and quinoxaline derivatives. Compound V does not form a bisulfite derivative, probably as a consequence of deactivation of the dicarbonyl system because of the mesomeric effect of the conjugated methoxy groups. The structure of V was confirmed by IR and mass-spectroscopic data.



I-V



VI



VII, VIII

R=H; I R′=CHO; II R′=CH_2OH; III R′=COCl; IX R′=$COCH_2O_2CCH_3$; R=OCH_3; IV R′=COCl; V R′=CHO; VII R=H; VIII R=CH_3O

Starting 4,5,6-trimethoxyindole was obtained by reduction of the corresponding isatin VI with diborane. The synthesis of VI was carried out using the data in [7-9] with modification of the step involving conversion of trimethylgallic acid to trimethoxyaniline.

EXPERIMENTAL

The melting points were determined with a Kofler apparatus and were not corrected. The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The mass spectrum was obtained with an MKh-1303 spectrometer at 110°C and an ionizing voltage of 30 eV.

3-Indolylglyoxal (I). A) A solution of 1 ml (11 mmole) of oxalyl chloride in 25 ml of dichloromethane was poured into a four-necked flask equipped with a stirrer, a thermometer, and two dropping funnels, one of which contained a solution of 1.7 ml (22 mmole) of dimethyl sulfoxide (DMSO) in 5 ml of dichloromethane, the other of which contained a solution of 1.75 g (10 mmole) of hydroxyacetylindole II in 5 ml of dichloromethane and 0.5 ml of DMSO. The contents of the first funnel were added slowly at −50 to −60°C, and the mixture was stirred for 2 min. After 5 min, the contents of the second funnel were added, and the mixture was stirred at −35°C for 45 min. A 7-ml (50 mmole) sample of triethylamine was then added, and, after 5 min, the mixture was allowed to warm up to room temperature. Water (50 ml) was then added, and the organic layer was separated and poured into a solution of sodium bisulfite. The precipitate that formed after prolonged stirring was removed by filtration and dried *in vacuo* to give 0.92 g (33%) of a product whose IR and UV spectra were identical to those described in the literature.

B) A solution of 1 mmole of trialkyltin hydride in 1 ml of ethyl acetate was added with stirring and ice cooling to a suspension of 207 mg (1 mmole) of indoylglyoxyl chloride (III) [10] in 1.5 ml of anhydrous ethyl acetate. After 5-10 min, the cooling bath was removed, and the mixture was stirred for 2 h. The resulting suspension was diluted with 4 ml of hexane, and the solid material was removed by filtration and washed with hexane. The yield was 0.11 g (63%).

4,5,6-Trimethoxy-3-indolylglyoxal (V). This compound was obtained in 75% yield by method B. IR spectrum: 3300 (NH), 2850 (OCH_3), 2830 (CHO), and 1630-1650 cm^{-1} (COCO). The product had mp 122°C (dec.).

2-(4,5,6-Trimethoxy-3-indolyl)quinoxaline (VIII). A solution of 2.64 g (0.01 mole) of o-phenylenediamine in 200 ml of tetrahydrofuran (THF) was stirred for 24 h, after which the solvent was evaporated, and the residue was chromatographed with a column filled with silica gel [elution with benzene–acetone (25:2)] to give 0.5 g (15%) of a product with mp 165°C (from benzene). Mass spectrum, m/z (relative intensity, %): M^+ 335 (100), 320 (22), 304 (15), 280 (19), 262 (27), 105 (12). Found, %: C 68.2; H 5.1; N 12.3. $C_{19}H_{17}N_3O_3$. Calculated, %: C 68.0; H 5.0; N 12.5.

Trimethylgallamide. A mixture of 1 g (5 mmole) of trimethylgallic acid and 1.1 g (5.2 mmole) of PCl_5 in ether was stirred for 1 h, after which the mixture was cooled and added slowly to a large excess of concentrated ammonium hydroxide. After 30 min, the ether was removed by distillation, and the amide was removed by filtration and dried *in vacuo* to give 0.95 g (91%) of a product with mp 177°C (mp 177°C [9]).

3,4,5-Trimethoxyaniline. A 46-g (0.22 mole) sample of trimethylgallamide was dissolved in 1 liter of methanol containing 24.9 g (0.46 mole) of $NaOCH_3$, the solution was cooled to 0°C, 36.8 g (0.23 mole) of bromine was added slowly, and the mixture was stirred at 0°C for 1 h and refluxed for 20 min. The methanol was removed *in vacuo*, the residue was dissolved in hot water containing 40 g of NaOH, and the solution was refluxed for 2 h. It was then cooled, and the precipitated crystals were removed by filtration and crystallized from benzene to give 26 g (65%) of a product with mp 116°C (mp 116°C [9]).

3-Acetoxyacetylindole (IX). A solution of 6.82 g (0.05 mole) of acetylglycolyl chloride in 25 ml of ether was added slowly dropwise with stirring to a cooled solution of indolylmagnesium iodide prepared from 2.72 g (0.11 mole) of magnesium and 17.7 g (0.11 mole) of ethyl iodide in 40 ml of ether. After 2 h, the mixture was cooled with ice and acidified with a solution of 15 ml of acetic acid in 50 ml of water, and the precipitate was removed by filtration and crystallized from water (with charcoal) to give 0.32 g (3%) of a product with mp 140°C (mp 139-140°C [11]).

LITERATURE CITED

1. G. Sanna, Gazz. Chim. Ital., 72, 363 (1942).
2. T. P. Karpetsky and E. H. White, J. Am. Chem. Soc., 93, 2333 (1971).
3. Y. Kishi, T. Goto, and Y. Hirata, Tetrahedron Lett., No. 37, 3427 (1966).
4. A. L. Vereshchagin and A. A. Semonov, Izv. Sibirsk. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk, No. 9, 133 (1981).
5. G. I. Zhungietu, V. A. Budylin, and A. N. Kost, The Preparative Chemistry of Indole [in Russian], Shtiintsa (1975), p. 189.
6. A. J. Mancuso, Shui-Lung Huang, and I. Swern, J. Org. Chem., 43, 2480 (1978).
7. J. R. Merchant and S. S. Salgar, J. Indian Chem. Soc., 40, 23 (1963).
8. A. Carlsson, H. Corrodi, and T. Magnusson, Helv. Chim. Acta, 46, 1231 (1963).
9. F. Benington, J. Org. Chem., 20, 1451 (1955).
10. K. N. F. Shaw, A. McMillan, A. G. Gudmundson, and A. D. Armstrong, J. Org. Chem., 23, 1177 (1958).
11. M. N. Preobrazhenskaya, L. M. Orlova, and S. S. Liberman, Khim.-farm. Zh., No. 1, 32 (1972).