LETTERS TO THE EDITOR

# REACTION OF AROMATIC ALDEHYDES WITH 1-METHYLINDOLE-2-CARBOXYLIC ACID AND ITS ESTERS

N. A. Kogan and M. I. Vlasova

UDC 547.756'778.4

In a large number of studies the reaction of aldehydes with 2-substituted indoles, including 2-carbethoxyindoles [1], it was established that the reaction products are diindolylphenylmethanes. In the present study we have isolated compounds that are products of a different trend of this reaction.

We found that 1-methylindole-2-carboxylic acid and its methyl ester react exothermically with aromatic aldehydes in ether saturated with hydrogen chloride to give 1-methyl-2-carboxy(carbomethoxy)-3-(α-chlorobenzyl)indoles (IV-XI, see Table 1). 1-Methyl-2-carboxy(carbomethoxy)-3-(α-bromobenzyl)indoles (I-III) are formed in glacial acetic acid saturated with hydrogen bromide. 1-Methyl-2-carboxy(carbo-

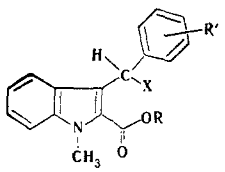

TABLE 1. 1-Methyl-2-carboxy(carbomethoxy)-3-(α-X-benzyl)-indoles

| Compound | R | X | R′ | mp, °C | Empirical formula |
|---|---|---|---|---|---|
| I | $CH_3$ | Br | H | 164—167 | $C_{18}H_{16}BrNO_2$ |
| II | $CH_3$ | Br | *p*-$NO_2$ | 145—148 | $C_{18}H_{15}BrN_2O_4$ |
| III | $CH_3$ | Br | *o*-Cl | 150—152 | $C_{18}H_{15}BrClNO_2$ |
| IV | $CH_3$ | Cl | *o*-$NO_2$ | 130—132 | $C_{18}H_{15}ClN_2O_4$ |
| V | $CH_3$ | Cl | *p*-$NO_2$ | 130—132 | $C_{18}H_{15}ClN_2O_4$ |
| VI | $CH_3$ | Cl | *o*-Cl | 132—134 | $C_{18}H_{15}Cl_2NO_2$ |
| VII | $CH_3$ | Cl | 2,4-Cl | 102—104 | $C_{18}H_{14}Cl_3NO_2$ |
| VIII | H | Cl | H | 150 | $C_{17}H_{14}ClNO_2$ |
| IX | H | Cl | *o*-Cl | 148 | $C_{17}H_{13}Cl_2NO_2$ |
| X | H | Cl | *o*-$NO_2$ | 140 | $C_{17}H_{13}ClN_2O_4$ |
| XI | H | Cl | *p*-$NO_2$ | 156 | $C_{17}H_{13}ClN_2O_4$ |
| XII | $CH_3$ | $OC_2H_5$ | H | 73 | $C_{20}H_{21}NO_3$ |
| XIII | $CH_3$ | $OC_2H_5$ | *o*-Cl | 128—130 | $C_{20}H_{20}ClNO_3$ |
| XIV | $CH_3$ | $OCH_3$ | *o*-Cl | 95—97 | $C_{19}H_{18}ClNO_3$ |
| XV | $CH_3$ | $OC_2H_5$ | *o*-$NO_2$ | 138—140 | $C_{20}H_{20}N_2O_5$ |
| XVI | $CH_3$ | $OC_2H_5$ | *p*-$NO_2$ | 90—93 | $C_{20}H_{20}N_2O_5$ |
| XVII | H | $OC_2H_5$ | *o*-Cl | 125 | $C_{19}H_{18}ClNO_3$ |
| XVIII | H | $OCH_3$ | *o*-Cl | 135 | $C_{18}H_{16}ClNO_3$ |
| XIX | $CH_3$ | O—Ac | H | 120—122 | $C_{20}H_{19}NO_4$ |
| XX | $CH_3$ | O—Ac | *p*-$NO_2$ | 138—140 | $C_{20}H_{18}N_2O_6$ |
| XXI | $CH_3$ | O—Ac | *o*-$NO_2$ | 134—136 | $C_{20}H_{18}N_2O_6$ |
| XXII | $CH_3$ | O—Ac | *o*-Cl | 158—160 | $C_{20}H_{18}ClNO_4$ |
| XXIII | H | OH | *o*-Cl | 125 | $C_{17}H_{14}ClNO_3$ |
| XXIV | H | OH | *p*-$NO_2$ | 185 | $C_{17}H_{14}N_2O_5$ |
| XXV | H | OH | *o*-$NO_2$ | 157 | $C_{17}H_{14}N_2O_5$ |
| XXVI | H | OH | H | 124 | $C_{17}H_{15}NO_3$ |

---

Leningrad Pharmaceutical Chemistry Institute. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 1003-1004, July, 1974. Original article submitted November 11, 1973; revision submitted February 11, 1974.

methoxy)-3-(α-alkoxybenzyl)indoles (XII-XVIII) are formed when the reaction is carried out in alcohol saturated with HCl. Compounds XIII and XIV are also obtained by crystallization of VI from ethanol (XIII) and methanol (XIV). Structure XIII was confirmed by PMR spectral data – aromatic protons (8H, 7.3 ppm), $OC_2H_5$ (q,* 3H, 3.53 ppm, t 2H, 1.19 ppm), $O-CH_3$ (s 3H, 3.79 ppm), $N-CH_3$ (s 3H, 3.97 ppm), benzyl group (1H, 6.52 ppm). 1-Methyl-2-carbomethoxy-3-(α-acetoxybenzyl)indoles (XIX-XXII) are formed by refluxing alkoxy derivatives XII-XV in acetic anhydride for 0.5 h. Acetoxy derivative XXII was also obtained by heating chloride VI in acetic anhydride. 1-Methyl-2-carboxy-3-(α-hydroxybenzyl)indoles (XXIII-XXVI) were obtained by dissolving halides VIII-X in dilute alkali and acidification of the resulting solutions with acetic acid. Chromatography of all of the synthesized compounds on Silufol with acyclohexane–ethyl acetate system (3 : 1) showed that the alkoxyacetoxy derivatives and the halides give one spot, while hydroxy derivatives XXIII-XXVI contain di(1-methyl-2-carboxy-3-indolyl)phenylmethanes as impurities. The elementary analyses of all of the compounds were satisfactory. The yields were 50-80%.

## LITERATURE CITED

1. C. Granacher, A. Mahal, and M. Gerb, Helv. Chim. Acta, 7, 579 (1924).

---

*Symbols: s is singlet, t is triplet, and q is quartet.