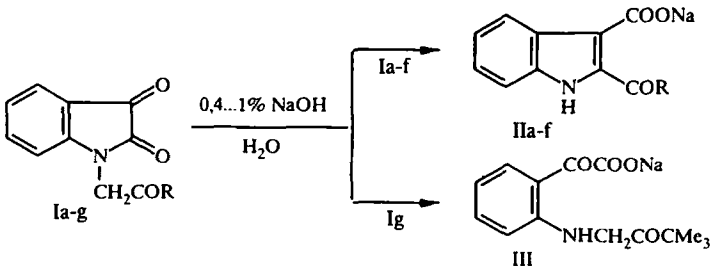
Chemistry of Heterocyclic Compounds. Vol. 34. No. 2, 1998

SYNTHESIS OF 2-(2,2-DIMETHYL-1-OXOPROPYL)-INDOLE-3-CARBOXYLIC ACID BY THE INDOLE-DIONE–INDOLE REARRANGEMENT METHOD IN NaOH/AQ. DMSO

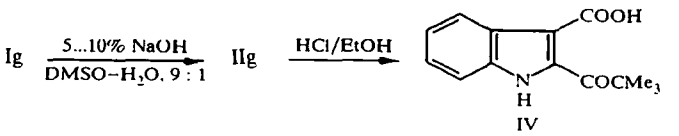
M. A. Rekhter, B. A. Rekhter, I. G. Yazlovetskii, and A. A. Panasenko

1-(2-Oxoalkyl)indole-2,3-diones (Ia-f) undergo the indoledione–indole rearrangement in 0.4-1% aq. NaOH to give the sodium salt of the corresponding 2-(1-oxoalkyl)indole-3-carboxylic acids (IIa-f) [1-4]. Under the same conditions, only opening of the heterocycle occurs in the case of 1-(3,3-dimethyl-3-oxobutyl)indole-2,3-dione (Ig) to give the Na salt of 2-(3,3-dimethyl-2-oxobutyl)phenyloxoacetic acid (III).



I, II a R = Me, b R = Et, c R = C_3H_7-*p*, d R = $CHMeCH_2Me_3$, e R = CH_2CHMe_2, f R = $CHEt_2$, g R = CMe_3

We have shown that Ig also undergoes the indicated rearrangement to the Na salt of 2-(2,2-dimethyl-1-oxopropyl)-indole-3-carboxylic acid (IIg) in superbasic medium (5-10% NaOH in 9:1 DMSO–water) [5, 6]. The action of ethanolic HCl on IIg leads to acid IV.



Indoledione Ig was obtained by hydrolysis of the β-ethylenacetal of 1-(3,3-dimethyl-2-oxobutyl)indole-2,3-dione (V).

Dione V was obtained by a reported procedure [7]. The bromine–pinacolin–β-ethylenacetal of 2,3-indoledione ratio was 1.8:5.3:1. This product dissolves poorly in ether and this permitted its crystallization instead of chromatography previously used in the synthesis of similar compounds. Extraction of the reaction mixture diluted with 10 volumes of water with ether leads to the removal of excess pinacolin and its bromination products. Product V crystallized out of the aqueous layer along with traces of the starting ethylenacetal of 2,3-indoledione. The yield of V was 40%, mp 113-115°C (from 1:1 benzene–hexane). PMR spectrum in $CDCl_3$: 1.26 (9H, s, CMe_3), 4.28-4.36 (4H, m, $-OCH_2CH_2O-$), 4.54 (2H, s, CH_2-N). 6.43-7.40 ppm (4H, m, H_{arom}).

Institute for the Biological Protection of Vegetation, Academy of Sciences of the Republic of Moldova, 2058 Kishinev. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 276-277, February, 1998. Original article submitted October 30, 1997.

 0009-3122/98/3402-0250$20.00

Dione Ig was obtained in 60% yield from ethylenacetal V by heating in ethanolic HCl at reflux, mp 84°C [7]. PMR spectrum in $CDCl_3$: 1.31 (9H, s, CMe_3), 4.71 (2H, s, CH_2), 6.51-7.58 ppm (4H, m, H_{arom}).

Acid IV. A sample of 2.0 g (8.13 mmoles) diketone Ig was added to 15 ml 9:1 DMSO–water containing 1.3 g (32.5 mmoles) NaOH. The blue color immediately observed turned to gray and then yellow–orange characteristic for III. The reaction mixture was stirred for 3.5 h at 20°C and then poured into 150 ml water acidified with 10 ml conc. hydrochloric acid. The crude precipitate of acid IV was removed, washed with two 30-ml portions of water, and purified through the sodium salt [1, 2]. Drying for 72 h at 20°C over P_2O_5 gave 1.2 g (55%) IV as $C_{14}H_{15}NO_3 \cdot H_2O$, mp 185-187°C. The yield when the reaction time was reduced to 2 h was only 20%. PMR spectrum in DMSO-d_6: 1.21 (9H, s, CMe_3), 3.35 (H, s, $NH+H_2O$), 8.05-7.25 (4H, m, H_{arom}), 12.17 ppm (1H, s, CO_2H). ^{13}C NMR spectrum in DMSO-d_6 at 20 MHz [3]: 135.33 ($C_{(12)}$), 105.45 ($C_{(3)}$), 121.63 ($C_{(4)}$), 120.99 ($C_{(5)}$), 120.69 ($C_{(6)}$), 112.24 ($C_{(7)}$), 125.22 ($C_{(8)}$), 141.49 ($C_{(9)}$), 165.30 ($\underline{C}O_2H$), 207.52 ($\underline{C}O$), 44.32 ($\underline{C}Me_3$), 28.58 ppm ($C\underline{Me}_3$).

The elemental analysis data for Ig, IV, and V were in accord with the calculated values.

REFERENCES

1. M. A. Rekhter, F. Z. Makaev, F. V. Babilev, G. N. Grushetskaya, and S. V. Rudakov, Khim. Geterotsikl. Soedin., No. 4, 483 (1996).
2. M. A. Rekhter, Khim. Geterotsikl. Soedin., No. 5, 642 (1993).
3. V. I. Gorgos, L. M. Zorin, G. I. Zhungietu, and M. A. Rekhter, Khim. Geterotsikl. Soedin., No. 11, 1490 (1983).
4. M. A. Rekhter, V. I. Gorgos, L. I. Zorin, and G. I. Zhungietu, USSR Inventor's Certificate No. 696,016; Byull. Izobret., No. 4 (1979).
5. M. A. Rekhter, Russian Federation Patent No. 2,047,603; Byull. Izobret., No. 3 (1995).
6. M. A. Rekhter, Khim. Geterotsikl. Soedin., No. 4, 472 (1996).
7. G. I. Zhungietu and M. A. Rekhter, Isatin and Its Derivatives [in Russian], Shtinitsa, Kishinev (1977).