INDOLE DERIVATIVES

CIII.* ESTERIFICATION OF ω-(3-INDOLYL)ALKANOIC ACIDS IN THE PRESENCE OF SULFONATE CATION-EXCHANGE RESINS

N. N. Suvorov, B. Ya. Eryshev,
L. E. Frumin, and A. G. Dubinin

UDC 542.951.3+547.752.29

Esters were obtained in satisfactory yields by reaction of ω-(3-indolyl)alkanoic acids with aliphatic alcohols of various structures in the presence of KU-2 and KU-36 sulfonate cation-exchange resins.

Esters of indolylalkanoic acids are of considerable interest as plant-growth stimulators. They are usually obtained by esterification of organic acids with alcohols in the presence of acid catalysts (for example, see [2, 3]). However, in the presence of mineral acids indolylalkanoic acids undergo a number of transformations, as a consequence of which the yields fall. Thus, in the esterification of 3-indolylacetic, β-(3-indolyl)propionic, and γ-(3-indolyl)butyric acids in the presence of sulfuric acid the yields of esters based on the crude products are 80-90%, but they fall sharply to 55-60% as a result of purification. The reaction does not take place in the presence of neutral catalysts or metal halides [4].

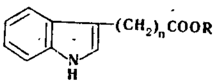
Our experiments have shown that indolylacetic acid reacts with ethanol in the presence of KU-2 to give the ester in quantitative yield. It is apparent from Fig. 1 that when the KU-2 catalyst is used better results are achieved when 3 g of the catalyst per 0.02 mole of the acid is used (curve 3). Moreover, equilibrium is reached after 3 h with 99.8% conversion of the acid. Better results are not obtained when the amount of catalyst is increased to 4 g (curve 4) because of acceleration not only of the forward but also of the reverse reaction. Equilibrium is established in only 6 h when a smaller amount of the catalyst (2 g) is used (curve 2). The optimum amount of KU-2 catalyst for the preparation of indolylacetic acid ester established in this way was also applied to the KU-36-catalyzed synthesis of esters of β-(3-indolyl)propionic and γ-(3-indolyl)butyric acids, inasmuch as the exchange capacities of the two resins differ only slightly. Alcohols of normal structure undergo reaction with indolylalkanoic acids more rapidly than alcohols with iso structures. Although the resins have approximately equal exchange capacities (KU-2 E = 3.5, KU-36 E = 3.0) the activity of KU-36 proved to be considerably weaker than KU-2. The yields of the esters did not increase even when the reaction was carried out with simultaneous removal of the water by distillation. In addition, KU-36 has increased resistance to temperature but is not stable with respect to organic solvents such as toluene. Thus when the esterification was carried out with benzyl alcohol at the boiling point of the reaction mixture, the exchange capacity and structure of the catalyst did not undergo significant changes (E = 3.0 prior to the reaction, and E = 2.55 after the reaction). However, when the reaction was carried out in the presence of toluene as an azeotrope-forming solvent, the structure of KU-36 changed markedly. The catalyst was converted to a fine powder, and the exchange capacity was reduced to 0.925; this indicates destruction of the KU-36 catalyst. When the esterification with lower alcohols was carried out 10 times, the catalyst did not lose its activity; this indicates the possibility of its repeated use, whereas the aggregate state and the moderate degree of swelling of the catalyst in this system indicate realization of the reaction under both periodic and continuous technological conditions.

---

* See [1] for communication CII.

D. I. Mendeleev Moscow Chemical-Engineering Institute. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1506-1508, November, 1974. Original article submitted January 14, 1974.

TABLE 1.



n	R	bp, °C (mm)	Empirical formula	N, %		Yield, % based on KU-36*
				found	calc.	
1	C_2H_5	170—174 (9,3·10⁻³)	$C_{12}H_{13}O_2N$	6,8	6,9	79,8 (97,5)
2	C_2H_5	188—195 (1·10⁻²)	$C_{13}H_{15}O_2N$	6,5	6,4	73,1 (98,2)
3	C_2H_5	215—222 (1·10⁻²)	$C_{14}H_{17}O_2N$	6,1	6,0	68,0 (96,9)
3	C_3H_7-*n*	185—205 (9,3·10⁻³)	$C_{15}H_{19}O_2N$	5,5	5,7	52,7
3	C_3H_7-*i*	190—215 (2,6·10⁻³)	$C_{15}H_{19}O_2N$	5,6	5,7	50,0
3	C_4H_9-*n*	195—205 (0,2·10⁻²)	$C_{16}H_{21}O_2N$	5,2	5,4	40,8
3	C_4H_9-tert	200—215 (2,0·10⁻³)	$C_{16}H_{21}O_2N$	5,6	5,4	35,4
3	C_5H_{11}-*i*	210—235 (1,02·10⁻²)	$C_{17}H_{23}O_2N$	4,7	5,1	40,0
3	$CH_2C_6H_5$	mp 133°	$C_{19}H_{19}O_2N$	4,8	4,8	27,7

*Data for KU-2 are given in parentheses.

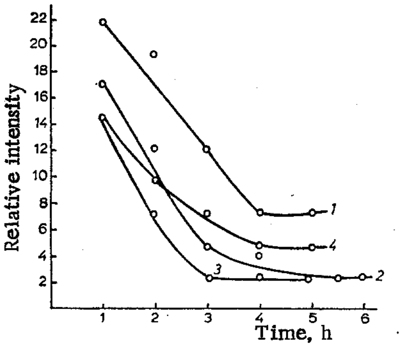


Fig. 1. Relative activity of KU-2 as a function of the amount used in the esterification of indolylacetic acid with ethanol: 1) 1 g; 2) 2 g; 3) 3 g; 4) 4 g.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer.

Preparation of the Catalyst. Commercial KU-2 and KU-36 in the salt form were placed in an Erlenmeyer flask and covered with 6% hydrochloric acid solution. The mixtures were allowed to stand for 24 h, after which the acid form (H^+) of the cation-exchange resin was sucked dry with a Büchner funnel and washed with distilled water until chloride ions were no longer present in the washings (as shown by tests with a silver nitrate solution). It was then washed with several portions of ethanol and dried on the funnel under vacuum; the product in this form was used as the catalyst.

Esters of ω-(3-Indolyl)alkanoic Acids (Table 1). A round-bottom flask equipped with a reflux condenser was charged with 0.02 mole of ω-(3-indolyl)alkanoic acid, 35 ml of alcohol, and 3 g of KU-2 or KU-36 catalyst.

The mixture was refluxed for 3 h, after which it was cooled to room temperature, and the catalyst was removed by filtration. The ester was isolated from the filtrate by the usual methods with allowance for the nature and properties of the alcohol used in the reaction. Lower alcohols, which are water-soluble, were removed with water, while higher alcohols were removed by vacuum distillation. Benzyl γ-(3-indolyl)butyrate was isolated by dissolving the residue from the reaction mixture, after removing the unchanged acid, in benzene (30 ml), and the benzyl ester was precipitated from the resulting solution by the addition of petroleum ether (200 ml). Absorption bands at 3340-3420 cm^{-1} (pyrrole ring NH) and 1720-1730 cm^{-1} (ester C=O) appear in the IR spectra of the esters obtained.

LITERATURE CITED

1. V. S. Rozhkov, Yu. I. Smushkevich, T. A. Kozik, and N. N. Suvorov, Khim. Geterotsikl. Soedin., 1502 (1974).
2. C. H. Fawsett, R. L. Wain, and F. Wightman, Proc. Roy. Soc., B452, 231 (1960).
3. A. K. Plisov and A. I. Bykovets, Zh. Obshch. Khim., 23, 613 (1953).
4. B. Ya. Eryshev and B. P. Yatsenko, Trudy MKhTI im. D. I. Mendeleeva, 66, 50 (1970).
5. N. N. Suvorov and B. Ya. Eryshev, USSR Author's Certificate No. 374300 (1972); Byul. Izobr., No. 15, 48 (1973).