BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 42 3340—3342 (1969)

Gamma-Ray-Induced Addition of Formamide and Aniline to Crotonic Acid and Its Ester

Mitsuomi ITOH, Masao TOKUDA, Yuji YOKOYAMA and Akira Suzuki*[1]

Department of Chemical Process Engineering, Hokkaido University, Sapporo, Hokkaido

(Received April 24, 1969)

Numerous reports on free radical addition reactions by various methods[1] are available, including peroxide induced reaction, photochemical reaction, and radiation-induced reaction. These varying methods tend to give different products. We reported previously on the photochemical addition of formamide and aniline to crotonic acid and its esters.[2] The present work was carried out using a γ-radiation technique on the same reactants in an attempt to compare the results with that obtained by photochemical method.

Light-induced amidation of olefins[3] and α,β-unsaturated esters,[4] and γ-radiation and electron induced amidation of olefins[5,6] and dienes[7] have been reported. According to the results, it was indicated that the light-induced addition of formamide to α,β-unsaturated esters such as methyl 2-octenoate, methyl 2-nonenoate and methyl 2-decenoate give only the β-adducts. On the other hand, we have pointed out that when crotonic acid and the esters are subjected to a photochemical addition of formamide, the α,- β- and γ-products were obtained and the product distribution between the acid and esters was different.

It was found that γ-ray-induced amidation of crotonic acid and its ethyl ester gives only the corresponding β-adduct, as summarized in Table 1.

1* Author to whom inquiries should be addressed.

1) For reviews, G. Sosnovsky, "Free Radical Reactions in Preparative Organic Chemistry," MacMillan Co., New York (1964).

2) M. Itoh, M. Tokuda, K. Kihara and A. Suzuki, *Tetrahedron*, **24**, 6591 (1968).

3) D. Elad and J. Rokach, *J. Org. Chem.*, **30**, 3361 (1965) and references cited therein.

4) J. Rokach and D. Elad, *ibid.*, **31**, 4210 (1966).

5) J. Rokach, C. H. Krauch and D. Elad, *Tetrahedron Letters*, **1966**, 3253.

6) D. P. Gush, N. S. Marans, F. Wessells, W. D. Addy and S. J. Olfky, *J. Org. Chem.*, **31**, 3829 (1966).

7) C. H. Krauch, J. Rokach and D. Elad, *Tetrahedron Letters*, **1967**, 5099.

TABLE 1. γ-RAY-INDUCED ADDITION OF FORMAMIDE TO CROTONIC ACID AND ETHYL CROTONATE

Substrate	Yield of 1:1-adduct, %	G-value	Distribution of products	
			α-Adduct	β-Adduct
$CH_3CH=CHCO_2H$	30[a]	10	0	100
	45[b]	8.6	0	100
$CH_3CH=CHCO_2Et$	36[a]	12	0	100

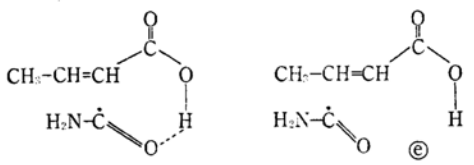
a) Irradiation time: 72 hr
b) Irradiation time: 144 hr

$$CH_3CH=CH-CO_2R + HCONH_2 \xrightarrow{\sim\sim} CH_3-\underset{\underset{CONH_2}{|}}{CH}-CH_2CO_2R$$

$R=H, C_2H_5$

Although detailed mechanistic studies were not undertaken, the reaction probably occurred by the attack of the carbamoyl radical which was produced by direct or indirect process.[5] The preference of β-adduct is in line with the generalization that the β-carbon is more easily attacked than the α-carbon in usual free radical addition to α,β-unsaturated carbonyl compounds having no phenyl linkage.[8]

The difference of the products obtained by photochemical procedure[2] and γ-ray-induced technique might be explained as follows: the orientation effect proposed in photochemical addition reactions need not be taken into account. A six-membered transition state such as A is not expected in γ-ray-induced reaction, because of the presence of the solvated electrons which interrupt the hydrogen bond with the carbonyl oxygen of the carbamoyl radical as described in B. Consequently, the addition of carbamoyl radical seems to occur readily at the β-carbon. On the other hand, the isomerization of the α,β-unsaturated ester to the corresponding β,γ-isomer observed in photochemical



reaction[2,9] was not observed in γ-ray-induced reaction. This is apparently the reason why the γ-adduct is not obtained in the latter reaction.

A γ-ray-induced addition of aniline to crotonic acid and ethyl crotonate was found to give a small amount of 1 : 1-adduct. The distribution of the product isomers is listed in Table 2. In the case of crotonic acid, only the β-adduct was obtained with a large amount of side reaction products which are probably a mixture of polymeric and fragmentated products. It is of interest that crotonic acid is readily converted, with a 66% conversion, as compared with the ethyl ester with a mere 2% conversion. When the sealed tube was opened after irradiation, an increase of the inside pressure was observed, suggesting a generation of carbon dioxide. The photochemical alkylation of nitrogen hetero-aromatics with alkyl radical resulting from carboxylic acid by decarboxylation has been reported.[10] Thus we attempted to examine decarboxylation during the γ-ray irradiation applied to a mixture of crotonic acid and aniline. When a mixture of crotonic acid (0.2 mol), aniline (0.4 mol) and benzene (25 m*l*) was irradiated for 72 hr, one hundred and fourteen milliliters of CO_2 gas (0.006 mol) was evolved. This indicates that 3% of crotonic acid was subjected to decarboxylation. Several carboxylic acids (acetic, propionic, butyric and benzoic acids) were also treated under the same condition, but generation of CO_2 was not observed.

TABLE 2. γ-RAY-INDUCED ADDITION OF ANILINE TO CROTONIC ACID AND ETHYL CROTONATE

Substrate	Yield of 1:1-adduct, %	G-value	Distribution of products	
			α-Adduct	β-Adduct
$CH_3CH=CHCO_2H$	5 (66[a])	4.3	0	100
$CH_3CH=CHCO_2Et$	2	1.6	42	58

a) Total converstion of crotonic acid, calculated from crotonic acid unreacted.

In the γ-ray-induced addition of aniline to ethyl crotonate, a yield of a small amount of α- and β-adducts without side reaction products was detected.

Experimental

Reagents and a General Procedure. All reagents were distilled or recrystallized before use. Benzene and *t*-butanol were dried over metal sodium and calcium oxide respectively.

A mixture of reactants was charged into a 30×100 mm tube and the inside atmosphere was replaced with nitrogen gas several times. The sealed sample was irradiated in a cobalt-60 cavity source at room temperature. The dose rate was approximately 4×10^5

8) R. Brown, W. E. Jones and A. R. Pinder, *J. Chem. Soc.*, **1951**, 2123; T. M. Patrick, *J. Org. Chem.*, **17**, 1269 (1952); R. L. Huang, *J. Chem. Soc.*, **1956**, 1749; M. Okawara, *Kogyo Kagaku Zassi (J. Chem. Soc. Japan, Ind. Chem. Sect.,)* **57**, 760 (1954).

9) M. Itoh, M. Tokuda, K. Seguchi, K. Taniguchi and A. Suzuki, *Kogyo Kagaku Zasshi (J. Chem. Soc. Japan, Ind. Chem. Sect.)*, **72**, 219 (1969).

10) H. Nozaki, M. Kato, R. Noyori and M. Kawanishi, *Tetrahedron Letters*, **1967**, 4259.

rad. hr^{-1}.

The irradiated sample was treated as described earlier.[2] Glpc analysis was made with a Yanagimoto Model GCG-220 and an Ohkura Type GT-360 (Apiezon Grease L 20% coated on Diasolid L).

γ-Ray-Induced Amidation of Crotonic Acid with Formamide. A mixture of crotonic acid (0.08 mol), formamide (1.20 mol) and *t*-butanol (20 m*l*) was irradiated for 72 hr. The total dose was 2.88×10^7 rads. Treatment of the reaction mixture gave 3.2 g of 1 : 1-adduct (yield, 30% based on crotonic acid employed). Glpc analysis (column temp., 170°C) of the esterified product indicated the presence of a large peak and two other small peaks, the former corresponding to β-adduct. Neither of the latter small peaks corresponded to α-adduct, β-adduct or oxamide.

Further irradiation (144 hr, total dose, 5.76×10^7 rads) to the same mixture gave 4.70 g of 1 : 1-adduct (45%) and the product was confirmed as the β-adduct by glpc analysis.

γ-Ray-Induced Amidation of Ethyl Crotonate with Formamide. A mixture of ethyl crotonate (0.08 mol), formamide (1.20 mol) and *t*-butanol (20 m*l*) was irradiated for 72 hr (total dose, 2.88×10^7 rads). The same treatment of the irradiated mixture gave 4.60 g of 1 : 1-adduct (36%) and glpc analysis (170°C) of the esterified product indicated the presence of only β-adduct.

γ-Ray-Induced Addition of Aniline to Crotnic Acid. A mixture of crotonic acid (0.2 mol), aniline (0.4 mol) and benzene (25 m*l*) was irradiated for 72 hr (total dose, 2.88×10^7 rads). The reaction mixture was treated by the procedure reported by Stoermer,[11] which gave 2.0 g of β-anilinobutyranilide (yield, 4% based on crotonic acid) and 0.2 g of ethyl β-anilinobutyrate (1%). Distribution of 1 : 1-adducts was determined by glpc (Apiezon Grease L, 250°C). The total conversion of this reaction was calculated as 66% from the recovered crotonic acid (5.8 g).

Decarboxylation during the irradiation was estimated by gas analysis of CO_2 evolved. When the sealed tube was destroyed in an autoclave, 116 m*l* of CO_2 (0.006 mol) was generated at 22°C, which indicated that 3% of crotonic acid used was decarboxylated during the irradiation.

γ-Ray-Induced Addition of Aniline to Ethyl Crotonate. The irradiation of a mixture of ethyl crotonate (0.07 mol), aniline (0.14 mol) and benzene (10 m*l*) for 72 hr (total dose, 2.88×10^7 rads) gave 0.08 g of ethyl anilinobutyrate (1%) and 0.12 g of anilinobutyranilide (1%). The distribution of 1 : 1-adducts was determined by glpc analysis (250°C).

The authors wish to thank the Nippon Gosei Kagaku Co. for the supply of pure crotonic acid.

11) R. Stoermer and E. Robert, *Ber.*, **55**, 1030 (1922).