Journal of Labelled Compounds — Vol. VIII, n°2, April-June, 1972

NOTE.

ON ALKENOIC ACIDS AND ALKENOLS FOR TRITIATED LONG-CHAIN COMPOUNDS.

received on February 25, 1972

It has been pointed out in the previous paper (1) that tritiated long-chain compounds of high purity, in terms of radiochemical criteria, could be better synthesized through the following route :

$$R.CH_2CH_2.COOH \xrightarrow[I_2]{Br_2} R.CH_2CHI\ COOH \xrightarrow{KOH} R.CH{=}CH.COOH$$

$$\xrightarrow{^3H_2} R.CH\ ^3H.CH\ ^3H\ COOH \xrightarrow{LiAlH_4} R.CH\ ^3H.CH\ ^3H.CH_2OH \quad \text{(Route i)}$$

rather than

$$\underset{(I)}{R{\cdot}CHO} \xrightarrow{CH_2\begin{smallmatrix}\diagup COOR'\\ \diagdown COOR''\end{smallmatrix}} \underset{(II)}{R{\cdot}CH{=}CH{\cdot}COOH} \xrightarrow{LiAlH_4} \underset{(III)}{R{\cdot}CH{=}CH{\cdot}CH_2OH}$$

$$\xrightarrow{^3H_2} \underset{(IV)}{R.CH\ ^3H.CH\ ^3H.CH_2OH} \qquad \text{(Route ii)}$$

with $R'=R''=C_2H_5$, which was employed originally by Tulus (2). This has been critisized for some uncertainty of the reaction, I ⟶ II (1, 3).

Koo et al. (4) reported that 2,3-dimethoxycinnamic acid is formed with 70 % yield by condensation of 2,3-dimethoxybenzaldehyde with malonic acid ($R'=R''=H$) when the reaction proceeds in a solution of piperidine in pyridine. To see whether the reaction is applicable to the tritiation of long-chain compounds, we have examined the behaviors of II and III with $R = C_9H_{19}$, $C_{11}H_{23}$, and $C_{13}H_{27}$ upon tritiation using Urushibara (5) or Raney nickel.

The product II obtained by the method of Koo (4) was subjected to reduction with $LiAlH_4$ to obtain III by the method of Nystrom and Brown (6). Both II and III were purified by repeated distillation to give the narrow ranges of boiling points cited in the third column of Table I.

TABLE 1. Boiling points of II, III, and their tritiation products.

Product	R =	Before	After
		Tritiation	
II	C_9H_{19}	168 °C/10 mm Hg	170 °C/2.5 mm Hg
	$C_{11}H_{23}$	164.7-169.0 °C/3.5 mm Hg	------------------------
(acids)	$C_{13}H_{27}$	145 -148 °C/1 mm Hg	204 -205 °C/5.5 mm Hg
III	C_9H_{19}	102.5-103.0 °C/2.5 mm Hg	102.6-103.0 °C/2.5 mm Hg
(alcohols)	$C_{11}H_{23}$	133 -135 °C/1 mm Hg	137 -139 °C/2 mm Hg

However, the hydrogen absorption for any of these products always reached saturation at ca. 50 % of the calculated value. A typical example is shown in Fig. 1.

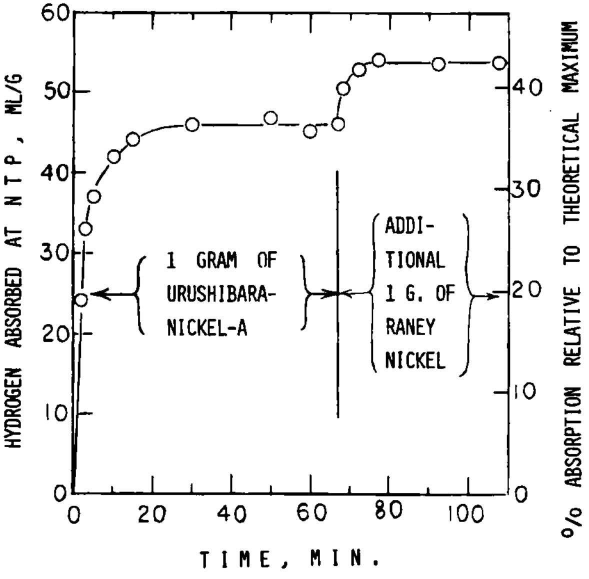

FIG. 1. Hydrogen absorption curve for III with R = C_9H_{19}
Dodecen-2,3-Ol-1, 1.045 g.
Solvent, 70 ml of ethanol
Initial catalyser, 1 g. of Urushibara Nickel A
Additional catalyser, 1 g. of Raney nickel

Evidently, the products, II and III, contained considerable amounts of some saturated compound(s) of similar nature as reflected by the same boiling point.

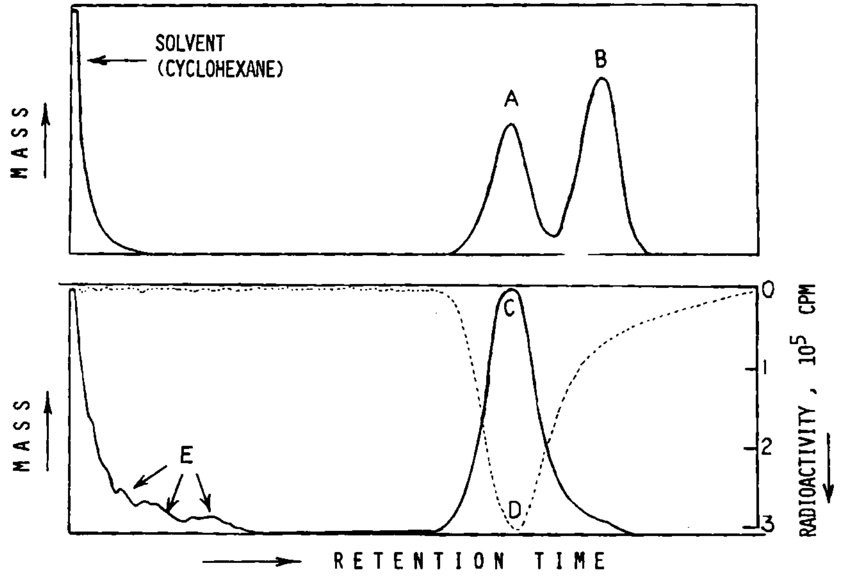

FIG. 2. (Upper part) Gaschromatogram of II with R = $C_{13}H_{27}$
(Lower part) Mass- (full curve) and radiogaschromatograms (dotted) a few days after tritiating the sample shown in the upper part. Specific activity of the tritiated compound, 84 m Ci/m mole. Both samples were methylated with diazomethane prior to the chromatography.

Fig. 2 illustrates the difference in radiogaschromatograms (Yanagimoto-Aloka, Type RD-4 for gas-phase proportional counting) before and after the tritiation of hexadecen-2,3-oic acid. Essentially the same chromatograms were obtained for any of the acids and alcohols examined. It can be seen in this figure that peak B, in the upper part, is erased by tritiation to merge with the peak A, which coincides with both the mass peak C and the radioactivity peak D in the lower part. It was shown in separate experiments that the peaks C and D represent tritiated hexadecanoic acid, suggesting that peak B is indicative of the corresponding unsaturated acid : the incomplete absorption of hydrogen (Fig. 1) can be ascribed to the saturated compound, which is identical to the hydrogenated product of II or III. The difference in retention time between the two peaks, A and B, is attributable to the difference not in boiling point (Table I, columns 3 and 4) but in molecular polarity due to the double bond.

It should be noted that the tritiation of II or III was accompanied always by the formation of impurities having tritium radioactivity, as appearing in the region E of Fig. 2. It is possible that either one or both of the original two peaks, A and B, included such substance(s) susceptible to degradation into small fragments upon tritiation. They were not very difficult to separate from the tritiated alcohols by fractional distillation. In the case of acids, however, it was rather difficult to eliminate these fragments, unless the acids had been methylated to the corresponding esters for fractional distillation, followed by saponification to recover the original acids in the pure form. The route, however, is too complicated and involves some procedures inadequate for handling labelled compounds. It seems, therefore, that Route ii is of use only for obtaining the tritiated alcohols, IV, which are separable from the fragmental impurities by distillation or other means pertinent to individual requirements. On the other hand, Route i is useful for obtaining not only alcohols, IV, but also the acids to be obtained by tritiation of II without special care for eliminating fragmental impurities which are found only with Route ii.

The authors thank Dr. I. Motoyama for his technical help in handling the catalysers.

Mitsuo MURAMATSU, Kazuo TAJIMA, Makio IWAHASHI, Kunio MASUMOTO and Teruo HORIUCHI

Department of Chemistry, Faculty of Science,
Tokyo Metropolitan University, Setagaya-Ku

Tokyo, Japan 158

REFERENCES

1. MURAMATSU, M., and TAJIMA, K. - *J. Labelled Compounds*, 2 : 304 (1966).
2. TULUS, R. - *Rev. Faculté sci. univ. Istanbul*, 9A : 105 (1944).
3. GENSLER, W. J. - *Chem. Rev.*, 57 : 191 (1957).
4. KOO, J., FISH, M. S., WALKER, G. N., and BLAKE, J. - Organic Syntheses, Collective Volume 4, edited by N. Rabjohn, John Wiley and Sons, Inc., New York, N.Y. 1963, p. 327.
5. URUSHIBARA, Y., NISHIMURA, S., and UEHARA, H. - *Bull. Chem. Soc. Japan*, 28 : 446 (1955).
6. NYSTROM, R. F., and BROWN, W. G. - *J. Am. Chem. Soc.*, 69 : 2548 (1947).