

TRITIUM LABELING OF HEXACHLOROCYCLOHEXANE ISOMERS

BY GAS EXPOSURE METHOD. I.

Masayuki Hamada and Eiko Kawano

Department of Chemistry, Radiation Center of Osaka Prefecture

Sakai, Osaka, Japan

(Received in Japan 18th September 1969; received in UK for publication 14th October 1969)

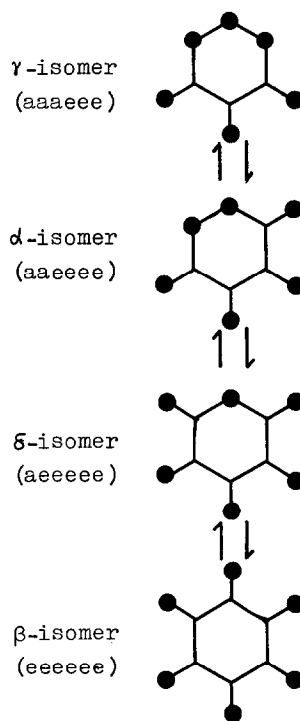
It is well known that organic compounds can be isotopically labeled by exposure to tritium gas. Recently, Angyal, Garnett and Hoskinson¹⁾ have reported the stereochemical investigation of tritiation of (-)-inositol and its hexa-O-methyl derivatives. Isomers of 1,2,3,4,5,6-hexachlorocyclohexane (benzene hexachloride) were chosen for this study, because both some stereochemical preference in the substitution by tritium and considerable stereochemical inversion at each carbon atom are expected to occur during tritiation.

α -, β -, γ - And δ -isomers of 1,2,3,4,5,6-hexachlorocyclohexane were exposed to 1 to 2 curies of tritium gas for 2 to 3 weeks. After exposure to tritium gas, certain amounts of appropriate isomers of hexachlorocyclohexane were added to the tritiated product, respectively. Each compound was then purified to constant specific activity by repeated column partition chromatography which was a modification of Ramsay and Patterson²⁾. Table 1 shows the tritium activity found in parent molecules and other labeled isomers, given as dpm/mg of irradiated parent molecule.

The ratio of radioactivity of a inversion compound at one carbon atom to that of retention (parent) one widely varies with the compound tritiated. For example, in the tritiation of γ -isomer, the activity of α -isomer which is obtained by the inversion at one carbon atom of γ -isomer, is approximately 30 % of the activity of the parent compound. However, the activity of γ -isomer separated from the tritiated product of α -isomer is very low compared with that of parent. This difference may be largely dependent on the meta-axial chlorine-

Table 1 Specific Activities of Hexachlorocyclohexanes

Compound exposed to Tritium	Compound Isolated	Specific Activity dpm/mg parent
γ -isomer	Crude	19.79
	γ (parent)	11.68
	α	3.505
α -isomer	Crude	6.006
	α (parent)	4.353
	γ	0.0136
	δ	0.0154
δ -isomer	Crude	14.76
	δ (parent)	9.621
	α	0.511
	β	1.694
	γ	0.0377
β -isomer	Crude	7.803
	β (parent)	1.542
	δ	0.893



carbon bond of γ -isomer. In general, it may be concluded that stereochemically unstable isomer of hexachlorocyclohexane is subject to inversion at one carbon of cyclohexane ring during tritiation.

In order to obtain the intramolecular distribution of tritium, α -, γ - and δ -isomers prepared by the tritiation of the corresponding isomer were chlorinated under appropriate conditions³⁾, respectively. Scheme of the chlorination is shown in Fig. 1. Hepta-, octa- and nona-chlorocyclohexane isomers whose configurations had been established were purified to constant specific activity by the column chromatography. The intramolecular distributions of activity in the original hexachlorocyclohexane isomers were calculated from the activities of those higher chlorinated compounds. The results are summarized in Table 2.

The reaction of He^3H^+ ions, formed from the β -decay of molecular tritium, with organic compound is known to predominate under conditions ensuring that the

Fig. 1 Scheme of Chlorination

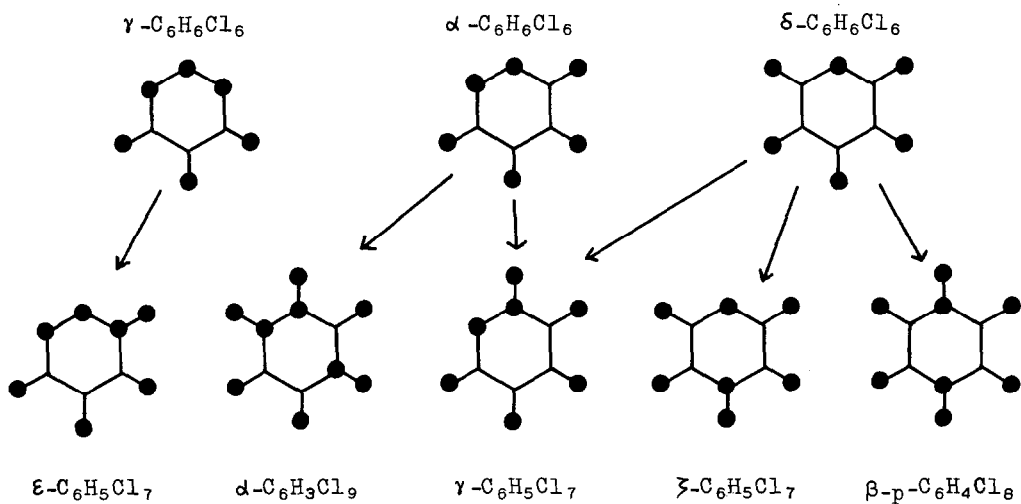
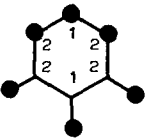
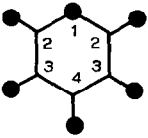
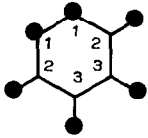


Table 2 Intramolecular Distribution

Isomer	Position	Specific Activity dpm/m mol.	Distribution
$\gamma\text{-C}_6\text{H}_6\text{Cl}_6$ 	1	1.76×10^6	1.00
	2	0.20×10^6	0.11
$\delta\text{-C}_6\text{H}_6\text{Cl}_6$ 	1	0.77×10^6	0.06
	2	3.38×10^6	0.27
	3	12.69×10^6	1.00
	4	12.18×10^6	0.96
$\alpha\text{-C}_6\text{H}_6\text{Cl}_6$ 	1	0.68×10^6	1.00
	2	0.28×10^6	0.41
	3	0.60×10^6	0.88

tritiated products formed through radiolytic process are reduced to an insignificant fraction by decreasing the concentration of tritium gas⁴). Assuming that each carbon of the cyclohexane ring is protonated by the ions in the initial stage of tritiation process under conditions employed here, such protonated intermediates decompose to produce the mixture of the observed labeled compounds such as retention, inversion and probably dechlorinated products.

In the case of γ -hexachlorocyclohexane, the distribution of tritium is shown as the values at only two different positions because of the ring conversion of the isomer. The data of Table 2 represent that the activity at C-1 is much more than that at C-2 position. Since in the tritiation of γ -isomer a considerable amount of tritiated α -isomer which is the inversion product at C-2 position is obtained as shown in Table 1, the observed difference between the activities at C-1 and C-2 positions in the tritiated γ -isomer seems reasonable. The result from δ -isomer shows that activities at C-1 and C-2 positions are less than those at C-3 and C-4 positions, probably because more inversions take place at C-1 and C-2 than at C-3 and C-4 of cyclohexane ring. In comparison with these results, the differences among the activities at three different carbon positions of α -isomer are relatively small, while the yields of the inversion compounds are very low as shown in Table 2. These facts indicate that α -isomer is stereochemically stable and there are few cases to lead to the inversion of the configuration during tritiation process. Alternatively, a close relation may exist between the distribution of the activity in parent compound and the yield of tritiated compounds other than parent.

REFERENCES

- 1) S.J.Angyal, J.L.Garnett and R.M.Hoskinson, Australian J.Chem. 16, 252 (1963)
- 2) L.L.Ramsey and W.I.Patterson, J.Off.Agr.Chem. 29, 337 (1946)
- 3) T.Oiwa, R.Yamada, M.Hamada, M.Inoue and M.Ohno, Botyu-Kagaku, 14, 42 (1949), 15, 32 (1950), 16, 11 (1951)
- 4) F.Cacace and S.Caroma, J.Am.Chem.Soc. 89, 6848 (1967)