HOT SYNTHESIS OF COMPOUNDS LABELLED WITH RADIOACTIVE CARBON

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1. METHODS OF SYNTHESISING LABELLED COMPOUNDS

During recent years great attention has begun to be paid to the investigation of physicochemical methods of synthesising labelled compounds, together with direct chemical synthesis and biosynthesis. Methods which have recently been developed are isotopic exchange, exchange synthesis under conditions of irradiation and self-irradiation, radiation synthesis, synthesis in a gaseous discharge, synthesis by means of accelerated ions, and hot synthesis. The last method has now been most thoroughly investigated, and in our opinion is the most promising in several cases.

(a) Simple Chemical Synthesis

The vast majority of the labelled compounds required in science and technology can be obtained by simple chemical synthesis. Only a few natural compounds form exceptions. However, the chemical synthesis of complicated labelled compounds is laborious, while the yield of the products is often low. These difficulties arise from the fact that the starting materials obtained in the nuclear reactor are carbonates in the case of carbon, and elementary tritium or water in the case of hydrogen. A great deal of work has been done on methods of direct chemical synthesis[1-3].

(b) Synthesis by Means of Isotopic Exchange

Synthesis can be achieved by means of isotopic exchange with chemically mobile atoms, such as halogen atoms in organic derivatives, hydrogen, metals in salts and oxides, ligands in complex compounds, etc. If the molecule undergoing labelling contains several identical atoms in identical positions, they are all labelled simultaneously. If the bonds are not identical, the extent to which the radioactive atoms enter into exchange is characteristic of each position, and the specific activity of the compound is not the same at different bonds. In several cases, isotopic exchange can be initiated by irradiation or by self-irradiation. Thus contact of various substances with gaseous tritium is accompanied by the exchange of hydrogen for tritium[3-13]. Exchange has been studied in methane, ethane, toluene, 3,5-dinitrobenzamide, vitamin B_{12}, 4,5-xylylene-1,2-diamine, trinitronaphthoic acid, 4-hydroxyphthalide, 2,4-dihydroxyacetophenone, α-methylglutamic acid, 2-deoxyribose phosphate, imidazoledicarboxyamide, and gibberellic acid.

As a result of the disintegration of tritium in the T_2 molecule, a number of other tritium-labelled products, both simpler and more complex in composition, are formed during the exchange. Methane in the presence of T_2, for example, yields tritium-containing hydrocarbon molecules with 1–6 carbon atoms[4]. The introduction of tritium into organic molecules by contact of the latter with T_2 has been called the Wilzbach method[5].

(c) Radiation Synthesis

The radiolysis of chemical compounds, especially organic compounds, involves the formation of radicals, which interact to yield a mixture of products. If a mixture including substances containing radioactive isotopes is subjected to radiolysis, a mixture of labelled compounds is obtained, among which are present the original molecules, simpler molecules, more complicated molecules, and structural isomers[4].

Radiochemical synthesis can take place both under the influence of external radiation[4] and under the influence of self-irradiation if the substance which acts as donor of radioactive atoms has a high specific activity[3,5-10]. Radiochemical synthesis results in a complex mixture of labelled compounds, which has its advantages and disadvantages. This complicates the isolation of labelled substances, but at the same time makes it possible to obtain a series of compounds by radiation synthesis. In this method it is difficult to predict the intramolecular distribution of the radioactive isotope.

(d) Synthesis by Means of Accelerated Ions

Several workers have shown[13-19] that it is possible to synthesise labelled compounds, for example, to label carbon in organic compounds, by means of accelerated ions containing radioactive atoms. Here it is difficult to expect that a specific tracer will be obtained in a definite position, or that the distribution of radioactive atoms will be the same, within the molecule. The specific activity of the parent substance at a current of the order of 100 μA is a fraction of a microcurie per gramme. It is even lower than the specific activity of the corresponding compounds formed by hot synthesis. The reaction products of accelerated ions are qualitatively similar to those of hot atoms.

(e) Synthesis in an Electric Discharge

Passage of an electric discharge through the vapour of an organic substance generates ions and radicals, which

interact to form new substances. If the discharge passes through the vapour of a radioactive substance or through a mixture of substances, formation of a mixture of labelled compounds can be expected[20-23]. This method has the same advantages and disadvantages as has radiation synthesis.

(f) "Hot" Synthesis†

The term "hot synthesis" is applied to a synthesis resulting from the interaction with surrounding molecules of radioactive recoil atoms obtained in nuclear reactions or by radioactive disintegration. Such interaction yields labelled molecules of the substance within which the recoil atom is produced, more complicated compounds (addition and condensation products), and simpler compounds (decomposition products of the original substance). Hot synthesis is attractive in its practical simplicity. Generation of the radioactive isotope and its introduction into molecules take place in a single process, so that in several cases this method may prove more efficient than other methods. A complex mixture of labelled products is formed, which requires effective and rapid methods of separation. Among such are firstly chromatography, and then fractionation and chemical separation by means of carriers.

2. MECHANISM OF REACTIONS INVOLVING HOT ATOMS

The interaction of recoil atoms with surrounding molecules can be regarded as occurring in three stages.

The first stage involves slowing down of the recoil atoms by collisions with the surrounding atoms and molecules, without the recoil atoms entering chemical compounds. In this stage the recoil atom causes ionisation of the atoms, their electronic excitation, displacement of atoms from their lattice positions, etc., the process which predominates depending on the recoil energy. Electronic excitation is the most probable at high recoil energies, but the energy losses due to this process become unimportant as the recoil atoms slow down, elastic collisions acquiring increasing significance during this period.

The transition to elastic collisions during the slowing down of the recoil atoms takes place gradually. An approximate calculation based on the equation $E = MI/8m$ (where M is the mass of the moving atom, m the mass of the electron, and I the energy of excitation of the electron)‡ shows that ionisation of the medium, for example, by recoil carbon atoms, ceases at energies of the order of 15–20 keV.

Elastic collisions can occur in the range of Rutherford scattering or as between billiard balls. In the former case the transfer of energy takes place in small amounts, so that the range of the recoil atom is large, reaching 10–100 Å with ^{14}C.

The critical energy below which the billiard-ball type of collisions takes place can be found from the equation

$$E_{cr} = 13.6 \frac{2(M_1 + M_2)}{M_2} Z_1 Z_2 \sqrt{Z_1^{2/3} + Z_2^{2/3}},$$

where M_1 and M_2 are the masses of the colliding atoms, and Z_1 and Z_2 their nuclear charges.

For carbon E_{cr} = 6 keV. Above this energy, Rutherford scattering takes place.

The second stage consists in interaction between the recoil atoms and the molecules of the medium in such a way that a molecule (usually excited) or an excited intermediate complex containing the recoil atom is formed.

Depending on the degree of cooling of the recoil atom, interaction takes place within the range of the so-called hot, epithermal, or thermal reactions. Hot reactions have already begun in the range of solid-sphere collisions, for which there is equal probability of any transfer of energy between zero and some maximum value from the recoil atom to an atom of the medium,

When the energy has fallen to 100–200 eV the recoil atom loses the whole of its remaining energy in the last few collisions. For a ^{14}C recoil atom in a hydrocarbon medium the number of such collisions is estimated at five or six.

According to the Seitz–Koehler model of retardation[24-27] described above, a hot zone, in which the temperature is raised to 10^5°K by the dissipation of 100–200 eV of energy, is formed by the ^{14}C recoil atom at a distance of a few hundred Ångström units from the point where it had been produced. The quantity of energy transferable here and the temperature of this region depend on the relative atomic weights of the recoil atom and the atoms of the surrounding medium. The volume of the hot zone and its life-time are determined not only by the energy but also by various properties of the medium, in particular its state of aggregation, thermal conductivity, etc.

The life of a zone with such a temperature does not exceed 10^{-10}–10^{-11} sec. During this short period of time, the disorder characteristic of a liquid may arise at the centre of the hot zone, which in the case of carbon comprises only a few atoms or ions, and as a result any fragments entering this region may approach the recoil atom. In contrast to the model described above, the retardation mechanism suggested by Libby ignores Rutherford scattering at high energies and postulates only solid-sphere collisions for the recoil atoms[28,29]. According to the Libby model, the recoil atoms transfer a great part of their energy within the space of one or more cages by solid-sphere collisions with the atoms forming the walls of the cages. Thus transfer by a ^{14}C atom of energy between 40 000 and 25 eV requires 5–10 collisions in a hydrocarbon medium, resulting in the formation of a hot zone with a temperature of ~ 10^7 °K and a life of ~ 10^{-5} sec, comprising a few hundred atoms or ions; the solid in the zone melts and is mixed up, so that even very remote fragments may approach the recoil atom. Since Libby's theory postulates the transfer of the greater proportion of the energy within the zone of stabilisation of the recoil atom, variation in the initial recoil energy should affect the radiochemical yields of the products. However, experiments with the recoil

† The term "hot" synthesis, as well as the terms "hot" reaction and "epithermal" reaction, will henceforward be used without quotation marks.

‡ The interested reader is advised to consult "Radiation Damage in Solids" by D.S. Billington and J.H. Crawford, O.U.P., 1961, pp. 31 *et seq.* (Ed. of Translation).

atoms ^{14}C having E = 40 keV and ^{11}C having E = 1000 keV did not show this effect, as could be expected on the Seitz–Koehler model for recoil energies exceeding the energy limit of solid-sphere scattering and that portion of the energy which can be transferred in the hot region (100–200 eV for carbon). Limitations in the Libby model are indicated also by other experimental results, the limits of its applicability being governed by the energy range within which Rutherford collisions are insignificant. At low initial recoil energies, at which Rutherford scattering can be disregarded, the Libby model agrees with the postulates of the Seitz–Koehler theory.

The hypothesis of a billiard-ball type of collision can be used to describe the mechanism of the formation of the primary labelled compounds when the energy of the recoil carbon atoms exceeds 25–50 eV. In collisions of this type, ^{11}C and ^{14}C recoil atoms having sufficient kinetic energy can effect elastic replacement of nitrogen, carbon (^{12}C), and other atoms of similar mass in molecules of the medium. On this basis Capron and Oshima showed[30] that such substitution becomes possible only when $E_0 > 2r$ and $r < \frac{1}{2}$, where E_0 is the energy of the recoil atom before the collision, and $r = [(M-m)/(M+m)]^2$ is the minimum fraction of the energy which can remain associated with the recoil atom of mass M after collision with an atom of mass m. Hence substitution is possible provided that $m/M = 0.17$: *i.e.* atoms of the isotopes ^{11}C and ^{14}C can replace atoms of carbon, nitrogen, etc., but cannot replace, by an elastic collision mechanism, hydrogen atoms, for example. The problems of the mass ratio and of the angular distribution of collisions belong to the "energetic" aspect of the consideration of solid-sphere collisions. The mass ratio governs the probability of a complete transfer of energy depending on the masses of the colliding atoms; apart from these factors, the collision frequency must be taken into account in calculating the yield of products of elastic substitution, and this is a function of the number of replaceable atoms, or more precisely of their concentration, dimensions, and steric factors. It has been demonstrated experimentally that the radiochemical yields and specific activities of the substitution products actually depend not only on the mass ratio of recoil and substituted atoms but also on the relative numbers of these atoms in the medium.

In the formation of a substance by a mechanism of elastic collisions, the molecule of the reaction product is obtained by combination of a radical with a recoil atom which has lost all (limiting case) or a considerable part of its energy. In this way a labelled parent molecule is formed as a product of the replacement of other atoms by the recoil atom. Only in the limiting case of zero energy of the recoil atom after the collision is an unexcited molecule formed: in all the remaining cases the product is a molecule having an excess of energy compared with the mean. The excitation may not spread throughout the molecule, but may be localised in some part of it before its decay.

If the recoil atom is cooled in the first stage to lower energies (below 25–50 eV), it can react with the surrounding molecules by a mechanism of inelastic collision, by so-called epithermal reactions[31,32]. This involves energy transfer to the molecule as a whole, and its excitation yields an intermediate complex with excess of energy or an excited molecule.

The energy of excitation is determined by the initial energy of the recoil atom colliding with the molecule and by the proportion of the energy which can be converted into excitation. The latter, as the work of Magee[33,34] has shown, is a function in particular of the relative masses of the recoil atom, the bombarded fragment of the molecule, and the whole molecule.

If during the first stage the collisions result in the recoil atoms being cooled to energies lower than the bonding energies of the atoms in the molecule, it is only in the limiting case that such atoms form unexcited molecules in subsequent thermal chemical reactions. In most cases an excited molecule containing the recoil atom is formed.

The third stage consists in stabilisation of the excited molecule or breakdown of the intermediate complex. Excited molecules formed as a result of hot and epithermal processes will in most cases be stabilised by dissipation of the energy among the surrounding molecules or by the emission of light. Such a process leads to the formation of simple products in which substitution by the recoil atom has occurred. However, reactions involving slight rearrangement, for example, isomerisation, may also occur. In the case of the formation of an intermediate complex by an epithermal mechanism the energy of excitation is large, and transition to the normal, non-excited state involves a fundamental change in the initial molecule, such as its decomposition, combination with other molecules, rupture or formation of double bonds between carbon atoms, etc. Formation of labelled molecules in the epithermal region obviously passes through successive stages of breakdown of the molecules and recombination of the fragments with recoil atoms in the reaction cage.

If the excited molecule decomposes so rapidly that the excitation does not have time to spread throughout the molecule, the result of such a process is formation of a product in which an atom or group of atoms has simply been replaced by the recoil atom.

It has been shown with the simplest molecules that more complicated compounds are obtained practically entirely by thermal reactions, and are suppressed by radical inhibitors[35,36].

Experimental determinations of the composition of the products from reactions involving recoil atoms indicate the final result of all three stages. Few attempts have yet been made to find the reaction products of a recoil atom in the second stage or the mechanism by which the intermediate compounds are transformed in the third stage. An exception is provided by Wolf's papers[37–39], in which the results are interpreted in terms of the formation of an intermediate complex.

The behaviour of the recoil atoms during the first stage, and the proportions of them which react in the hot, epithermal, and thermal regions, depend on the initial energy of the recoil atom and the nature of the surrounding medium, on the masses of its atoms and the structure of its molecules. The governing factors in the second stage are the probability of the formation of an intermediate complex of a particular composition and the structure and degree of excitation of the molecule or complex. Important factors in the third stage are competition between several modes for removal of the excitation energy and the probability of the occurrence of several chemical reactions yielding chemically stable molecules. The radiation stability of the compounds plays a quite significant part in this.

(a) Energy and Charge of Radioactive Carbon Recoil Atoms

In order to obtain ^{14}C-labelled compounds, substances containing nitrogen, alone or mixed with other compounds,

are irradiated with neutrons. Compounds containing the radioactive isotope ^{11}C can be obtained by means of the recoil atoms arising from the nuclear reactions: $^{12}C(n,2n)^{11}C$ and $^{12}C(\gamma,n)^{11}C$. The heat of formation of ^{14}C from nitrogen by the reaction $^{14}N(n, p)^{14}C$ is 0.6 MeV, and that for the formation of ^{11}C by neutron irradiation is $Q = 7.15$ MeV. Hence the recoil energies of the ^{14}C and ^{11}C atoms are respectively $Q/15 = 0.04$ and $2Q/13 = 1.1$ MeV; a similar calculation for the reaction $^{12}C(\gamma,n)^{11}C$ gives a value of the order of 0.5 MeV.[40-43]

Such a high recoil energy of ^{14}C and ^{11}C atoms results in complete rupture of their bonds with the parent molecules and the formation of hot carbon atoms having great kinetic energy. In the case of ^{14}C the speed of the recoil atom corresponds to that of electrons of 1.56 eV energy, the speed of ^{11}C recoil atoms being considerably higher. At such energies and speeds, the carbon recoil fragments must lose those orbital electrons with velocities below what would correspond to the kinetic energies and speeds of the fragments[3]. The outer electrons are stripped by the electrostatic fields of the atoms in the path of the recoil fragment. Owing to this stripping of the outer electrons from the ^{14}C ions formed initially at the instant of splitting off from the parent molecule, the recoil fragments are neutralised after the first few collisions. When the recoil atom has cooled down, it can again acquire extra electrons, thus becoming negatively charged, if ions having a negative electron affinity are present in the surrounding medium. In the case of carbon recoil atoms, the energies at which a neutral fragment can acquire electrons are of the order of 30 keV.

(b) Interaction of Radioactive Carbon Recoil Atoms with Matter

Table 1 gives data on the radioactivity of the reaction products formed by hot ^{14}C and ^{11}C atoms with various substances. Table 2 contains information on the distribution of radioactive carbon in the labelled compounds obtained by hot synthesis. The data in these tables indicate the distribution of radioactive carbon between labelled molecules and individual atomic groupings in molecules.

Substitution forms one of the main reactions of hot carbon atoms. With carbon recoil atoms the replacement of carbon, nitrogen, oxygen, and halogens can occur in collisions of the billiard-ball type. Substitution of hydrogen is possible only by an epithermal reaction mechanism. Whole groups of atoms can also be replaced by the latter mechanism. The yields and the specific activities of the substitution products depend on the relative masses of the colliding atoms and on their relative numbers. If G is the ratio of the number of ^{12}C atoms to the number of ^{14}N atoms from which the ^{14}C recoil atoms are produced, the specific activities of the substitution products are proportional to the ratios $G/(G + 1)$.[2] The maximum values correspond to $G = 1$. The correctness of these conclusions has been demonstrated in the case of several examples[71]. In particular, neutron irradiation of 1-butyltetrazole-5-amine ($G = 1$) and of 1-hexyltetrazole-5-amine ($G = 1.4$) yielded specific activities of 2.0 and 1.2 $\mu c\ mg^{-1}$.

The role of such factors as the frequency and efficiency of collisions are exemplified by the oxalates of nitrogen bases. The distribution of ^{14}C recoil atoms between the base and the oxalate radical has been studied by Zifferero and coworkers[51]. They showed experimentally that a considerable proportion of the parent labelled products is formed by a solid-sphere collision mechanism. Taking the numbers

TABLE 1. Reaction products of carbon recoil atoms.

Irradiated system	Radioactive products	Activity of reaction products		Reference
		%	$\mu c\ g^{-1}$	
Butane + 2-methylpyrazine	n-butane	3.0	–	44
	n-pentane	5.0	–	
	isopentane	5.0		
n-Pentane + 2-methylpyrazine	n-pentane	2.8	0.04	45
	n-hexane	6.5	0.09	
	2-methylpentane	4.3	0.03	
	3-methylpentane	2.1	0.03	
n-Pentane + aniline	light gases	12	–	46
	n-pentane	25		
	isopentane	1	–	
	n-hexane	12	–	
	hexane isomers	6	–	
n-Pentane + aniline or propylamine	light gases	2.1	–	47
	butane	5.7	–	
	neopentane	2.4	–	
	isopentane	3.6	–	
	n-pentane	2.1	–	
	2,2-dimethylbutane	0.1	–	
	2,3-dimethylbutane	0.2	–	
	2-methylpentane	4.5	–	
	3-methylpentane	8.3	–	
	n-hexane	12.2	–	
Methanol + aniline	methane	34.3	–	48
	methanol	15.9	–	
	ethanol	8.4	–	
	n-propanol	9.1	–	
	n-butanol	6.2		
	isopentyl alcohol	4.9		
	higher alcohols	11.3		
	aniline	9.9		
Methylammonium fluoride	light gases	18.5		48
	n-pentylamine	10.0		
	n-hexylamine	1.8		
	3-(isopropylamino)propylamine	4.0		
	tributylamine	21.7		
	ethylamine	16.0		
	n-propylamine	10.0		
Ethylamine	methane	6.8	–	48
	ethylamine	21.5		
	n-propylamine	10.9		
	n-butylamine	12.1		
	di-n-propylamine	10.5		
	t-octylamine	8.2		
	3-(isopropylamino)propylamine	10.1		
	tributylamine	14.0		
	di-2-ethylhexylamine	5.5		
	N-methyldiphenylamine	0.4		
Ethylammonium fluoride	light gases	2.1	–	48
	ethylamine	16.1		
	n-propylamine	14.7		
	n-butylamine	7.8		
	di-n-propylamine	5.0		
	n-hexylamine	3.1		
	t-octylamine	3.5		
	3-(isopropylamino)propylamine	9.8		
	tributylamine	9.8		
	diethylamine	9.0		
	methyldiphenylamine	14.8		
Acetamide	acetic acid	6.44	0.215	49,50
	propionic acid	6.52	2.180	
	acetone	0.13	0.068	
Hydrazinium oxalate	carbon monoxide	3.2	–	51
	carbon dioxide	5.0		
	oxalic acid	10.4		
	formic acid	12.5		
	methylamine	10.7		
	formaldehyde	5.7		

TABLE 1 (cont'd).

Irradiated system	Radioactive products	Activity of reaction products		Reference
		%	$\mu c\ g^{-1}$	
Alanine	alanine	0.2	0.06	38
1,1-Dimethylcyclopentane + 2-methylpyrazine	1,1-dimethylcyclopentane	0.1	–	38
trans-1,2-Dimethylcyclopentane + 2-methylpyrazine	*trans*-1,2-dimethylcyclopentane	0.3	–	38
trans-1,3-Dimethylcyclopentane + 2-methylpyrazine	*trans*-1,3-dimethylcyclopentane	0.4	–	38
Benzene + aniline	methane benzene toluene diphenylmethane triphenylmethane polymers	1.5 2.5 1.7 3.2 2.0 12.2	–	48
Benzene + 2-methylpyrazine	benzene toluene	2.5 1.9	0.065 0.17	50
Benzene clathrate	carbon monoxide carbon dioxide oxalic acid benzene hydrogen cyanide	0.2 0.4 6.7 4.0 2.5	–	52
Benzene clathrate	benzene	1.4	0.63	53
Benzene + aliphatic amines	benzene toluene	2.6 2.25–3.3	– –	54
Toluene + 2-methylpyrazine	toluene *o*-xylene *m*-xylene *p*-xylene ethylbenzene	3.30 0.96 1.35 0.46 0.85	0.13 0.27 2.22 0.13 0.12	38
Toluene + 2-methylpyrazine	toluene *o*-xylene *m*-xylene *p*-xylene ethylbenzene	1.6 0.33 0.37 0.16 0.50	0.1 0.04 0.02 0.04 0.06	44
Aniline	methane aniline benzene toluene toluidine (*o*, *p*, *m*) benzylamine methylaniline *o*-methylbenzidine methyldiphenylamine (*o*, *m*, *p*)	1.5 3.0 0.1 0.7 3.2 0.8 2.0 2.6 1.6	– –	48
Aniline	aniline benzene toluene	2.8 0.35 0.074	0.10 0.03 0.006	55
Methylanilinium oxalate	methylaniline oxalic acid	11.8 3.3		56, 57
Anilinium oxalate	aniline oxalic acid	8.0 2.7		56, 57
Isohexanoanilide	isohexanoic acid aniline	1.0 2.0		38
Phenylalanine	phenylalanine aspartic acid glutamic acid serine lysine α-aminobutyric acid α-aminovaleric acid formic acid propionic acid malonic acid succinic acid glutaric acid β-phenylpropionic acid	2.8 4.7 2.9 1.0 1.4 1.2 2.0 4.2 1.8 2.9 1.4 3.6 3.7		58
Benzamide	benzamide acetophenone benzoic acid	4.1 0.7 3.8		60

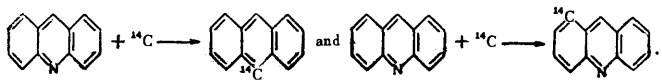
TABLE 1 (cont'd).

Irradiated system	Radioactive products	Activity of reaction products		Reference
		%	$\mu c\ g^{-1}$	
Benzanilide	benzanilide benzoic acid aniline bibenzoyl oxalic acid hydrogen cyanide carbon monoxide carbon dioxide	1.5 0.4 0.9 0.9 0.7 2.6 11.7 5.0		60
Stilbene + azobenzene	stilbene	1.3	0.65	61
Azobenzene	azobenzene	2.3	0.65	55
Naphthalene + hydrazinium oxalate	naphthalene	0.0	–	55
Anthracene + ammonia (liq.)	anthracene	0.009	0.01	55
1-Butyltetrazole-5-amine	1-butyltetrazole-5-amine	14.4	–	61
1-Decyltetrazole-5-amine	1-decyltetrazole-5-amine	1.6	–	61
1-Ethyltetrazole-5-amine	1-ethyltetrazole-5-amine	5.5	–	61
1-Hexyltetrazole-5-amine	1-hexyltetrazole-5-amine	7.7	–	61
1-Phenyltetrazole-5-amine	1-phenyltetrazole-5-amine	1.0	–	61
Pyridine	pyridine	0.5	–	62
Methylpyridine	4-methylpyridine toluene	1.7 0.26	–	39
Pyridinium oxalate	pyridine benzene phenol oxalic acid	2.0 7.6 5.4 1.7	– – – –	56 57 63
Ethylpyridine	ethylpyridine	1.0	–	38, 64
Ammonium nicotinate	nicotinic acid benzoic acid propionic acid valeric acid malonic acid glutaric acid	4.1 1.5 2.3 1.5 16.3 3.2	–	65
Nicotinamide	nicotinamide benzoic acid	3.4 0.4	0.03 1.81	38
Hydrazide of nicotinic acid	benzoic acid	–	0.43	38
Quinolinium oxalate	quinoline naphthalene 1-naphthol oxalic acid carbon dioxide carbon monoxide	1.6 8.4 2.2 7.1 0.01 0.02	–	56, 66
Quinoline	isoquinoline quinoline naphthalene 1-naphthol oxalic acid	0 5.0 0.15 0 0	–	67
Isoquinoline	isoquinoline naphthalene	8.0 0.15	–	67
Quinoline oxalate	quinoline naphthalene 1-naphthol oxalic acid	10.0 0.2 0.2 0.37	–	67
Isoquinoline oxalate	isoquinoline oxalic acid	10.0 1.5	–	56, 57
1,2-Benzacridine	1,2-benzacridine 1,2-benzanthracene	4.0 0.2	–	68, 69
Acridine	acridine anthracene	3.5 0.2	0.22 0.32	38, 70
Reserpine + tetrazoleamine	reserpine	–	0.16	71

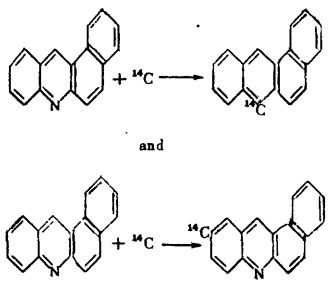
TABLE 2. Distribution of activity in ^{14}C-labelled molecules.

Substance irradiated	Suggested basic mechanism of formation of labelled substance	Product	Activity (%) in given position: theor.	Activity (%) in given position: expt.	Specific activity, $\mu c\ g^{-1}$	Ref.
Acetamide $CH_3.CO.NH_2$	elastic collision, replacement of ^{12}C	acetic acid CH_3	50	38	0.536	49
		$COOH$	50	62	0.840	50
Alanine $CH_3-CH(NH_2)COOH$	ditto	alanine CH_3	33.3	14	—	38
		$CH(NH_2)$	33.3	7	—	
		$COOH$	33.3	79	—	
Benzene C_6H_6	»	benzene C_6H_6	100	100	0.068	50
Toluene $C_6H_5-CH_3$	»	toluene C_6H_5	85.7	89	—	38
		CH_3	14.3	11	—	
Benzamide $C_6H_5-CO-NH_2$	»	benzoic acid C_6H_5	85.7	87.2	—	38
		$COOH$	14.3	12.8	—	
trans-Stilbene $C_6H_5.CH:CH.C_6H_5$ + + azobenzene	»	*trans*-stilbene C_6H_5	42.9	37.5	—	39
		CH	7.1	12.5	—	
		CH	7.1	12.5	—	
		C_6H_5	42.9	37.5	—	
Acetamide $CH_3-CO-NH_2$	elastic collision, replacement of ^{14}N	acetone CH_3	50	40	—	49, 50
		CO	0	20	—	
		CH_3	50	40	—	
Aniline $C_6H_5-NH_2$	ditto	toluene C_6H_5	0	14	—	48
		CH_3	100	86	—	
Azobenzene $C_6H_5-N=N-C_6H_5$	»	benzylideneaniline C_6H_5	0	15	—	61
		CH	100	85	—	
		N	0	0	—	
		C_6H_5	0	0	—	
Methanol CH_3-OH	inelastic replacement of H	ethanol CH_3	100	95	—	39
		CH_2OH	0	5	—	
Pentane $CH_3-(CH_2)_3-CH_3$	ditto	hexane CH_3	100	97	—	39
		$(CH_2)_4$	0	3	—	
		CH_3				
		3-methylpentane				
		$CH_3-CH_2-CH_3$	0	3	—	
		$CH_3\ CH_3\ CH_3$	100	97	—	
Acetamide $CH_3-CO-NH_2$	»	propionic acid CH_3	100	52	3.30	49, 50
		CH_2	0	24	1.44	
		$COOH$	0	24	1.49	
Benzene C_6H_6	»	toluene C_6H_5	0	12	0.024	50
		CH_3	100	88	1.01	
Benzene C_6H_6	»	toluene C_6H_5	0	16	—	19
		CH_3	100	84	—	
Toluene $C_6H_5-CH_3$	»	xylene C_6H_4	0	15	—	38
		$(CH_3)_2$	100	85	—	
		ethylbenzene C_6H_5	0	7	—	
		CH_2	0	13	—	
		CH_3	100	80	—	
Methanol CH_3-OH	thermal replacement of H by fragment containing two carbon atoms	n-propanol CH_3	50	43	—	39
		CH_2	50	55	—	
		CH_2OH	0	2	—	

of ^{12}C and ^{14}N atoms in the molecular volumes of the basic and acidic groups as measures of the probabilities of the ^{14}C entering a given group, these workers calculated the ratio of the activity of the base to that of the acid. With aniline oxalate, for example, the molecular volume of the base is 1.67 times that of oxalic acid and since in the aniline and oxalic acid molecules the ratios of the ^{12}C atoms to the total number of atoms similar in mass to ^{14}C are 6 : 7 and 2 : 6 respectively, the probability of the formation of labelled aniline is 4.3 times that of the formation of the labelled acid. This value agrees comparatively well with the experimental data. With other bases the difference between calculated and experimental values is so large that the assumption of hot substitution probably has little justification in their cases. Among the best studied examples of hot substitutions are the substitution of ^{12}C and ^{14}N in aromatic rings. When acridine is bombarded with neutrons in a nuclear reactor, labelled anthracene and acridine having specific activities of 0.4 and 0.22 $\mu c\ g^{-1}$ of the substance can be isolated[68] from the irradiated specimen. Another paper[70] gives the specific activities of acridine and anthracene as 0.22 and 0.32 $\mu c\ g^{-1}$ of carbon with yields of 0.5 and 0.2% respectively of the total activity. The two products can be formed by replacement of carbon and nitrogen atoms in the original compound by ^{14}C:



In a similar manner neutron irradiation of 1,2-benzacridine yielded labelled 1,2-benzanthracene and the labelled initial product[69], the yields being 4 and 0.2% respectively of the total activity:



The distribution of activity between the products of the above hot reactions is close to the statistical value, in conformity with the character of substitution produced by elastic collision and the closeness of the masses of ^{12}C and ^{14}N to that of ^{14}C.

The most probable result of the hot mechanism with carbon compounds is the formation of labelled parent molecules. Cases are known, however, in which the latter are formed[37] by reactions other than hot elastic collisions. Thus several experiments have shown that, in the neutron irradiation of benzene mixed with molecules containing nitrogen, labelled benzene is obtained not only by hot reactions but also by thermal recombination of recoil fragments with free radicals, as shown by the dependence of the yield of labelled benzene on the preserve of radical-acceptors (1,1-diphenyl-2-picrylhydrazyl, etc.). Another example is the formation of labelled products in the irradiation of quinoline and isoquinoline. If it is assumed that the labelled parent compounds and naphthalene are formed

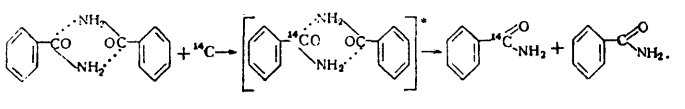
by hot substitutions of ^{14}C for ^{12}C and ^{14}N, the ratio of the yield of quinoline to that of naphthalene, for example, should correspond to the ratio of the number of carbon atoms to that of nitrogen atoms in the quinoline molecule. The yields of labelled compounds obtained by irradiation of isoquinoline and quinoline and its oxalate have been shown[56,67,72] to contradict this hypothesis, and are explained in these papers by the difference in chemical properties between quinoline and isoquinoline, or more precisely by the difference in the bonds and also in the position of the carbon atoms in the molecules of these substances. Such a dependence of the yield of labelled compounds on molecular structure indicates that in this case the labelled molecules of the parent compound are not products of a simple hot substitution.

With azobenzene–stilbene solid solutions a linear relation has been found[61] between the yield of labelled parent compound and the mole fraction. The yield of stilbene did not extrapolate to zero at zero mole fraction of it in the original solution. This suggests that part of the labelled stilbene has arisen as a result of secondary recombination of fragments which had been formed from only the one component, azobenzene: *i.e.* on irradiation of azobenzene–stilbene solutions, part of the parent compound (stilbene) is formed by thermal or epithermal processes involving recombination of the fragments. The deviations of the intramolecular distribution of activity in stilbene from that calculated on the hypothesis that substitution takes place at random also demonstrates the possibility that stilbene can be formed by thermal or epithermal reactions. An important factor is the contribution made by secondary processes, involving the stabilisation of intermediate complexes and excited molecules, to the distribution of activity in products of the postulated hot substitution of ^{14}C atoms for those of similar mass. In aromatic compounds labelled by replacement of ^{12}C and ^{14}N by ^{14}C recoil atoms, for example, the distribution is statistical only to a first approximation, discrepancies always being observed. These deviations show definite regularities.

In the formation of labelled toluene from toluene mixed with 2-methylpyrazine and of labelled benzoic acid from benzamide, the deviations from a statistical distribution are of the order of a few per cent higher content of ^{14}C in the ring. A probable cause of this phenomenon in the former case may be removal of the excess excitation energy of the molecules by elimination of the methyl group:

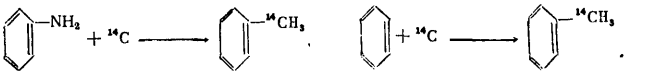


Since this process is especially probable in the case of substitution of carbon in the side-chain, it should lead to a relatively high content of ^{14}C in the ring of toluene. A similar explanation can also be given for benzoic acid obtained from benzamide, the excess excitation energy in this case perhaps being expended also in the rupture of intermolecular hydrogen bonds (bond strength 10–5 kcal × × mole^{-1}); this results in a molecule of benzoic acid being split off without dissociating, and the deviation from a statistical distribution is smaller in this case:

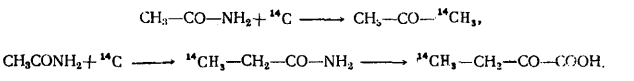


Analogous explanations can be given for the deviations from a statistical distribution of activity in molecules of acetic acid obtained from acetamide, and of labelled alanine from alanine (Table 2).

Replacement of hydrogen by carbon atoms differs both in mechanism and in rules from the hot substitution of atoms of similar mass to carbon. This can be illustrated by results obtained for the irradiation of aniline and of a mixture of benzene with 2-methylpyrazine[48,50]. Labelled toluene is a product in both cases



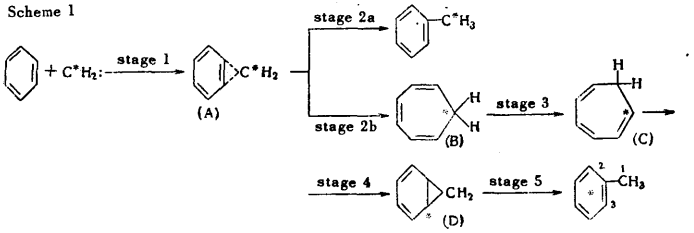
If the substitution of hydrogen in benzene were assumed to take place, like that of nitrogen in aniline, by hot reactions, the yield of toluene from benzene would be six times its yield from aniline. The experimental value of this factor is only 2.7. Irradiation of acetamide provides another example confirming that the substitution of hydrogen by ^{11}C and ^{14}C recoil atoms differs in mechanism from that of nitrogen and inactive carbon atoms. The irradiated acetamide yielded[49] acetone containing 0.13% of the total activity and propionic acid containing 6.52%, the latter being obtained by treating the irradiated mixture with alkalis or acids



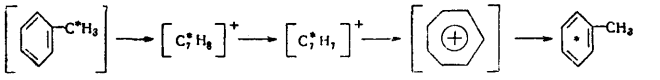
The radiochemical yield of the latter is 50 times that of acetone, whereas the random character of hot reactions would suggest only a threefold difference in yield.

The substitution of hydrogen differs to a considerable extent also from thermal reactions involving radicals. The yield of toluene in the irradiation of benzene is unaffected by the addition of radical-acceptors[37], which tends to refute the possibility that the labelled toluene is formed by thermal recombination of radicals with recoil fragments. According to Wolf, toluene is formed in an epithermal process, independently of additions of radical-acceptors, according to one of the following schemes:

Scheme 1



Scheme 2



In Wolf's view, inelastic collisions result in this case in the formation of an intermediate complex containing seven carbon atoms and possessing sufficient excitation energy for its further conversion into labelled toluene in which the distribution of activity is either fixed or fortuitous. The possibility of the excited methylene reacting with rupture of a C–C bond and formation of a compound of type A

(Scheme 1) is probably not excluded under certain conditions. Interaction of methylene with rupture of a C–H bond has been observed by several investigators[73]. The intermediate compound rearranges to form toluene either by a simple, single-stage process (stage 2a) or along a multistage path including redistribution of hydrogen and rupture of several bonds (stages 2b–5). A more or less uniform distribution of active carbon atoms in positions 1–3 is probable for a multistage process.

Reaction with rupture of a C–H bond may result in the formation of strongly excited toluene. In such a case the toluene molecule can lose hydrogen and ionise to form a tropylium ion $[(C_7H_7)^+]^*$. On losing its excitation energy, this ion is converted into toluene having a uniform distribution of active carbon.

From the above mechanism for the formation of labelled toluene it is evident that the distribution of activity not only among groups of atoms in a molecule but also among groups of molecules (*i.e.* among substances) may depend on the nature of the processes by which the intermediate compound is stabilised.

Epithermal reactions may involve replacement by recoil atoms not only of individual atoms in the molecule but also of entire fragments of molecules, when the yield of labelled products will depend in particular on the size and the structure of the fragment. For example, the yield of labelled benzamide was greater when sulphonated benzamide was irradiated than from the irradiation of benzamide itself. A similar conclusion as to the role of the size of the fragment and the structure of the species was reached from the irradiation of three homologous azobenzenes *p*-ethoxy-*p'*-methoxy-, *p*-methoxy-*p'*-propoxy-, and *p*-ethoxy-*p'*-propoxy-azobenzene. The relative activities of the methoxy, ethoxy, and propoxy groups in the corresponding compounds were 1.00/1.07, 1.00/1.12, and 1.00/1.04.

A method has been suggested[79] for the quantitative measurement of the yields of labelled compounds which is analogous to the calculation of the yields of neutron-capture reactions, *i.e.* the use as the main variables of the flux of recoil atoms and their capture cross-section by components of the medium. The capture cross-section is determined by the chemical properties of the substance, the geometrical dimensions of the fragment undergoing collision, etc. The results can be explained in terms not only of the geometrical dimensions but also of the masses of the fragments colliding with the recoil atom. In fact, in conformity with Magee's conclusions, the fraction of the energy transferred on collision with the recoil atom which is used in increasing the internal energy of the molecule depends on the ratio of the masses of the molecule and the colliding fragment. In particular, for a diatomic molecule

$$\Delta E_{int} = \Delta E_{coll}\, m/(M + m),$$

where ΔE_{coll} is the energy transferred to an atom of mass M on collision with the recoil atom, ΔE_{int} the part of the energy which goes to increase the internal energy of the molecule, m the mass of the molecular residue, and $(M + m)$ is the molecular weight. Thus ΔE_{int} and hence the probability of dissociation of the molecules and its converse, the probability of a labelled molecule being formed without fundamental degradation, depend on the mass ratio of the colliding atom and the rest of the molecule. This relation probably holds also for molecules more complex than diatomic. On this basis the results mentioned above[74] can be explained in just the same way as those on the activity of the alkyl phenyl ethers.

The role of particular processes in the reactions of hot atoms can be analysed with the irradiation of pentane and isopentane (Table 1) as example[47]. In the case of n-pentane the low yield of the labelled starting material (2.1%) indicates that reactions like the hot substitution of carbon atoms are not very probable. A considerably greater part is played by epithermal substitutions of the ^{14}C atom, or fragments containing it, for hydrogen in the pentane molecule, leading to the formation of hexane in yields of up to 12% (with respect to activity).

In considering the distribution of activity among products (radiochemical yield and specific activity) and the distribution of active atoms within molecules of a given kind, account must be taken not only of the nature of the primary reactions of the recoil atoms, leading to the formation of labelled compounds, but also of secondary processes in which excited molecules and intermediate complexes are stabilised. The chemical nature of the molecules and separate fragments, bond strengths, the stabilities of molecules, etc., will play a special part in the distribution of activity at the stage of stabilisation of the intermediate excited complex[64]. Thus in xylenes formed by the irradiation of toluene ~15% of the active carbon is in the ring and 85% in the methyl groups, the greatest number of active carbon atoms being concentrated in the *meta*-position with respect to the first methyl group, and the smallest number in the *para*-position. The difference in radiochemical yields and specific activities of the individual xylenes is probably associated with the greater thermodynamic stability of *m*-xylene. Interpretation of the experimental results is complicated by the fact that the same labelled molecules can be formed by different mechanisms, while the distribution of activity within molecules obtained by different mechanisms will not be the same.

(c) Factors Influencing the Yields of Labelled Products

Temperature. Lowering the temperature has been found[31] to increase the yield of several compounds, which are mainly complicated products of the condensation and cross-linking of molecules, radicals, and fragments. The yield of ^{11}C-labelled benzene from the irradiation of benzene with fast neutrons increases as the temperature is lowered from 0° to -195°. These results are explained[38] by a lengthening, with fall in temperature, of the life of those fragments, the products of hot reactions, which combine with one another in the course of thermal reactions to give benzene. Consequently, temperature has a marked influence on the yields of the products of thermal reactions. Nevertheless, the yield of toluene formed at the same time as benzene, but in the epithermal region, is little affected by temperature. The yields of hot reactions depend still less on temperature. A decrease in yield of the most complicated products with rise in temperature has also been observed[15,16], in the irradiation of cholesterol, paraffin wax, and stearic and benzoic acids with accelerated $^{14}C^+$ and $^{14}CO^+$ ions, in which cases the thermal stabilisation of the fragments containing ^{14}C is similar in character to the thermal reactions with recoil atoms. It is pointed out that the synthesis of complicated labelled compounds should be most efficient at low temperatures.

It is interesting that the yield of labelled products is affected not only by the temperature at which the specimen has been irradiated but also by the processing temperature to which it has been subjected after irradiation[76,77].

Sharman and McCallum observed a variation in the distribution of activity in products, formed by the irradiation of sodium carbonate and of oxalic, glyoxylic, and glycollic acids, with the temperature to which the irradiated preparation had been heated [78].

These phenomena are most often associated with the thermal stability of the products, the effect of annealing leading to disorientation of the molecules in crystal lattices, and the corresponding variation in the rates of thermal recombination. For the carbon isotopes they are similar in character as with the isotopes of other elements.

It follows from this account that, in the choice of temperature of irradiation, due regard must be had to the thermal stability of the specimens. Irradiation at temperatures at which cracking becomes appreciable may substantially change the distribution of activity among the products owing to the change in composition of the irradiated mixture involved in cracking. Furthermore, the choice of temperature of irradiation is important in the synthesis of products formed by thermal reactions.

State of aggregation. The yield of the products of hot synthesis is affected also by the state of aggregation. The difference in the reactions of hot atoms is especially marked between condensed phases and the gas phase: in the latter such processes as, for example, the recombination of fragments and the transfer of energy from excited molecules to the medium become improbable. The phase state does not affect the yield of products obtained by elastic collisions, as in the replacement by a carbon recoil atom of atoms of similar mass. The yields of epithermal and thermal reactions are greatly dependent on the phase state of the irradiated material. On transformation into a solid phase, the probability of energy transfer on collision is markedly changed, and both the cell effect and the probability of the recombination of radicals and recoil fragments, are increased. The difference in thermal conductivity between liquid and solid materials is also important, since the conductivity can determine to a considerable extent the dimensions of the liquid cell [26,27]. The difference in thermal conductivity between different crystalline structures may also play some part. Owing to the greater thermal conductivity and higher melting-points of ionic crystals compared with molecular crystals, for example, the volume of the hot molten zone is considerably smaller in the former. All this makes it possible for recoil atoms in molecular crystals to react with the more remote fragments, which in the case of ionic crystals have insufficient time to diffuse to the recoil atom.

Interesting results have been obtained by Muxart, who found a lower yield of parent compound in the irradiation of liquid quinoline (5.4%) than in that of its solid oxalate (10%). These results were explained by the phase effect in epithermal reactions.

The experimental results confirm the dependence of the yield of labelled products on the phase state. Thus Royland and Libby [43] studied the distribution of activity among the products of the neutron irradiation of solid and liquid specimens of CO_2 and carbonates, and found that on passing from the liquid to the solid state the yield of CO decreased from 95–100 to 50%, while the yield of CO_2 increased under the same conditions from 2–3 to 50%. The increase in the yield of CO in the liquid phase is attributed to an increase in the rate of diffusion of the recoil atom from its track, where it can recombine with oxygen to form CO_2, into the external medium, where it undergoes ordinary thermal reactions with the medium and CO molecules are formed:

$$^{14}C + CO_2 = {}^{14}CO + CO; \qquad {}^{14}C + H_2O = {}^{14}CO + H_2.$$

In the case of the irradiation of benzene with fast neutrons — the nuclear reaction $^{12}C\,(n,2n)\,^{11}C$ — changing from the liquid to the solid state results in a decreased yield of labelled benzene but hardly affects the yield of toluene. Such behaviour can be explained on the hypothesis that formation of toluene takes place at comparatively high energies, whereas that of benzene is a result not only of hot reactions but also of thermal recombination. Toluene is synthesised at energies of 25–50 eV, when the recoil atom transfers to the system so much energy that the solid in a small volume along the track fuses, and the boundary between liquid and solid states of the system disappears.

A considerable quantity of labelled benzene is formed at low energies, so that the phase effect is appreciable, *i.e.* because of the limited diffusion in a solid medium and the short life of the recoil atom, it recombines with fragments from the immediate vicinity. This results in the formation of products differing from benzene. In the solid phase the recoil atom has insufficient time to react with species suitable for the formation of benzene. The interpretation of data for the solid phase must take into account various defects produced by recoil atoms in solids, in particular the intrusion and substitution of atoms, formation of vacancies, and thermal dislocation spikes [26,79]. In view of the different numbers of defects in single crystals and in fine powders, for example, differences can be expected in these cases in the retention and in the dependence of the change in the latter on thermal annealing. Retention should be greater in single crystals than in the powder, but on the other hand, it grows more rapidly on annealing after irradiation in the powder than in the single crystals [80]. Thus the experimental data on phase effects with ^{14}C show that, if the product is formed as a result of hot substitution, the irradiated specimen can be in any state of aggregation. Epithermal reactions occur best when solids are irradiated. Irradiation of liquid phases is the most effective for ensuring a maximum yield in thermal processes.

Recoil energy. It is difficult to reach final conclusions concerning the role of the initial energy of recoil atoms in the synthesis of labelled products. Comparison of data for various recoil atoms obtained from the reactions $^{12}C\,(n,2n)\,^{11}C$, $^{12}C\,(\gamma,n)\,^{11}C$, and $^{14}N\,(n,p)\,^{14}C$ [37,48,50] gives no precise picture, since the experimental conditions varied, among these being the radiation dose, radiation intensity, temperature, phase state of the specimens, and the composition of the irradiated mixtures.

Data are available [37] for solid and liquid benzene on the yield of labelled substances in the nuclear reaction $^{12}C\,(n,2n)\,^{11}C$, and cases have been described of the irradiation of solid benzene with accelerated ions and the irradiation with slow neutrons in a reactor — $^{14}N\,(n,p)^{14}C$ reaction — of a mixture of benzene and 2-methylpyrazine (see Table 1). Unfortunately, slight discrepancies in the results of different workers can be attributed not only to the initial energy but also to several other causes. Among these are firstly the dilution of the benzene with 2-methylpyrazine, which reacts with fragments and radicals, thereby affecting the yields of labelled benzene and toluene, that of the former being especially markedly diminished. Results from different sources are difficult to compare also because of the considerable difference in radiation effects, since the total

doses and intensities of irradiation also differed greatly. This view is supported by data on the irradiation of benzene with $^{14}C^+$ ions in an ion-accelerator, the design of which enabled the energy of the ions to be changed and the variation in other parameters to be fixed[19]. The results show that even slight variations in the conditions of irradiation change the yields of labelled benzene from 0.46 to 1.92%, of labelled toluene from 0.20 to 0.94% and of cycloheptatriene from 0.24 to 1.96%. The results of this work on the dependence of radiochemical yields on the energy of the bombarding ions are most complete, although they are fundamentally qualitative in character; they show that a change in the energy of $^{14}C^+$ from 5000 to 90 eV increases the yield of degradation products and decreases that of benzene, toluene, and cycloheptatriene. The cause of this is probably a diminution in the proportion of products of hot substitution at low energies of the ions. The distribution of activity within the toluene molecule (87 ± 5% in the methyl group, 16 – 15% in the ring) shows that the mechanism of the formation of labelled molecules by the interaction of accelerated ions with the medium is analogous to the interaction of the medium with recoil atoms.

In spite of the considerable obscurities associated with the effect of the initial energy with benzene and other compounds labelled with carbon by means of various recoil atoms and ions, it can nevertheless be suggested that the most probable effect would be an increase in the yield of labelled products other than the parent substance on passing from the reactions (γ,n): (n,γ) to the reactions (n,2n) and (n,p), at least partly owing to the more intense decomposition of the medium.

It is interesting that the yield of products may be influenced not only by the energy but also by the charge and configuration of the ion or fragments, since dimensions and hence steric factors can vary considerably, and these must be taken into account in calculating the number of collisions. This is shown especially clearly in the case of stearic acid exposed to $^{14}C^+$ and $^{14}CO_2^+$ ions (see Table 3).

TABLE 3. Radiochemical yields of products from the irradiation of stearic acid with $^{14}C^+$ and $^{14}CO_2^+$ ions.

Product	Yield on irradiation, %	
	$^{14}C^+$	$^{14}CO_2^+$
Stearic acid	5.7	0.6
Formic acid	2.0	1.0
Formaldehyde	none	1.0
Oxalic acid	none	0.2
3-Oxostearic acid	none	0.3
Activity adsorbed on charcoal	87.2	72.9

Radiolysis. There are no consistent and verified data on the effect of radiolysis in the stabilisation of carbon recoil atoms. However, it can be expected that radiation effects with ^{11}C and ^{14}C will be similar to those in the stabilisation of recoil atoms of other isotopes. The main ways in which radiolysis affects the distribution of activity among products of hot synthesis are firstly decomposition and other radiation-induced reactions of labelled products, in particular their hydrogenation, or dehydrogenation, polymerisation, etc. An important part is played also by radiation changes in the initial specimens, resulting in the appearance of new radicals, excited molecules, which take part in the stabilisation of recoil atoms. The principal factors causing radiolysis of irradiated systems include, apart from the γ-radiation and the neutrons of the nuclear reactor, elementary particles and recoil atoms, the effect of these last being especially strong since they possess not only great energy but also considerable mass. Study of the way in which the yield of various labelled products depends on the dose and the flux of ionising radiation enables the role of radiolysis in hot synthesis to be established. Table 4 gives data on the yields of stabilisation products of ^{14}C recoil atoms in aniline under various conditions of irradiation. They show that a tenfold change in the n/γ flux intensity ratio produces some change in the distribution of activity. The yields of polymer, of fractions soluble in hydrochloric acid, and of the fraction soluble in benzene are especially strongly affected, but the yields of labelled methane and of the acetic-acid fraction are hardly affected. The influence on the activity of the latter of the duration of irradiation is also very weak.

In 1955 it was found[41,42] that doubling the total dose or intensity of γ-radiation in the exposure of anhydrous Na_2CO_3 to a flux of γ-quanta of energy 23 MeV, which produces the reaction $^{12}C(\gamma,n)^{11}C$, left the distribution of active carbon in the products unchanged. The conclusion that radiolysis is absent is probably correct only for variations in intensity of irradiation within narrow limits. This suggestion is supported by the observation[81] of radiation effects with brominated hydrocarbons.

In view of the considerable influence of radiolysis on the distribution of activity in irradiated systems, the choice of materials for irradiation is very important for the solution of practical problems of hot synthesis. If molecules of the initial substance react directly with hot atoms, the irradiated compound should be stable to radiation, while the conditions of irradiation should guarantee minimum radiation effects. If, however, the labelled compound to be synthesised is a product of interaction of a hot atom with fragments of the initial molecules, which have undergone preliminary radiolysis, it is desirable that the starting material should give the maximum number of such fragments, and the mechanism of the formation of this product should be taken into account in selecting the conditions of irradiation. The chief variables in irradiation are time, intensity, and total dose. Radiation effects due to nuclei and recoil particles can be varied by irradiating heterogeneous systems with particles of different sizes. Increase in their dimensions produces a diminution in the

TABLE 4. Influence of conditions of irradiation on yields of products formed by reaction of ^{14}C recoil atoms with aniline[48].

Irradiation conditions	*Neutron flux, 10^{-5} counts min^{-1}	2.7	1.3	0.63	0.31	3.4
	Flux of γ-rays, 10^{-3} counts × min^{-1}	2.0	2.0	2.0	2.0	7.0
	Time of irradiation, days	4.3	4.3	4.3	4.3	0.65
Activity	total × 10^{-5} counts min^{-1}	64	31	15	18	12
Activity	CH_4, %	1.5	1.7	1.5	1.5	2
Activity of fractions dissolved in	acetic acid, %	17.0	18.1	17.8	17.5	17.1
	0.1 *N* HCl, %	40.1	39.6	39.3	39.6	36.7
	1.0 *N* HCl, %	13.9	11.7	11.6	11.1	15.1
	6.0 *N* HCl, %	11.4	12.5	—	—	11.3
	12.0 *N* HCl, %	7.1	9.2	—	—	9.1
	benzene, %	3.0	3.3	24.4	26.8	4.2
Activity	insoluble residue, %	6.2	4.0	3.5	3.3	3.8

* These headings in the original paper were respectively: neutron flux, n.cm.$^{-2}$ sec.$^{-1}$ × 10^{-11}; γ-intensity r min^{-1} × 10^{-3}; time (full power), sec. × 10^{-5} (Ed. of Translation).

dose from recoil fragments. However, it is difficult to use this method with the carbon isotopes because of the short range of the recoil atoms. Apart from the radiation effect due to the recoil energy, radiolysis can be produced in irradiated systems by the radiation of the radioactive isotope itself. Table 5 gives data on the degrees of degradation§ of various classes of organic compounds[81]¶. They show that, at moderate values of the degradation factor (5–20), considerable decomposition can be expected only at comparatively high doeses, of the order of 10^6–10^9 rad, which corresponds to considerable specific activities or very prolonged standing.

Table 6 shows the doses of intrinsic radiation of the ^{14}C isotope at definite specific activities and times of storage of labelled preparations[81].

Additives. The yield of labelled products is determined to a considerable extent by the additives present. Their action can differ in mechanism and hence in effectiveness. Inert diluents diminish the yield of products obtained by a mechanism of elastic collisions, and their influence can be calculated. Substances which remove excitation (energy and charge) and thereby prevent the decomposition of labelled molecules and radicals, the yield of which is correspondingly increased, affect mainly the yield of products obtained by epithermal reactions. A study of the radiolysis of hydrocarbon mixtures[82,83] showed that, in a binary mixture, charge is transferred from the component which is excited first (the main component) by the material of lower ionisation potential (additive), and thus the primary component is protected from radiation-induced decomposition. The mechanism by which excitation is degraded may vary. In particular, diffusion of excited solvent molecules, migration of excitation energy to neighbouring molecules, and single-stage transmission of excitation energy to considerable distances, are possible. Effects of this type have been detected in the benzene–toluene, benzene–cyclohexane, benzene–cyclohexene, and cyclohexane–cyclohexene systems. The most efficient additives are acceptors of radicals, which markedly diminish the yields of labelled compounds formed by thermal reactions

TABLE 5. Degrees of degradation of organic compounds.

Compounds	G*	Compounds	G
Saturated hydrocarbons	6–9	Ketones	7
Unsaturated hydrocarbons	14–2000	Carboxylic acids	5
Aromatic hydrocarbons	1	Esters	4
Alcohols	4–12	Halogenated derivatives	4
Ethers	7	Amino-acids	2–30

* G = degradation factor.

TABLE 6. Doses of intrinsic radiation of ^{14}C isotope and degrees of decomposition of organic substances.

Specific activity, counts g^{-1}	Dose after 1 month, rad	Degree of decomposition of substance at $G = 20$, %
1	$7 \cdot 10^4$	—
10	$7 \cdot 10^5$	0.17
100	$7 \cdot 10^6$	1.17
1000	$7 \cdot 10^7$	15.2

Wolf and coworkers[37] have studied the effect of additives on the yield of labelled benzene and labelled toluene from the irradiation of benzene and the activation of carbon by the reaction (n,2n). Additions of quinol were found to have little effect, but addition to the irradiated benzene of the radical-acceptors 1,3,5-trinitrobenzene and especially 1,1-diphenyl-2-picrylhydrazyl greatly diminishes the yield of benzene, that of toluene being slightly increased. The distribution of activity between toluene and benzene is considerably changed in the presence of 2-methylpyrazine, the yield of toluene increasing while that of benzene falls, as in the case of radical-acceptors. The effect of additives has not yet been entirely elucidated. There is little agreement, for example, between the above facts and the results of several workers[37,48,50,53] who obtained identical yields of ^{14}C-labelled benzene and toluene by the irradiation of benzene to which had been added various compounds containing nitrogen: 2-methylpyrazine, aniline, etc. Results given by MacKay and Libby[47] also suggest that the distribution of activity in the products of the irradiation of n-pentane is unaffected by additions of aniline or propylamine. On the other hand, there are indications[84] of a difference in the yields of gaseous and polymeric products of the irradiation of CCl_4 solutions with pyridine and with aniline. The effect of additives is important not only at the instant of localisation of the active atom and formation of the labelled compound, but also during the following moments of existence of the labelled substance in the medium, since it is they which, to a considerable extent, create the conditions under which the products may be either stable or unstable. If a labelled substance is unstable in a given system containing certain components, it will undergo further conversion into a product which is stable under these conditions. All that has been stated above applies to the influence of substances added to the system before irradiation. The action of substances added after irradiation is also important, being based mainly on ordinary chemical interaction, isotopic exchange, and other effects. In general, the distribution of activity in the products should depend on the method of treatment of the irradiated system. Interesting results have been obtained by Wolf *et al.*[54], who found the yield of toluene from benzene to be greatest in solutions in which the amines used as sources of nitrogen contain the greatest quantity of hydrogen in the molecule, data obtained with bis-(3-aminopropyl)amine and 2-methylpyrazine being compared. Further examples are provided by data[85,86] on the distribution of activity in specimens of crystalline Be_3N_2 irradiated in a reactor and then treated in various ways, and also on irradiated acetamide subjected to acid or alkaline hydrolysis.

The available data show that variation in solution pH after irradiation affects not only the yields of individual labelled components but also the intramolecular distribution of activity. However, it is difficult at the present time, owing to the insufficiency of the experimental data, to derive specific rules governing the effect of a method of treatment.

§ This is termed the energy yield, G, by Western authorities. It is the number of molecules changed per 100 eV of energy absorbed in the system (Ed. of Translation).

¶ This reference appears to be incorrect (Ed. of Translation).

The regularities observed in the interaction of recoil atoms and of ions with matter described above make it possible to select the most suitable procedure for the synthesis of labelled compounds. Choice of the initial mixture to be irradiated and the conditions for its subsequent processing to isolate the labelled products is governed not only by the mechanism of formation from the starting material. An individual approach must be made to each irradiated mixture and each product in deciding the question of additives, methods of irradiation and separation, etc. Nevertheless, there are several general principles, attention to which may provide some assistance in carrying out the hot synthesis of labelled compounds.

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THE CHEMISTRY OF THE SILICIDES OF THE RARE-EARTH ELEMENTS

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CONTENTS

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1. INTRODUCTION

One of the most important conditions for the development of modern technology is the production of new high-temperature materials with special physical and chemical properties — semiconducting, magnetic, nuclear, refractory, emission, and high-temperature strength properties. In this connection the silicides of the rare-earth metals are attracting attention. Compounds of the rare-earth elements are also of theoretical interest, since, unlike the transition metals, in which the d levels are being filled, lanthanum and the lanthanides have incomplete inner $4f$ levels, which cannot participate directly in chemical bonding, but which can exert an influence on the nature of the chemical bond formed by the electrons in the outermost levels. In particular, since the $4f$ and $5d$ states are close to one another, the latter may arise in crystals of the compounds as a result of $f \rightarrow d$ transitions.

Because of this and the simultaneous existence, in the silicide lattices, of covalent bonds between the silicon atoms and metallic bonds between the atoms of the metals and silicon, the bonding in silicides is of complex character, and this makes it possible to vary the physical and chemical properties of these compounds over wide limits. Scandium and yttrium resemble the lanthanides extremely closely in many of their properties, their geochemical features, and their behaviour in compounds. These two elements are intermediate between the d and f transition elements; their silicides exhibit features characteristic both of the silicide phases of transition metals of Groups IV–VIII and of the silicides of the lanthanides.

The problems of the further study of the electronic structure and physical properties of the silicides of the rare-earth elements and the extension of the range of their application makes it necessary to summarise the available information on this group of inorganic compounds.

2. STRUCTURE AND PROPERTIES

The characteristic type of crystal structure shown by the disilicides of the rare-earth metals is the α-$ThSi_2$ structure, in which the silicon atoms form a three-dimensional framework (Fig.1) and the metal atoms are situated in the spaces in this framework (the unit cell contains 4 atoms). This type of structure is produced when the silicon: metal radius ratio $r_{Si} : r_M = k$ is greater than 0.7 and less than 0.8 ($0.7 < k < 0.8$). This corresponds to the silicides of almost all the rare-earth metals, since for the latter $k = 0.69_5–0.75_5$. In this case the significant difference in atomic radii does not favour the close packing of silicon and metal, as in the silicides MSi_2 of the iron disilicide type. Every silicon atom in silicides of the α-$ThSi_2$ type is surrounded by three neighbouring silicon atoms and six metal atoms. The Si–Si distances indicate the existence of covalent bonding (close to $2r_{Si} = 2.35$ Å). The configuration of the bonds corresponds to sp^3 hybridisation. On the other hand, the M–Si distances indicate the absence of covalency, or the existence of weak covalent bonds, between the atoms of metal and silicon in a structure of this type. This bond is apparently metallic in character.

The silicides of lanthanum, cerium, praseodymium, and europium have this type of structure, but the silicides of neodymium, samarium, gadolinium, dysprosium, and yttrium crystallise in a slightly different orthorhombic