cyclo[2.2.1]heptane (I), b.p. 52.5–54° (25 mm.), $n^{25}D$ 1.5007; 42 g. (37%) of 2-methylene-3-acetoxymethylbicyclo[2.2.1]heptane (IX), b.p. 75–83° (4.0 mm.), $n^{25}D$ 1.4767; and 7.2 g. (5% recovery) of the starting diacetate VI. There was a small fraction of high refracting material that distilled at a temperature intermediate between that of the olefin acetate IX and the diacetate VI. The total recovery of material was 88% and the yield of the diene I was 79%, based on unrecovered VI and IX.

Anal. Calcd. for C_9H_{12}: C, 89.93; H, 10.07. Found: C, 90.06; H, 10.10.

5,8-Endomethylene-$\Delta^{9(10)}$-octalin-2,3-dicarboxylic Anhydride (X).—A solution of 0.816 g. (0.00834 mole) of maleic anhydride and 1.00 g. (0.00834 mole) of 2,3-dimethylenebicyclo[2.2.1]heptane (I) in 7 ml. of anhydrous benzene was allowed to stand overnight at 0°. The benzene was removed by evaporation and the residue was recrystallized three times from cyclohexane to yield 1.05 g. (62%) of 5,8-endomethylene-$\Delta^{9(10)}$-octalin-2,3-dicarboxylic anhydride (X), m.p. 118.2–120.2°.

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.37; H, 6.70.

1,4,8,11-Di-endomethylene-6,13-diketo-$\Delta^{4a(14a),7a(11a)}$-octadecahydropentacene (XI).—A solution of 2.0 g. (0.017 mole) of 2,3-dimethylenebicyclo[2.2.1]heptane (I) and 0.90 g. (0.0083 mole) of 1,4-benzoquinone in 20 ml. of ethanol was heated under reflux for 12 hours. After the solution was cooled to 0°, 0.89 g. of light yellowish crystals, m.p. 182–202° dec., was removed by filtration. This solid was undoubtedly a mixture of isomeric forms of XI. Several recrystallizations of this solid from methyl ethyl ketone produced white needles of 1,4,8,11-diendomethylene-6,13-diketo-$\Delta^{4a(14a),7a)11a)}$-octadecahydropentacene (XI), m.p. 219–227° dec. (evacuated capillary), whose m.p. range did not change on repeated recrystallization. A small amount of a higher melting form also was obtained.

Anal. Calcd. for $C_{24}H_{28}O_2$: C, 82.72; H, 8.10. Found: C, 82.55; H, 7.86.

Ozonolysis of 2,3-Dimethylenebicyclo[2.2.1]heptane (I). A solution of 2.0 g. (0.017 mole) of 2,3-dimethylenebicyclo-[2.2.1]heptane (I) in 75 ml. of ethyl acetate was ozonized at 0°. Formaldehyde that was evolved during the ozonization was collected in a water trap and identified by odor and conversion to its dimethone derivative, m.p. 190° (reported[10] m.p. 191–191.5°).

The ethyl acetate was removed under reduced pressure and the residual ozonide was decomposed by heating for 2 hours on a steam-bath with 25 ml. of 30% hydrogen peroxide and 40 ml. of glacial acetic acid. The excess peroxide was decomposed and the reaction mixture was evaporated to dryness under reduced pressure. Since the *cis*-cyclopentane-1,3-dicarboxylic acid (XII) could not be easily purified from the reaction product, the residue was heated under reflux for 12 hours with acetic anhydride. Removal of the acetic anhydride under reduced pressure, followed by recrystallization from a mixture of ethyl acetate and cyclohexanone, gave 0.40 g. (17%) of *cis*-cyclopentane-1,3-dicarboxylic anhydride, m.p. 163–164° (reported[11] 160–161.5°). A small portion of the anhydride was heated with water and the water removed by evaporation to give the *cis*-cyclopentane-1,3-dicarboxylic acid (XII), m.p. 120.5–123° (reported[11] m.p. 120–121.5°). Heating a small sample of the anhydride for 12 hours with aniline followed by recrystallization from methanol produced the corresponding dianilide, m.p. 223–225° (reported[11] m.p. 222–224°).

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(10) E. C. Horning and M. G. Horning, *J. Org. Chem.*, **11**, 95 (1946).

(11) K. T. Pospischill, *Ber.*, **31**, 1950 (1898).

COLLEGE PARK, MARYLAND

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, BROOKHAVEN NATIONAL LABORATORY]

Radioactive Anthracene-C^{14} and Acridine-C^{14} from the Neutron Irradiation of Acridine[1]

BY ALFRED P. WOLF AND R. CHRISTIAN ANDERSON

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Anthracene-C^{14} has been produced by neutron irradiation of the nitrogen analog, acridine. The recoiling carbon-14 entities produced by the $N^{14}(n,p)C^{14}$ reaction also were found in acridine molecules, where the nitrogen had not undergone neutron capture during the course of irradiation. The ratio of activity as acridine to the activity as anthracene was about 19/1. Of the total activity produced in the samples, 3.5% was found as acridine and 0.2% was found as anthracene.

Prior to the advent of nuclear reactors, production of carbon-14 was severely limited by the lack of adequate sources of neutrons. The high neutron fluxes available from nuclear reactors allow the production of carbon 14 on a much larger scale.

Equation 1 represents the nuclear transformation taking place in carbon-14 production.

$$N^{14} + n \longrightarrow (N^{*15}) \longrightarrow C^{14} + p \qquad (1)$$

The ejection of a proton from the compound nucleus, N^{*15}, imparts a recoil energy[2] of 45,000 e.v.[3] to the carbon-14 as it is formed.

The chemical consequences of such an act afford a novel approach to the reactivity of organic molecules. It seems certain that the tremendous energy (with respect to bond energies) imparted to carbon-14 would result in bond rupture in every event. The recoiling fragment can lose energy by various means such as elastic and inelastic collisions and dissipation as vibrational energy in the crystal lattice. The fate of the carbon-14 when it has lost most of its recoil energy then becomes of chemical interest. The mechanism of entry into a molecular species whether by physical or chemical means depends on the precise nature of the carbon-14 fragment just prior to reaction. The question may only be resolved by knowing its energy and structure at this point.

The present work is the first part of a systematic study of the nature of the recoil processes occurring in organic compounds *via* the $N^{14}(n,p)C^{14}$ reaction. A consequence of exploring the recoil processes may be the development of useful techniques for labeling organic compounds without involving organic synthesis.

Acridine was irradiated in the Brookhaven nuclear reactor. This compound was chosen for study because of its high chemical and thermal stability, and its resistance to radiation decomposition, which

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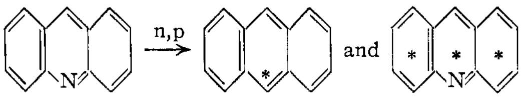
(1) Research carried out under the auspices of the U. S. Atomic Energy Commission. Presented before the Organic Division at the 123rd National Meeting, Los Angeles, Calif., March, 1953. This paper is the first of a series on the chemical consequences of a recoiling C^{14} fragment in organic compounds.

(2) H. Huber and A. Stebler, *Phys. Rev.*, II **73**, 85 (1948).

(3) 1 e.v. = 1.602×10^{-12} erg. A value of 6.02×10^{23} e.v./mole is equivalent to 23.1 kcal./mole. Normal bond energies are in the 3-5 e.v. region.

can be high under the intense bombardment received in a nuclear reactor.

Anthracene (II),[4] the carbon analog of acridine (I), was isolated containing carbon 14. Significantly, acridine (III) containing carbon-14 also is isolated.



I II III

Anthracene-9-C^{14} was removed from the reaction mixture by a carrier technique. The total number of active carbon atoms formed during irradiation is small compared to the total number of molecules present. Irradiation of approximately 8×10^{22} (neutron flux about 5×10^{12} neutrons/cm.^{2}) molecules of acridine for three weeks in the Brookhaven reactor will result in approximately 8×10^{17} atoms of carbon-14. Less than 1% of these replace nitrogen to give anthracene. Consequently it would have been inconvenient to attempt the isolation of the anthracene-9-C^{14} carrier free.

A unique problem which appears in the investigation of chemical systems of this sort is the extraordinary care that must be taken in order to ensure the radiochemical purity of the products. Acridine could not be brought to constant specific activity by physical methods of purification. A reaction cycle then was devised which subjected acridine and analogs of acridine to a variety of chemical conditions, while not affecting the basic structure of acridine itself. The end product was again acridine which was demonstrably at constant specific activity. It should be emphasized that a single method of purification which seemingly results in constant specific activity is not sufficient evidence for the purity of products obtained by neutron bombardment of nitrogen-containing material. The radio-assays on acridine and its analogs are given in Table I. Careful purification gives a good yield of material at constant specific activity.

TABLE I

SEQUENTIAL PURIFICATION OF ACRIDINE

Compound	Activity mμc./mg. C Sample A[a]	Sample B[b]
Crude acridine	0.94	4.73
Acridine, one sublimation	.100	0.345
Acridine, two sublimations	...	.291
Thioacridone	.076	.275
Thioacridone, one recrystallization	...	.243
Acridone	...	.253
Acridane	.058	.228
Acridane, one recrystallization	...	.213
Acridine	...	.227
Acridine, one sublimation	...	.220
Acridine, two sublimations	.057	.222
Acridine, one recrystallization	...	.221
Acridine, three recrystallizations	...	.218
Acridine, five recrystallizations	...	.217

[a] Irradiation ~ 6 days. [b] Irradiation ~ 20 days.

Synthesis by nuclear recoil was used by Reid[5] who prepared an active $C_5H_{11}I^{128}$ fraction from the reaction between pentane and iodine-128. As a result of the work of Ruben and Kamen[6] and Yankwich, Rollefson and Norris,[7] Maddock[8] suggested the neutron irradiation of nitrogen-containing organic compounds in order to produce carbon-14 containing compounds. Edwards[9] reported that irradiation of pyridine and aniline yielded pyridine and aniline containing carbon-14. Giacomello,[10] and Croatto, Giacomello and Maddock[11] also have reported the formation of compounds containing carbon-14 produced by such a process. The results of this latter work is given in Table II. Recently Schrodt and Libby[12] have reported on the neutron irradiation of a 5 mole per cent. solution of aniline in *n*-pentane.

TABLE II

NEUTRON IRRADIATION OF PYRIDINE AND QUINOLINE OXALATES (DATA OF CROATTO, GIACOMELLO AND MADDOCK[10,11])

Compound irradiated	Products	Activity % of total found in product
Pyridine oxalate	Benzene	7.6
	Phenol	5.4
Quinoline oxalate	Naphthalene	8.4
	α-Naphthol	2.2
	Quinoline	1.6
	Oxalic acid	7.1

Our results are consistent with the view that the reactive carbon-14 fragment not only replaces nitrogen to give labeled anthracene, but also replaces carbon to give labeled acridine. If this replacement is random, one would expect to find a greater percentage of the total carbon-14 activity as acridine than as anthracene, since acridine has 13 potentially replaceable sites, whereas anthracene can only result by the replacement of nitrogen. A purely statistical replacement would result in a ratio of activities of 13/1. This figure compares favorably with the most probable value obtained in this work of

$$\frac{\text{activity as acridine}}{\text{activity as anthracene}} = 17/1, \text{A}; \quad 19/1, \text{B}; \quad \text{(see Table IV)}$$

The data of Giacomello, and Croatto, Giacomello and Maddock are not in agreement with this result. Their experimental ratio, act. as quinoline/act. as naphthalene is 1/5. The statistical ratio for these compounds is 9/1.

The percentage of the total activity isolable as acridine-C^{14} is small, being 3.5% of the total activity produced. Anthracene-9-C^{14} accounts for 0.2% of the total. About 3% of the activity was found in gaseous fragments. The remaining activity is mainly contained in polymeric material isolated during the beginning of the acridine purification.

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[4] The anthracene is presumed to be labelled in the 9 position, since only the replacement of nitrogen would result in anthracene.

[5] A. F. Reid, *Phys. Rev.*, **69**, 530 (1946).

(6) S. Ruben and M. D. Kamen, *ibid.*, **59**, 349 (1941).

(7) P. E. Yankwich, G. K. Rollefson and T. H. Norris, *J. Chem. Phys.*, **14**, 131 (1946).

(8) A. G. Maddock, *Research*, **2**, 556 (1949).

(9) R. Edwards, A.C.S. Sixth Southwest Regional Meeting, San Antonio, Texas, 1949.

(10) G. Giacomello, *La Ricerca Scientifica*, **21**, 1211 (1951).

(11) U. Coratto, G. Giacomello and A. G. Maddock, *ibid.*, **21**, 1598 (1951).

(12) A. G. Schrodt and W. F. Libby, THIS JOURNAL, **76**, 3100 (1954).

Some of the activity also may be found in other chemical species, probably formed by reaction between acridine and the carbon-14 fragment.

These results indicate a new and unique way of obtaining a specific label if a nitrogen analog of the desired compound is available. If random labeling is required then the compound desired may be mixed with a suitable nitrogen-containing material before irradiation. The recoiling carbon-14 fragments then will be incorporated into the compound in question. This would prove especially advantageous in the random labeling of complex natural products such as alkaloids and steroids. The low activity yield in random labeling may be balanced by the relative ease of preparation of a labeled compound difficult to obtain synthetically. It is hoped that the level of activity may be increased by proper choice of nitrogen-containing materials. A high nitrogen-to-carbon ratio in the diluent will serve this end. Similarly the yield of carbon analogs may be increased to the level where they can be isolated carrier free. These compounds would have specific activities heretofore unattainable.

The specificity of the label is under investigation at the present time. Work is also in progress to obtain accurate values for the C/N replacement ratio, to evaluate the effect of bond strengths on the replacement, to compare the solid and liquid state with regard to product yield, and to obtain information pertinent to the mechanism of replacement.

Experimental[13]

Irradiation.—The samples were irradiated in the Brookhaven reactor at an approximate flux of 5 × 10^{12} neutrons/cm.^{2}/sec. In order to correct for fluctuations in neutron density during irradiation, an integrated value for the total irradiation is reported in megawatt hours.[14] Irradiation could be carried out in either of two facilities, one operating at 80–100° and the other at 30°. After irradiation, one to two weeks was allowed for decay of short lived activities arising from impurities in the quartz containers.

Packaging.—Irradiation containers were made of clear quartz in varying widths and lengths. The samples used for measuring the activity of the gaseous fragments were enclosed in containers with breakseals at one end.

The powdered acridine was tamped in the container. The assembly was evacuated to a pressure of 1 × 10^{-5} mm. and flushed with helium three times. After outgassing the acridine by melting under vacuum, a final flushing with helium was carried out. The containers were sealed under a pressure of 1 × 10^{-5} mm. or less.

Processing of Samples.—Containers with breakseals were opened in a vacuum system. The volume of released gases was measured in a gas buret and after suitable dilution, transferred to gas counting tubes (see Table III). There was no difference in physical appearance between those samples irradiated at 80° and those irradiated at 30°. The acridine was black but still crystalline in appearance. The black material was dissolved in benzene. The crushed container was leached with boiling benzene. All fractions were then combined. Insoluble polymeric material formed during irradiation was included in the combined fraction. In order to get a representative assay of the activity in the gross solids, the benzene solution was shaken so as to suspend the insoluble material. A number of aliquots were taken for each series. The irradiation data and initial processing results are given in Table III.

TABLE III

RADIOCHEMICAL RESULTS; NEUTRON IRRADIATION OF ACRIDINE

Sample[a]	Weight in grams	Irradiation in megawatt hours[b]	Activity in gas as % of total[c]	Activity, μc. Calculated[d]	Activity, μc. In gross solid[e]	Activity, μc. In soluble solid[f]
A-1	0.44	2449	2.8	0.39	0.44	..
1	0.839	3398	..	1.00	1.26	4.06
2	1 182	3398	3.6	1.41	1.24	
3	1.653	3398	2.3	1.96	2.15	
4	24.336	11578	..	0.101 mc.	0.112 mc.	0.103 mc.

[a] Temperature of samples A-1, 1, 2 and 3 during irradiation was 80–100°. Temperature of sample 4 was ~30° during irradiation. [b] See footnote 13. A normal day of pile operation results in 576 megawatt hours of irradiation. [c] These values are based on the calculated activity. [d] Total C^{14} activity produced by irradiation. [e] Activity of all solid material recovered. The error in these values is high because of the difficulty in obtaining consistent results, due to active impurities from the quartz and materials adhering to the outside walls of the container. [f] Activity of gross material soluble in benzene.

Samples 1, 2 and 3 were combined after the activities of the gross solids had been determined. The experimental procedures used were essentially the same for 1, 2 and 3 (hereafter called A) and sample 4 (hereafter called B). Exceptions are noted as such. Yields and assays are given separately. Numerical values used in the descriptive part of the experimental are for sample A.

Purification of Acridine Prior to Irradiation.—Matheson practical grade, m.p. 95–100°, was recrystallized twice from benzene–hexane. Upon sublimation, the first 25% of the sublimate was removed from the cold finger and discarded. The sublimed material was recrystallized again, m.p. 110–111°. A final sublimation in which the first 10–15% of material was discarded was then carried out. The procedure was varied slightly from one batch to another. A typical sample of the purified acridine was analyzed.

Anal. Calcd. for $C_{13}H_9N$: C, 87.1; H, 5.1; N, 7.8. Found: C, 87.2; H, 4.8; N, 7.8.

Anthracene-9-C^{14}.—Highly purified anthracene[15] (207 mg.) was added to the benzene solution (298 cc., 3.67 g. of irradiated material) of sample A. The solution was filtered. Gaseous hydrochloric acid was passed into the iced filtrate for ten minutes. The solution was filtered several times. The filtrate was extracted with two 100-cc. portions of 4 *N* HCl, followed by two 50-cc. portions of saturated K_2CO_3 solution and finally washed with two 50-cc. portions of water.

The precipitated acridine hydrochloride, the two acid washes and the water washes were combined and set aside for later work.

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[13] Microanalyses were performed by F. Schwarzkopf, Woodside, 77, N. Y. Radioassays were performed by N. E. Day and D. Christman of this Laboratory. The method of R. C. Anderson, Y. Delabarre and A. A. Bothner-By, *Anal. Chem.*, **24**, 1298 (1952), was used. The radioassays were usually performed at least in duplicate. The standard deviation for any given assay is 1–2% ($\sigma = \sqrt{\text{TOT. COUNTS}} \times 100/\text{TOT. COUNTS}$). The root mean square error encompassing all errors inherent in the analysis is not greater than 5%. All melting points were taken on a Kofler hot-stage.

[14] In order to calculate yield of active atoms during any given irradiation, use is made of the equation

$$N^* = \frac{N(nv)\sigma}{\lambda}(1 - e^{-\lambda t})$$

where N^* represents the number of active atoms at time t (C^{14} in this case), N represents the number of atoms of the species undergoing bombardment (N^{14} in this case), nv represents the reactor flux in neutrons/cm.^{2}/sec., σ represents the capture cross section for neutrons of the element undergoing bombardment, λ represents the characteristic decay constant for the active species, and t is the time of bombardment in seconds. If the half-life of the species produced is large compared with the time of irradiation then this equation may be put in the form

$$N^* = N(nv)\sigma t$$

where nvt = megawatt hours × 6.5 × 10^{14} × 0.79. The factor 0.79 corrects for the position of the sample in the reactor.

[15] The appropriate quantity of carrier anthracene to be added was determined by assuming that 1% of the total activity was in this form and by considering the limits of our assay method. On this basis dilution was made to a point where an accuracy of 5% could still be expected.

The dried benzene solution was concentrated to 2 cc. This was evaporated to dryness at 10 mm. After taking up the faint yellow residue in a solution of 100 cc. of hexane (Phillips 99% pure, refractionated in a 15-plate column) and 25 cc. of dry benzene, the solution was placed on an activated alumina column. Benzene (75%)-hexane (25%) was used to develop the column. The bands were followed using an ultraviolet lamp. The first and last 10% of the anthracene coming through was discarded. After removing the benzene-hexane by vacuum distillation, a residue (A, 0.159 g. 77%; B, 0.506 g. 84%) with a violet fluorescence was obtained, m.p. 215-216°.

Anal. A. Found: 0.043 mμc./mg. C. B. Found: 0.512 mμc./mg. C.

Recrystallization of the anthracene (0.029 g.) from an ethanol-benzene mixture, gave anthracene (0.016 g.) with an intense violet fluorescence, m.p. 215-215.5°.

Anal. A. Found: 0.048 mμc./mg. C. B. Found: 0.319 mμc/mg. C.

A small sample of crude anthracene from A was sublimed.

Anal. Found: 0.049 mμc./mg. C.

A small sample of the recrystallized material from B was sublimed.

Anal. Found: 0.320 mμc./mg. C.

9,10-Anthraquinone-9-C^{14}.—The method was essentially that of Beisler and Jones.[16] The following description is for the procedure used on sample B. Anthracene (0.073 g.) which had been sublimed from the chromatographed anthracene was mixed with sodium dichromate (0.180 g.) and 0.3 cc. of boiling water. Dropwise addition of 0.25 cc. of concd. H_2SO_4 in 0.2 cc. of boiling water then followed. The solution was boiled and stirred for one hour. The solution was cooled to 80° and centrifuged. The solid remaining after the supernatant liquid had been removed was washed twice with boiling water. The light yellow powder was taken up in concd. H_2SO_4 and heated for two hours at 120°. Hot water was added to precipitate the product. After centrifugation, and removal of the supernatant liquid, the product was washed with hot water, sodium hydroxide solution and finally hot water. The crystals were washed in ice cold methanol and then dried. A chloroform solution of the product was taken to dryness after first having filtered the solution hot. Crystallization from a minimum quantity of chloroform gave 0.032 g. of fine yellow needles, m.p. 285°.

Anal. A. Found: 0.044 mμc./mg. C. B. Found: 0.32 mμc./mg. C.

Total activity as anthracene-9-C^{14} found in A was 9.17 mμc. Total activity as anthracene-9-C^{14} found in B was 183 mμc.

Initial Acridine Isolation.—The total acridine hydrochloride sample was brought to a *p*H 8-9 with potassium carbonate solution with both sample and solution at 0°. The tan precipitate was collected and dried.

Anal. A. Found: 0.94 mμc./mg. C. B. Found: 4.73 mμc./mg. C.

A portion (1.072 g.) of the crude product (2.84 g.) was sublimed. The sublimate (0.778 g.) was used in all subsequent steps.

Anal. A. Found: 0.100 mμc./mg. C. B. Found: 0.345 mμc./mg. C.

Sample B was sublimed again.

Anal. B. Found: 0.291 mμc./mg. C.

At this point the major purification takes place. After the first sublimation had taken place, a black cake was left behind in the sublimer.

Anal. B. Found: 16.2 mμc./mg. C.

For sample B, this cake was subjected to two further sublimations to remove all the acridine that may still have been present. This procedure established that the polymer (9.5 g.) still contained 42 to 58% of acridine. Therefore the minimum total acridine recovered at this point was 14.02 g. This material can be considered to be chemically pure but not radiochemically pure. The figure used as the basis for minimum activity as radioactive acridine is then equal to the weight of chemically pure acridine times the assay on radiochemically pure acridine.

Thioacridone.—The method used was essentially the one described by Albert.[17] A mixture of 0.712 g. of acridine and 0.165 g. of flowers of sulfur was sealed in a bomb tube and kept at 195 ± 5° for four hours. The tube was cooled to −30° and then opened. The product formed an extremely hard cake which was dissolved in 40 cc. of boiling 0.5 *N* sodium hydroxide. The solution was filtered through glass wool. The product precipitated from the cooled solution. After centrifugation of the solution, the supernatant liquid was removed by pipet. Additional product was obtained by passing CO_2 into the separated liquid. The solid was dried for one hour at 105° and 55 mm. The product, 0.663 g. had a m.p. 261-264°.

Anal. A. Found: 0.076 mμc./mg. C. B. Found: 0.275 mμc./mg. C.

A small sample from B was recrystallized from 95% ethanol. B. Found: 0.243 mμc./mg. C.

Acridone.—The method described by Albert[17] was used here. Thioacridone (0.540 g.) was dissolved in 10 cc. of 95% ethanol. To this was added 0.33 g. of sodium hydroxide in 20 cc. of water. The thioacridone solution was heated on the steam-bath. Sodium hypochlorite solution (12 cc. of Baker and Adamson hypochlorite plus 100 cc. of water) was slowly added. The reaction mixture was kept hot for another 30 minutes. The *p*H of the solution was adjusted to 4-5 with hydrochloric acid. After cooling, the solution was filtered. The solid obtained was dried at 105° and 30 mm. to give 0.550 g. of crude product. A small sample recrystallized from *n*-amyl alcohol gave a melting point of 347-349°.

Anal. B. Found: 0.253 mμc./mg. C.

Acridane.—The method described by Albert[17] was used. Acridone (0.454 g.) was dissolved in 20 cc. of boiling *n*-amyl alcohol. Sodium (1.5 g.) was added in small pieces over a half-hour period. Boiling was continued for an additional half-hour. The excess sodium was then removed. On cooling, a sludge was obtained which was treated with 20 cc. of water. The *n*-amyl alcohol was removed by steam distillation. The cooled solution was filtered. The crude acridane was dried at 80° and 100 mm. for two hours. A yield of 0.248 g. was obtained.

Anal. A. Found: 0.058 mμc./mg. C. B. Found: 0.228 mμc./mg. C.

A small sample from B was recrystallized from 95% ethanol.

Anal. B. Found: 0.213 mμc./mg. C.

Acridine.—Acridine was prepared from acridane by the method described in Albert.[17] Acridane (0.200 g.) was stirred in a solution of 23 cc. of boiling water and 1.11 cc. of dilute sulfuric acid (d. 1.19) until a homogeneous suspension was obtained. A solution of potassium dichromate (0.108 g. in 1.7 cc. of boiling water) was added in two parts, allowing five minutes to pass before the second addition was made. A solution of 0.276 g. of dichromate in 2.8 cc. of water was then added and boiling was continued for five more minutes. It was cooled rapidly and then stored in the refrigerator overnight. The salt was suspended in 7.7 cc. of hot water. The solution was treated with concentrated ammonium hydroxide solution (1.9cc.), brought to a boil, cooled quickly and filtered. After washing with water, the precipitate was dissolved in a little over one equivalent of hot 0.5 *N* hydrochloric acid. A trace of acridane was removed at this point. Acridine was reprecipitated with ammonium hydroxide. The product was dried over calcium chloride in a vacuum desiccator. Two sublimations gave 0.106 g., m.p. 108-109°.

Anal. A. Found: 0.057 mμc./mg. C (resublimed material). B. Found: 0.227 mμc./mg. C (crude material).

Crude acridine from B was resublimed.

Anal. B. Found: 0.220 mμc./mg. C.

This sample was sublimed a second time to give acridine with a melting point of 109-110°.

Anal. B. Found: 0.222 mμc./mg. C.

Further Purification of Sample B.—Material which had gone through the chemical purification cycle and had been sublimed twice was used in each case. All crystallizations were carried out so that only a small part of the acridine would precipitate. This afforded maximum purification in each process.

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[16] W. H. Beisler and L. W. Jones, THIS JOURNAL, **44**, 2296 (1922).

[17] A. Albert, "The Acridines," Edward Arnold & Co., London, 1951, pp. 17-18.

Acridine dissolved in hexane–benzene was filtered hot; slow cooling gave hair-like, pale yellow crystals.

Anal. Calcd. for $C_{13}H_9N$: C, 87.1; H, 5.1; N, 7.8. Found: C, 87.2; H, 4.9; N, 7.5; radioassay, 0.214 mμc./mg. C.

Another sample was recrystallized first from benzene. These crystals were then recrystallized from absolute ethanol. The crystals from ethanol were then recrystallized from absolute ether. Analyses are given in corresponding order.

Anal. Found: 1. 0.220 mμc./mg. C; 2. 0.211 mμc./mg. C; 3. 0.217 mμc./mg. C.

A five-step crystallization using hexane–benzene was then carried out on sublimed material. Analyses are given for the first, third and fifth steps.

Anal. Found: 1. 0.221 mμc./mg. C; 3. 0.218 mμc./mg. C; 5. 0.217 mμc./mg. C.

Total Activity in Acridine.—The total activity in the form of acridine was estimated as follows. A minimum figure is obtained by using that weight of acridine actually recovered. These figures are A, 2.064; B, 14.02 g. Considering losses in sublimation, transfer, etc., an estimate can be made of the most probable value for recoverable acridine. These figures are A, 3.14 g.; B, 18.42 g. The maximum figure can be considered to be that ignoring any radiation damage. These figures are A, 3.674 g.; B, 24.336 g., and are useful only insofar as they place an upper limit on the total activity as acridine.

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Action of Grignard Reagents. VII. Benzoxazones, Benzoxaz-2,4-diones and 2,3-Diphenylquinazolone-4

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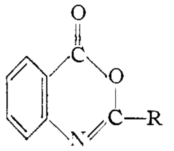
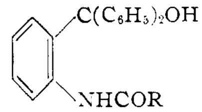
Treatment of benzoxazones with phenylmagnesium bromide brought about cleavage of the hetero ring in the case of 2-phenyl-3,1-benzoxaz-4-one (Ib), 2,3-benzoxaz-1-one (IVa) and its 4-aryl derivatives (IVb,c), and addition to the carbonyl group in the case of 2-phenyl-1,3-benzoxaz-4-one (VII). Addition of the Grignard also occurred with the benzoxazdiones, 1,3-benzoxaz-2,4-dione (Xa) and its benzoyl derivative Xb, which yielded a compound believed to have the structure represented by XIa, together with triphenylcarbinol in the case of Xb. Treatment with phenylmagnesium bromide, followed by hydrolysis, caused opening of the hetero ring in 2,3-diphenylquinazolone-4 (XIIb) to give III and aniline.

Mustafa and co-workers[1] have shown that the treatment of 1,8-naphthosultone, N-phenylsulfonylnaphthosultam, 2-phenyl-1,2-benzisothiazol-3-one-1,1-dioxide, 2-phenylsulfonyl-1,2-benzisothiazol-3-one and N-phenylsulfonylphthalimide with Grignard reagents results in opening of the hetero five-membered ring. We have now investigated the reaction of the hetero six-membered ring in benzoxazones (Ia-b, IVa-c and VII), benzoxaz-2,4-diones (Xa,b) and 2,3-diphenylquinazolone-4 (XIIb) with these reagents. It has been shown that the reactions of Grignard reagents with 2-methyl-3,1-benzoxaz-4-one (Ia)[2] and coumarin[3] are not strictly analogous. Thus, Ia reacted with phenylmagnesium bromide by the inverse method to give the acetyl derivative of *o*-aminobenzophenone (33%) and with this reagent by direct addition to give only 2-acetamidophenyldiphenylcarbinol (IIa, 23%); in the case of coumarin, the carbinol is the only product formed by either method. We obtained the carbinol IIa in almost quantitiative yield by addition of Ia to the Grignard.

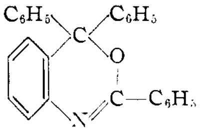
Treatment of 2-phenyl-3,1-benzoxaz-4-one (Ib) with phenylmagnesium bromide, by both the inverse method and normal addition, gave only 2-benzamidophenyldiphenylcarbinol (IIb) and its dehydration product 2,4,4-triphenyl-3,1-benzoxazine (III). Treatment of Ib with phenyllithium gave results similar to those obtained with phenylmagnesium bromide.



Ia, R = CH_3
b, R = C_6H_5



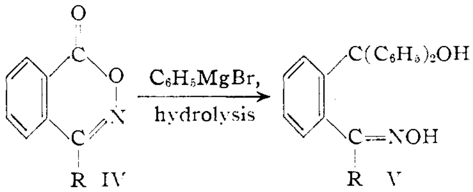
IIa, R = CH_3
b, R = C_6H_5



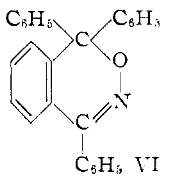
III

The structure of II and III was determined by the benzoylation of *o*-aminotriphenylcarbinol which yielded IIb; dehydration of IIb yielded III.[4]

Treatment with phenylmagnesium bromide brought about opening of the oxazone ring in the 2,3-benzoxaz-1-ones, IVa-c, which yielded the corresponding oximes of 2-formyl- (Va), 2-benzoyl- (Vb) and 2-(α-naphthoyl)-triphenylcarbinol (Vc), respectively.



IV and V: a, R = H; b, R = C_6H_5; c, R = α-$C_{10}H_7$



C_6H_5 VI

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