TABLE I

Starting compd	R	Mp, °C	Complex											
			Mol wt		Anal., %				Chemical shift (multiplicity[a]) (relative intensity)					
					C		H							
			Calcd	Found	Calcd	Found	Calcd	Found	CH_3	τ_1	τ_2	τ_3	τ_4	R
IVa	CH_3	170–173	546.9	536	30.74	30.30	4.42	4.59	8.70 (s) (3.0)	7.20 (q) (1.0)	7.06 (t) (1.0)	8.30 (m) (1.8)	6.65 (q) (2.0)	9.13 (d) (3.0)
IVb	C_6H_5	139–140	671.1	660	42.95	43.20	4.21	4.50	8.48 (s) (3.0)	6.24 (s) (1.0)	6.82 (t) (1.2)	8.30 (m) (2.4)	6.60 (q) (2.0)	
IVc	$COOC_2H_5$	171–173	660.8	658	32.61	32.63	4.26	4.03	8.00 (s) (3.0)	7.23 (s) (1.0)	7.06 (t) (1.0)	8.30 (m) (2.3)	6.70 (q) (2.3)	

[a] Abbreviations used were s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

these by-products was not performed in the present study.[8]

That the complexes IIa,b are formed at room temperature, whereas the formation of the complex IIc from IVc, in which the double bond would be electron deficient, requires a higher temperature would suggest that in the initial step of the formation of the complexes IIa–c an intermediate similar to a cyclopropylcarbinyl cation would be formed by donation of an electron pair from the olefin to the palladium component. Thus, the cyclopropane ring would be opened through the usual cyclopropylcarbinyl–homoallyl rearrangement.

Experimental Section

2-Cyclopropylbutene-2 (IVa).—To an ethereal solution of the Wittig reagent, prepared from 37 g (0.1 mole) of ethyltriphenylphosphonium bromide, was added 8.4 g (0.1 mole) of cyclopropyl methyl ketone at room temperature. A white precipitate was formed immediately. The suspension was refluxed for 10 hr and filtered. The filtrate was washed with water, dried, and distilled to give 4.1 g of IVa, the yield being 48.9%, bp 102°.

Anal. Calcd for C_7H_{12}: C, 87.42; H, 12.58. Found: C, 87.21; H, 12.47.

1-Phenyl-2-Cyclopropylpropene-1 (IVb).—To an ethanolic solution of the Wittig reagent, prepared from 47.5 g (0.123 mole) of benzyl-triphenylphosphonium chloride, was added 10.3 g (0.123 mole) of cyclopropyl methyl ketone at room temperature over a period of 10 min. The reaction mixture was refluxed for 3.5 hr and worked up in usual way. The product, IVb, was obtained in a yield of 31% (6 g), bp 108° (15 mm).

Anal. Calcd for $C_{12}H_{14}$: C, 91.08; H, 8.92. Found: C, 91.17; H, 8.95.

Ethyl 3-Cyclopropyl-2-butenoate (IVc).—To a suspension of 1.2 g (0.05 mole) of sodium hydride in 100 ml of 1,2-dimethoxyethane was added 11.2 g (0.05 mole) of diethyl carboethoxymethylphosphonate over a period of 50 min. After the reaction mixture was stirred for 2 hr at room temperature, 4.2 g (0.05 mole) of cyclopropyl methyl ketone was added to the mixture over a period of 5 min, and then it was heated at 55° for 19 hr. The reaction mixture was poured into 300 ml of water and the organic layer was extracted with ether. The ethereal solution was distilled to give 5.6 g of IVc, the yield being 73%, bp 82–85° (17 mm).

Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.88; H, 9.18.

Complexes IIa–c.—An equimolar solution of IVa–c and bis-benzonitriledichloropalladium in benzene was refluxed (IVc) for 60 hr or was allowed to stand at room temperature (IVa,b) for 19 hr and was then poured into a large excess of petroleum ether. The precipitate formed was filtered and the filtrate was concentrated to give the complex which was purified by recrystallization from toluene (IIa,c) or benzene (IIb).

Registry No.—IVa, 5860-30-0; IVb, 15353-03-4; IVc, 825-78-5.

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(8) The type II′ complex might exist in the by-products.

The Preparation of 4-Substituted Bicyclo[2.2.1]heptane-1-carboxylic Acids[1]

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In a recent paper, the p*K*'s of several 4-substituted bicyclo[2.2.2]octane- and bicyclo[2.2.1]heptanecarboxylic acids in various solvents were reported.[2] This paper presents the syntheses of the bicycloheptane acids, which were all new compounds. The corresponding bicyclooctane acids were either available from earlier work or were prepared by known literature methods.

The key to the synthesis of the bicycloheptane acids was the conversion of 1,4-dichlorobicyclo[2.2.1]heptane[3] (1) into the 1,4-diacid, 2, since the methods already developed[4] for the synthesis of the bicyclooctane acids could be applied to the heptane diacid. The obvious method for conversion of the dichloride into the diacid was by carbonation of some metallic derivative. Several analogous reactions had been reported for the conversion of 1-chloro compounds into monoacids.[5–8]

Our early experiments in this direction were unsuccessful.[9] The dichloride did not react with lithium or sodium–potassium alloy in cyclohexane or decalin. In tetrahydrofuran or dibutyl ether, a reaction did occur, but apparently the intermediate anion abstracted hydrogens from the solvents since the only product isolated was norbornane. With sodium–potassium alloy in cyclohexane–benzene only benzoic acid was isolated. An attempt to carry out a lithium–halogen exchange on the dichloride with butyllithium in diethyl ether failed as did an attempt to form a transient Grignard reagent in cyclohexane–pyridine mixtures.

In the present work it was confirmed that 1-chlorobicyclo[2.2.1]heptane was readily converted into the

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(1) Based on the Ph.D. Dissertation of C. Leung to be submitted to the Cornell Graduate School, Ithaca, N. Y., Sept 1967. This material was presented in part at the 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967.

(2) C. F. Wilcox, Jr., and C. Leung, submitted for publication.

(3) C. F. Wilcox, Jr., and J. G. Zajacek, *J. Org. Chem.*, **29**, 2209 (1964).

(4) C. F. Wilcox, Jr., and J. S. McIntyre, *ibid.*, **30**, 777 (1965), and references therein.

(5) R. Bixler and C. Niemann, *ibid.*, **23**, 742 (1958).

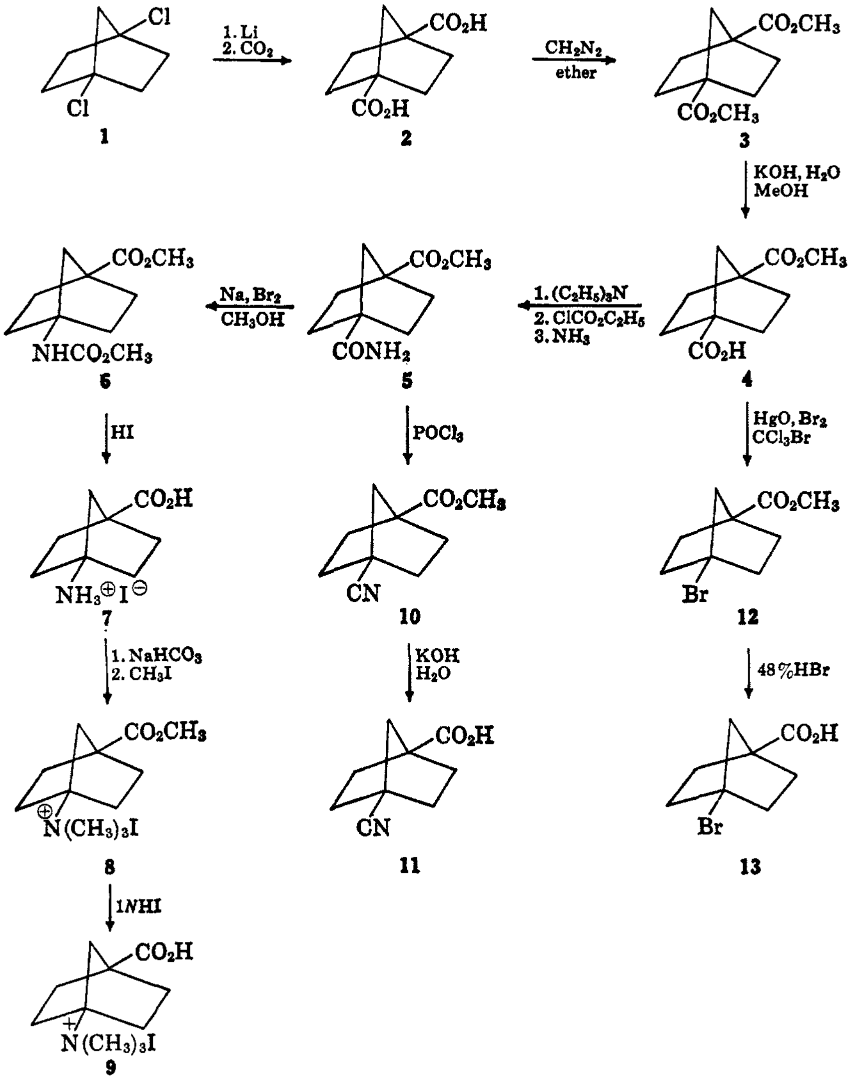
(6) S. Winstein and T. G. Traylor, *J. Am. Chem. Soc.*, **78**, 2597 (1956).

(7) W. von E. Doering and E. F. Schoenewaldt, *ibid.*, **73**, 2333 (1951).

(8) P. T. Lansbury and L. D. Sidler, *Tetrahedron Letters*, 691 (1965).

(9) J. G. Zajacek, Ph.D. Dissertation, Cornell University, Ithaca, N. Y., 1962.

Chart I



monoacid in good yield by either metallation with ordinary lithium or by exchange with *s*-butyllithium but that under the same conditions the dichloride did not react. The dichloride also did not form a Grignard reagent in ether, tetrahydrofuran, di-*n*-butyl ether, or diglyme.

Despite these negative results metalation did occur when the dichloride in refluxing cyclohexane was treated with excess lithium alloyed with 1% sodium; subsequent carboxylation with carbon dioxide gave the desired diacid in about 25% yield. There are numerous reports of the necessity of alloyed sodium for the success of the lithium reaction.[10] It was found that alkyllithium formation depended critically on the slow addition of the dichloride. Addition of the dichloride in a single batch gave only a 0.2% yield of diacid. Somewhat surprisingly in none of the carbonation experiments tried was there ever any evidence of the 4-chloro acid that would be formed from a monolithium derivative. The experiments carried out do not distinguish between the chloro anion being unstable relative to dissociation to the dianion or the alternate possibility of the chloro anion decomposing competitively to other products.

Formation of the monochloro anion is presumably aided by the dipole of the remaining chloro substituent; however, this substituent also tends to induce an unfavorable hybridization at the anion center.[11] With the dianion, however, the opposite is true and there is a synergistic stereochemical effect acting to offset the large anion–anion repulsion. The larger the 1,4 separation the greater the s character in the external orbitals at C_1 and C_4 and the greater the stabilization of the dianion.[12]

The preparation of the other 4-substituted bicyclo[2.2.1]heptanecarboxylic acids is outlined in Chart I. The procedures were patterned after those used with the bicyclooctane homologs.[4] The diacid was methylated with diazomethane. The basic half-hydrolysis of the diester **3** to the half-ester worked best at room temperature and gave a 75% yield of **4**. The favorable relative rates of hydrolysis of the monoester and the diester reflect the rate-enhancing character of the carbomethoxy group in the diester and the strongly rate-retarding negative charge of the carboxylate anion in

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[10] J. A. Beel, W. G. Koch, G. E. Tomasi, D. E. Hermansen, and P. Fleetwood, *J. Org. Chem.*, **24**, 2036 (1959); J. B. Wright and E. S. Gutsell, *J. Am. Chem. Soc.*, **81**, 5193 (1959); C. W. Kamienski and D. L. Esmay, *J. Org. Chem.*, **25**, 1807 (1960).

[11] For example, norbornane has a $C_1C_7C_4$ bridge angle of 96.0°, whereas the 1,4-dichloride has a bridge angle of 92.8° (unpublished electron diffraction data with S. H. Bauer and J. Chiang). These and other data are consistent with increased p character in the carbon orbitals forming bonds to the more electronegative chlorine atoms.

[12] Models suggest that was the C_1–C_4 distance to increase 20% from the observed 2.23 Å of the dichloride the ring bonds would form *ca.* 90° angles and the electron pairs at C_1 and C_4 would reside in purely s orbitals.

the half-ester.[2] The two acids, after removal of the unhydrolyzed diester, were separated by extraction of an acidified aqueous solution by CCl_4. The diacid is virtually insoluble in this solvent.

The amide **5** was converted into the urethan **6** by the modified Hofmann reaction.[13] A better yield was obtained when the bromine dissolved in methanol was added slowly and the reaction flask was protected from light.[14] Hydrolysis of the urethan with hydriodic acid gave the amino hydriodide **7**. Methylation[4] of **7** with methyl iodide gave a good yield of quaternary iodide **8** which could be hydrolyzed by hydriodic acid to the corresponding acid **9**.

The 4-cyano ester **10** was obtained by dehydration of the amide with phosphorus oxychloride in ethylene dichloride.[13] The cyano acid, **11**, was obtained from the ester by basic hydrolysis.

The 4-bromobicyclo[2.2.1]heptane-1-carboxylate ester, **12**, was prepared from the half-ester by the Hunsdiecker reaction using bromine and mercuric oxide in bromotrichloromethane.[14] The corresponding bromo acid **13** was prepared by hydrolysis of the bromo ester with 48% hydrobromic acid.

Experimental Section

Bicyclo[2.2.1]heptane-1,4-dicarboxylic Acid (2).—The reagents employed were carefully purified. Cyclohexane (Matheson Coleman and Bell Co. CX 2290) was passed through a 3 ft × 1.2 in. column of silica gel and distilled from sodium immediately before use. *n*-Pentane (Fisher Scientific Co. Certified Reagent) was passed through a 3-ft column of reagent grade aluminum oxide and distilled from sodium immediately before use. Analytical reagent grade benzene was refluxed over sodium for 24 hr and distilled from sodium before use. The nitrogen employed was passed over calcium chloride and activated silica gel, then through concentrated sulfuric acid, and then through two empty traps. The 1,4-dichlorobicyclo [2.2.1]heptane (1) was recrystallized three times from purified cyclohexane. The equipment was flamed and flushed with dry nitrogen for 1 hr. A dispersion (30% by weight in paraffin wax) of lithium alloyed with 1% Na (Lithium Corporation of America) (8.4 g Li, 1.2 g-atoms), and 50 ml of dry benzene were placed in a 1-l. round bottomed three-necked flask equipped with a Vibro-mixer, condenser with attached drying tube, and a Y inlet for nitrogen. The mixture was heated gently by means of a heating mantle until the paraffin wax dissolved. A medium-porosity sintered-glass gas dispersion tube (1-cm diameter) with joint was placed under the benzene solution surface. The benzene–wax solution was siphoned into a suction flask. The removal was aided by slightly reduced pressure at the sintered-glass tube outlet and positive nitrogen pressure inside the reaction flask. The lithium dispersion was washed three times with 50-ml portions of benzene and twice with 50-ml portions of purified cyclohexane. Then the sintered-glass tube was replaced by an addition funnel, 60 ml of purified cyclohexane was added to the lithium, and the suspension was heated to gentle reflux while being vigorously agitated by the Vibro-mixer. A solution of 10 g (0.06 mole) of 1,4-dichlorobicyclo-[2.2.1]heptane (1) which had been dissolved in 30 ml of cyclohexane and dried over magnesium sulfate for 2 hr before use, was added dropwise to the mixture during the course of 0.5 hr. The mixture was refluxed for an additional 4 hr and then cooled, and 200 ml of *n*-pentane was added to the mixture. Excess Dry Ice was added to the vigorously agitated suspension. After 8 hr the excess lithium was destroyed by the addition of ethanol followed by water. The layers were separated and the aqueous layer was washed with two 50-ml portions of ether, then saturated with sodium chloride, and acidified with concentrated HCl. The aqueous solution was extracted with four 100-ml portions of ether. The combined ethereal extracts were extracted with four 100-ml portions of aqueous sodium bicarbonate. The combined sodium bicarbonate extracts were saturated with common salt, acidified with dilute HCl, and extracted with four 100-ml portions of ether. The ethereal extracts were dried over magnesium sulfate; the solvent was removed by distillation to give 4 g (36.7%) of crude product (60–70% pure). The product was sublimed at 126° (0.5 mm). The sublimate was recrystallized twice from acetic acid and twice from acetone to yield, finally, 0.5 g of colorless needles, mp 248°. The infrared spectrum (KBr disk) of this diacid showed broad bands at 2.9–3.9 μ (acid OH) and absorption at 5.95 μ (C=O). The 60-Mc nmr spectrum (10% Na_2CO_3 in D_2O), using TMS as an external standard, showed a multiplet at τ 8.03–8.42 (10 H, methylene hydrogens) and a sharp singlet at 5.24 (2 H, attributable to water from the acidic protons).

Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.73; H, 6.63.

Dimethyl Bicyclo[2.2.1]heptane-1,4-dicarboxylate (3).—To 25 ml of diethyl ether was added 7.5 ml of 40% aqueous KOH and the mixture was cooled to 5°. To this mixture was added, with continuous cooling and shaking, 0.7 g (0.004 mole) of finely powdered nitrosomethylurea[15] in small portions over a period of 5 min. The deep yellow ether layer was decanted and dried over KOH, ready for use.

Diacid **2** (0.8 g, 0.004 mole) was dissolved in 25 ml of ether contained in a 100-ml erlenmeyer flask. The ethereal solution of diazomethane was added in small portions with stirring; the resulting pale yellow mixture was allowed to stand at room temperature for 1 hr. The solution was warmed in a water bath until it was colorless; then it was washed with water, saturated $NaHCO_3$, and NaCl aqueous solutions, and finally dried over magnesium sulfate. After the solvent was removed, 0.9 g of the diester (96%) was obtained. This diester was sublimed at 55°, mp 62°. The infrared spectrum (KBr disk) showed absorption at 5.80 μ (C=O). The 60-Mc nmr spectrum in carbon tetrachloride showed a multiplet at τ 7.9–8.6 (10 H) and a sharp singlet at 6.35 (6 H) from TMS.

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.24; H, 7.61. Found: C, 62.36; H, 7.63.

Methyl Hydrogen Bicyclo[2.2.1]heptane-1,4-dicarboxylate (4).—A solution of 0.21 g of diester **3** (0.001 mole), 1.25 ml of 0.8 *N* KOH in 87% MeOH (0.001 mole KOH), and 1.75 ml 87% MeOH were added to a 25-ml flask. The solution was allowed to stand at room temperature for 42 hr. Then the mixture was poured into 10 ml of ice water and the solution was washed with ether. From the ether layer 0.026 g (12.4%) of the starting diester was recovered. The aqueous solution was saturated with sodium chloride and acidified with dilute HCl. A white solid separated from the aqueous solution. The mixture was extracted three times with 20-ml portions of carbon tetrachloride. The carbon tetrachloride solution was filtered and washed with water, then with saturated aqueous sodium chloride solution, and dried over magnesium sulfate. After the removal of the solvent, the residue was sublimed at 95° to yield 0.15 g of the monoester, **4**, (76%), mp 114–115°. The infrared spectrum (KBr disk) showed absorptions at 5.80 and 5.95 μ (C=O). The 60-Mc nmr spectrum in carbon tetrachloride showed a multiplet at τ 7.8–8.4 (10 H) and two singlets at 6.32 (3 H) and −2.2 (1 H) from TMS.

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.57; H, 7.12. Found: C, 60.42; H, 7.05.

The aqueous layer was extracted with three 20-ml portions of ether. The ether extracts were combined with the precipitate from the carbon tetrachloride filtration to yield after evaporation 0.012 g (7%) of the diacid **2**.

Methyl 4-Carboxamidobicyclo[2.2.1]heptane-1-carboxylate (5).—A solution of the half-ester **4** (1.05 g, 0.0053 mole) and triethylamine (0.745 ml, 0.0053 mole) in 30 ml of chloroform was cooled in an ice–salt bath, and the ethyl chloroformate (0.506 ml, 0.0053 mole) added to the solution in one portion with continuous stirring. After 15 min, anhydrous ammonia gas was bubbled through the mixture (1 hr). The mixture was removed from the cooling bath, stirred at room temperature for 1 hr, and allowed to stand overnight. The dispersion was filtered and the chloroform in the filtrate was removed by gentle heating on a steam bath. The residue was boiled with 15 ml of benzene and filtered hot. The benzene solution was diluted with 25 ml of *n*-hexane. After cooling, filtration gave 0.95 g (90.9%) of the amide **5**.

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[13] J. D. Roberts, W. T. Moreland, Jr., and W. Frazer, *J. Am. Chem. Soc.*, **75**, 637 (1953); J. D. Roberts and W. T. Moreland, Jr., *ibid.*, **75**, 2167 (1953).

[14] H. D. Holtz and L. M. Stock, *ibid.*, **86**, 5183, 5188 (1964).

[15] Material kindly supplied by H. Klingele, Cornell University.

After two recrystallizations from a benzene–*n*-hexane mixture, the colorless crystals had mp 112–113° and infrared absorptions (KBr disk) at 5.75 (ester C=O) and 6.00 μ (amide C=O).

Anal. Calcd for $C_{10}H_{15}O_3N$: C, 60.89; H, 7.67; N, 7.10. Found: C, 60.93; H, 7.65; N, 7.05.

Methyl 4-(N-Carbomethoxy)aminobicyclo[2.2.1]heptane-1-carboxylate (6).—A mixture of 1.6 g (0.0081 mole) of amide **5** and 32 ml of a solution of 0.64 g of sodium in 48 ml of methanol (0.019 g-atom of sodium) was cooled in an ice–salt bath. The solution was stirred magnetically while 2.9 ml of a solution of 0.9 ml of bromine in 4.1 ml of methanol (0.012 mole bromine) was added dropwise for 3 hr. Stirring was maintained for another 5 hr, during which period the ice had melted and the mixture had become room temperature. The mixture was poured over 200 ml of water, the water extracted with hexane, and the hexane solution dried over magnesium sulfate. After evaporation of the hexane, a colorless oil was obtained. An attempt to crystallize this oil failed. The infrared absorption spectrum (liquid film), with maxima at 5.8, 5.9 (C=O) and 6.55 μ (N–H), of the crude product supported the proposed structure, and the urethan was used for the next preparation without purification.

4-Aminobicyclo[2.2.1]heptane-1-carboxylic Acid Hydriodide (7).—A mixture of the urethan, **6**, obtained from 1.6 g (0.0081 mole) of amide and 7 ml of hydriodic acid (analytical reagent grade) in a 25-ml round-bottomed flask was heated in an oil bath at 100° for 6 hr and allowed to stand overnight. The excess hydriodic acid was removed on a flash evaporator. The residue was dried *in vacuo* at room temperature and washed with two small portions of acetone. Filtration gave 1.2 g of the acid hydriodide (52%, based upon the amide **5**). After recrystallization from ethanol–ethyl acetate mixture, the product (mp 270° dec) was obtained. The infrared absorption spectrum (KBr disk) showed a strong peak at 5.86 (C=O) and broad complex peaks at 2.8–4 μ (acid OH). The acid hydriodide was used without further purification.

4-Carbomethoxybicyclo[2.2.1]heptane-1-trimethylammonium Iodide (8).—A solution of 0.15 g (0.00053 mole) of the acid hydriodide **7**, 0.11 ml (0.0018 mole) of methyl iodide, 0.15 g (0.0018 mole) of sodium bicarbonate, and 6 ml of methanol was heated under reflux for 70 hr. At the end of 24 and 48 hr, 0.5 ml of methyl iodide was added. The excess methyl iodide and methanol were evaporated on a steam bath and the residue was extracted with six 10-ml portions of boiling chloroform. The chloroform was evaporated and the residue recrystallized from ethanol. The colorless crystals (0.13 g, 72%), mp 240°, had infrared absorption (KBr disk) at 5.78 μ (C=O). An nmr spectrum showed peaks at τ 7.75–8.20 (complex multiplet, 10 H), 6.9 (singlet, 9 H), and 6.40 (singlet, 3 H).

Anal. Calcd for $C_{12}H_{22}NO_2I$: C, 42.48; H, 6.59; N, 4.13; I, 37.41. Found: C, 42.67; H, 6.66; N, 4.20; I, 37.63.

4-Carboxybicyclo[2.2.1]heptane-1-trimethylammonium Iodide (9).—A solution of 4-carbomethoxybicyclo[2.2.1]heptane-1-trimethylammonium iodide (0.5 g, 0.0015 mole) and 3 ml of 1 *N* hydriodic acid was heated in a sealed tube at 100° for 10 hr. After the mixture was cooled and filtered, 0.35 g (73%) of the product **9** was isolated. Recrystallization from absolute ethanol yielded colorless crystals, mp 265° dec. The infrared spectrum (KBr disk) showed carbonyl absorption at 5.80 μ. The nmr spectrum showed peaks at τ 7.75–8.2 (multiplet, 10 H), 6.9 (singlet, 9 H), and 5.5 (singlet, 1 H).

Anal. Calcd for $C_{11}H_{20}NO_2I$: C, 40.63; H, 6.20; N, 4.31; I, 39.03. Found: C, 40.50; H, 6.05; N, 4.45; I, 39.24.

Methyl 4-Cyanobicyclo[2.2.1]heptane-1-carboxylate (10).—A solution of amide ester **5** (0.3 g, 0.0015 mole), 5 ml of ethylene dichloride, and 0.5 ml of phosphorus oxychloride was refluxed on a steam bath for 20 min. The solvent and excess phosphorus oxychloride were removed under slightly reduced pressure. The residue was treated with ice-cold 2 *N* sodium hydroxide and then extracted with *n*-pentane. The *n*-pentane solution was washed with water and dried over magnesium sulfate. After the *n*-pentane was removed *ca.* 0.2 g of a colorless oil was obtained and used for the next preparation without purification. The infrared absorption spectrum (liquid film) showed maxima at 4.43 (C≡N) and 5.75 μ (C=O).

4-Cyanobicyclo[2.2.1]heptane-1-carboxylic Acid (11).—A solution of cyano ester **10** prepared from the preceding reaction, 0.7 ml of 0.8 *N* KOH in 87% methanol, and 4 ml of 87% methanol was refluxed for 1 hr. The solution was cooled, diluted with 15 ml of water, washed with ether to remove the starting cyano ester saturated with sodium chloride, acidified with 6 *N* hydrochloric acid, and finally extracted with ether. The ether solution after drying over magnesium sulfate was evaporated and the product crystallized from an ether–*n*-hexane mixture. The colorless crystals (0.18 g, 73%, based upon the amide ester), mp 137°, had infrared absortions (KBr disk) at 4.43 (C≡N) and 5.90 μ (C=O). The nmr spectrum (perdeuterioacetone) showed absorptions at τ 5.33 (broad singlet, 1 H) and 7.6–8.3 (complex multiplet, 10 H).

Anal. Calcd for $C_9H_{11}NO_2$: C, 65.43; H, 6.71; N, 8.48. Found: C, 65.26; H, 6.79; N, 8.31.

Methyl 4-Bromobicyclo[2.2.1]heptane-1-carboxylate (12).—A solution of bromine (0.4 ml, 0.0075 mole) in 6 ml of bromotrichloromethane in a 50-ml, three-necked flask fitted with magnetic stirrer, reflux condenser, and dropping funnel was heated to 45° in an oil bath. A slurry of half-ester **4** (0.7 g, 0.0035 mole), mercuric oxide (0.5 g, 0.0023 mole), and 20 ml of bromotrichloromethane in a 50-ml addition funnel was added dropwise to the reaction flask with vigorous stirring. After the addition was completed, the temperature of the oil bath was maintained at 70° for 1 hr. The mixture was cooled and filtered. The filtrate was washed with aqueous sodium thiosulfate and potassium hydroxide solution and dried over calcium sulfate. The solvent was removed under reduced pressure. The infrared absorption spectrum (KBr disk) of the crude product showed a single carbonyl band at 5.76 μ. The nmr spectrum showed peaks at τ 7.8–8.4 (complex multiplet, 10 H) and 6.35 (singlet, 3 H).

4-Bromobicyclo[2.2.1]heptane-1-carboxylic Acid (13).—A solution of bromo ester in 10 ml of 48% hydrobromic acid was stirred magnetically in a stoppered 50-ml, round-bottomed flask for 14 hr, and then heated at 67° for 1 hr. After cooling, the mixture was diluted with 20 ml of water and extracted with ether. The ether solution was extracted with aqueous sodium bicarbonate. The aqueous solution was saturated with sodium chloride, acidified with hydrobromic acid, and then extracted with ether. This ether solution was dried over magnesium sulfate and then evaporated. Recrystallization of the product from a benzene–hexane mixture yielded 0.4 g of colorless crystals (51%), mp 148°, which sublimed at 85°. The infrared absorption spectrum (KBr disk) showed a maximum at 5.9 μ (C=O), and the nmr spectrum (CCl_4) showed peaks at τ 7.8–8.2 (complex multiplet, 10 H) and −1.4 (broad, 1 H).

Anal. Calcd for $C_8H_{11}O_2Br$: C, 43.86; H, 5.06; Br, 36.48. Found: C, 43.76; H, 5.10; Br, 36.50.

Registry No.—**2**, 15544-51-1; **3**, 15448-76-7; **4**, 15448-77-8; **5**, 15448-78-9; **6**, 15448-79-0; **7**, 15448-80-3; **8**, 15448-81-4; **9**, 15448-82-5; **10**, 15448-83-6; **11**, 15448-86-9; **12**, 15448-84-7; **13**, 15448-85-8.

Dakin–West Reactions on 2-(Purin-6-ylthio)propionic Acid[1]

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In connection with studies on the acylation of various purines,[2] attempts were made to cyclize 2-(purin-6-ylthio)propionic acid (**1**) with acetic anhydride. Ring closure could be expected to occur at the 7- or 1-nitrogen atoms. However, analytical and spectral data showed the compound to be ketone **2**. The presence of the 2-acetyl-2-ethyl group on the sulfur of compound **2** was confirmed by its hydrolysis under mild conditions to compound **3**, which was synthesized from purine-6-thione and 3-chloro-2-butanone in dimethylformamide

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[1] This investigation was supported by Public Health Service Research Grant No. CA-03477 from the National Cancer Institute.

[2] E. Dyer, J. M. Reitz, and R. E. Farris, Jr., *J. Med. Chem.*, **6**, 289 (1963).