3-Methylenebicyclo[2.1.0]pentane-1-carbonitrile and 3-Vinylbicyclobutane-1-carbonitrile

H. K. Hall, Jr.,* and R. E. Yancy, III

Department of Chemistry, University of Arizona, Tucson, Arizona 85721

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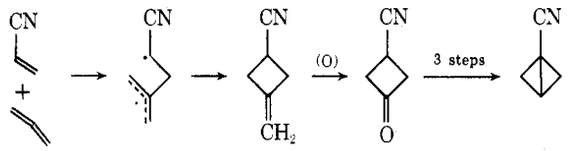
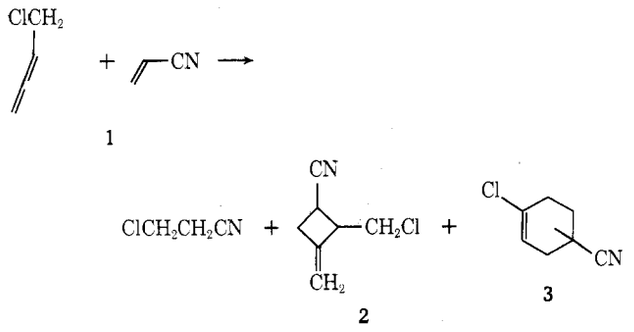
4-Chloro-1,2-butadiene reacted with acrylonitrile at 210–225° and autogenous pressure to yield the [$_\pi$2 + $_\pi$2] cycloadduct, 2-chloromethyl-3-methylenecyclobutanecarbonitrile (**2**). The equilibrium constants allene + acrylonitrile ⇌ 3-methylenecyclobutanecarbonitrile were calculated for various temperatures by assigning infrared fundamentals to the latter and calculating the thermodynamic properties of each component. The yield of cycloadduct was not limited by equilibrium considerations. Dehydrochlorination of **2** with potassium *tert*-butoxide in ether gave 3-methylenebicyclo[2.1.0]pentanecarbonitrile (**4**). This polymerized readily. This sequence represents the synthesis of a new bicyclic monomer in two steps from industrially available materials. Vinylmagnesium chloride added to 3-cyanocyclobutanone to yield 3-vinyl-3-hydroxycyclobutanecarbonitrile (**5**). Reaction of **5** with triphenylphosphine in carbon tetrachloride occurred with partial allylic rearrangement to give tertiary chloride **6** and primary chloride **7**. Dehydrochlorination of **6** afforded 3-vinylbicyclobutanecarbonitrile (**8**); this polymerized readily. Dehydrochlorination of **7** gave a mixture of **8** and 3-vinyl-2-cyclobutene-1-carbonitrile (**9**).

Synthesis of 3-Methylenebicyclo[2.1.0]pentane-1-carbonitrile. In earlier work, we have synthesized and polymerized bicyclobutane-1-carbonitrile[1–7] and bicyclo[2.1.0]pentane-1-carbonitrile,[8] each containing a C–C single bond of high p character. Further development in this new field of ring-opening polymerization through strained C–C single bonds requires facile syntheses from readily available starting materials. For two compounds of this class, our present work describes convenient syntheses, one from industrially available materials.

Cycloaddition of 4-Chloro-1,2-butadiene ("Isochloroprene") to Acrylonitrile. Our earlier, rather lengthy synthesis of bicyclobutane-1-carbonitrile began with the biradical cycloaddition of allene to acrylonitrile.[9] In the

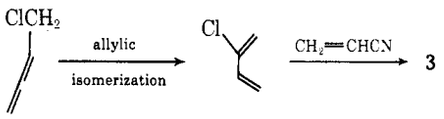


present work we have utilized 4-chloro-1,2-butadiene (chloromethylallene, "isochloroprene," **1**) in the acrylonitrile cycloaddition reaction. The isochloroprene is easily obtained by the 1,4-addition of hydrogen chloride to monovinylacetylene.[10] Four compounds were obtained from the reaction with acrylonitrile. A little 3-chloropropionitrile, proba-



bly formed by generation of HCl in some unknown fashion, followed by addition to acrylonitrile, was obtained as the first fraction. The second fraction contained the remaining three components. Two of these were the desired cis and trans cycloadducts **2**. Although a cycloadduct bearing the chloromethyl group on the *exo*-methylene carbon was expected as well, comparison of our cycloaddition product with authentic material (see below) showed its absence.

The fourth compound crystallized from the second fraction on storage. From its melting point of 53–54° and its nmr spectrum (one vinyl H), this was the Diels–Alder adduct **3** of chloroprene to acrylonitrile (lit.[11] mp 51°). Evi-



dently isochloroprene isomerizes to chloroprene (2-chloro-1,3-butadiene) and then undergoes the Diels–Alder reaction with acrylonitrile. Whether this isomerization occurs thermally or is catalyzed by traces of impurities is not known at present.

Reaction conditions were varied to optimize the yield of cycloadduct **2**. Best results were obtained in sealed glass ampoules heated under pressure-equalizing conditions within a rocker bomb. A limited amount of benzene served as solvent, and a substantial quantity of 2,5-di-*tert*-butylhydroquinone was the inhibitor. Conversions of 40–45% were obtained at 210–225° during reaction periods of 3–8 hr. These conditions are similar to those used for the cycloaddition of allene itself to acrylonitrile.[9] Higher temperature and longer reaction times led in our hands to tar or charred material.

The [$_\pi$2 + $_\pi$2] cycloadduct mixture could be separated cleanly from the [$_\pi$2 + $_\pi$4] product by preparative gas chromatography if required; however, separation of the individual cis and trans isomers of the former has not been accomplished. Because **3** is inert to the basic conditions used in the next step (see below), the mixture of **2** and **3** could be used as such.

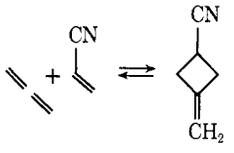
Calculation of the Equilibrium Constants for Cycloaddition of Allenes to Acrylonitrile. We were interested in knowing whether the cycloaddition of a typical allene to acrylonitrile reached equilibrium under our conditions, or whether the conversion was controlled by kinetic factors. In a previous investigation of the cycloaddition of ethylene to acrylonitrile to give cyclobutanecarbonitrile,[12] this problem was approached by assigning the fundamental infrared absorptions of the components and calculating their thermodynamic properties. The same procedure has been used here. The heat of formation of 3-methylenecyclobutanecarbonitrile was taken from the paper of Hall and Baldt.[3] The laser Raman and mid-infrared spectra were measured and the fundamental frequencies were identified (Table I). With the help of these identifications,

Table I
Fundamental Vibrations for 3-Methylenecyclobutanecarbonitrile

Type of vibration	Fundamental vibration frequency, cm^{-1}	Description
A_1 (13); A′	510	C–CN stretching
	612	Ring deformation
	910	Ring deformation
	1005	Ring breathing
	1225	CH_2 wagging (α)
	1410	Olefinic CH_2 deformation
	1430	CH_2 deformation (β)
	1440	CH_2 deformation (α)
	1689	C=C stretching
	2244	C≡N stretching
	2900	CH_2 stretching (α)
	2995	CH_2 stretching (β)
	3080	Olefinic CH_2 stretching
A_2 (5); A″	640	CH_2 rocking (α)
	950	Olefinic CH_2 twisting
	1200	CH_2 twisting (β)
	1200	CH_2 twisting (α)
	2900	CH_2 stretching (anti, α)
B_1 (10); A″	260	C–CN wagging
	490	C=C in-plane bending
	690	Ring deformation (anti)
	840	Ring stretching (anti)
	1160	CH_2 wagging (β)
	1200	CH_2 wagging (α)
	1325	Olefinic CH_2 rocking
	1450	CH_2 deformation (α)
	2900	CH_2 stretching (α)
	3080	Olefinic CH_2 stretching
B_2 (8); A′	195[a]	Ring puckering
	275	C–CN rocking
	370	C=C out-of-plane bending
	690	CH_2 rocking (α)
	780	CH_2 rocking (β)
	880	Olefinic CH_2 out-of-plane wagging
	1055	CH_2 stretching (a, α)
	2950	CH_2 stretching (a, β)
Total 36		

[a] Estimated from the observed far-infrared transitions as the harmonic frequency needed to represent the contributions to the thermodynamic functions of the ring-puckering vibration.

the thermodynamic quantities were calculated (Table II). They were insensitive to the effect of the ring puckering angle in the range 0–30° on the moments of inertia. The free energies and equilibria of the reaction of allene with acrylonitrile were calculated as follows.



$$\Delta G^\circ_T = -28{,}870 + 47.38T$$

Dehydrochlorination of 2. Cycloadduct **2** was rapidly dehydrochlorinated by sublimed potassium *tert*-butoxide in ether to give 3-methylenebicyclo[2.1.0]pentane-1-carbonitrile (**4**) in 50% yield.

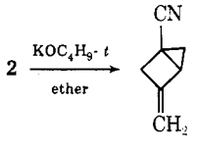


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Table II
Thermodynamic Properties of 3-Methylenecyclobutanecarbonitrile

Assumptions: Symmetry C_s, $\sigma = 1$; electronic contributions negligible; all vibrations are harmonic oscillations; ring puckering angle 30°; $\Delta H^\circ_{f,g,298} = +60.27$ kcal mol^{-1}

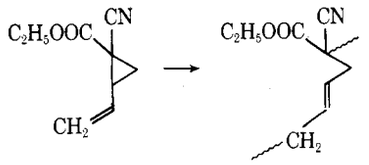
Molecular parameters: $I_A = 0.921134 \times 10^{-38}$ g cm^{-2}
$I_B = 0.552016 \times 10^{-37}$ g cm^{-2}
$I_C = 0.603078 \times 10^{-37}$ g cm^{-2}
Mol wt 93.120

Temp, °K	$(H_T^\circ - E_0^\circ)/T$[a]	H°_T[b]	$(G^\circ - E_0^\circ)/T$[a]	G_T°[b]	S°	C_p
0	0	65.45	0	65.45	0	0
298.2	14.91	69.90	−62.35	46.86	77.25	25.96
400	18.75	72.96	−67.26	38.55	86.01	33.89
500	22.46	76.68	−71.85	29.53	94.31	40.46
600	25.93	81.00	−76.25	19.70	102.17	45.84
700	29.09	85.82	−80.49	9.11	109.58	50.26

[a] Cal mol^{-1} deg^{-1}. [b] kcal mol^{-1}.

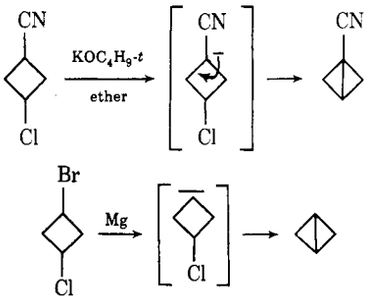
No substantial difference in the reactivity of the cis–trans isomers of **2** was noted. The Diels–Alder adduct **3** was inert under these conditions. After cycloadduct **2** had reacted to the extent of ~95%, the mixture was worked up and compound **4** was separated by vacuum distillation from unreactive **3**. Nitrile **4** polymerized rapidly under ambient conditions or at 0° (probably caused by light and/or air) to a glassy solid. Accordingly this new monomer was stored at −80° in the presence of inhibitors.

Synthesis of 3-Vinylbicyclobutane-1-carbonitrile. Monomer **4** contains a vinylcyclopropanecarbonitrile moiety incorporated into a bicyclic structure. This moiety has been shown by Lishanskii and his colleagues[13] to be polymerizable even in acyclic cases. In this work, for purposes of

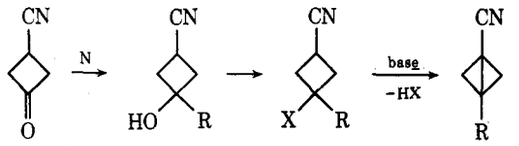


comparison, a second bicyclic monomer containing this moiety has been synthesized.

Addition of Vinylmagnesium Chloride to 3-Cyanocyclobutanone. Bicyclobutane syntheses in this series[1,2] have involved the generation of a carbanion on the cyclobutane ring in a 1,3 relationship to a leaving group. If an activating group (CN, $COOCH_3$) were present at C_1, abstraction of H^+ by strong bases yielded the requisite carbanion; if none were present,[14] abstraction of positive halogen by metals served the same purpose. Our present route to 3-



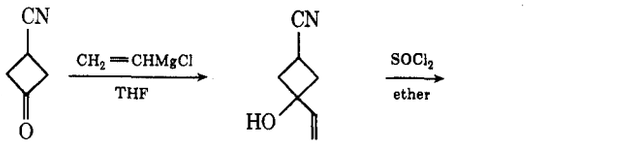
vinylbicyclobutane-1-carbonitrile utilized the former of these modes. 3-Cyanocyclobutanone, available as described above, has already been shown to be a prolific source of the required 1,3-disubstituted cyclobutanes. Attack of a nucleophile R^- at carbonyl, conversion of the resulting hydroxyl to a leaving group X, and elimination have been



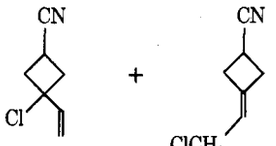
R = CN, C_6H_5
X = Cl, $OSO_2C_6H_5$.

demonstrated for two cases. We have carried out this sequence with R = vinyl. Addition of vinylmagnesium chloride to 3-cyanocyclobutanone in tetrahydrofuran at −25 to −30° proceeded smoothly in yields of 85–90%.

Replacement of Hydroxyl by Chlorine. Although it is reputed to be the reagent favoring SNi[1] reaction,[15] thionyl chloride in ether converted cyano alcohol to an allylically rearranged mixture of chlorides **6** and **7**. Triphenylphosphine in carbon tetrachloride led to a similar, but much cleaner, mixture in 70% yield. Sieja[14] encountered a similar allylic rearrangement in his synthesis of 1-vinylbicyclobutane. The primary chloride **7** could be separated by fractional distillation from the cis–trans mixture of tertiary isomers **6**. Spectral and gas chromatographic studies of the rearranged product **7** indicated that it was different from the isomeric [$_\pi$2 + $_\pi$2] cycloadduct **2** described above, and confirms the absence of **7** from the cycloaddition reaction mixture.

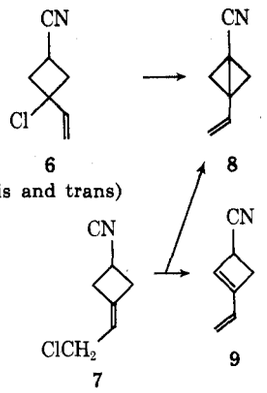


5
(cis and trans)



6 (cis and trans) **7**

Dehydrochlorination of 6 and of 7. The dehydrochlorination of tertiary chloride **6** and primary chloride **7** was carried out with potassium *tert*-butoxide in ether as before. The tertiary chlorides gave a 90% yield of 3-vinylbicyclobutanecarbonitrile (**8**). The primary chloride gave a mixture of **8** and 3-vinyl-2-cyclobutenecarbonitrile (**9**) in about equal amounts, for a combined yield of 60%. These could not be separated by fractional distillation or glc, but were clearly visible by nmr spectroscopy. This differs from Sieja's results; both his tertiary and primary chlorides gave only 1-vinylbicyclobutane.



6 (cis and trans) **8** **7** **9**

The new bicyclobutane monomer **8**, like other bicyclobutane-1-carbonitriles,[1,2] underwent ready polymerization (probably by light and air) and was stored at −80° in the presence of inhibitor.

Discussion

Synthesis of 3-Methylenebicyclo[2.1.0]pentane-1-carbonitrile. Like allene itself, 4-chloromethyallene has been found to cycloadd readily to acrylonitrile. The reason why only **2**, and not **7**, is formed in this reaction is not clear at present. A referee has suggested that the regiospecificity may be due to higher odd-electron localization on the internal end of the allylic radical.[16] The cycloadduct has been obtained in conversions of 40–50%. That this is limited by side reactions, rather than by equilibrium considerations, is clear from the thermodynamic data obtained. Thus for the allene–acrylonitrile cycloaddition, the temperature at which $\Delta G° = 0$ is 336°. These calculations should apply to 4-chloromethyallene as well.

In our earlier work[12] on the ethylene–acrylonitrile reaction, $\Delta G° = 0$ at 175°, and cycloadduct could be obtained at temperatures well above that value. These calculations suggest that increased conversions and reaction rates should be achievable if side reactions could be minimized, possibly in a vapor-phase reactor.

The practical significance of these results is that a novel monomer has been synthesized in two steps from industrially available chemicals.

Synthesis of 3-Vinylbicyclobutane-1-carbonitrile. The facile synthesis of monomer **8** provides another example of the generality of the synthesis. The only departure from previous results lies in the dehydrochlorination of primary chloride **7** to a mixture of **8** and **9**. Possibly the inductive effect of the 1-cyano group activates the β hydrogen as well as α hydrogen to attack by base.

Polymerization studies of **8**, and also of **4**, will be described at a later date.

Experimental Section

All boiling points and melting points were uncorrected. Capillary melting points were determined on a Thomas-Hoover melting point apparatus. Infrared spectra were determined with a Perkin-Elmer Model 337 spectrophotometer in KBr or between NaCl plates. Nmr spectra were obtained on a Varian T-60 spectrometer. Mass spectral data were collected on a Hitachi Perkin-Elmer RMU-6E double-focusing instrument at an ionization potential of 70 eV. All gas–liquid chromatography, analytical and preparative, was done on a Varian Aerograph 1700 instrument using the following columns: (A) 3% SE-30 on 80–100 mesh Chromosorb W AW/DMCS HP, 5 ft × 0.25 in., (B) 15% Fluorosilicon QF-1-0065 on 80–100 mesh Anakron SD, 5 ft × 0.25 in., (C) 5% Carbowax 20 M on 80–100 mesh Chromosorb W AW/DMCS, 5 ft × 0.25 in. Elemental analyses were performed by Galbraith Laboratories.

Isochloroprene (4-Chlorobutadiene-1,2) (1). The procedure of Carothers, Berchet, and Collins[10] was followed. Separation of the desired allene derivative from the by-product chloroprene (2-chlorobutadiene-1,3) was accomplished with a 3-ft glass helix-filled column. The isochloroprene, bp 86–88° (700 mm), was stored in a refrigerator over 2,5-di-*tert*-butylhydroquinone inhibitor.

3-Methylene-2-chloromethylcyclobutanecarbonitrile (2). All experiments in this series were carried out at the University High Pressure Laboratory.

Heavy-walled glass tubes with interior diameters of 25–30 mm and with a constriction at the neck about 3 in. below the mouth were prepared. In a typical experiment, a tube was charged with 10 g of isochloroprene, 20 g of acrylonitrile, and 0.5 g of 2,5-di-*tert*-butylhydroquinone. The resulting mixture contained the nitrile and the chloride in a molar ratio of 4:1. To this mixture was added 15 ml of benzene as a diluent, and the contents of the tube were degassed. This was accomplished by freezing the mixture in a Dry Ice–acetone bath, reducing pressure in the tube to 0.3–0.2 mm, and alternately thawing and refreezing the contents until no gas bubbles were observed escaping in the liquid state. The cycle was usu-

ally repeated three or four times. While the mixture was frozen and under reduced pressure, the tube was sealed by heating at the constriction until the walls slowly collapsed. The tube was then subjected to temperatures of 180–200° for 10–15 hr, after which time it was opened and the darkened, slightly viscous liquid was poured into 200 ml of anhydrous ethyl ether. This precipitated acrylonitrile oligomers and polymers. Filtration and concentration of the filtrate on the rotary evaporator yielded 9 g of yellow liquid. Distillation of this residue through the spinning-band column resulted in two fractions. The first component, 2.3 g, bp 29–30° (1.2 mm), was shown by glc to be composed of one compound, which was shown spectrally to be 3-chloropropionitrile: ir superimposable on that of authentic 3-chloropropionitrile found in Sadtlers Collective Indices; nmr ($CDCl_3$) τ 6.0 (triplet, 2 H, α cyano), 6.9 (triplet, 2 H, α chloro).

The second fraction from the spinning-band column was collected at a head temperature of 46–56° (0.1 mm). This fraction was shown by glc to contain three components. Separation of these compounds by preparative gas–liquid chromatography was accomplished and both materials were analyzed.

3-Methylene-2-chloromethylcyclobutanecarbonitrile (Cis and Trans) (2) had ir (NaCl) 2250 (CN), 1625 cm^{-1} (C=C); nmr ($CDCl_3$) τ 4.7 (broad singlet, 2 H, olefinic), 6.0)multiplet, 3 H, α to cyano and chloro), 6.8 (multiplet, 3 H, chloromethyl and methine α to chloromethyl); mass spectrum *m/e* 141, parent peak (calcd mol wt, 141).

Anal. Calcd for C_7H_8NCl: C, 59.34; H, 5.69; N, 9.88; Cl, 25.09. Found: C, 59.40; H, 5.63; N, 9.84; Cl, 25.31.

1-Chloro-1-cyclohexene-4-carbonitrile (3). On standing at below 0° temperature for several days, the mixture of cycloadducts contained a crystalline precipitate. Filtration and recrystallization from hot hexane afforded pure crystals, mp 53–54°. Preparative glc of the binary mixture that constituted fraction 2 of the spinning-band distillation showed that the compound having the longer retention time was identical with the solid recrystallized from hexane: ir (KBr) 2250 (CN), 1660 (olefinic), 740 cm^{-1} (CCl); nmr ($CDCl_3$) τ 4.4 (multiplet, 1 H, olefinic), 7.3 (multiplet, 1 H, α to cyano), 7.5 (multiplet, 4 H, α to double bond), 8.0 (multiplet, 2 H, C-5 methylene); mass spectrum *m/e* 141, parent peak (calcd mol wt, 141).

Anal. Calcd for C_7H_8NCl: C, 59.34; H, 5.69; N, 9.88; Cl, 25.09. Found: C, 59.21; H, 5.74; N, 9.79; Cl, 25.20.

3-Methylenebicyclo[2.1.0]pentane-1-carbonitrile (4). The mixture of cycloadducts **2** and **3**, 1.5 g (106 mmol), was dissolved in 20 ml of anhydrous ethyl ether, placed in an ice–methanol bath, and chilled to −8°. A gentle nitrogen bleed was applied and 1.3 g (115 mmol) of potassium *tert*-butoxide was added all at once. The color of the resulting mixture darkened to a brownish purple and the temperature rose to 3–4° before beginning to fall. At this point, 1.0 g of powdered CO_2 was added to the reaction mixture followed by 2–3 ml of saturated potassium chloride solution. Filtration of the slurry of salt and drying over $MgSO_4$ was followed by rotary evaporation and distillation. The distillate, 0.6 g, bp 38–56° (0.1 mm), was found to contain a new lower boiling component along with the unreacted Diels–Alder adduct. Separation of the two substances was accomplished through preparative glc and the new compound, present in 80% yield based on starting reactive adduct, was analyzed: ir (NaCl) 2250 (CN), 1660 cm^{-1} (C=C); nmr ($CDCl_3$) τ 5.0 (doublet, 2 H, olefinic), 6.8 (multiplet, 2 H, cyclobutylmethylene), 8.0 (triplet, 3 H, cyclopropyl); mass spectrum *m/e* 105, parent peak (calcd mol wt, 105).

Anal. Calcd for C_7H_7N: C, 80.03; H, 6.66; N, 13.30. Found: C, 80.13; H, 6.78; N, 13.22.

3-Hydroxy-3-vinyl-1-cyclobutanecarbonitrile (5) Vinylmagnesium chloride was prepared from magnesium turnings and vinyl chloride.[17] We found it necessary to heat the mixture of vinyl chloride, magnesium turnings (ground), and THF to 60° before reaction could be sustained. The reagent, when stored under nitrogen at room temperature, was stable for months. The concentration of the solution of Grignard reagent in THF was determined by acidification with known acid (excess) followed by back titration with standard NaOH. The Grignard reagent, 50 ml of 2.0 *M* solution, was placed in a 250-ml three-necked flask fitted with a motor-driven stirrer, 50-ml addition funnel, and gas inlet adaptor. The flask and contents were cooled to −30° in a controlled Dry Ice–acetone bath. A solution of 5.3 g (0.056 mol) of 3-cyanocyclobutanone in 30–40 ml of dry THF was placed in the addition funnel and added dropwise to the Grignard reagent over a period of 30–45 min. After addition was complete, stirring was continued for 2 hr while the temperature was maintained at −30°. At this point about 15 ml of saturated KCl solution was added to the mixture (carefully!). Formation of a light yellow crystalline precipitate was observed during the addition of the salt. The resulting organic layers were washed with 5 ml of saturated KCl, dried over $MgSO_4$, and rotary evaporated to a clear yellow-orange residue. Distillation in a short-path distillation apparatus afforded 4.1 g (60%) of a clear, colorless distillate: bp 70–73° (0.1 mm); ir (NaCl) 3420 (OH), 2240 (CN), 1630 cm^{-1} (C=C); nmr ($CDCl_3$) τ 3.8–4.2 (multiplet, 1 H, vinyl), 4.5–4.9 (multiplet, 2 H, vinyl), 6.0 (singlet, 1 H, hydroxyl), 7.4 (broad singlet, 5 H, cyclobutyl). Deuteration of the sample resulted in the disappearance of the singlet at τ 6.0 while leaving the remainder of the spectrum virtually unchanged. The mass spectrum of the vinyl alcohol behaved anomalously, giving repeatedly a parent peak of *m/e* 220 (calcd mol wt, 123); we were unable to account for this. The overwhelming majority of the data, however, assures us that the compound we have is 3-hydroxy-3-vinyl-1-cyclobutanecarbonitrile.

Anal. Calcd for C_7H_9NO: C, 68.27; H, 7.37; N, 11.28. Found: C, 68.35, H, 7.47; N, 11.28.

3-Chloro-3-vinyl-1-cyclobutanecarbonitrile (6) and 3-(β-chloroethylidene)-1-cyclobutanecarbonitrile (7). A solution of 26 g (0.1 mol) of triphenylphosphine in 75 ml of CCl_4 was placed in a 200-ml round-bottomed flask fitted with an air-cooled reflux condenser and Teflon-coated magnetic stirring bar. To this solution was added 6.0 g (0.05 mol) of 3-hydroxy-3-vinyl-1-cyclobutanecarbonitrile (**5**). The mixture was stirred and brought to 60–65° and maintained at this temperature for 24 hr. At the end of this period the reaction mixture was added to 30 ml of cold hexane, effecting the precipitation of much of the triphenylphosphine oxide. Filtration and rotary evaporation yielded 9 g of reddish, clear liquid. When this liquid was placed under full oil pump vacuum and the residual carbon tetrachloride removed, more of the triphenylphosphine oxide precipitated. At this point an additional 10 ml of hexane was added to the thick slurry and the filtration and rotary evaporation were repeated. Distillation of this second residue yielded 4.9 g (71%) of clear, colorless liquid, bp 53–56° (0.08 mm). Gas–liquid chromatography indicated that three new components were present in addition to a small amount of unreacted alcohol. The two components of shorter retention time were the cis and trans isomers of tertiary chloride **6;** the component of longest retention time was primary chloride **7.** Spinning-band distillation was used to separate the isomeric 3-chloro-3-vinyl-1-cyclobutanecarbonitriles (**6**) from the higher boiling **7.** We were, however, unable to separate the isomeric tertiary chlorides from each other.

3-Chloro-3-vinyl-1-cyclobutanecarbonitrile (6) had ir (NaCl) 2200 (CN), 1550 and 1620 (C=C), 757 cm^{-1} (CCl); nmr ($CDCl_3$) τ 3.8–4.1 (multiplet, 1 H, vinyl), 4.6–4.9 (multiplet, 2 H, vinyl), 7.1 (singlet, 5 H, ring protons); mass spectrum *m/e* 141, parent peak (calcd mol wt, 141).

Anal. Calcd for C_7H_8NCl: C, 59.31; H, 5.65; N, 9.90; Cl, 25.10. Found: C, 59.35; H, 5.63; N, 9.83; Cl, 24.93.

3-(β-Chloroethylidene)-1-cyclobutanecarbonitrile (7) had ir (NaCl) 2240 (CN), 1630 (C=C), 750 cm^{-1} (CCl); nmr ($CDCl_3$) τ 4.4–4.7 (multiplet, 1 H, methylene), 6.0 (doublet, 2 H, chloromethyl), 6.9 (broad singlet, 5 H, ring H's); mass spectrum *m/e* 141 parent peak (calcd mol wt, 141).

Anal. Calcd for C_7H_8NCl: C, 59.31; H, 5.65; N, 9.90; Cl, 25.10. Found: C, 59.13; H, 5.74; N, 10.04; Cl, 25.27.

3-Vinylbicyclobutanecarbonitrile (8). A solution of 1.0 g (71 mmol) of 3-vinyl-3-chlorocyclobutanecarbonitrile (cis–trans mixture) in 30 ml of anhydrous ethyl ether was placed in a 50-ml three-necked round-bottom flask fitted with a nitrogen gas inlet adaptor and Teflon-coated magnetic stirring bar. The flask and its contents were then cooled to −6° in an ice–methanol bath. At this point 1.0 g (88 mmol) of potassium *tert*-butoxide was added to the flask all at once. The color of the mixture instantly became a dark brownish purple and the temperature rose from −6° to about 4° over a 3-min period. Over the next 4–5 min the temperature tapered off and began to drop. At this point the reaction mixture was treated with 1.0 g of powdered CO_2 and approximately 2 ml of saturated KCl solution. The resulting slurry of salts was rapidly filtered, and the filtrate was dried over a little magnesium sulfate and concentrated on the rotary evaporator. Distillation of the residue yielded 0.7 g (92%) of a clear, colorless liquid: bp 45–48° (0.08 mm); ir (NaCl) 2210 (CN), 1550 and 1610 cm^{-1} (C=C); nmr ($CDCl_3$) τ 3.8–4.2 (multiplet, 1 H, vinyl), 4.5–4.8 (multiplet, 2 H, vinyl), 7.6 (singlet, 2 H, ring protons), 8.4 (singlet, 2 H, ring protons), the last two signals (τ 7.6 and 8.4) are attributed to the exo and endo protons, respectively; mass spectrum *m/e* 105, parent peak (calcd mol wt, 105).

Anal. Calcd for C_7H_7N: C, 80.02; H, 6.66; N, 13.30. Found: C, 79.97; H, 6.83; N, 13.02.

A 15% solution of **8** in sulfolane yielded polymer when subjected to uv radiation for 8 hr at room temperature.

3-Vinyl-1-cyanocyclobut-2-ene (9) 3-(β-Chloroethylidene)cyanocyclobutane, 1.0 g (71 mmol), was dissolved in 15 ml of anhydrous ethyl ether. The resulting solution was placed in a 50-ml three-necked round-bottomed flask fitted with a nitrogen gas inlet adaptor and a 0.5-in. magnetic stirring bar (Teflon coated). The flask and contents were then cooled to −7° in an ice–methanol bath. At this point, 1.0 g (88 mmol) of potassium *tert*-butoxide was introduced into the flask all at once. The color of the solution turned dark brownish purple as the temperature rose slightly above 0°. After 10–12 min the temperature began to fall and the reaction mixture was worked up by adding *ca.* 0.5 g of powdered CO_2 and 1–2 ml of saturated KCl solution. The resulting slurry of salts was filtered and the filtrate was dried over a little $MgSO_4$ and distilled. The distillate (0.8 g), collected over a temperature range of 37–63° (0.1 mm), was found to contain, in addition to 20% unreacted starting material, a 55:45 (glc) mixture of two new lower boiling components. These two substances were separated from the unreacted chloride and their nmr spectrum was taken. When the spectrum (nmr) of pure 3-vinylbicyclobutanecarbonitrile was compared with that of the mixture of products of this reaction, it was evident that the conjugated diene **9** was present along with the bicyclic isomer. The yield of diene based on a 45:55 diene to bicyclic ratio was about 29%: nmr ($CDCl_3$) τ 6.5 (broad multiplet, 1 H, α to cyano), 7.0 (multiplet, 2 H, methylene), 3.5–4.8 (multiplet, 4 H, olefinic protons) (absorptions caused by 3-vinylbicyclobutane-1-carbonitrile not mentioned).

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Pyrimido[5,4-*e*]-*as*-triazines. VII. Synthesis of 7-Aza Analogs of Pteroic and Folic Acids[1]

Carroll Temple, Jr.,* and Conrad L. Kussner, and John A. Montgomery

Kettering-Meyer Laboratory, Southern Research Institute Birmingham, Alabama 35205

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An investigation of the preparation and stability of dihydropyrimido[5,4-*e*]-*as*-triazines indicated that electron-donating groups in the dihydro-*as*-triazine ring promoted the air oxidation of these compounds to the corresponding heterocyclic derivatives. Work was also carried out in the preparation and reactions of a number of substituted anilinoacetonitriles. Conversion of [*p*-(ethoxycarbonyl)anilino]acetonitrile (**6a**) and diethyl *p*-[(cyanomethyl)amino]benzoyl-L-glutamate (**6c**) to the corresponding ethyl imidates and condensation of the latter with 2,5-diamino-4-(benzylthio)-6-hydrazinopyrimidine (**7**) provided directly ethyl *p*-[[[7-amino-5-(benzylthio)-pyrimido[5,4-*e*]-*as*-triazin-3-yl]methyl]amino]benzoate (**10a**) and the corresponding diethyl L-glutamate (**10b**), respectively. Nucleophilic replacement of the benzylthio group of **10a** with the appropriate reagent gave the 5-oxo (**11a,** ethyl 7-azapteroate), the 5-thione (**12a**), and the 5-amino (**13a**) derivatives. Similarly, **10b** was converted to the 5-oxo (**11c,** 7-azafolic acid) and 5-thione (**12c**) derivatives. Reaction of **10b** with sodium azide lead to the corresponding diethyl ester of the 5-amino derivative (**13b**).

Previously, we reported the development of synthetic methods for the preparation of 4-substituted 2-amino-7-azapteridines (5-substituted 7-aminopyrimido[5,4-*e*]-*as*-triazines).[2] Further modification of these procedures have now provided methods for the preparation of 7-azapteroic and 7-azafolic acids and related compounds.[3] These compounds, especially 7-azafolic acid and the corresponding 4-thio compound, are of interest as potential substrates for the folic reductase enzyme, which on interaction might produce biologically interesting 7-aza derivatives that are analogs of the tetrahydrofolate coenzymes.[4]

Earlier we showed that reaction of **2a** with NaSH not