7,8-Dicyanotricyclo[4.2.2.0^{2,5}]deca-3,7,9-triene (XIV).—Cyclooctatetraene (10 g., 0.096 mole) and dicyanoacetylene (7.6 g., 0.1 mole) were refluxed in tetrahydrofuran (60 ml.) for a period of 43 hr. Removal of the solvent left a semisolid residue which was taken up in chloroform; after filtration through aluminum oxide, the filtrate was evaporated to dryness. Recrystallization of the slightly oily crystals (2.9 g., 16.8%) from 90% methanol (charcoal) gave almost white crystals which after sublimation at 130–140°, 1 mm., melted at 148–149°.

Anal. Calcd. for $C_{12}H_8N_2$: C, 79.97; H, 4.48; N, 15.48. Found: C, 79.85; H, 4.53; N, 15.55.

7,8-Dicyanotricyclo[4.2.2.0^{2,5}]-3,4-dihydrodeca-3,9-diene (XVI).—XIV (0.125 g., 0.0007 mole) was hydrogenated in methanol with platinum. The hydrogen uptake (17.3 ml., calcd., 17.4 ml.) was a very rapid one, but became rather slow after one mole had been consumed. Evaporation of the solvent and sublimation at 130°, 1 mm. with subsequent recrystallization from methanol afforded white crystals, m.p. 134.5–135.5°.

Anal. Calcd. for $C_{12}H_{10}N_2$: C, 79.10; H, 5.54; N, 15.38. Found: C, 78.96; H, 5.66; N, 15.27.

The Retrodiene Cleavage of 7,8-Dicyanotricyclo[4.2.2.0^{2,5}]-3,4-Dihydrodeca-3,9-diene (XVI).—XVI (0.397 g., 0.00218 mole) was placed in a sealed tube and kept at 185° for a period of 40 min. The butadiene formed (46 ml., at S.T.P., 93%) showed the following characteristic data: pressure, 10 mm. at −78° (by standard high vacuum technique); lit.[17]: 10 mm. at −79.7° for 1,3-butadiene and 10 mm. at 75° for cyclobutene. Mol. wt., 53.6; calcd. 54.

The infrared spectrum was superimposable over the one of a known sample of 1,3-butadiene. No absorption belonging to cyclobutene could be detected. The solid residue (0.2742 g., 97.3%) was identified by m.p. and by infrared spectrum as phthalonitrile.

2,3,5,6-Tetramethyl-7,8-dicyanobicyclo[2.2.2]octa-2,5,7-triene (XVII).—Durene (2 g., 0.015 mole) and dicyanoacetylene (2.6 g., (0.034 mole) were placed in a sealed tube and heated to 132° (1-nitropropane as a heat exchange medium) for a period of 6 hr. The excess of dicyanoacetylene was evaporated and the semisolid residue added to methanol (10 ml.). The tarry material was well dispersed, the solution cooled in ice, and the solid (0.57 g.) filtered off. Then it was added to ether (5 ml.) and the insoluble part (0.19 g.) filtered off. Sublimation at 120–150°/1 mm. through a thin layer of glass wool gave traces of durene and 120 mg. of XVII as a light yellow sublimate, m.p. 231–232.5°.

Anal. Calcd. for $C_{14}H_{14}N_2$: C, 79.95; H, 6.71; N, 13.33. Found: C, 80.06; H, 6.66; N, 13.03.

The infrared spectrum showed CN absorption at 4.49 μ and a band for C═C at 6.25 μ (KBr wafer). Absorption in the ultraviolet occurred at $\lambda_{\max}^{\text{ethanol}}$ 241 mμ (ε 5120) shoulder at 250 mμ (ε 4440), 358 mμ (ε 299).

The n.m.r. spectrum contained peaks at 107 c.p.s. (60 Mc/sec.) characteristic for allylic methyl of intensity (6), and at 256 c.p.s. (60 Mc./sec.) characteristic for tertiary allylic hydrogen of intensity (1).

4-Benzo-2,3-dicyanoisoxazole (XVIII).—Dicyanoacetylene (1.4 g., 0.018 mole) was added to an ethereal solution of benzonitrile oxide[18] (approximately 2.3 g., 0.019 mole) and refluxed for a period of 40 min. Evaporation of the solvent and recrystallization of the residue (2.92 g., 81%) from carbon tetrachloride yielded slightly yellow crystals, m.p. 84–86°.

Anal. Calcd. for $C_{11}H_5N_3O$: C, 67.69; H, 2.58; N, 21.53. Found: C, 67.64; H, 2.57; N, 21.50.

Bis(1,2-dicyano-1-chloroethene)mercury (XIX).—Dicyanoacetylene (5 g., 0.0658 mole) was added to a solution of mercuric chloride (18 g., 0.066 mole) in water (50 ml.) saturated with sodium chloride. The suspension was shaken for 20 min. with occasional cooling. The yellow precipitate (8.5 g., 61%) was filtered off, washed with water, and dried.

It was dissolved in acetone, chloroform added, and precipitation of yellow crystals, m.p. 185–190° dec., brought about by cooling the mixture in ice–water.

Anal. Calcd. for $C_8Cl_4N_4Hg$: C, 22.68; Cl, 16.73; N, 13.22; Hg, 47.35. Found: C, 22.79; Cl, 16.54; N, 13.19; Hg, 47.27.

***N*-Methyl-3,4-dicyanopyrazole (XXI).**—An ethereal solution of diazomethane was slowly added to a solution of dicyanoacetylene (3.8 g., 0.05 mole) in ether until a yellow color persisted. The temperature during the reaction was kept at about 5°. (The reaction becomes a very violent one without external cooling.) Evaporation of the solvent left a crystalline residue (6.9 g., 99%). Sublimation at 200°, 20 mm. gave white crystals, m.p. 195–196.5°. The compound is slightly soluble in boiling water.

Anal. Calcd. for $C_6H_9N_4$: C, 54.55; H, 3.05; N, 42.41. Found: C, 54.51; H, 2.88; N, 42.08.

1,2-Dicyano-1-phenylaminoethene (XXIIa).—A solution of dicyanoacetylene (1.52 g., 0.02 mole) in ether (10 ml.) was added with external cooling to a solution of aniline (1.86 g., 0.02 mole) in ether (20 ml.). It was allowed to remain at room temperature for 30 min. Evaporation of the solvent gave a tan residue (3 g., 88%). Recrystallization from chloroform yielded light yellow needles, m.p. 126.5–127.5°.

Anal. Calcd. for $C_{10}H_7N_3$: C, 70.93; H, 4.17; N, 24.83. Found: C, 71.01; H, 4.59; N, 24.52.

1,2-Dicyano-1-benzylaminoethene (XXIIb).—A solution of dicyanoacetylene (1.52 g., 0.02 mole) in ether (10 ml.) was added with external cooling to a solution of benzylamine (2.1 g., 0.02 mole) in ether (20 ml.). The solution remained at room temperature for 30 min. and was then evaporated to dryness. The residue (3.3 g., 92%) was dissolved in chloroform and filtered through aluminum oxide and finally recrystallized from the same solvent. The colorless crystals melted at 119–120°.

Anal. Calcd. for $C_{11}H_9N_3$: C, 72.11; H, 4.95; N, 22.94. Found: C, 71.79; H, 4.91; N, 22.64.

Acknowledgment.—The author is indebted to Dr. B. C. McKusick for helpful discussions and to Dr. T. H. Regan for the n.m.r. spectra.

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(17) "Handbook of Chemistry and Physics," 38th ed., Chemical Rubber Publishing Co., Cleveland, Ohio, 1956–1957.

(18) F. Montforte, *Gazz. chim. ital.*, **82**, 130 (1952).

Aromatic Cyclodehydration. L. Some Bisacridizinium Systems[1]

C. K. BRADSHER AND NANCY L. YARRINGTON[2]

Department of Chemistry, Duke University, Durham, North Carolina

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Starting from 2,2′- (V), 3,3′- (VI), and 4,4′-bisbromomethylbiphenyls (VII) and using the cyclization methods previously developed, the first bisacridizinium systems have been synthesized. In addition, a bis(9-acridizinium)methane (XVI) and a bis(9-acridizinium)ethane have been prepared. In contrast to the presumably planar 9,9′-bisacridizinium system, the sterically hindered 7,7′-system has an ultraviolet absorption spectrum closely resembling that of the acridizinium ion.

The current interest in the pharmacology of bisquaternary nitrogen systems, especially with regard to their application as hypotensive, ganglionic, and neuromuscular-blocking agents,[3] made it desirable to study the possibility of synthesizing some bisacridizinium

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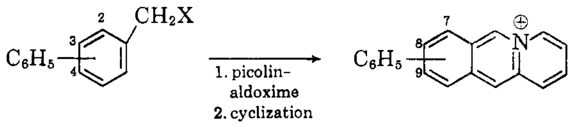
[1] For the preceding communication of this series see *J. Org. Chem.*, **26**, 4944 (1961).

[2] This research was supported by a research grant (H-2170) of the National Heart Institute of the National Institutes of Health.

[3] *E.g.*, A. P. Gray, W. L. Archer, E. E. Spinner, and C. J. Cavallito, *J. Am. Chem. Soc.*, **79**, 3805 (1957); A. P. Phillips, *ibid.*, **79**, 5754 (1957).

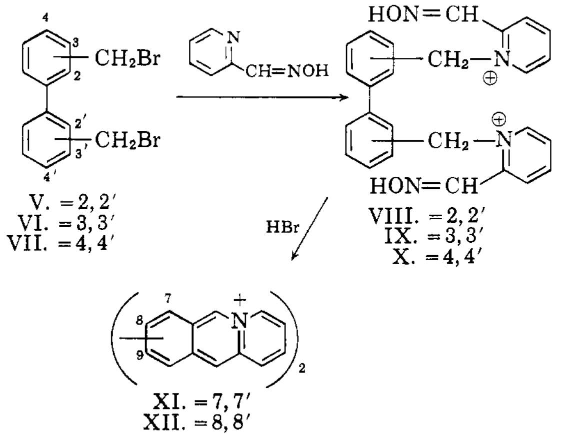
compounds. This class of diaryls has not been synthesized previously.

Since it appeared that the most logical route to the synthesis of such salts would involve cyclization of quaternary salts derived from bis(bromomethyl)-biphenyls (V–VII), model experiments were carried out using 2-bromomethyl- and 4-iodomethylbiphenyl (I and II). The hitherto unknown 7- and 9-phenylacridizinium salts were obtained without difficulty.



I. $2\text{-}C_6H_5, X = Br$ III. $7\text{-}C_6H_5$
II. $4\text{-}C_6H_5, X = I$ IV. $9\text{-}C_6H_5$

It has been shown by several workers[4–6] that biphenyl derivatives which are capable of assuming a configuration in which the rings are coplanar can transmit electronic effects across the pivot bond. It was not known whether the positive charge on the acridizinium nucleus first formed would be sufficiently transmitted to make the second cyclization impossible. The first synthesis started with 2,2′-bis(bromomethyl)-biphenyl[7] (V), selected because the expected arylacridizinium intermediate could not easily assume the coplanar position needed for transmission of electronic effects. In any event, 2,2′-bis(bromomethyl)biphenyl (V) was quaternized by reaction with two equivalents of 2-picolinaldoxime and the crude hygroscopic salt (presumably VIII) cyclized with 48% hydrobromic acid to yield a yellow-orange product having the properties expected for 7,7′-bis(acridizinium bromide).



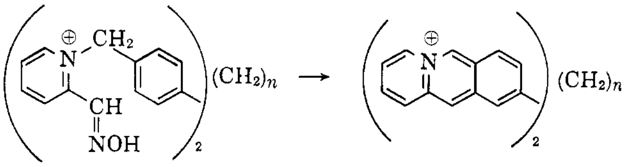
V. =2,2′
VI. =3,3′
VII. =4,4′

VIII. =2,2′
IX. =3,3′
X. =4,4′

XI. =7,7′
XII. =8,8′
XIII. =9,9′

In the same way, starting from 4,4′-bis(bromomethyl)-biphenyl (VII), 9,9′-bis(acridizinium bromide) (XIII), was prepared via the intermediate quaternary salt (X). The quaternary salt (IX) from 3,3′-bis(bromomethyl)biphenyl (VI) in theory could afford 8,8′-, 8,10′-or 10,10′-bis(acridizinium bromide), on cyclization, but it seems most probable that the product which we have isolated is the 8,8′-salt.[8]

From 4,4′-bis(bromomethyl)diphenylmethane and 4,4′-bis(bromomethyl)bibenzyl, *via* the quaternary salts XIV and XV, 9,9′-methylenebis(acridizinium bromide) (XVI) and 9,9′-ethylenebis(acridizinium bromide) (XVII) were obtained.



XIV. $n = 1$ XVI. $n = 1$
XV. $n = 2$ XVII. $n = 2$

The ultraviolet absorption spectra of the 7,7′- and 9,9-′acridizinium salts make an interesting comparison with that of acridizinium perchlorate (Table I).

Table I

Ultraviolet Absorption Spectra of Some Bisacridizinium Salts

	Max.		Min.	
	λ, mμ	$\log_{10} \epsilon$	λ, mμ	$\log_{10} \epsilon$
Acridizinium perchlorate[a]	242	4.68	311	3.15
	361	3.99	369.5	3.88
	379.5	4.01	389.5	3.81
	399	3.93		
7,7′-bis(bromide) (XI)	244	4.93	315	3.55
	363	4.27	372	4.13
	383	4.24	392	4.14
	406	4.32		
9,9′-bis(bromide) (XIII)	243	4.74	255	4.52
	266	4.60	279	4.51
	302	4.78	307	4.76
	310	4.77	347	3.95
	366	4.15	374	4.11
	410	4.38	417	4.34
	431	4.42		

[a] Bradsher and Beavers, *J. Am. Chem. Soc.*, **77**, 4812 (1955).

It would be expected that 7,7′-bis(acridizinium bromide) would be nonplanar, and as a result, its ultraviolet absorption spectrum would closely resemble that of the simple acridizinium ion. This is essentially true, there being only a slight bathochromic shift.

It seems probable that the 9,9′-bisacridizinium (XIII) would have no serious impediment to the achievement of planarity, and as in biphenyl[6] or the dimethochloride of γ,γ′-dipyridyl[9] the pivot bond would develop double bond character. In any case, the spectrum of the 9,9′-bisacridizinium system is more complex than that of simple acridizinium salts and shows significant absorption at higher wave lengths.

The bisacridizinium systems form an interesting new class of compounds worthy of additional study.

Experimental

All analyses were carried out by Dr. Ing. A. Schoeller, Microanalytisches Laboratorium, Kronach, Germany. The melting points were determined using the Mel-Temp apparatus and are uncorrected. Ultraviolet absorption spectra were determined in 95% ethanol using the Cary model 11 recording spectrophotometer and 1-cm. silica cells. Wave lengths are expressed in millimicrons and shoulders are designated by use of an asterisk (*).

1-(2-Biphenylmethyl)-2-oximidomethylpyridinium Bromide.—A mixture containing 2.47 g. (0.01 mole) of 2-bromomethylbi-

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(4) M. T. O'Shaughnessy and W. H. Rodebush, *J. Am. Chem. Soc.*, **62**, 2906 (1940).

(5) E. Berliner and E. A. Blommers, *ibid.*, **73**, 2479 (1951).

(6) D. W. Sherwood and M. Calvin, *ibid.*, **64**, 1350 (1942).

(7) C. W. Muth, W. Sung, and Z. B. Papanastassiou, *ibid.*, **77**, 3393 (1955).

(8) Alkaline permanganate oxidation did not appear to yield any biphenyltetracarboxylic acid. Work is in progress on the development of a suitable general method for the degradation of acridizinium derivatives.

(9) P. Krumholz, *J. Am. Chem. Soc.*, **73**, 3487 (1951).

phenyl (I. X = Br)[10] 1.22 g. (0.01 mole) of picolinaldoxime and 1.5 ml. of N-methylpyrrolidone was heated on the steam bath in a stoppered flask for 15 min. The resinous product was triturated with ethyl acetate to effect crystallization. Recrystallization from methanol–ethyl acetate yielded 2.45 g. (66%) of colorless hexagonal platelets m.p. 167–168°.

Anal. Calcd. for $C_{19}H_{17}BrN_2O$: C, 61.81; H, 4.54; N, 7.59. Found: C, 61.76; H, 4.76; N, 7.65.

7-Phenylacridizinium Salts (III).—A solution of 1.6 g. of 1-(2-biphenylylmethyl)-2-oximidomethylpyridinium bromide in 15 ml. of 48% hydrobromic acid was refluxed. At the end of 1.5 hr. yellow crystals formed in the boiling solution and (after the mixture had been cooled) were collected, 0.78 g. The mother liquor on vacuum evaporation afforded and additional 1.0 g. The combined crude product was crystallized from methanol–ethyl acetate yielding 1.34 g. (89%) of a bright yellow powder, m.p. about 271°. The analytical sample of the bromide formed a bright yellow powder from methanol–ethyl acetate, m.p. 276–278°. The analysis indicated that the product was a double salt[11] containing hydroxylamine hydrobromide.

Anal. Calcd. for $(C_{19}H_{14}NBr)_2 \cdot NH_3OHBr$: C, 58.03; H, 4.10; N, 5.34. Found: C, 57.94; H, 4.17; N, 5.09.

The **picrate** was prepared in ethanol as bright yellow microcrystalline needle clusters, m.p. 141.5–143.5° (from ethanol); λ_{max} (log ϵ), 249 (4.79), 365 (4.45), and 386 (4.38); λ_{min} 225 (4.62), 311 (3.86), and 380 (4.37).

Anal. Calcd. for $C_{25}H_{16}N_4O_7$: C, 61.98; H, 3.33; N, 11.57. Found: C, 62.01; H, 3.39; N, 11.53.

1-(4-Biphenylylmethyl)-2-oximidomethylpyridinium Iodide.—Two grams of 4-chloromethylbiphenyl[12] was converted to crude 4-iodomethylbiphenyl, m.p. 95–96°, by the action of potassium iodide in methanol–water. The reaction of 1.24 g. of the crude iodomethylbiphenyl with 0.51 g. of 2-picolinaldoxime was carried out in 6 ml. of dimethylformamide at refrigerator temperature over a period of 8 days. Addition of ethyl acetate caused the precipitation of the yellow salt, m.p. 145–147°; yield 0.96 g. (57%). The analytical sample formed pale yellow irregular platelets from methanol–ethyl acetate, m.p. 157–158°.

Anal. Calcd. for $C_{19}H_{17}IN_2O \cdot {}^1/_4CH_3COOC_2H_5$: C, 54.88; H, 4.38; N, 6.40. Found: C, 55.26; H, 4.64; N, 6.38.

9-Phenylacridizinium (IV) **Picrate.**—After conversion in the usual way of 0.96 g. of 1-(4-biphenylylmethyl)-2-oximidomethylpyridinium iodide to the corresponding chloride (by the action of silver chloride) the resulting chloride was cyclized by refluxing it for 3 hrs. in 48% hydrobromic acid. Vacuum evaporation of the acid and conversion of the residue to the picrate yielded 0.81 g. (71%), m.p. 237–240°. This material crystallized from ethanol-water as bright yellow needles, m.p. 243–245°.

Anal. Calcd. for $C_{25}H_{16}N_4O_7$: C, 61.98; H. 3.33; N, 11.57. Found: C, 61.76; H, 3.31; N, 11.20.

7,7′-Bis(acridizinium Bromide) (**XI**).—The quaternization of 3.40 g. (0.01 mole) of 2,2′-bis(bromomethyl)biphenyl (V)[7] with 2.44 g. (0.02 mole) of 2-picolinaldoxime in 3 ml. of N-methylpyrrolidone was carried out in the usual way. The white solid (5.43 g.) obtained by trituration of the mixture with ethyl acetate, proved too hygroscopic for crystallization by conventional procedures, and was used directly in the cyclization. From 2.47 g. of the crude bromide (VIII), after 4 hr. refluxing in 48% hydrobromic acid, followed by the usual isolation procedure, 0.96 g. (40% over-all) of yellow-orange crystals of the bromide (m.p. 305° dec.) were obtained. The analytical sample was crystallized from ethanol–water as bright yellow microcrystalline parallelograms, m.p. 310° dec.

Anal. Calcd. for $C_{26}H_{18}Br_2N_2 \cdot {}^1/_2H_2O$: C, 59.22; H, 3.63; N, 5.31. Found: C, 59.41; H, 3.63; N, 5.03.

The **picrate** crystallized from acetonitrile as bright yellow irregular platelets, m.p. 248° d.

Anal. Calcd. for $C_{38}H_{22}N_8O_{14}$: C, 56.03; H, 2.72; N, 13.76. Found: C, 55.68; H, 2.67; N, 13.39.

The **perchlorate** crystallized from ethanol–water as pale yellow elongated rectangular crystals, m.p. 372° (with detonation).

Anal. Calcd. for $C_{26}H_{18}N_2Cl_2O_8$: C, 56.03; H, 3.25; N, 5.03. Found: C, 56.05; H, 3.18; N, 5.05.

3,3′-Bis(1-methylene-2-oximidomethylpyridinium Picrate)-biphenyl (IX).—The quaternization of 3.40 g. of 3,3′-bis(bromomethyl)biphenyl (VI)[13] was carried out essentially as in the case of the isomer (V) except that all heating was avoided. When the contents of the flask became solid, ethyl acetate was added and the bromide collected. The yield was 5.5 g. (94%), m.p. 187–190°. The best sample crystallized from methanol–ethyl acetate as colorless microcrystalline needle clusters, m.p. 205–207°, but was not of analytical purity.

The **picrate** crystallized from ethanol as well defined bright yellow needles, m.p. 119–121°.

Anal. Calcd. for $C_{38}H_{28}N_{10}O_{16} \cdot {}^1/_2C_2H_5OH$: C, 51.83; H, 3.46; N, 15.51. Found: C, 51.63; H, 3.40; N, 15.52.

8,8′(?)-Bis(acridizinium Bromide).—The cyclization of 2 g. of the crude bromide (IX) was carried out in the usual way (5 hr.) yielding 0.56 g. (32%) of yellow solid, m.p. above 375°. The analytical sample was crystallized from ethanol–water as a yellow microcrystalline powder, m.p. above 380°, λ_{max} (log ϵ) 242 (4.70) 318–326* (3.95), 3.67 (4.26), 380* (4.18), 397* (3.60); λ_{min} 331 (3.94).

Anal. Calcd. for $C_{26}H_{28}Br_2N_2 \cdot {}^1/_2 H_2O$: C, 59.22; H, 3.63; N, 5.31. Found: C, 59.21; H, 3.83; N, 5.69.

The **picrate** was obtained from acetonitrile as a yellow microcrystalline powder, m.p. >400°.

Anal. Calcd. for $C_{38}H_{22}N_8O_{14} \cdot H_2O$: C, 54.81; H, 2.90; N, 13.46. Found: C, 54.51; H, 3.24; N, 13.39.

The **perchlorate** crystallized from acetonitrile as a pale yellow microcrystalline powder, m.p. above 390°.

Anal. Calcd. for $C_{26}H_{18}Cl_2N_2O_8$: C, 56.03; H, 3.25; N, 5.03. Found: C, 56.39; H, 3.50; N, 5.29.

4,4′-Bis(1-methylene-2-oximidomethylpyridinium Picrate)-biphenyl (X).—The quaternization of 3.40 g. of 4,4′-bis(bromomethyl)biphenyl (VII)[14] with picolinaldoxime was carried out in dimethylformamide. Trituration of the reaction mixture with ethyl acetate yielded 5 g. of a hygroscopic solid (presumably the bromide of X) suitable for further reactions.

The **picrate** was crystallized from ethanol as a bright yellow microcrystalline powder, m.p. 197–198°.

Anal. Calcd. for $C_{38}H_{28}N_{10}O_{16}$: C, 51.82; H, 3.20; N, 15.91. Found: C, 52.06; H, 3.43; N, 15.47.

The **perchlorate** was crystallized from methanol–ethyl acetate as a cream-colored microcrystalline powder, m.p. 198–200°.

Anal. Calcd. for $C_{26}H_{24}Cl_2N_4O_{10} \cdot {}^1/_2CH_3COOC_2H_5$: C, 51.00; H, 4.28; N, 8.50. Found: C, 50.94; H, 4.30; N, 8.72.

9,9′-Bis(acridizinium Bromide) (**XIII**).—The cyclization of 2.7 g. of the bromide (X) in the usual way afforded 1.0 g. (37%) of orange product, m.p. above 390°. The analytical sample crystallized from ethanol–water as aggregates of flat orange needles, m.p. above 390°.

Anal. Calcd. for $C_{26}H_{18}Br_2N_2 \cdot {}^1/_2H_2O$: C, 59.22; H, 3.63; N, 5.31. Found: C, 59.30; H, 3.85; N, 5.12.

The **perchlorate** crystallized from acetonitrile as a bright yellow powder, m.p. above 390° d.

Anal. Calcd. for $C_{26}H_{18}N_2Cl_2O_8$: C, 56.03; H, 3.25; N, 5.03. Found: C, 56.44; H, 3.54; N, 4.95.

4,4′-Bis(1-methylene-2-oximidomethylpyridinium Bromide)-diphenylmethane (XIV).—The quaternization of 2-picolinaldoxime by 4,4′-bis(bromomethyl)diphenylmethane[15] was carried out in N-methylpyrrolidone at steam bath temperature. Worked up as usual it afforded 5.0 g. of crude bromide (XIV) suitable for further reactions. The analytical sample crystallized from ethanol–ethyl acetate as a colorless microcrystalline powder, m.p. 202–203° dec.

Anal. Calcd. for $C_{27}H_{26}Br_2N_4O_2 \cdot {}^1/_2H_2O$: C, 54.12; H, 4.70; N, 9.02. Found: C, 54.40; H, 4.61; N, 8.86.

9,9′-Methylenebis(acridizinium Bromide).—The crude quaternary salt (XIV) obtained from 1.77 g. of 4,4′-bis(bromomethyl) diphenylmethane was cyclized in hydrobromic acid by heating the solution overnight at steam bath temperature. A total of 1.08 g. (41%) of product, m.p. 289° dec., was recovered. The analytical sample crystallized from ethanol–water as yellow needle clusters, m.p. 289° dec., λ_{max} (log ϵ), 244 (4.96), 250* (4.93), 277* (4.74), 362 (4.42), 374 (4.50), and 394 (4.41); λ_{min} 318 (3.72), 366 (4.38), 385 (4.29).

Anal. Calcd. for $C_{27}H_{20}Br_2N_2$: C, 60.92; H, 3.79; N, 5.26. Found: C, 60.75; H, 4.13; N, 5.54.

The **picrate** crystallized from ethanol–water as bright yellow felted needles, m.p. 247–248°.

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(10) J. von Braun and G. Manz, *Ann.*, **468**, 258 (1929).

(11) A forthcoming publication will discuss some earlier observations on double salt formation in the acridizinium series.

(12) J. von Braun, G. Irmisch, and J. Nelles, *Ber.*, **66**, 1471 (1933).

(13) W. Werner, *J. Org. Chem.*, **17**, 523 (1952).

(14) D. D. Reynolds and K. R. Dunham, U. S. Patent 2,789,971; *cf.*, *Chem. Abstr.*, **51**, 14814b (1957).

(15) H. Steinberg and D. J. Cram, *J. Am. Chem. Soc.*, **74**, 5388 (1952).

Anal. Calcd. for $C_{39}H_{24}N_8O_{14}\cdot{}^1/_2C_2H_5OH$: C, 56.41; H, 3.20; N, 13.16. Found: C, 56.50; H, 3.11; N, 12.71.

4,4′-Bis(1-methylene-2-oximidomethylpyridinium Picrate)-bibenzyl (XV).—The quaternization of picolinic aldoxime with 4,4′-bis(bromomethyl)bibenzyl[16] was carried out in N-methylpyrrolidone in the usual way. A portion of the crude product was converted to the picrate which formed a bright yellow powder from ethanol, m.p. 130–131°.

Anal. Calcd. for $C_{40}H_{28}N_{10}O_{16}\cdot C_2H_5OH$: C, 53.05; H, 3.60; N, 14.73. Found: C, 52.75; H, 3.50; N, 14.41.

9,9′-Ethylenebis(acridizinium Bromide) (XVII).—The cyclization of 2.5 g. of the crude bromide (XV) was carried out as in the case of the homolog (XIV). The product consisted of 1.1 g. (40%) of small bright orange needles from ethanol–water, m.p. above 390°, λ_{max} (log ϵ), 245 (4.79), 252 (4.80), 362 (4.52), 376 (4.20), 393 (4.26), and 395* (4.12); λ_{min}, 249 (4.78), 314 (3.34), 368 (4.17), and 388 (4.03).

Anal. Calcd. for $C_{28}H_{22}Br_2N_2$: C, 61.56; H, 4.06; N, 5.13. Found: C, 61.37; H, 4.11; N, 5.41.

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[16] J. L. R. Williams and K. R. Dunham, U. S. Patent 2,843,567; *cf.*, *Chem. Abstr.*, **52**, 16798h (1958).

Aromatic Cyclodehydration. LI.[1] Phenanthridizinium Derivatives Bearing a Carboxyethyl Group

C. K. BRADSHER AND NANCY L. YARRINGTON[2]

Department of Chemistry, Duke University, Durham, North Carolina

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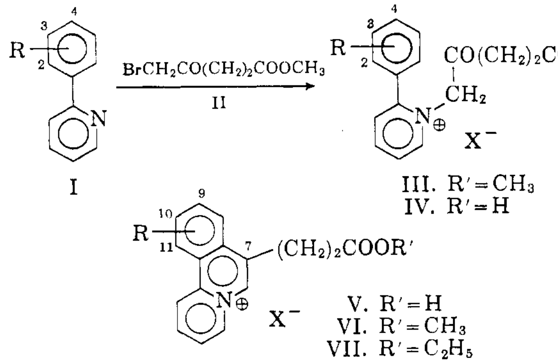
The quaternary salt formed by the reaction of methyl δ-bromolevulinate with 2-phenylpyridine may be cyclized to afford the 7-(β-carboxyethyl)benzo[*a*]quinolizinium ion. The synthesis was extended to two of the 2-tolylpyridines.

Analogy suggests that any extensive application of phenanthridizinium[3] salts in medicinal chemistry will require that there be one or more functional groups in addition to the quaternary nitrogen. To date, fully aromatic phenanthridizinium salts bearing a methoxyl[4] or hydroxyl[3] group have been prepared, but with the exception of the 1,2,3,4-tetracarbomethoxyphenanthridizinium ion reported by Diels and co-workers[5,6] it appears that no derivatives having functional groups have been synthesized. The present communication describes some experiments directed toward the introduction of the carboxyl or a carboxylalkyl group into the 7-position of the phenanthridizinium nucleus.



I

III. $R' = CH_3$
IV. $R' = H$

V. $R' = H$
VI. $R' = CH_3$
VII. $R' = C_2H_5$

It seemed probable that the carboxyl function could be introduced into the phenanthridizinium nucleus by quaternization of a 2-phenylpyridine with a suitable ω-bromoketo ester, $BrCH_2CO(CH_2)_nCOOR$ followed by cyclization. Preliminary attempts at quaternization using ethyl bromopyruvate[7] ($n = 0$) were unsuccessful, the major product being the hydrobromide of the base I. The next higher homolog, γ-bromoacetoacetic ester ($n = 1$) was not studied since it seemed obvious that in boiling mineral acid, rapid hydrolysis and decarboxylation of the quaternary salt would occur. The next higher homolog, methyl δ-bromolevulinate (II. $n = 2$) is easily obtained[8] and quaternizes readily with 2-phenyl- and 2-tolylpyridines (I) to afford ether-insoluble liquid salts (III). The crude salts were not purified, but used directly in the cyclization reaction. Cyclization in boiling hydrobromic acid proved slower (6–16 days) than was the case with the simple 1-acetonyl-2-arylpyridinium salts (2–3 days) studied earlier.[9] In nearly all cyclization attempts, uncyclized keto acid (IV) was recovered along with the product (V). Where the methyl group was in the *ortho* position of the phenyl ring (I. R = 2-CH_3), no cyclization product was detected, even after a reflux period of fifteen days, 39% of starting material being recovered as uncyclized keto acid (IV. R = 2-CH_3). This was not too surprising since the methyl at the 2-position impedes the achievement of the coplanarity essential for cyclization. The related 1-acetonyl-2-(*o*-tolyl)pyridinium salt cyclized in only 9% yield under the conditions which produced a 71% yield from the *p*-tolyl analog.[9]

The 7-(β-carboxyethyl)phenanthridizinium (V) perchlorates melted above 200° and showed the characteristic instability toward alkali. Efforts to prepare the zwitterion either by addition of potassium hydroxide to an alcoholic solution of the perchlorate or by action of silver oxide on the bromide yielded unstable products which showed the characteristic carboxylate anion absorption at 1575 cm.$^{-1}$, but were not analytically pure. Esterification of the new acids (V) in absolute methanol (hydrogen chloride catalyst) occurred in good yield. In one case (V. R = 9-CH_3) esterification was likewise brought about *via* the acid chloride, which was formed as a milky suspension by stirring a suspension of the acid in carbon tetrachloride with oxalyl chloride at room temperature. If the resulting milky suspension

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[1] For the preceding communication of this series see C. K. Bradsher and N. L. Yarrington, *J. Org. Chem.*, **28**, 78 (1963).

[2] Taken from part of a dissertation submitted by N. L. Y. in partial fulfillment of the requirements for the Ph.D. degree, Duke University. This investigation was supported by a research grant (H-2170) from the National Heart Institute of the National Institutes of Health.

[3] The name phenanthridizinium has been proposed [C. K. Bradsher and K. B. Moser, *J. Am. Chem. Soc.*, **81**, 1941 (1959)] as a simpler alternative to the *Chem. Abstr.* designation, benzo[*a*]quinolizinium.

[4] L. E. Beavers, Ph.D. dissertation, Duke University, 1955.

[5] O. Diels and J. Harms, *Ann.*, **525**, 73 (1936).

[6] O. Diels and K. Alder, *ibid.*, **498**, 16 (1932).

[7] C. F. Ward, *J. Chem. Soc.*, **123**, 2207 (1923).

[8] H. Dannenberg and S. Läufer, *Ber.*, **89**, 2242 (1956).

[9] C. K. Bradsher and K. B. Moser, *J. Am. Chem. Soc.*, **81**, 1941 (1959).