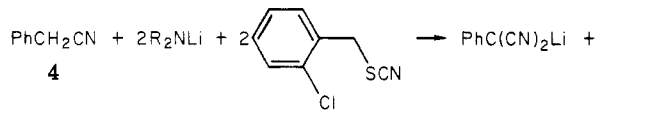
Table I. Synthesis of Arylmalononitriles from Aromatic Acetonitriles

arylacetonitrile	aryl-malono-nitrile	yield, %	mp, °C
phenyl	1	94	67–68
4-methoxyphenyl	7	77	71–72
4-bromophenyl	9	91	86–87.5
3,4-(methylenedioxy)phenyl	10	92	131–133
3-pyridyl	11	56	250 dec
1-naphthyl	12	100	165–166
2-methylphenyl	13	95	49–50
2-chlorophenyl	14	92	62–63

aqueous base, followed by acidification. The overall reaction is shown in eq. 7. Seven additional arylmalononitriles were synthesized in excellent yield by the same general procedure. The results are summarized in Table I.



(7)

2-Chlorobenzyl thiocyanate (8), unlike cyanogen chloride, is a selective cyanating agent and does not react with highly stabilized anions. Thus, the anion of phenylmalononitrile does not react with thiocyanate 8, although it can be further cyanated to phenyltricyanomethane by cyanogen chloride[10] (eq 8).

$$PhCH(CN)_2 \xrightarrow[ClCN]{NaH} PhC(CN)_3 \quad (8)$$

Similarly, thiocyanate 8 did not react with the anion of ethyl α-cyanophenylacetate, whereas the reaction of anions of this type with cyanogen chloride proceeds readily.

Experimental Section

General Methods. Melting points were determined on a Thomas-Hoover apparatus and are uncorrected. Mass and infrared (KBr) spectra were recorded with a Hitachi Perkin-Elmer RMH-2 and a Perkin-Elmer Model 137 spectrometer, respectively. NMR spectra were recorded on a Bruker 250 FT machine with $CDCl_3$ solution containing Me_4Si as an internal standard unless otherwise noted and are reported in δ units (J values are in hertz). Elemental analyses were carried out by Galbraith Laboratories.

General Procedure for the Cyanation of Arylacetonitriles. To a solution of LDA (11.0 mmol) in benzene (75 mL) at 5 °C under nitrogen was added a solution of the arylacetonitrile (5.00 mmol) in benzene (25 mL), and the reaction mixture was stirred for 15 min. A solution of 2-chlorobenzyl thiocyanate (11.0 mmol) in benzene (50 mL) was added over 15 min, and the reaction mixture was stirred for an additional hour. The reaction was worked up by washing the benzene solution with water and 10% aqueous sodium hydroxide. The combined aqueous solution was cooled in an ice bath and acidified to pH 1 with concentrated hydrochloric acid. The product was extracted into methylene chloride, and the solution was dried over $MgSO_4$ and evaporated to give the arylmalononitrile. Arylmalononitriles **7**, **9–12**, and **14** were crystallized from ethanol, and **1** and **13** were distilled at reduced pressure.

Phenylmalononitrile (1): mp 67–68 °C (lit.[1,4] mp 68–69 °C); IR (KBr) 2900, 1480, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) 5.08 (s, 1 H), 7.50 (s, 5 H); *m/e* (relative intensity) 142 (M^+, 58), 115 (100).

(2-Methylphenyl)malononitrile (13): mp 49–50 °C; IR (KBr) 2900, 1480, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) 2.48 (s, 3 H), 5.05 (s, 1 H), 7.38–7.60 (m, 2 H); MS, *m/e* (relative intensity) 156 (M^+, 35), 141 (15), 129 (100), 91 (23). Anal. Calcd for $C_{10}H_8N_2$: C, 76.92; H, 5.13; N, 17.95. Found: C, 76.75; H, 5.28; N, 17.76.

(2-Chlorophenyl)malononitrile (14): mp 62–63 °C (lit.[1] mp 60–62 °C) IR (KBr) 2900, 1475, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) 5.38 (s, 1 H), 7.40–7.75 (m, 4 H); MS, *m/e* (relative intensity) 176 (M^+, 41) 141 (100), 114 (19).

1-Naphthylmalononitrile (12): mp 165–166 °C (lit.[5] mp 166–167 °C); IR (KBr) 2900, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) 5.58 (s, 1 H), 7.54–8.05 (m, 7 H); MS *m/e* (relative intensity) 192 (M^+, 100), 191 (31), 165 (47).

(4-Bromophenyl)malononitrile (9): mp 86–87.5 °C; IR (KBr) 2900, 1490 cm^{-1}; ^1H NMR ($CDCl_3$) 5.05 (s, 1 H), 7.39 (d, J = 8.5 Hz, 2 H), 7.65 (d, J = 8.5 Hz, 2 H); MS, *m/e* (relative intensity) 222 (18), 220 (M^+, 19), 141 (100); high-resolution mass spectrum, calcd for $C_9H_5BrN_2$ *m/e* 219.9636 and 221.9616, found 219.9664 and 221.9626.

(4-Methoxyphenyl)malononitrile (7): mp 71–72 °C (lit.[1] mp 67–69 °C; IR (KBr) 2850, 1600, 1510 cm^{-1}; ^1H NMR ($CDCl_3$) 3.84 (s, 3 H), 5.01 (s, 1 H), 7.41 (d, J = 8.5 Hz, 2 H), 7.98 (d, J = 8 Hz, 2 H); MS, *m/e* (relative intensity) 172 (M^+, 100), 161 (30), 157 (39), 102 (34).

3-Pyridylmalononitrile (11): decomposes at 250 °C (lit.[10] mp 246–248 °C); IR (KBr) 3100, 2175, 2125 cm^{-1}; ^1H NMR (Me_2So-d_6) 7.60 (s, 2 H), 7.91 (s, 2 H), 13.0 (br s, 1 H); MS, *m/e* (relative intensity) 143 (M^+, 100), 116 (80); high-resolution mass spectrum, calcd for $C_8H_5N_3$, *m/e* 143.0483, found 143,0483.

[3,4-(Methylenedioxy)phenyl]malononitrile (10): mp 131–133 °C; IR (KBr) 2950, 1500, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) 4.96 (s, 1 H), 6.06 (s, 2 H), 6.84–6.98 (m, 3 H); MS, *m/e* (relative intensity) 186 (M^+, 100), 185 (96), 156 (40), 128 (99). Anal. Calcd for $C_{10}H_6N_2O_2$: C, 64.52; H, 3.23; N, 15.05. Found: C, 64.73; H, 3.43; N, 15.04.

Acknowledgment. This work was supported by the National Science Foundation MRL program under Grant DMR 7923647.

Registry No. **1**, 3041-40-5; **4**, 140-29-4; **5**, 104-47-2; **7**, 33534-87-1; **9**, 86239-14-7; **10**, 86239-15-8; **11**, 25230-06-2; **12**, 5518-09-2; **13**, 86239-16-9; **14**, 32122-65-9; 4-bromophenylacetonitrile, 16532-79-9; 3,4-(methylenedioxy)phenylacetonitrile, 4439-02-5; 3-pyridylacetonitrile, 6443-85-2; 1-naphthylacetonitrile, 132-75-2; 2-methylphenylacetonitrile, 22364-68-7; 2-chlorophenylacetonitrile, 2856-63-5; 2-chlorobenzyl thiocyanate, 2082-66-8.

(10) Wagner, H.,; Gompper, R. *Angew Chem., Int. Ed. Engl.* **1969**, *8*, 986.

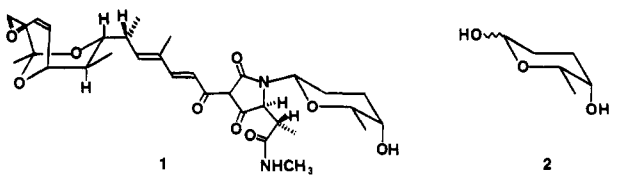
A Simple Synthesis of Rhodinose from (*S*)-Ethyl Lactate

T. Ross Kelly* and Pushkar N. Kaul

Department of Chemistry, Boston College, Chestnut Hill, Massachusetts 02167

Received November 23, 1982

In conjunction with a program directed toward the synthesis of the antibiotic streptolydigin (**1**),[1] we sought a convenient supply of the trideoxyhexose subunit rhodinose (**2**).[2] Two syntheses of rhodinose, both from car-

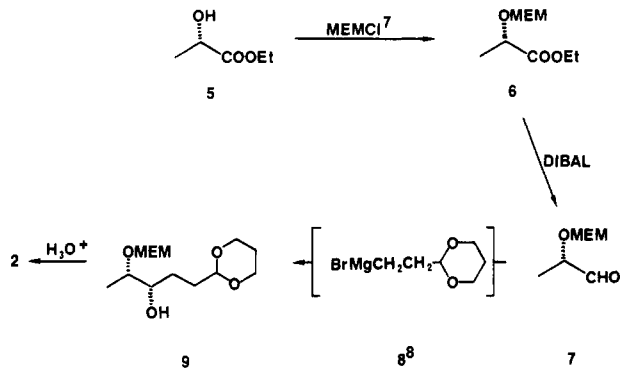


(1) Rinehart, K. L., Jr.; Borders, D. B. *J. Am. Chem. Soc.* **85**, 4083 (1963).

(2) (a) Stevens, C. L.; Blumbergs, P.; Wood, D. L. *J. Am. Chem. Soc.* **86**, 3592 (1964). (b) Rhodinose is also a component of the oligosaccharides present in the rhodomycin family of anthracycline antibiotics: Brockmann, H.; Greve, H. *Tetrahedron Lett.*, 831 (1975) and references therein.

0022-3263/83/1948-2775$01.50/0

Scheme I



bohydrate precursors [L-rhamnose (**3**),[3] L-xylose (**4**)[4]], have been reported,[5,6] but they are low yield and quite lengthy by current standards, especially if the lack of complexity of **2** is taken into account.

We now report a four-step synthesis of **2** from readily available (*S*)-ethyl lactate (**5**), which proceeds in 31% overall yield (Scheme I). The key reaction in the sequence takes advantage of the precedented[9] propensity of chiral α-alkoxy aldehydes to suffer "chelation-controlled"[9c] addition of Grignard reagents and proceeds with a diastereoselectivity of 19:1 at −100 °C.[10]

Experimental Section

General Procedures. Melting points were determined in Pyrex capillaries and are uncorrected; specific rotations were obtained with a Perkin-Elmer 141 polarimeter and IR spectra were taken on a Perkin-Elmer 599B spectrophotometer. ^{1}H NMR spectra were recorded at 60 MHz on an Hitachi Perkin-Elmer R-24 NMR spectrometer and mass spectra on an Hitachi Perkin-Elmer RMS-4 mass spectrometer. High-pressure liquid chromatographic (HPLC) separations were performed on a Varian Model 5000 chromatograph equipped with a Varian Varichrome UV–vis detector and a 4 mm × 30 cm C_{18}-μBondapak column. Thin-layer chromatography (TLC) was performed on 0.25-mm Machery-Nagel Sil G/UV_{254} plastic sheets; spots were visualized with phosphomolybdic acid. Column chromatography was carried out according to the procedure of Still et al.[11] Elemental analyses were performed by Galbraith Laboratories.

Except for the hydrolysis of **9** to **2**, all reactions were conducted under an atmosphere of nitrogen.

(*S*)-Ethyl 2-[(2-Methoxyethoxy)methoxy]propionate (6). *N,N*-Diisopropylethylamine (48.5 g, 65 mL, 0.375 mol) was added to dry distilled methylene chloride (ca. 250 mL) and the mixture cooled in an ice bath. (*S*)-Ethyl lactate (29.5 g, 29.0 mL, 0.25 mol) was added in one portion and the mixture stirred at room temperature for 15 min. (2-Methoxyethoxy)methyl chloride (46.75 g, 46 mL, 0.375 mol, Aldrich) was added dropwise over 0.5 h and the mixture stirred for an additional 4 h. The mixture was then washed successively with distilled water (3 × 150 mL), 10% hydrochloric acid (150 mL), and water (150 mL) and dried over anhydrous sodium sulfate. Removal of solvent in vacuo gave 50 g (90%) crude ester that was over 90% pure as judged by TLC (chloroform/methanol, 95:5) and NMR and was ordinarily used without further purification. Analytically pure material was obtained by distillation: bp 75–76.5 °C (5 torr); NMR ($CDCl_3$) δ 1.30 (3 H, t, *J* = 7 Hz), 1.54 (3 H, d, *J* = 8 Hz), 3.35 (3 H, s), 3.4–3.9 (4 H, m), 4.16 (2 H, q, *J* = 7 Hz), 4.24 (1 H, q, *J* = 8 Hz), 4.77 (2 H, s); $[\alpha]^{23}_D$ −42.5° (*c* 1.0, absolute EtOH). Anal. Calcd for $C_9H_{18}O_5$: C, 52.42; H, 8.73. Found: C, 52.59; H, 8.83.

(*S*)-2-[(2-Methoxyethoxy)methoxy]propanal (7). Crude ester **6** (80 g, 0.386 mol) was dissolved in 500 mL of dry distilled methylene chloride at −78 °C and the mixture mechanically stirred. Diisobutylaluminum hydride (56.8 g, 0.40 mol, 1 M solution in hexane, Aldrich) was added over a period of 15 min and the mixture stirred for 1 h at −78 °C followed by quenching at −78 °C with 100 mL of a saturated solution of ammonium chloride. Hydrochloric acid (4%, 200 mL) was added, the cooling bath removed, and the mixture stirred for $^1/_2$ h. The mixture was subsequently extracted with methylene chloride (4 × 200 mL), and the extracts were dried over anhydrous sodium sulfate. Removal of solvent gave 55 g of crude aldehyde. Distillation gave 53 g (85%) of pure **7**: bp 53–54 °C (0.6 torr); NMR δ 1.32 (3 H, d, *J* = 7 Hz), 3.38 (3 H, s), 3.48–3.9 (4 H, m), 4.1 (1 H, q of d, *J* = 7, 2 Hz), 4.81 (2 H, s), 9.62 (1 H, d, *J* = 2 Hz); $[\alpha]^{23}_D$ −29.3° (*c* 1.0, absolute C_2H_5OH). Anal. Calcd for $C_7H_{14}O_4$: C, 51.84; H, 8.70. Found: C, 51.90; H, 8.72.

(*S,S*)-α-[1-((2-Methoxyethoxy)methoxy)ethyl]-1,3-dioxane-2-propanol (9). Magnesium turnings (12 g, 0.5 mol) were taken in dry tetrahydrofuran (400 mL) in a flask provided with a condenser. 2-(2-Bromoethyl)-1,3-dioxane (71 g, 50 mL, 0.36 mol, Fluka) was added over a period of 5 min. The exothermic reaction was controlled by cooling periodically in ice. The mixture was subsequently refluxed for 15 min and then stirred at room temperature for an additional 30 min.

The clear solution of the Grignard reagent (**8**)[8] was added via syringe over 1 h to a solution of 8.0 g (0.050 mol) of aldehyde **7** in 200 mL of dry tetrahydrofuran maintained at −100 °C (*internal*[10] temperature, a liquid N_2/dry ice bath was employed). The mixture was stirred at −100 °C for an additional 1 h and the solvent removed. The residue was poured cautiously into 500 mL of 0.5% hydrochloric acid and extracted with ether (4 × 200 mL). The organic layer was dried over anhydrous sodium sulfate and the solvent removed to give the crude alcohol that was purified by column chromatography, using 1:1 acetone/chloroform as eluent to afford the desired product (**9**) and the undesired isomer in a 95:5 ratio (10 g, 75%) as determined by HPLC.[12] The desired **9** can be separated from its epimer by careful flash chromatography (1:1 acetone/chloroform). Analytically pure **9** was obtained by HPLC, using methanol as the eluent: NMR δ 1.20 (3 H, d, *J* = 6 Hz), 1.45–1.9 (4 H, m), 3.12 (1 H, br s, OH), 3.35 (3 H, s), 3.4–4.2 (11 H, m), 4.57 (1 H, t, *J* = 3 Hz), 4.75 (2 H, s); $[\alpha]^{23}_D$ −6.5° (*c* 1.0, absolute C_2H_5OH). Anal. Calcd for $C_{13}H_{26}O_6$: C, 56.10; H, 9.42. Found: C, 56.25; H, 9.32.

2,3,6-Trideoxy-L-*threo*-hexose (2, Rhodinose). Alcohol **9** (2.78 g, 10 mmol) was dissolved in a mixture of 50 mL of acetone, 10 mL of water, and 10 mL of 10% hydrochloric acid and heated at 55 °C for 2 h at which time the reaction was judged completed by TLC (1:1 CH_3COCH_3/CH_3OH). The acidic solution was neutralized with 15 mL of 3% sodium bicarbonate solution and the solvent removed in vacuo. The crude product was purified by column chromatography (silica gel, 1:1 $CH_3COCH_3/CHCl_3$) to give 760 mg (57%) of **2** as a pale-yellow oil. Analytically pure material was obtained by HPLC, using 1:1 methanol/water as solvent. The NMR and IR spectra of **2** are in agreement with those reported.[4] Anal. Calcd for $C_6H_{12}O_3$: C, 54.55; H, 9.15. Found: C, 54.50; H, 9.30. The (2,4-dinitrophenyl)hydrazone derivative of **2** was prepared in 30% yield.[13] After recrystallization

(3) Haines, A. H. *Carbohydr. Res.* **21**, 99 (1972).
(4) Knollman, R.; Dyong, I. *Chem. Ber.* **108**, 2021 (1975).
(5) The antipode of **2** has been prepared from triacetylglucal (see ref 2a).
(6) The preparation of benzyl 4-*O*-acetyl-2,3,6-trideoxy-L-*threo*-hexopyranoside (a protected form of **2**) from L-rhamnose has also been described: El Khadem, A. H.; Cermak, R. C. *Carbohydr. Res.* **75**, 335 (1979).
(7) Corey, E. J.; Gras, J.-L.; Ulrich, P. *Tetrahedron Lett.*, 809 (1976).
(8) Stowell, J. C. *J. Org. Chem.* **41**, 560 (1976).
(9) (a) Wolfrom, M. L.; Hanessian, S. *J. Org. Chem.* **27**, 1800 (1962). (b) Nakati, T.; Kishi, Y. *Tetrahedron Lett.*, 2745 (1978). (c) Still, W. C.; Schneider, J. A. *Ibid.* **21**, 1035 (1980).
(10) The degree of stereoselectivity is temperature dependent. The **9**/*epi*-**9** ratio is 80:20 and 90:10 at −30 and −78 °C (internal temperatures), respectively. Use of temperatures below 100 °C was precluded by the freezing of the reaction mixture. The degree of stereoselectivity is also dependent on the molar ratio of substrate to Grignard reagent. In simultaneous experiments conducted at −78 °C using the same stock solution of **8**, reaction of **7** with **8** prepared from **4** and 7.2 equiv of the halide gave **9**/*epi*-**9** product ratios of 80:20 and 90:10, respectively.
(11) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **43**, 2923 (1978).
(12) The UV–vis detector (see general comments at beginning of Experimental Section) was set at 250 nm. Calibration studies at several different wavelengths indicated that relative peak areas of **9** and its epimer did not vary with detector wavelength.

from 95% ethanol it melted at 120–122 °C [lit.[2a] mp 121–122 °C (for enantiomer[14])].

Acknowledgment. Support of this work by a grant (GM 28968) from the National Institutes of Health is gratefully acknowledged. We also thank Professor W. C. Still and Mr. J. A. Schneider[9c] for helpful information and Dr. K. L. Loening (Chemical Abstracts Service) for an illuminating discussion.

Registry No. **2**, 35903-48-1; **5**, 687-47-8; **6**, 86163-00-0; **7**, 86163-01-1; **9**, 86163-02-2; 2-(2-bromoethyl)-1,3-dioxane, 33884-43-4.

(13) Shriner, R. L.; Fuson, R. C.; Curtin, D. Y. "The Systematic Identification of Organic Compounds"; 5th ed.; Wiley: New York, 1964; p 253.

(14) Haines[3] encountered dimorphism and/or isomerism and reports various melting points. We did not experience this complication.

The [12]Annulene Anion Radical

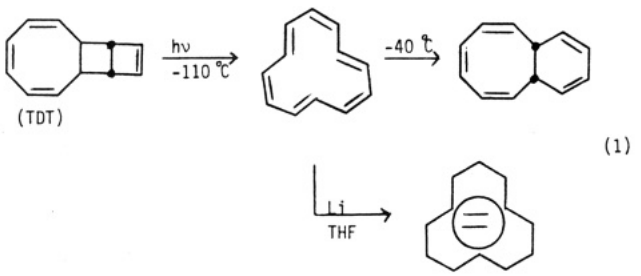
Gerald R. Stevenson,* Rosario Concepcion, and Richard C. Reiter

Department of Chemistry, Illinois State University, Normal, Illinois 61761

Received July 22, 1982

There has been considerable interest in the addition of a single electron to annulenes that are antiaromatic in the Hückel sense. However, only two such anion radicals (containing $4n + 1$ π electrons) have been generated and observed. Both [8]annulene and [16]annulene readily accept an additional electron from either an alkali metal or an electrode to yield the respective anion radical.[1,2] Here, we report the preparation and ESR observation of the missing annulene anion radical that lies between the anion radicals of [8]annulene and [16]annulene.

Neutral [12]annulene has been observed at low temperature and was prepared via the photoirradiation of *syn*-tricyclo[6.4.0.0^{9,12}]dodeca-2,4,6,10-tetraene (TDT) at −110 °C.[3] At −40 °C [12]annulene rearranges irreversibly to its bicyclic tautomer as shown in eq 1.



(1)

The unstable [12]annulene can be reduced either polarographically or via alkali metal in THF (tetrahydrofuran) to give the [12]annulene dianion (eq 1).[4] This dianion is very stable, and its ^{1}H NMR signal remains unaltered at temperatures between −90 and +30 °C (NMR signals at 6.98, 6.23, and −4.6 ppm).

(1) (a) Strauss, H. L.; Katz, T. J.; Fraenkel, G. K. *J. Am. Chem. Soc.* **1963**, *85*, 2360. (b) Katz, T. J.; Fraenkel, G. K. *Ibid.* **1960**, *82*, 3785. (c) Stevenson, G. R.; Concepcion, J. G. *J. Phys. Chem.* **1972**, *76*, 2176.

(2) (a) Oth, J. F. M.; Baumann, H.; Gilles, J. M.; Schröder, G. *J. Am. Chem. Soc.* **1972**, *94*, 3498. (b) Concepcion, J. G.; Vincow, G. *J. Phys. Chem.* **1975**, *79*, 2037.

(3) Oth, J. F. M.; Rottele, H.; Schröder, G. *Tetrahedron Lett.* **1970**, *1*, 61.

(4) Oth, J. F. M.; Schröder, G. *J. Chem. Soc. B* **1971**, 904.

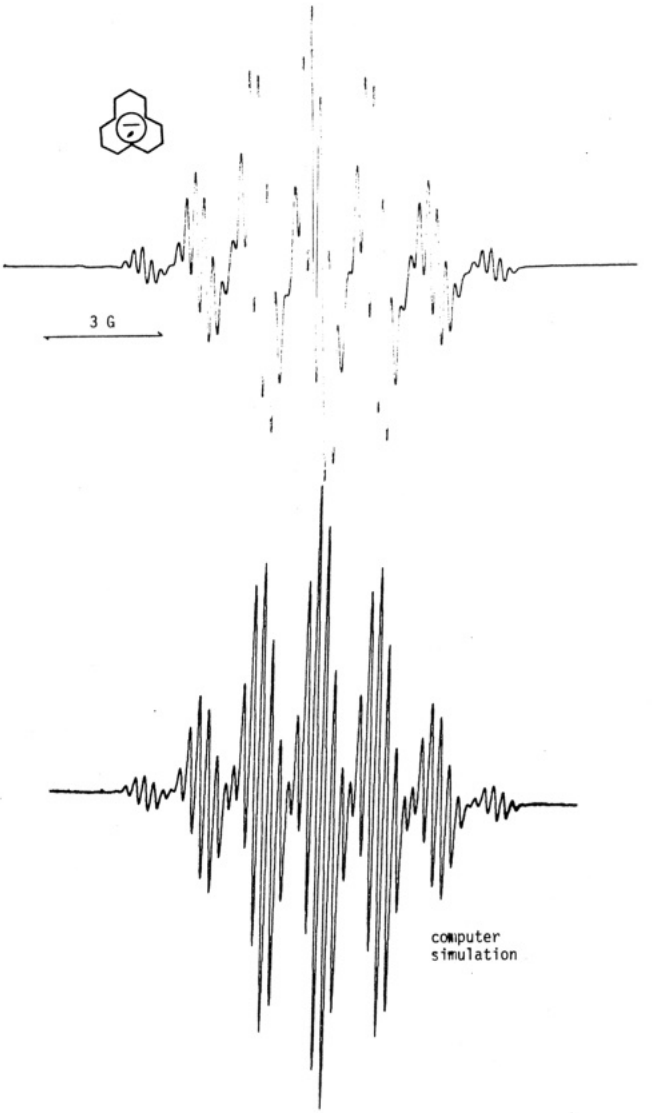


Figure 1. ESR spectrum (upper) of the [12]annulene anion radical recorded at −100 °C. The lower spectrum is a computer simulation generated by using the experimental coupling constants listed in Table I. This spectrum looks very similar to the small picture of the ESR spectrum in ref 4 that was recorded during the generation of the annulene dianion. No mention of the spectrum appears in this paper[4] or in any other to our knowledge. Continued reduction of the solution results in the disappearence of the ESR signal and simultaneous appearance of the NMR spectrum for the [12]annulene dianion. Under high-gain conditions, no further lines can be observed either at lower or higher fields.

Experimental Section

Samples of TDT dissolved in THF were sealed under vacuum in a 4-mm quartz EPR tube. A potassium mirror was deposited at the top of the tube out of contact with the solution. The frozen solution was irradiated at liquid nitrogen temperature with a high-pressure mercury lamp for 40 h. After each hour of irradiation the solution was allowed to thaw at −100 °C in an acetone slush bath. The sample was then replaced in liquid nitrogen and the irradiation continued. At the end of the irradiation period, the quartz tube was inverted, allowing the [12]annulene solution to come into contact with the potassium mirror at −100 °C. Low-temperature EPR experiments were then carried out on the potassium-reduced solutions with a Varian E-4 EPR spectrometer.

Results and Discussion

The EPR pattern from the reduction of [12]annulene with potassium metal results from two sets of three equivalent protons with coupling constants of 1.53 and 1.30

0022-3263/83/1948-2777$01.50/0