Reactions of Delocalized Dicarbanions with Dihalides

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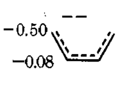
The reaction of butadiene dianion, hexatriene dianion, 2-methyleneallyl dianion, and 2-methylenepentadienyl dianion with dihalides $X(CH_2)_{1-4}X$ gave, in variable yield, products with three-to seven-membered rings as well as some acyclic products. The predominant cyclic products generally came from initial alkylation at the most negatively charged carbon of the dianion to give the most stable monoanion intermediate, followed by cyclization to give the smallest ring possible. These reactions appear to provide the most convenient route to some of the observed products.

The reaction of a carbanion with an alkyl halide is one of the most commonly used carbon–carbon bond-forming reactions. Recently delocalized dicarbanions **1–4** have been prepared and shown to react in good yield with 2 equiv of alkyl halide.[1] The current study was undertaken to determine the feasibility of treating dianions **1–4** with dihalides to give a series of cyclic hydrocarbons, some of which are currently available only by multistep procedures using unusual starting materials.[2]



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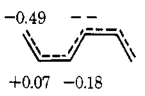
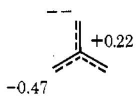


2



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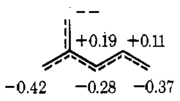

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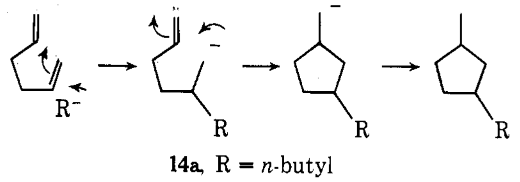
Results

Dianions **1–4** were prepared in 25–90% yield as crystalline dilithium salts solvated with two tetramethylethylenediamine (TMEDA) molecules[3] by metalating the appropriate alkene or diene.[1] Although dianion yields would have been higher if the dianion in the supernatent liquid were included, it was considered desirable to avoid contamination from the intermediate monoanion which remains in solution. The salts of **1** and **3** had not been crystallized previously.

The dihalides used were $ClCH_2Cl$, ICH_2I, and $Br(CH_2)_{2-4}Br$. To favor ring formation over polymerization, high dilution techniques were indicated. After it was determined in one case that simultaneous addition of dilute solutions of the two reactants to a large volume of vigorously stirred solvent[5] gave only slightly better yields than adding a dilute dianion solution to a vigorously stirred 0.1 M dihalide solution, the latter technique was employed.

The products obtained are summarized in Table I. They were isolated by distillation and preparative GC, and characterized by ^1H NMR, mass spectrometry, and in many cases by comparison with authentic samples. The *E* configurations of **8b** and **8c** were demonstrated by oxidation to (*E*)-cyclopentane-1,2-dicarboxylic acid[6] and (*E*)-cyclohexane-1,2-dicarboxylic acid,[7] respectively. The 1,2-divinylcyclopropane isolated must have the *E* configuration as shown in **8a** since it is stable to at least 125 °C, whereas the *Z* isomer Cope rearranges above 0 °C.[8]

During the reactions involving **2** prepared by dimetalating 1,5-hexadiene with *n*-butyllithium, 1-methyl-3-*n*-butylcyclopentane (**14a**) was noted among the products. That this is a minor by-product in the dimetalation step was shown by isolating it in 7% yield from the mother liquors from the preparation of **2**. Similarly, when *tert*-butyllithium was substituted for *n*-butyllithium, 1-methyl-3-*tert*-butylcyclopentane (**14b**) was formed in 7% yield. These reactions may occur as follows, or perhaps with the first two steps concerted:



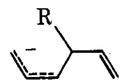
14a, R = *n*-butyl
b, R = *tert*-butyl

Discussion

Of the products listed in Table I, **5a–c**, **7a–c**, **8a–c**, **11a–b**, **12a–c**, and **13**, with three- to seven-membered rings, were from the desired reactions. Where total yields of these cyclization products were low, it was not due to the formation of further isomeric cyclization products (e.g., cyclopentene in the first reaction), but to side reactions. Most of the by-products were higher boiling and no doubt arose from two intermolecular alkylations rather than an intermolecular alkylation followed by an intramolecular one; these side reactions could have been lessened by employing higher dilution.

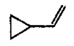
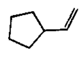
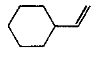
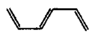
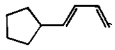
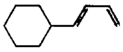
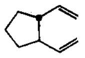
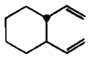
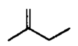
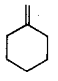
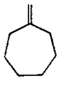
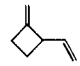
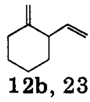
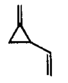
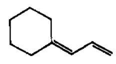
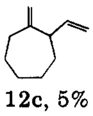
The diethylations of these same four dianions[1] are far from perfect models for these cyclizations, especially in the case of **2**, which gives only 1,4 and 1,6 diethylation, but only 1,2 and 3,4 dialkylation in its cyclic reactions. However, it might be expected that the formation of the *first* carbon–carbon bond would occur with essentially the same distribution over the carbons of the dianion, whereas in the *second* alkylation, the distribution pattern could differ greatly between the intermolecular and intramolecular cases. The diethylation products could in all cases be rationalized by initial attack at an end of the dianion system to give the most stable monoanion intermediate, e.g., pentadienyl anion **15a** from **2**.[1] However, although no 3,4-diethyl-1,5-hexadiene was found in the diethylation of **2**, **8a–c**, the analogous cyclic products, were found in significant amounts and prove that some of the initial alkylation of **2** by a dihalide occurs at carbon 3, the site of *second* highest electron density,[9] giving an ene-allylanion intermediate **15b**. Probably some of the 81% of diethylation products of **2** which could have come from initial attack at either carbon 1 or 3 similarly came from initial attack at carbon 3 rather than all at 1 as was previously assumed. All of the cyclization products other than **8a–c** can be rationalized as coming from *initial alkylation at the most negatively charged carbon of the dianion to give the most stable monoanion intermediate, followed by cyclization to give the smaller of two possible ring sizes,* i.e., three rather than

15a



15b

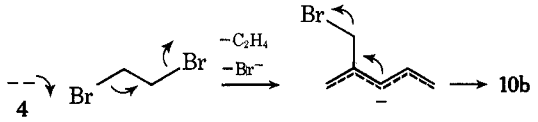
Table I. Isolated Products and Yields

Starting Materials	ICH_2I	$Br(CH_2)_2Br$	$Br(CH_2)_3Br$	$Br(CH_2)_4Br$
1	 5a, 3% 6a, 7%	 6a, 33%	 5b, 8%	 5c, 3%
2	 7a, 20%[a] 6b, 10%	 6b, 61%	 7b, 8%	 7c, 0.6%
	 8a, 8%		 8b, 9%	 8c, 4%
3	 9, 5% 10a, 6%	 10a, 70%	 11a, 96%	 11b, 15%
4	 12a, 14%		 12b, 23%	
	10b, 10%	 10b, 100%	 13, 5%	 12c, 5%

[a] In this case, $ClCH_2Cl$ was used instead of ICH_2I; yields of these products might have been higher with ICH_2I. Other products included chlorobenzene (5%), 2,4,6-octatriene (3%), and 1,3,5-octatriene (2%).

five, four than six, five than seven, six than eight, and seven than nine. **12b** and **13** can arise via competing cyclizations of the same precursor to give the same size ring.

Instead of giving cyclization products, ethylene dibromide (and to a minor extent, the methylene halides) oxidized the dianions, giving two halide ions, 1 mol of ethylene, and, in relatively high yield, **6a, 6b, 10a,** or **10b,** obtained by the loss of two electrons from the dianion. These reactions may proceed by displacement on bromine as indicated below for **4**:



These displacements on bromine occur readily with ethylene dibromide because the leaving group is bromide ion, and most of the time this dihalide is in the anti conformation, favoring this reaction and hindering displacement on carbon. Only the *E* stereoisomer of **6b**[10] was observed, probably reflecting a very large predominance of *E* configuration for the central bond of **2**.[1,4] Dianions are oxidized similarly by I_2, but the yield of **6b** from **2** with I_2 was only 8%, probably because **6b** reacts further with I_2.

The methylene halides are sufficiently acidic to protonate these dianions, especially the very basic **1** and **3**. Yields of diprotonation products from **1–4** were 30, 10, 60, and 15%, respectively. With methylene *chloride*, **4** gave a 25% yield of diprotonation products and virtually no **10b** or **12a**. An unusual product from **3** was 2-methyl-1-butene (**9**), apparently formed by alkylation of the monoanion with methyl iodide formed from methylene iodide.

Among the unexpected products was chlorobenzene, obtained in 5% yield from the reaction of **2** with methylene chloride; this is reminiscent of the formation of biphenyl (77% yield) by heating 3-phenylhexatriene dianion at 60 °C.[11] Other unusual products from the reaction of **2** with methylene chloride were 1,3,5- and 2,4,6-octatrienes (2 and 3%, respectively).

Owing to the shortness of these syntheses and the ease in separating the products (most side reactions lead to higher molecular weight substances readily removed by distillation), these reactions may serve as the most convenient ways of preparing some of these substances. For example, the previous syntheses of **8a**,[12] **8b**,[13] and **8c**[13] each required many steps. **6b** was prepared previously in considerably lower yield by a several-step procedure which gives a mixture of stereoisomers rather than *E* only.[14] **10b** and its thermolysis product 3-methylenecyclopentene may be more readily prepared by the procedure described herein than by earlier methods.[15] **7b, 12a, 12b,** and **12c** have to our knowledge not been prepared previously.

Experimental Section

All solvents and starting alkenes were distilled from either CaH or $LiAlH_4$ and stored under argon over molecular sieves. The gases, (*Z*)-2-butene and isobutylene, were distilled from lecture bottles just prior to use and not further purified. *n*-Butyllithium and *tert*-butyllithium solutions in hexane or pentane were used as received from Alfa Inorganics. Columns for preparative GC were 15–25 ft × 0.25 in., packed with 20% Carbowax 20M on Chromosorb P, and operated at 50–160 °C.

Preparation of Dicarbanions 1–4. Each dianion was prepared and crystallized in 18 × 150 mm test tubes filled with argon and tightly capped with a rubber septum. To these tubes was added 10.0 ml (24 mmol) of 2.4 M *n*-butyllithium. The tubes were cooled in an ice–acetone bath and 3.6 ml (24 mmol) of anhydrous TMEDA was added. Upon warming to room temperature, the white, crystalline 1:1 complex dissolved whereupon 12 mmol of the corresponding precursor alkene was added via syringe. This mixture was set aside at room temperature until crystallization was complete. Just prior to use, the crystallized dianion was purified by removing the supernatent solution by syringe, washing the residue with hexane (optional), and drying in a stream of dry argon. The yield, necessary for the determination of the amount of dihalide to be used, was determined by weighing the dried anion. The precursor, crystallization time, solvent(s), and yield for each dianion follow: 1 [(*Z*)-2-butene; 3–5 weeks; TMEDA; 25–35%];[16] 2 (1,5-hexadiene; overnight; TMEDA or THF or ether; 80–90%); 3 (isobutylene; 3–7 days; TMEDA or THF; 50–70%); 4 (2-methyl-1,4-pentadiene; 2–4 weeks; TMEDA or THF; 30–40%).

Reaction of Dianions 1–4 with Dihalides. To an argon-filled, septum-capped, 250-ml round-bottomed flask equipped with a magnetic stirring bar and cooled by a dry ice–acetone bath was added 30–50 ml of anhydrous solvent and a 10% excess of dihalide. The solvent used depended on the properties of the desired products. For products boiling below 50 °C (**5a, 6a, 9,** and **10a**) dibutyl ether was used. Diethyl ether was suitable for materials boiling above 50 °C, while THF and hexane were used for products with boiling points above 90 °C.

The reaction was conducted with rapid stirring at −78 °C by adding dianion solution dropwise via syringe through the septum cap. Dibutyl ether tended to crystallize at these temperatures but this problem was avoided by either conducting the reaction rapidly or warming to no higher than −50 °C. The product was worked up in different ways depending on the product's boiling point. The low-boiling **5a, 6a, 9,** and **10a** were isolated by fractional distillation through a short Vigreux column, collecting all material until the distillation head temperature exceeded 100 °C. A slow stream of argon swept out further product, which was collected in a series of traps cooled in acetone–dry ice baths. The crude product was further purified by preparative GC. Products boiling above 50 °C were worked up by quenching with 20 ml of water unless the solvent was THF. The organic layer was separated and the aqueous phase was discarded after being extracted with 2 × 15 ml of ether. The combined organic phases were washed with dilute sulfuric acid to extract amines. An emulsion generally formed when the washings became acidic but the problem could be minimized by making the acid wash emulsion slightly basic, separating the aqueous phase and backwashing it with 2 × 15 ml of ether, combining the organic phases and extracting the combined solution with one final 10-ml wash of dilute sulfuric acid. If an emulsion still formed, it was separated by centrifuging. The organic layer was then washed with water, recentrifuged if necessary, and the separated organic layer washed with 5% aqueous sodium bicarbonate. The product solution was dried over sodium hydroxide pellets and filtered into a round-bottomed distillation flask and the solvent was removed by careful fractional distillation through a 3-ft tantalum wire column. When solvent removal was nearly complete, the distillation was interrupted, the residue was cooled and drawn into a syringe, and the material was flash distilled under vacuum. The purified product, free from polymer, was collected in a dry ice cooled trap and was suitable for preparative GC.

If THF was used as the initial solvent, the aqueous workup was avoided since much of the product was carried into the aqueous washes and thereby lost. Instead the crude reaction product was fractionally distilled, removing further THF by periodically adding spectrograde hexane and continuing the distillation until all THF had codistilled. The cooled residue was then diluted with 20 ml of ether and worked up as described in the preceding paragraph.

The structure of **7b** was deduced from its spectral properties:[17] MS *m/e* 122 (m), 107, 93, 79, 67 (base); NMR δ 6.3 (ddd, 1, J = 8.5, 9.5, 16.5 Hz), 5.9 (m, 2), 5.0 (dd, 1, J = 2.0, 16.5 Hz), 4.9 (dd, 1, J = 2.0, 9.5 Hz), 2.4 (m, 1), 1.6 (m, 8).

For **12a**: NMR δ 6.0 (ddd, 1, J = 7.0, 9.5, 17.0 Hz), 5.1 (d, 1, J = 17.0 Hz), 5.1 (d, 1, J = 9.5 Hz), 4.9 (m, 2), 3.7 (m, 1), 2.7 (m, 2), 2.1 (m, 2).

Anal. Calcd for C_7H_{10}: C, 89.29; H, 10.71. Found: C, 89.13; H, 10.57.

For **12b**: MS *m/e* 122 (m), 107, 93, 79 (base), 67; NMR δ 6.0 (ddd, 1, J = 7.0, 9.0, 18.0 Hz), 5.1 (dd, 1, J = 2.0, 9.0 Hz), 5.1 (dd, 1, J = 2.0, 18.0 Hz), 4.8 (m, 2), 2.8 (m, 1), 2.3 (m, 2), 1.7 (m, 6).

Anal. Calcd for C_9H_{14}: C, 88.45; H, 11.55. Found: C, 88.36; H, 11.51.

The structure of **12c** was deduced from the similarity of its NMR spectrum to those of **12a** and **12b**.[17] For **12c**: NMR δ 6.0 (ddd, 1, J = 6.0, 9.5, 17.5 Hz), 5.1 (d, 1, J = 9.5 Hz), 5.1 (d, 1, J = 17.5 Hz), 5.0 (m, 2), 3.1 (m, 1), 2.3 (m, 2), 1.8 (m, 8).

Preparation of Compounds 14a and 14b. The reaction was set up as for the preparation of dianion **2**, using *n*-butyllithium for preparing **14a** and *tert*-butyllithium for **14b**. After 12 h at room temperature, the dark red-black liquid was removed by a syringe and quenched into 30 ml of water. The organic layer was separated and treated as above to remove impurities except that the flash distillation was unnecessary. Starting with 1.0 g (12 mmol) of 1,5-hexadiene, the yield of both **14a** and **14b** after preparative GC was 115 mg (7%).

Stereochemistry of 8b and 8c. According to the method of Arai and Crawford,[12] 58.5 mg (0.48 mmol) of **8b** was added to a septum-capped 50-ml Erlenmeyer flask containing a stirring bar, 1.65 g (7.67 mmol) of sodium periodate, 20 mg (0.13 mmol) of potassium permanganate, and 45 ml of water. After 6 days, the reaction was worked up by filtering off the inorganic solids, extracting the organic phase exhaustively with ether, evaporating the ether, and dissolving the solid residue in 1 ml of hot water. In a few days crystals of acid formed which had mp 160–162 °C [lit. for (*Z*)-1,2-cyclopentanedicarboxylic acid, 139–140 °C; (*E*)-1,2-cyclopentanedicarboxylic acid, 162–163 °C].[6] These crystals showed no melting point depression on mixing with an authentic sample of (*E*)-1,2-cyclopentanedicarboxylic acid.

The identical procedure using 65.5 mg (0.48 mmol) of **8c** gave product with mp 223–226 °C [lit. for ((Z)-1,2-cyclohexanedicarboxylic acid, 192 °C; (*E*)-1,2-cyclohexanedicarboxylic acid, 227–229 °C].[6,7]

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Registry No.—**1,** 53721-70-3; **2,** 53721-71-4; **3,** 53721-69-0; **4,** 53721-72-5; **7b,** 58298-55-8; **12a,** 58298-56-9; **12b,** 19995-92-7; **12c,** 58298-57-0; (*Z*)-2-butene, 590-18-1; 1,5-hexadiene, 592-42-7; isobutylene, 115-11-7, 2-methyl-1,4-pentadiene, 763-30-4; ICH_2I, 75-11-6; $Br(CH_2)_2Br$, 106-93-4; $Br(CH_2)_3Br$, 109-64-8; $Br(CH_2)_4Br$, 110-52-1.

References and Notes

(1) R. B. Bates, W. A. Beavers, M. G. Greene, and J. H. Klein, *J. Am. Chem. Soc.*, **96**, 5640 (1974).

(2) For the preparation of a cyclooctane ring in 25% yield by reaction of a delocalized dianion with a dihalide, see M. P. Cooke, Jr., and R. Goswami, *J. Am. Chem. Soc.*, **95**, 7891 (1973).

(3) Only one carbanion (**2**) is positively known to have this composition,[4] but the others appear to from quenching studies.

(4) S. K. Arora, R. B. Bates, W. A. Beavers, and R. S. Cutler, *J. Am. Chem. Soc.*, **97**, 6271 (1975).

(5) E. J. Corey and E. Block, *J. Org. Chem.*, **31**, 1663 (1966).

(6) S. F. Birch, R. A. Dean, N. J. Hunter, and E. V. Whitehead, *J. Org. Chem.*, **20**, 1178 (1955); "Dictionary of Organic Compounds", Vol. 2, Oxford University Press, London, 1965, p 728.

(7) D. E. Applequist and N. D. Werner, *J. Org. Chem.*, **28**, 48 (1963).

(8) J. M. Brown, B. T. Golding, and J. J. Stofko, *J. Chem. Soc., Chem. Commun.*, 319 (1973).

(9) The charge calculated on each carbon atom in dianions **1–4** is shown on its formula; an INDO program was used and since hydrogens were included, the sums of charges on carbon do not total 2.

(10) J. C. H. Hwa, P. DeBenneville, and H. Sims, *J. Am. Chem. Soc.*, **82**, 2537 (1960).

(11) R. M. Magid and S. W. Wilson, *Tetrahedron Lett.*, 19 (1971).

(12) M. Arai and R. J. Crawford, *Can. J. Chem.*, **50**, 2158 (1972).

(13) E. Vogel, K. H. Ott, and K. Gajek, *Angew. Chem.*, **71**, 172 (1961).

(14) "Organic Syntheses", Collect. Vol. V, Wiley, New York, N.Y., 1973, p 608.

(15) T. C. Shields, W. E. Billups, and A. R. Lepley, *J. Am. Chem. Soc.*, **90**, 4749 (1968); W. E. Billups, T. C. Shields, W. Y. Chow, and N. C. Deno, *J. Org. Chem.*, **37**, 3676 (1972).

(16) The crystalline form of **1** referred to here is red. In some runs, orange crystals, relatively insoluble, formed first; on longer standing they were replaced by the red solid.

(17) Elemental analyses on **7b** and **12c** were 2–3% low on carbon, presumably owing to partial oxidation on exposure to air.