

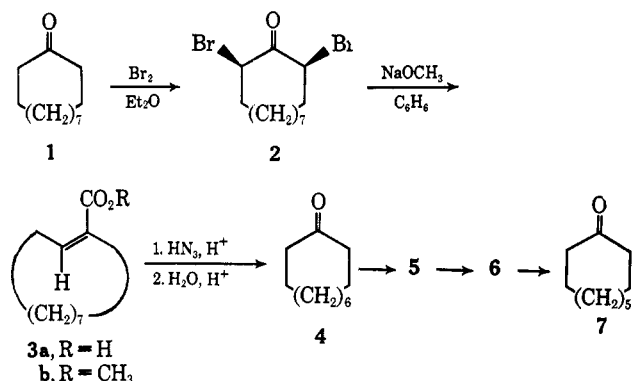
A Convenient Synthesis of Cycloundecanone and Cyclodecanone

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Cycloundecanone (4) and cyclodecanone (7) have been synthesized by several approaches.¹ The generally preferred one involves the acyloin condensation; however, recently Schank and Eistert synthesized 4 in about 25% over-all yield by ring contraction of cyclododecanone (1).^{1b} Their reaction sequence was initiated by the dibromination of 1 giving 2, which underwent the Favorskii rearrangement to 3a, the azide of which was converted into the isocyanate (Curtius rearrangement) which upon hydrolysis gave 4. At this time,^{1b} the configurations of 2 and 3a were unknown.



We report here a synthesis of 4 from 1 in over-all yields consistently ranging between 85 and 90%. The improvement in this synthesis as compared with that reported by Schank and Eistert^{1b} is ascribed to (1) modifying their procedure for the bromination of 1 to give 2, (2) carrying out the Favorskii rearrangement on 2 under anhydrous conditions to give 3b,² and (3) substituting the Schmidt for the Curtius reaction in the conversion of 3 into 4. A repetition of this reaction sequence starting with 4 but, without purification of the 2,11-dibromocycloundecanone (5) and methyl 1-cyclodecene-1-carboxylate (6), led to 77% (over-all yield) of 7.

The configurations of 2 and 3a,b have been established as *cis* and *trans*, respectively.³ Under the conditions described below, the Favorskii rearrangement proceeds essentially quantitatively on either the *cis* or *trans* dibromo ketones.

Experimental Section

Cyclododecanone (1), melting at 61.5–62° cor, was obtained by recrystallizing commercial 1 from ethyl acetate (70 g/100 ml) followed by washing with cold (0°) petroleum ether (bp 30–60°) and drying under vacuum over phosphorus pentoxide.

(1) (a) E. H. Rodd, Ed., "Chemistry of Carbon Compounds," Vol. II, Elsevier Publishing Co., New York, N. Y., 1953, p 270 f; K. Schank, B. Eistert, and J. H. Felzmann, *Chem. Ber.*, **99**, 1414 (1966); Rhone-Poulenc S. A., Netherlands Patent 6,605,908 (1966); see *Chem. Abstr.*, **66**, 85538s (1967); K. C. Brannock, R. D. Burpitt, V. W. Goodlett, and J. Y. Tweatt, *J. Org. Chem.*, **29**, 818 (1964); E. Müller and M. Bauer, *Ann.*, **654**, 92 (1962); (b) K. Schank and B. Eistert, *Chem. Ber.*, **98**, 650 (1965); (c) A. C. Cope, J. W. Barthel, and R. D. Smith in "Organic Syntheses, Coll. Vol. IV, N. Rabjohn, Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, p 218.

cis-2,12-Dibromocyclododecanone (2).—Bromine (160 g, 1 mol) was added during *ca.* 15 min to a stirred and cooled solution of 182.1 g (1 mol) of 1 in 1.2 l. of anhydrous ethyl ether contained in a 2-l. erlenmeyer flask over a period of about 15 min (the rate of addition was comparable to that of bromine uptake by the solution). The ice bath then was removed and a second 160-g (1 mol) portion of bromine was added dropwise at the uptake rate. After the addition was about two-thirds complete, 2 crystallized suddenly and to the extent that the reaction mixture no longer could be stirred efficiently. At this point the addition of bromine was discontinued. The reaction mixture was cooled in an ice bath for 15 min and then filtered through a Buchner funnel. The solid was washed twice with 100 ml of anhydrous ether giving fraction one (*ca.* 100 g) of 2. The remainder of the bromine was added dropwise to the combined filtrate and washings over a period of 20 min. The reaction mixture was cooled and filtered, providing fraction two (*ca.* 120 g) of 2. The filtrate was concentrated under reduced pressure to *ca.* 150 ml giving fraction three (*ca.* 50 g) of 2 after filtration. This filtrate was concentrated further to about 100 ml and was left overnight in a glass-stoppered flask. The accumulated crystals were then collected by filtration giving fraction four (*ca.* 50 g) of 2.⁴ Fractions one to four of 2 were combined and recrystallized (by dissolving 2 in warm benzene (230 ml/100 g), filtering the resulting solution, and then adding an equal volume of petroleum ether (bp 30–60°) to the filtrate) to give 321.6 g of 2. An additional 11.5 g of 2 was obtained after equilibration⁴ in ether-HBr of the crude dibromo ketone isomers that were recovered from the mother liquors of all of the above operations to give a total yield of 333.1 g (98%), mp 126.5–172° cor (lit.⁵ mp 125°).

Cycloundecanone (4).—To a well-stirred suspension of 189 g (3.5 mol) of powdered sodium methoxide in 1.5 l. of dry benzene was added 340.1 g (1 mol) of 2 over a period of 35 min while maintaining the reaction temperature between 25 and 30° by means of an ice bath. After the addition of 2 was complete, the reaction mixture was stirred for 10 min at room temperature and then washed with 500 ml of water. The aqueous phase was extracted twice with ether. The combined organic phases were washed with 5% hydrochloric acid and concentrated sodium chloride solution, dried over anhydrous sodium sulfate, and finally the solvent was evaporated under reduced pressure to give 3b which by glpc and nmr was configurationally homogeneous and void of any major impurities.

Without further treatment, 3b was added through a long-stem funnel to 600 ml of slowly stirred sulfuric acid (97%), cooled to 0°, and contained in a three-necked flask fitted with a reflux condenser, drying tube, and thermometer. After stirring for several minutes, 500 ml of chloroform was added and the temperature of the mixture was raised to 35°. (*Caution:* The following operation is accompanied by the evolution of hydrazoic acid (bp 37°) which is toxic and may be violently explosive in its condensed state. Consequently it is recommended that the operation be conducted in a hood under the guard of a safety shield.) Sodium azide (78 g, 1.2 mol)⁶ was added to the reaction mixture in small portions over a period of 40 min while maintaining the reaction temperature between 35 and 40° through cooling.⁷ Stirring was continued for 5 min at 40° followed by cooling the reaction mixture to below 5° and then pouring it onto about 1 kg of crushed ice. Water (1.5–2 l.) was added and the chloroform was distilled from the aqueous mixture. The residue was steam distilled and the distillate extracted with the recovered chloroform and then twice with ether. The combined extracts were dried over anhydrous sodium sulfate and then evaporated

(2) The improvement here is that the yield of 3b which is obtained under anhydrous conditions has been for us consistently higher than that of 3a^{1b} which is obtained under aqueous conditions. However, the Schmidt reaction on 3a gave as good results as on 3b.

(3) E. W. Garbisch, Jr., and J. Wohllebe, *Chem. Commun.*, in press.

(4) At configurational equilibrium in ether at 26–30° (HBr catalyzed) the ratio *cis* 2/*trans* 2 is 80:20. The solubility of *cis* 2 is less than that of *trans* 2 in ether to the extent that the former crystallizes exclusively upon concentration of the ether solution. If the ether mother liquor is saturated in HBr, the remaining *trans* 2 undergoes equilibration leading to the gradual crystallization of *cis* 2. It is possible, therefore, to obtain *cis* 2 in yields up to 98% from the bromination of 1 which initially leads to a mixture of about 70% *cis* 2 and 30% *trans* 2.

(5) W. Ziegenbein, *Chem. Ber.*, **94**, 2989 (1961).

(6) The yield of 4 was not markedly changed by increasing the molar excess of sodium azide from 20 to 150%.

(7) Maintaining the reaction temperature at 25° led to the recovery of a substantial amount of unreacted 3a.

under reduced pressure. Distillation of the residue gave 154.9 g of **4** (92% yield): bp 109–110° (7 mm); mp 16° uncor; n_D^{25} 1.4794 (lit. bp 117°–118° (10 mm),^{1b} mp 15°,⁸ n_D^{20} 1.4810⁹). The infrared spectrum of **4** compared well with its published⁸ one.

Cyclodecanone (7).—Bromine, 162 g (ca. 1 mol), was added dropwise to a stirred solution of 84.1 g (0.5 mol) of **4** in 350 ml of anhydrous ether at roughly the bromine uptake rate while cooling the reaction mixture. After the addition was completed,¹⁰ the reaction mixture was poured onto 200 g of crushed ice followed by the addition of 100 ml of water and 150 ml of benzene. The aqueous phase was separated and extracted with 100 ml of benzene. The combined organic phases were washed successively with dilute aqueous solutions of sodium sulfite and sodium hydrogen carbonate and a concentrated aqueous solution of sodium chloride, and finally dried over anhydrous sodium sulfate. The ether then was evaporated and the resulting benzene solution was added dropwise to a stirred suspension of 95 g (1.75 mol) of sodium methoxide in 300 ml of dry benzene over a period of 30 min while maintaining the reaction temperature between 20 and 25°. The mixture was stirred for an additional 5 min at room temperature followed by work-up as described for **3b**. The crude **6** was added to 350 ml of sulfuric acid (97%) followed by the addition of 350 ml of chloroform. Sodium azide, 42 g (0.65 mol) was added to the stirred reaction mixture over a period of about 20 min while maintaining the reaction temperature between 35 and 38° through cooling. Work-up as described for **4** gave on distillation 59.2 g (77% yield) of **7**: bp 94.5–95° (6 mm); mp 26° uncor, n_D^{25} 1.4801 (lit. bp 99–101° (8 mm),^{1c} mp 25°,⁸ n_D^{25} 1.4806).^{1c} The infrared spectrum of **4** compared well with that previously published.⁸

Registry No.—**4**, 878-13-7; **7**, 1502-06-3.

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(8) Th. Burer and Hs. H. Gunthard, *Helv. Chim. Acta*, **39**, 356 (1956); **40**, 2054 (1957).

(9) H. C. Brown and K. Ichikawa, *Tetrahedron*, **1**, 221 (1957).

(10) The composition of the stereoisomeric 2,11-dibromocycloundecanones obtained is about 80% *cis* and 20% *trans*.

On the Structure of the Cycloheptatriene–Tetracyanoethylene Diels–Alder Adduct

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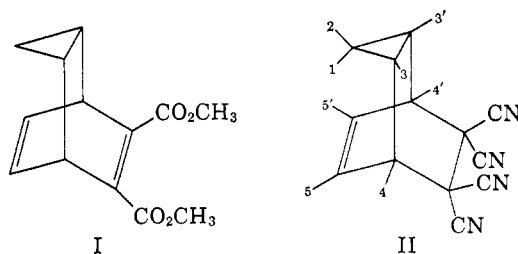
The reports¹ of novel reactivity of tetracyanoethylene (TCNE) with *N*-carbethoxyazepine prompt us to report our findings on the reactivity of the parent hydrocarbon with TCNE.

Only recently has the stereochemistry of a Diels–Alder adduct of cycloheptatriene (CHT) been rigorously established.² Goldstein and Gevirtz² combined an analysis of spectral properties and chemical correlations to demonstrate that the originally assumed³ structure (I) of the CHT–dimethylacetylenedicarboxylate adduct was correct. These authors² further pointed out that the mechanism of Diels–Alder addition to cyclohepta-

(1) J. E. Baldwin and R. A. Smith, *J. Amer. Chem. Soc.*, **87**, 4819 (1965); A. S. Kende, P. T. Izzo, and J. E. Lancaster, *ibid.*, **87**, 5044 (1965).

(2) M. J. Goldstein and A. H. Gevirtz, *Tetrahedron Lett.*, 4417 (1965).

(3) K. Alder and G. Jacobs, *Chem. Ber.*, **86**, 1528 (1953).



triene was not yet firmly established. For this reason, and also because tetracyanoethylene has shown unusual reactivity,⁴ we thought it important to establish conclusively the nature of the CHT–TCNE adduct.

Jordan and Elliott in the course of other work⁵ reacted TCNE and CHT and obtained a product which gave the proper elemental analysis and displayed infrared absorption consistent with the presence of the nitrile group and a three-membered ring. No additional proof was offered for the proposed structure, II.

We have repeated the reaction of TCNE with CHT using benzene as solvent. The adduct II, produced in good yield, possessed physical properties which agreed with the published data.⁵ The 100-MHz H^1 nmr spectrum of an acetone-*d*₆ solution of II containing internal TMS (see Table I), however, provides strong support for the proposed structure.

TABLE I
100-MHz NMR DATA OF II

Chemical shift (τ)	Relative area	Signal appearance	Assignment
9.65	1	Doublet of triplets $J_{1,2} = -6.1$ Hz $J_{1,3} = +3.8$ Hz	H-1
9.25	1	Doublet of triplets $J_{1,2} = -6.1$ $J_{2,3} = +7.5$	H-2
8.33	2	Complex	H-3, H-3'
5.77	2	Complex ^a	H-4, H-4'
3.77	2	Complex	H-5, H-5'

^a Irradiation at 5.77 causes the 3.77 signal to collapse to a singlet and the 8.33 signal to change into a doublet of doublets ($J_{1,3} = +3.8$ Hz; $J_{2,3} = +7.5$ Hz). (All signs of coupling constants are assigned in accordance with the assumption of a positive sign for 1J (C^{13} – H^1)).

The τ 9.65 and 9.25 signals are assigned to the *endo* (H-1) and *exo* (H-2) geminal cyclopropyl hydrogens, respectively. The higher field position of the resonance of the *endo* hydrogen is ascribable to the shielding effect of the double bond.⁶

Additional evidence for the assigned stereochemistry of II is provided by relative magnitudes of the coupling constants. The τ 9.65 signal is split by only 3.8 Hz as would be expected for *trans* vicinal coupling in a three-membered ring. The τ 9.25 signal, split by 7.5 Hz, is in accord with its assignment to the *exo* hydrogen

(4) J. K. Williams and R. E. Benson, *J. Amer. Chem. Soc.*, **84**, 1257 (1962); C. A. Stewart, Jr., *ibid.*, **84**, 117 (1962); A. T. Blomquist and Y. C. Meinwald, *ibid.*, **81**, 667 (1959); C. D. Smith, *ibid.*, **88**, 4273 (1966); E. LeGoff and R. B. LaCount, *Tetrahedron Lett.*, 277 (1965); D. N. Dhar, *Chem. Rev.*, **67**, 611 (1967).

(5) N. W. Jordan and I. W. Elliott, *J. Org. Chem.*, **27**, 1445 (1962).

(6) We have attempted to strengthen this argument by hydrogenating the double bond. If our logic was correct we would expect to find no signal above τ 9.50 in the nmr spectrum of the dihydro derivative. However, all attempts at hydrogenation have failed! Examination of a molecular model of II indicates severe crowding above and below the double bond.