The Diels-Alder Reaction of Cyclopentadiene with Nitroölefins. With 1-Nitroheptene and 1-Nitroöctene

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Cyclopentadiene is known to undergo Diels-Alder reactions with several 1-nitroalkenes: β-nitrostyrene in 86[1] to 95%[2,3] yield, nitroethylene[4] in 61[5] to 66%[6] yield, 1-nitropropene in 55[4] to 59%[7] yield, and 1-nitropentene in 72% yield,[4] giving adducts containing secondary nitro groups. Furthermore, cyclopentadiene reacts with some nitroolefins, giving adducts containing tertiary nitro groups, as in the reaction with 2-nitropropene,[8,9] 2-nitro-1-butene,[8] and 2-nitro-2-butene.[9] The report of Nightingale and Janes[10] that all efforts to condense 1-nitroheptene with cyclopentadiene were negative would appear, therefore, to be anomalous.

We have now obtained the corresponding adducts from reactions of 1-nitroheptene and 1-nitroöctene with excess refluxing cyclopentadiene. With this removal of the last remaining contrary evidence, the conclusion now appears justified that the Diels-Alder reaction of 1-nitroalkenes with cyclopentadiene is a general reaction.

EXPERIMENTAL

5-Nitro-6-pentylbicyclo-[2,2,1]-2-heptene. Matheson, Coleman and Bell technical grade *n*-hexaldehyde was distilled and purified through the bisulfite addition compound.[11] *n*-Hexaldehyde and nitromethane were condensed in the presence of an equivalent amount of sodium hydroxide to form 1-nitro-2-heptanol[10] in 83% yield by the method of Sprang with Degering[12] for 1-nitro-2-octanol, except that it was found desirable, after adding the sodium hydroxide over a period of 4 hours, to leave the reaction mixture at 10° for 2 more hours before diluting and neutralizing it with acetic acid. 1-Nitro-2-heptanol was acetylated by the method of Tindall[13] and dehydroacetylated in 78% yield to 1-nitroheptene[10] by refluxing in ether solution with potassium bicarbonate for 13 hours by the method of Schmidt and Rutz.[14]

1-Nitroheptene (13.0 g., 0.0907 mole, n^{25}_{D} 1.4551) and freshly cracked cyclopentadiene (34.0 g., 0.514 mole) were warmed on the steam-bath until refluxing of the cyclopentadiene ceased (3 hours) and for 2 more hours. The solution was vacuum-distilled, removing dicyclopentadiene and a considerable forerun and yielding a pale yellow liquid (12.5 g., 0.0598 mole, 66%), b.p. 122–123° (~5 mm.), n^{28}_{D} 1.4788. Redistillation gave 5-nitro-6-pentylbicyclo-[2,2,1]-2-heptene as an almost colorless liquid, b.p. 121° (~3–4 mm.), n^{25}_{D} 1.4800; ν_{NO_2} (cm.$^{-1}$) 1544, 1375.

Anal. Calc'd for $C_{12}H_{19}NO_2$ (209.28): C, 68.86; H, 9.15; N, 6.69. Found: C, 68.64; H, 9.37; N, 6.66.

5-Nitro-6-hexylbicyclo-[2,2,1]-2-heptene. 1-Nitro-2-octanol[12] was acetylated and pyrolyzed to 1-nitroöctene[14 15] by the method of Cerf de Mauny.[15] Crude 1-nitroöctene (37.1 g., 0.236 mole, n^{25}_{D} 1.4501) and freshly cracked cyclopentadiene (72.0 g., 1.09 moles) were warmed on the steam-bath until refluxing of the cyclopentadiene ceased (2 hours) and for 2 more hours. The solution was vacuum-distilled, removing dicyclopentadiene and a considerable forerun and yielding several fractions of pale yellow liquid (17.2 g., 0.0771 mole, 33%), b.p. 112–131° (~1.5–2 mm.), n^{25}_{D} 1.4707. Redistillation gave 5-nitro-6-hexylbicyclo-[2,2,1]-2-heptene as a pale yellow liquid, b.p. 103° (~0.5 mm.), n^{25}_{D} 1.4792; ν_{NO_2} (cm.$^{-1}$) 1543, 1373.

Anal. Calc'd for $C_{13}H_{21}NO_2$ (223.31): C, 69.92; H, 9.48; N, 6.27. Found: C, 70.09; H, 9.55; N, 6.22.

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[11] (a) G. B. Bachman in A. H. Blatt, *Org. Syntheses*, **Coll. Vol. 2**, 324 (1943); (b) A. I. Vogel, *A Textbook of Practical Organic Chemistry*, Longmans, Green and Co., London, England, 1948, p. 320, note 2.

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The Base-Catalyzed Reaction of Benzyl Mercaptan with Styrene Oxide

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In connection with another problem, the reaction of benzyl mercaptan with styrene oxide in basic solution was investigated briefly. Styrene oxide normally reacts with basic reagents B to give the secondary alcohol $C_6H_5CHOHCH_2B$.[1] Alkali mer-

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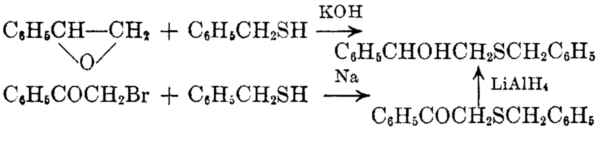
[1] Zuidema, Cook and Van Zyl, *J. Am. Chem. Soc.*, **75**, 294 (1953); Adams and VanderWerf, *J. Am. Chem. Soc.*, **72**, 4368 (1950); Guss, *J. Org. Chem.*, **17**, 678 (1952), and other papers by these authors.

captides react with aliphatic oxides in the same fashion.[2]

In keeping with prediction, we observed that potassium benzyl mercaptide opened the oxide ring to form 1-phenyl-2-benzylmercaptoethanol in good yield. The product was identical with an authentic sample prepared from 1-phenyl-2-benzylmercaptoethanone by reduction with lithium aluminum hydride.



$$C_6H_5CH\text{—}CH_2(\text{—}O\text{—}) + C_6H_5CH_2SH \xrightarrow{KOH} C_6H_5CHOHCH_2SCH_2C_6H_5$$

$$C_6H_5COCH_2Br + C_6H_5CH_2SH \xrightarrow{Na} C_6H_5COCH_2SCH_2C_6H_5 \xrightarrow{LiAlH_4} C_6H_5CHOHCH_2SCH_2C_6H_5$$

EXPERIMENTAL

Reaction of styrene oxide with benzyl mercaptan. A suspension of 11.2 g. (0.2 mole) of powdered potassium hydroxide in 75 ml. of dioxane was treated with 24.8 g. (0.2 mole) of benzyl mercaptan, and the mixture was stirred for 30 min. Then 24.0 g. (0.2 mole) of styrene oxide (Dow Chemical Co.) was added dropwise during 30 min. to the stirred suspension. The mixture was heated on the steam-bath during the addition, following which it was stirred for an additional 2 hours at room temperature.

Addition of water to the dark suspension caused the separation of two layers. The aqueous layer was extracted with ether, and the combined organic extracts were washed successively with dilute sulfuric acid, water, and a saturated sodium chloride solution, and then were dried with potassium carbonate. The product was purified by distillation, giving 37.6 g., 77%, b.p. 172–175° (1.5 mm.). An additional 2.3 g., b.p. 175–178° (1.5 mm.), distilled subsequently.

The main fraction solidified on chilling. When crystallized from ether-petroleum ether, there was obtained 20.6 g., m.p. 40–46°, and a second crop, 7.3 g., m.p. 42–47°. When recrystallized, the m.p. was 47–48°. The various mother liquors were combined, redistilled, and the main fraction was recrystallized. The total yield of pure material, m.p. 47–48°, was 23.4 g., 48%.

Another experiment using 0.4 g.-atom of potassium metal, 0.4 mole of benzyl mercaptan, and 0.1 mole of styrene oxide in 300 ml. of dioxane gave 56% of pure material when processed in the same way.

Synthesis of 1-phenyl-2-benzylmercaptoethanol. 1-Phenyl-2-benzylmercaptoethanone was prepared in 70% yield by the reaction of sodium benzylmercaptide with phenacyl bromide in alcohol by the procedure of Wahl[3]; m.p. 86–87°, reported,[3] 89°. Its dinitrophenylhydrazone was prepared by Brady's method[4]; m.p. 168.9-169.7° (acetic acid).

Anal. Calc'd for $C_{21}H_{18}N_4O_4S$: C, 59.70; H, 4.25. Found: C, 60.03; H, 4.33.

The ketone was reduced to the carbinol in 75% yield by refluxing it in ether with a slight excess of lithium aluminum hydride. The product was recrystallized from ether-petroleum ether, m.p. 46–47°. A mixture of this material with that prepared above melted at 46–47°, and their infrared spectra were identical.

Anal. Calc'd for $C_{15}H_{16}OS$: C, 73.73; H, 6.60. Found: C, 74.00; H, 6.40.

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On the *O*-Methylation of α-Propionyl-*p*-chlorophenylacetonitrile

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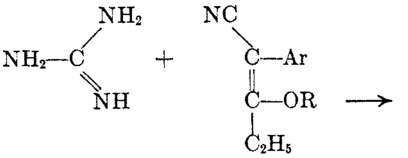
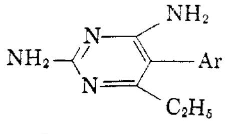
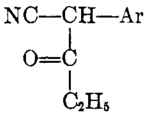
The important antimalarial 2,4-diamino-5-*p*-chlorophenyl-6-ethylpyrimidine (pyrimethamine; Daraprim; I)[1] is prepared by the cyclization-condensation of guanidine with a β-alkyloxy-α-*p*-chlorophenyl-β-ethylacrylonitrile (II).[2] The compound II is the enol ether of the ketonitrile III. These enol ethers were originally prepared by treatment of the ketonitriles with diazomethane[2]



II (Ar = —C_6H_4Cl-*p*)



I (Ar = —C_6H_4Cl-*p*)



III

(giving II; R = Me); subsequently the reaction with ortho esters was employed[3] while more recently the Walker method, an acid catalyzed etherification, has been utilized.[4] This last method may be operated commercially although, at times, difficulties have been encountered.

The *O*-alkylation of the ketonitriles III with alkyl iodides and sulfates in aqueous or alcoholic potassium hydroxide solution[2,3] or in acetone solution in the presence of sodium carbonate[4a] met with indifferent success. Matti and Reynaud,[5] however, reported that under mild conditions cyandesoxybenzoin (IV) was converted by treatment with methyl sulfate and alkali into good yields of a mixture of the geometrically isomeric enol ethers Va and Vb. The findings of the French authors sug-

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(3) Wahl, *Ber.*, **55**, 1454 (1922).

(4) Brady, *J. Chem. Soc.*, 756 (1931).

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(4) (a) Chase, Thurston, and Walker, *J. Chem. Soc.*, 3439 (1951); (b) Chase and Walker, *J. Chem. Soc.*, 3518 (1953).

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