over silica gel (12 × 1 in.). A 1:1 mixture of hexane–benzene (33 ml) eluted 2.2 mg of a pink residue which was found to contain, by gc (5% SE-30)–mass spectral analysis, four volatile fractions with molecular ions m/e 139, 226 ($C_{16}H_{34}$),[5] 173 ($C_{10}H_7NO_2$),[6] and 253 (probably $C_{18}H_{23}N$) in their order of appearance. A mixture of hexane–benzene (1:2, 400 ml) eluted 2-azido-3-nitronaphthalene (55 mg, 28%): mp and mmp (with the authentic sample) 101–102°; ir (CH_2Cl_2) superposable with that of the authentic material. A 1:3 mixture of the same solvents (600 ml) eluted 2-amino-3-nitronaphthalene (3.8 mg, 3.9%). Gc analysis over a 3% SE-30 column (6 ft × 1/8 in., at 200°, Varian-1800 gas chromatograph) confirmed the presence of 2-amino-3-nitronaphthalene associated with trace amounts of an unidentified impurity. Further elutions with chloroform and a chloroform–ethanol mixture (9:1) gave a dark intractable solid which charred upon vacuum sublimation.

Registry No.—**2**, 22496-30-6; **5**, 13115-28-1; **6**, 31417-80-8.

(5) Assumed to be a combination of solvent radicals.
(6) Assumed to be β-nitronaphthalene.

The Reaction of Dithiazolium Cations with Sodium Azide

JAMES E. OLIVER

Entomology Research Division, Agricultural Research Service, U. S. Department of Agriculture, Beltsville, Maryland 20705

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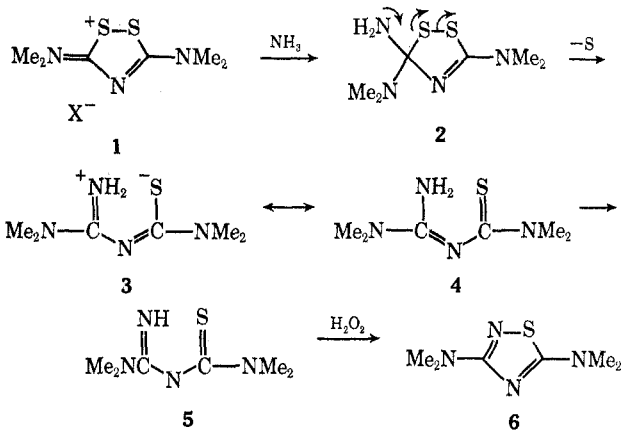
3,5-Bis(dimethylamino)-1,2,4-dithiazolium chloride (**1**, X = Cl) and a number of closely related dithiazolium salts are chemosterilants against house flies (*Musca domestica* L.).[1] To see whether similar biological activity might be found in geometrically similar, uncharged heterocyclic compounds, we wished to prepare a series of bis(dimethylamino) heterocyclic compounds including the 1,2,4-thiadiazole **6**. Various syntheses of amino-1,2,4-thiadiazoles have been developed,[2] but many of them give only mono- or unsubstituted amino groups. 3,5-Diamino-1,2,4-thiadiazoles can be prepared by oxidation of amidinothioureas,[2,3] and, since amidinothioureas can be made by reacting iminodithiazolidine salts and amines,[3] we were able to prepare **6** from **1** as shown in Scheme I. The overall yield of **6** was about 25%.[1b] The probable mechanism[3,4] of the addition of ammonia presumably involves ring opening and extrusion of elemental sulfur, assisted by an electron pair from either the amino or dimethylamino group of **2**.

The immediate species after loss of sulfur is interesting. Resonance form **3** suggests that the remaining sulfur should be rather nucleophilic, and we reasoned that, if the ring opening were initiated by a nucleophile that contained an inherent electrophilic center, direct cyclization might occur. To test this hypothesis we reacted **1** with sodium azide (NaN_3).

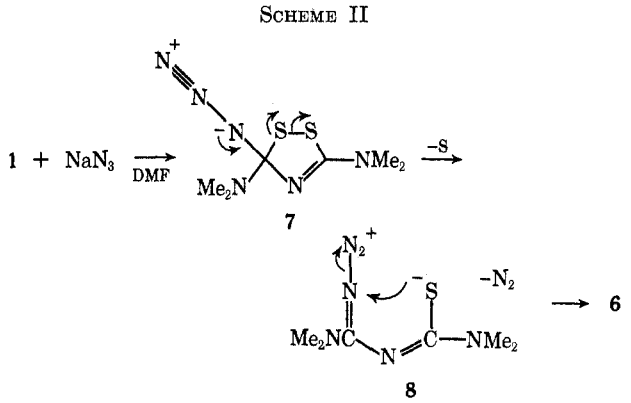
When **1** and NaN_3 were heated together in water, no reaction occurred. However, in dimethylformamide

SCHEME I



(DMF), an intense blue color quickly developed, and at about 80° nitrogen was evolved. In a few minutes the color was discharged, and the product, obtained in 75% yield after distillation, was the same 1,2,4-thiadiazole prepared earlier. The rationale is shown in Scheme II.

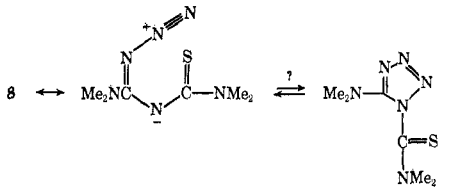
SCHEME II



The N_2^+ end of the azide function evidently creates the desired electrophilic center and also serves as a good leaving group.[5]

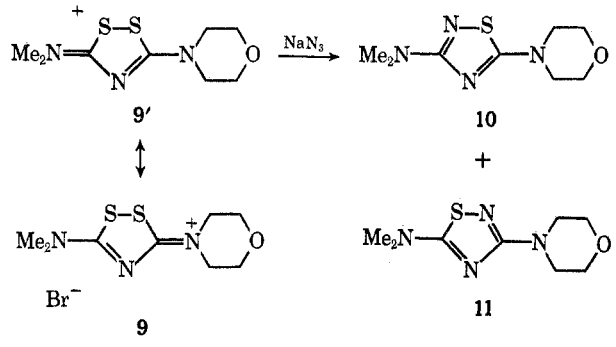
3,5-Dipiperidino-1,2,4-dithiazolium bromide reacted analogously with NaN_3 to give a good yield of 3,5-dipiperidino-1,2,4-thiadiazole. We then tried the reaction on an unsymmetrically substituted dithiazolium salt and chose the dimethylaminomorpholino compound **9,9′** with the hope that the rather large difference in basicity[6] between dimethylamine (pK_B = 3.36) and morpholine (5.64) might result in selective nucleophilic attack at one of the two ring carbons. Although **9,9′** was somewhat less reactive than **1**, it did react smoothly

(1) (a) R. L. Fye, G. C. LaBrecque, A. B. Bořkovec, and J. Morgan, Jr., *J. Econ. Entomol.* **62**, 522 (1969); (b) J. Oliver, S. C. Chang, R. T. Brown, J. B. Stokes, and A. B. Bořkovec, unpublished results.
(2) F. Kurzer, *Advan. Heterocycl. Chem.*, **5**, 119 (1965).
(3) (a) S. N. Dixit, *J. Indian Chem. Soc.*, **37**, 151 (1960); (b) *ibid.*, **38**, 221 (1961).
(4) Nucleophilic additions to the closely related 1,2-dithiolium cations have been studied in some detail. For a review see H. Prinzbach and E. Futterer, *Advan. Heterocycl. Chem.*, **7**, 39 (1966).
(5) The editor has pointed out that intermediate **8** is very similar to the proposed intermediates in the thermal isomerizations of 5-aminotetrazoles: R. A. Henry, W. G. Finnegan, and E. Lieber, *J. Amer. Chem. Soc.*, **76**, 88 (1954); **77**, 2264 (1955). Thus **8** could possibly have closed to a thiocarbamoyltetrazole. We have no evidence that such a reaction occurred; however, the isolated thiadiazoles were usually much more soluble than most tetrazoles, and small amounts of the latter could have escaped detection.



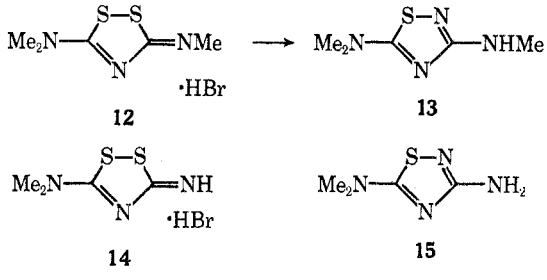
(6) H. K. Hall, *ibid.*, **79**, 5441 (1957).

with NaN_3 in dimethyl sulfoxide (DMSO) to give a 76% yield of crude thiadiazoles (**10** + **11**). The anticipated selectivity was not observed, however, as a 1:2 mixture of the two isomers was obtained. Pure samples of both **10** and **11** were obtained by preparative gas



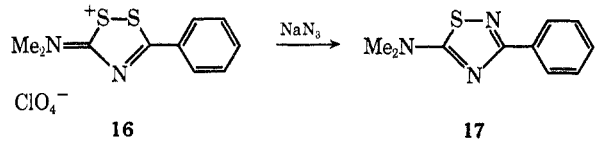
chromatography, but the physical data have not allowed us to unambiguously distinguish which isomer is which. More important, we feel, is the lack of selectivity in spite of the difference in basicities of the substituents.

Dimethylaminomethylimino- and dimethylaminoimino-1,2,4-dithiazolidines (as their hydrobromides **12** and **14**) similarly reacted with NaN_3 in DMF to give the 5-(dimethylamino)-3-(methylamino)- and 3-amino-5-(dimethylamino)-1,2,4-thiadiazoles (**13** and **15**, respectively). The yields of pure **13** and **15** were 40–60%; the other isomers were not detected. These products



correspond to attack by N_3^- at the carbon bearing the less highly substituted amine.

Finally we reacted NaN_3 with 5-(dimethylamino)-3-phenyl-1,2,4-dithiazolium perchlorate (**16**). The product was the known[7] 5-(dimethylamino)-3-phenyl-1,2,4-thiadiazole (**17**). Though the yield of recrystallized **17** was only about 25%, we were unable to detect any of the other isomer in the crude reaction mixture. It is in-



teresting that nucleophilic attack has occurred on the phenyl-substituted carbon instead of on the carbon adjacent to the exocyclic nitrogen (which must bear most of the positive charge).[8]

An interesting aspect of these reactions is the color that usually accompanied them. The color normally began to develop almost immediately upon heating a mixture of a dithiazolium salt and NaN_3 in DMF or DMSO, well before the reactants had completely dissolved. Often a pale green color developed first that rather quickly changed to an intense blue. Although the color was occasionally discharged in a few minutes, this was frequently not the case and intensely colored solutions sometimes remained after the reactions had gone to completion, although a deep red-brown usually replaced the original blue. This phenomenon is not specific to dithiazolium salts, however; we have found that a variety of sulfur-containing compounds—dithiobiurets, monothiobiurets, tetralkylthioureas, 1,2,4-dithiazolidine-3-thiones—and sulfur itself also produce blue or blue-green colors when heated with NaN_3 in DMF. Although we do not know the cause of the colors, we feel that they are not necessarily associated with any of the intermediates between the dithiazolium salts and thiadiazoles. For example, the reaction of **14** and NaN_3 did not produce a blue solution although the expected product was obtained.

(7) J. Goerdeler and K. H. Heller, *Chem. Ber.*, **97**, 225 (1964).

(8) Nucleophiles have been reported to similarly attack C-5 of 5-phenyl-1,2,4-dithiazole-3-thione: J. Vialle, *Quart. Rep. Sulfur Chem.*, **5**, 151 (1970).

Experimental Section[9]

Melting points were obtained on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded on a Varian Model T-60 spectrophotometer and infrared spectra were obtained on a Perkin-Elmer Model 137 sodium chloride prism spectrophotometer. Gas chromatographic separations were achieved on an Aerograph Autoprep Model A-700 gas chromatograph. Mass spectra were recorded on a Finnigan Model 1015 quadrapole mass spectrometer. Magnesium sulfate was used as a drying agent. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

Caution: Although we experienced no difficulties with any of these reactions, normal precautions should be observed when heating azides and perchlorates.

Preparation of Dithiazolium Bromides.—The general procedure was that described for the preparation of 3,5-bis(dimethylamino)-1,2,4-dithiazolium bromide (**1**, X = Br).[10] A mixture of dimethylthiocarbamoyl chloride (0.1 mol) and KSCN (0.1 mol) in acetone (90 ml) was stirred and refluxed 15 min and then cooled. The KCl was removed by filtration and the bright yellow filtrate was cooled in an ice bath. The appropriate amine (Me_2NH, morpholine, $MeNH_2$, or NH_3, 0.1 mol) in water or acetone was added dropwise; after *ca.* 30 min HBr (48%, 0.1 mol) and H_2O_2 (30%, 0.1 mol) were added dropwise in that order. The dithiazolium bromides were collected by filtration, washed with acetone, and recrystallized (usually EtOH–H_2O). Yields were 50–70%.

(Dimethylamino)morpholino-1,2,4-dithiazolium bromide (**9**,**9′**) had mp 208–210° dec.

Anal. Calcd for $C_8H_{14}N_3OS_2Br$: C, 30.77; H, 4.52; N, 13.45; S, 20.54. Found: C, 30.54; H, 4.83; N, 13.40; S, 20.57.

(Dimethylamino)(methylimino)-1,2,4-dithiazolidine hydrobromide (**12**) had mp 248–249°.

Anal. Calcd for $C_5H_{10}N_3S_2Br$: C, 23.44; H, 3.93; N, 16.40. Found: C, 23.28; H, 3.89; N, 16.44.

(Dimethylamino)imino-1,2,4-dithiazolidine hydrobromide (**14**) had mp 215–219°.

Anal. Calcd for $C_4H_8N_3S_2Br$: C, 19.84; H, 3.33; N, 17.35. Found: C, 19.60; H, 3.28; N, 17.49.

3,5-Dipiperidino-1,2,4-dithiazolium bromide was prepared in the same way from pentamethylene thiocarbamoyl chloride.[11] It had mp 258–260° dec.

Anal. Calcd for $C_{12}H_{20}N_3S_2Br$: C, 41.14; H, 5.75; N, 11.99. Found: C, 40.97; H, 5.87; N, 11.89.

5-(Dimethylamino)-3-phenyl-1,2,4-dithiazolium Perchlorate (**16**).—Aqueous Me_2NH (1.7 ml, 40%) was added to glacial HOAc (90 ml), and then 5-(methylthio)-3-phenyl-1,2,4-dithi-

(9) Mention of a proprietary product or company does not necessarily imply endorsement by the U. S. Department of Agriculture.

(10) W. R. Diveley, U. S. Patent 3,166,564 (Jan 19, 1965); *Chem. Abstr.*, **62**, 9145*g* (1965).

(11) W. Ried, H. Hillenbrand, and G. Oertel, *Justus Liebigs Ann. Chem.*, **590**, 123 (1954).

azolium perchlorate[12] (4.35 g) was added. The mixture was stirred and heated to reflux at which time a homogeneous solution resulted. The solution was filtered and cooled; **16** was collected and recrystallized again from HOAc to give 1.01 g, mp 189–190.5° (23%; another modification has mp 176°).

Anal. Calcd for $C_{10}H_{11}ClN_2O_4S_2$: C, 37.21; H, 3.44; N, 8.68; S, 19.87. Found: C, 37.21; H, 3.33; N, 8.85; S, 20.00.

After collection of **16**, the HOAc filtrate was evaporated to dryness, and the residue was extracted with $CHCl_3$. The material thus obtained was recrystallized from hexane–EtOAc to give 0.55 g (20%) of methyl benzoyldithiocarbamate, mp 133–135°, that was identical with the authentic material.[13]

Reaction of 1 (X = Br) with NaN_3.—A mixture of **1** (8.46 g, 0.0314 mol) and NaN_3 (2.2 g, 0.034 mol) in DMF (75 ml) was stirred under nitrogen while the flask was heated in an oil bath. A deep blue color quickly developed. At 80–85° vigorous gas evolution was observed. The solution was kept at 85–90° for 1 hr, and the most of the DMF was removed *in vacuo*. Benzene was added, and the solution was filtered and distilled to give 4.1 g (76%) of 3,5-bis(dimethylamino)-1,2,4-thiadiazole [**6**, bp 120–126° (0.5–0.6 mm)], identical with that synthesized previously).[1b]

Reaction of 3,5-Dipiperidino-1,2,4-dithiazolium Bromide with NaN_3.—The reaction was run as described for the reaction of **1**; a 94% crude yield of 3,5-dipiperidino-1,2,4-thiadiazole was obtained as a light yellow oil. Partial decomposition occurred on attempted distillation [>150° (0.15 mm)] and the distillation was interrupted. Upon cooling, the material remaining in the flask solidified. Two recrystallizations from MeOH–H_2O gave the pure compound, mp 65–66°.

Anal. Calcd for $C_{12}H_{20}N_4S$: C, 57.10; H, 7.99; N, 22.20; S, 12.71. Found: C, 57.24; H, 8.03; N, 22.14; S, 12.51.

Reaction of 9 with NaN_3.—This reaction was run similarly except DMSO was used as the solvent (heated to 100°). The product was obtained by adding H_2O and extracting thoroughly with ether; a 76% yield of crude 3-(dimethylamino)-5-morpholino-1,2,4-thiadiazole (**10**) and 5-(dimethylamino)-3-morpholino-1,2,4-thiadiazole (**11**) was obtained from which samples of the pure compounds were obtained by preparative gas chromatography (5 ft × 0.25 in. 10% Carbowax 20M on 60–80 Chromosorb W, 190°). The collected samples were each recrystallized from hexane:

Isomer **A** (*ca.* 33%), mp 89–90°, had retention time 25 min; δ ($CDCl_3$) 3.04 (Me_2N).

Anal. Calcd for $C_8H_{14}N_4OS$: C, 44.84; H, 6.58; N, 26.15; S, 14.92. Found: C, 44.63; H, 6.61; N, 26.02; S, 15.02.

Isomer **B** (*ca.* 67%), mp 79°, had retention time 32.5 min; δ ($CDCl_3$) 3.08.

Anal. Calcd for $C_8H_{14}N_4OS$: C, 44.84; H, 6.58; N, 26.15; S, 14.92. Found: C, 44.97; H, 6.65; N, 25.94; S, 14.99.

Reaction of 12 with NaN_3.—A mixture of **12** (2.56 g) and NaN_3 (0.75 g) in DMF (20 ml) was heated at *ca.* 130° until no more gas evolution was visible. The deep blue color disappeared; the DMF was stripped; and the residue was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ was dried and evaporated to give 0.67 g (43%) of crude 5-(dimethylamino)-3-(methylamino)-1,2,4-thiadiazole (**13**) as a light yellow oil that solidified in a distillation apparatus [105–110° (0.15 mm)]. Recrystallization from hexane–EtOAc gave the pure material, mp 77–79°.

Anal. Calcd for $C_5H_{10}N_4S$: C, 37.95; H, 6.37; N, 35.41. Found: C, 37.91; H, 6.16; N, 35.67.

The structural assignment (**13** as opposed to the other possible isomer) is made partly by analogy to the formation of **15** from **14** (*vide infra*) and also by a strong peak in the mass spectrum at *m/e* 88 [$Me_2NC(=S)^+$].

Reaction of 14 with NaN_3.—A mixture of **14** (7.27 g) and NaN_3 (2.09 g) in DMF (40 ml) was heated at reflux 20 min (only a yellow color developed in this case). The solvent was stripped and the residue was extracted with several portions of warm MeOH; these extracts were filtered and evaporated and the remaining solid was washed with water and dried to give 2.44 g (56%) of 3-amino-5-(dimethylamino)-1,2,4-thiadiazole (**15**), mp 225–227.5°. An analytical sample was recrystallized from absolute ethanol, mp 230–232°.

Anal. Calcd for $C_4H_8N_4S$: C, 33.31; H, 5.58; N, 38.86; S, 22.24. Found: C, 33.43; H, 5.63; N, 39.01; S, 21.98.

(12) M. Ahmed and D. M. McKinnon, *Can. J. Chem.*, **48**, 2142 (1970).

(13) J.-L. Derocque and J. Vialle, *Bull. Soc. Chim. Fr.*, 1183 (1966).

The nmr spectrum (DMSO-d_6) was consistent with an amino(dimethylamino)thiadiazole [δ 3.00 (s, 6) and 5.98 (s, 2, exchangeable)] as was the mass spectrum (*m/e* 144). The opposite isomer, 5-amino-3-(dimethylamino)-1,2,4-thiadiazole, has been reported[14] to have mp 161°.

Reaction of 16 with NaN_3.—A mixture of **16** (1.00 g) and NaN_3 (0.269 g) in DMF (28 ml) was refluxed 45 min. The DMF was stripped and the residue was partitioned between benzene and water. The benzene solution was dried and evaporated leaving 0.380 g of an oily tan solid that was extracted with several small portions of MeOH (to remove sulfur). Treatment of the MeOH solution with water precipitated a light tan solid, mp 88–90°, that was again taken up in MeOH to remove a little more sulfur. Evaporation of the MeOH and recrystallization of the residue from hexane gave 0.153 g (24%) of 5-(dimethylamino)-3-phenyl-1,2,4-thiadiazole (**17**), mp 89–90° (reported[7] mp 89°).

Registry No.—**9**, 31354-27-5; **9′**, 31354-28-6; **10**, 31354-29-7; **11**, 31354-30-0; **12**, 31354-31-1; **13**, 31354-32-2; **14**, 31354-33-3; **15**, 31354-34-4; **16**, 31354-35-5; NaN_3, 12136-89-9; 3,5-dipiperidino-1,2,4-dithiazolium bromide, 31354-36-6; 3,5-dipiperidino-1,2,4-thiadiazole, 31354-37-7.

Acknowledgment.—We thank Miss Barbara Bierl for the mass spectra and Mr. R. T. Brown for the preparation of some starting materials.

(14) J. Goerdeler and M. Willig, *Chem. Ber.*, **88**, 1071 (1955).

Preparation of 2-Alkoxyiminoalkyl Bromides by the Bromination of *O*-Alkyl Oximes with *N*-Bromosuccinimide[1]

SOU-YIE CHU[2] AND DOMINICK A. COVIELLO*

Department of Medicinal Chemistry, College of Pharmacy, University of Illinois at the Medical Center, Chicago, Illinois 60612

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Several methods are available for the preparation α-halo ketoximes and α-halo aldoximes; these include the reduction of nitro olefins with zinc chloride,[3] the reaction of an olefin with nitrosyl chloride,[4] and the direct oximation of α-halocarbonyls.[5] Reactions of these compounds with certain nucleophiles have also been explored.[3,6] The corresponding *O*-alkyl ethers, however, have not been described.

N-Bromosuccinimide (NBS) can be used to brominate various types of compounds[7] including cyclohexanone and cyclopentanone oximes which yield the

(1) This investigation was supported by U. S. Public Health Service Research Grant RH 00293, National Center for Radiological Health.

(2) Abstracted from the Ph.D. dissertation, University of Illinois at the Medical Center, 1970.

(3) A. Dornow, H. D. Jordan, and A. Muller, *Chem. Ber.*, **94**, 67 (1961).

(4) (a) L. J. Beckham, W. A. Fessler, and M. A. Kise, *Chem. Rev.*, **48**, 369 (1951); (b) M. Ohno, N. Naruse, S. Torimitsu, and M. Okamoto, *Bull. Chem. Soc. Jap.*, **39**, 1119 (1966).

(5) E. T. Bailey, Ph.D. Thesis, University of Illinois, 1965.

(6) (a) A. Dornow and H. D. Jordan, *Chem. Ber.*, **94**, 76 (1961); (b) A. Dornow, H. H. Marquardt, and H. Paucksch, *ibid.*, **97**, 2165 (1964); (c) M. Ohno and N. Naruse, *Bull. Chem. Soc. Jap.*, **39**, 1125 (1966); (d) M. Ohno, S. Torimitsu, N. Naruse, M. Okamoto, and I. Sakai, *ibid.*, **39**, 1129 (1966); (e) M. Masaki, M. Sugiyama, S. Tayama, and M. Ohta, *ibid.*, **39**, 2745 (1966).

(7) (a) L. Horner and E. H. Winklemann in "Newer Methods of Preparative Organic Chemistry," Vol. III, W. Foerst, Ed., Academic Press, New York, N. Y., 1964, p 151; (b) C. Djerassi, *Chem. Rev.*, **43**, 271 (1948).