formamide was refrigerated (5°) for 3 hr. During this time triethylamine hydrobromide crystallized. The mixture was triturated with 10 ml. of ice–water and the resulting precipitate was filtered and dried. This material was suspended in 25 ml. of petroleum ether (b.p. 40–60°) and stirred for 10 min. The crude product (0.117 g.) was then filtered and recrystallized from ethanol to give 0.051 g. of colorless needles, m.p. 144–145°. The infrared spectrum in methylene chloride had strong carbonyl maxima at 1710, 1730, 1760, 1780, and 1800 cm.$^{-1}$.

Anal. Calcd. for $C_{24}H_{20}N_2O_6S$: C, 62.1; H, 4.32; N, 6.04. Found: C, 61.6; H, 4.35; N, 6.04.

Phenacyl 6-Tritylaminopenicillanate.—A mixture of 0.531 g. of 6-tritylaminopenicillanic acid diethylamine salt[29] and 0.199 g. of phenacyl bromide in 10 ml. of tetrahydrofuran was stirred at room temperature for 18 hr. The precipitated diethylamine hydrobromide (0.117 g., 76%) was removed and the filtrate was evaporated to dryness. The residue was triturated with petroleum ether; the solid material was removed by filtration and recrystallized from a mixture of methylene chloride and ethanol to yield 0.223 g. (39%) of fine colorless platelets, m.p. 184–185°. The infrared spectrum (methylene chloride) exhibits strong carbonyl maxima at 1710, 1760, and 1780 cm.$^{-1}$.

Anal. Calcd. for $C_{35}H_{32}N_2O_4S$: C, 72.7; H, 5.56; N, 4.86. Found: C, 72.6; H, 5.73; N, 5.23.

Phenacyl Phthaloylglycinate.—A mixture of 4.0 g. of phthaloylglycine,[28] 3.1 g. of phenacyl chloride, and 2.0 g. of triethylamine in 150 ml. of 95% ethanol was heated under reflux for 3 hr. and allowed to cool. The product which crystallized was collected and recrystallized from ethanol to yield 2.2 g. of colorless needles, m.p. 149–150°.

Anal. Calcd. for $C_{18}H_{13}NO_5$: C, 66.9; H, 4.02; N, 4.34. Found: C, 67.0; H, 4.01; N, 4.41.

Notes

The Synthesis and Configuration of *cis*- and *trans*-3-Hydroxystachydrine

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Received December 3, 1963

The mature fruit of *Courbonia virgata* has been shown to contain the two betaines of 3-hydroxyproline, *cis*- and *trans*-3-hydroxystachydrine.[2] These two isomers, distinguished by the letters a and b, had reported melting points of *ca.* 250° and 209–210°, respectively, with the latter being provisionally assigned the *cis* configuration "because of its greater solubility and slighter tendency to form crystalline salts."[2]

Recently, both *cis*- and *trans*-3-hydroxyproline have been synthesized in this laboratory and the configurations unambiguously assigned by conversion of a precursor, *trans*-3-methoxy-L-proline, to L-methoxysuccinamide.[3]

We have now synthesized *cis*- and *trans*-DL-3-hydroxystachydrine by treatment of the silver salts of *cis*- and *trans*-3-hydroxyproline with methyl iodide in methanol at room temperature. Under these mild conditions epimerization was not observed, in agreement with the analogous 4-hydroxyproline series.[4]

The comparison of the synthetic isomers with authentic samples of stereoisomers a and b revealed that isomer a corresponded to the *trans* configuration and isomer b corresponded to the *cis* configuration. Comparisons were made of melting points, infrared spectra, the relative electrophoretic mobilities, and by paper chromatography in three different solvent systems.

Experimental

Preparation of *cis*-3-hydroxy-DL-stachydrine.—A mixture of 50 mg. (381 µmoles) of *cis*-3-hydroxy-DL-proline, 100 mg. (433 µmoles) of silver oxide, and 125 µl. of water in a 3-ml. centrifuge tube was stirred occasionally at room temperature for 3.25 hr. Approximately one-half of the water was evaporated by means of a stream of nitrogen and 1.0 ml. of methanol was added followed by 50 µl. (113.5 mg., 800 µmoles) of methyl iodide. After 24 hr., an additional 37.5 µl. (85.5 mg., 602 µmoles) of methyl iodide was added and the mixture was stored at room temperature for 48 hr.

The liquor was withdrawn from the centrifuged suspension and the residue washed twice with methanol. Removal of the solvent gave a mixture of pale orange oil and colorless crystals which was triturated with a 2:1 mixture of ethyl alcohol and acetone. The crystalline material was washed twice with a 1:1 mixture of ethyl alcohol and acetone and then dried to give 125 mg. of *cis*-3-hydroxy-DL-stachydrine (41.3%). Two recrystallizations from ethyl alcohol gave small colorless elongated prisms, m.p. 222–222.5°.

Anal. Calcd. for $C_7H_{13}NO_3$: C, 52.8; H, 8.2; N, 8.8. Found: C, 52.66; H, 8.46; N, 8.31.

Analogous treatment of *trans*-3-hydroxy-DL-proline yielded 47.2 mg. of *trans*-3-hydroxy-DL-stachydrine (77.6%). Recrystallization from ethanol gave colorless prisms, m.p. 232.5–233°.

Anal. Calcd. for $C_7H_{13}NO_3$: C, 52.8; H, 8.2; N, 8.8. Found: C, 53.47; H, 8.64; N, 8.69.

By comparison, the melting point of isomer a was 251.5–252° dec. and of isomer b was 216.5–217° dec. All melting points were determined under nitrogen in sealed capillaries.

Comparison of *cis* and *trans*-3-Hydroxy-DL-stachydrine with Cornforth's Stereoisomers a and b.—The infrared spectrum of *trans*-3-hydroxy-DL-stachydrine was substantially identical with the spectrum of isomer a with peaks occurring at 3400, 1635, 1468 cm.$^{-1}$ and more than a score in the fingerprint region. The infrared spectrum of *cis*-3-hydroxy-DL-stachydrine was substantially identical with the spectrum of isomer b with peaks occurring at 3530, 1670, 1625, 1485 cm.$^{-1}$ and more than a score in the fingerprint region.

The relative mobilities of the compounds were as follows: paper electrophoresis[5] isomer a, 0.87; *trans*-3-hystach, 0.87; isomer b, 1.00; and *cis*-3-hystach, 1.00.

Paper chromatography was carried out in three different solvent systems [(a) *n*-butyl alcohol–acetic acid–water (4:1:5), 24.5 hr., Whatman No. 1 paper; (b) *n*-propyl alcohol–water (65:35), 19 hr., Whatman No. 1 paper; (c) ethyl alcohol–acetic acid–water (6:1:3), 15.5 hr., Whatman No. 1 paper] on isomer

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(1) U. S. Public Health Service Ref. No. 1-F1-GM-14,275-01A1.

(2) J. W. Cornforth and A. J. Henry, *J. Chem. Soc.*, 597 (1952).

(3) J. C. Sheehan and J. G. Whitney, *J. Am. Chem. Soc.*, **84**, 3980 (1962); **85**, 3863 (1963).

(4) A. A. Patchett and B. Witkop, *ibid.*, **79**, 185 (1957).

(5) pH 1.9, 3 kv; 4 hr.

a (0.19, 0.54, 0.68), *trans*-3-hystach (0.19, 0.54, 0.68), isomer b (0.21, 0.57, 0.70), and *cis*-3-hystach (0.21, 0.57, 0.70).

Acknowledgment.—The authors wish to thank Dr. J. W. Cornforth for the samples of 3-hydroxystachydrine and isomers a and b.

Fluoroolefins. X. The Reaction of Propynyllithium with Fluoroolefins

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Received September 27, 1963

England and his associates[1] reported briefly that the sodium salt of 1-hexyne and phenylacetylene reacted with tetrafluoroethylene to give, respectively, 30 and 9% of the corresponding difluoroethylene derivative.

$$2R{-}C{\equiv}CNa + CF_2{=}CF_2 \longrightarrow RC{\equiv}CCF{=}CFC{\equiv}CR + 2NaF$$

We now wish to report an extension of this reaction to other fluoroolefins in which propynyllithium was employed as the acetylenic compound and yields of product as high as 73% were realized.

The reactions were carried out by passing the gaseous fluoroolefin into a solution of the acetylide in tetrahydrofuran (THF) at either 0 or −22°. The products were separated by distillation and characterized by elemental analysis and n.m.r. and infrared analysis. The absorption at 4.49 μ served as an indication of the $C{\equiv}C$ system while peaks at 5.90 to 6.15 μ showed the $C{=}C$ group with varying amounts of fluorine.

The infrared absorption due to the triple bond is shifted toward lower wave lengths in the conjugated systems over that in methylacetylene which is noted at 4.67 μ, the values for the $C{\equiv}C$ absorption varying from 4.46 to 4.49 μ. On the other hand the absorption in the double-bond region is shifted toward higher wave lengths; thus chlorotrifluoroethylene exhibits $C{=}C$ absorption at about 5.6 μ whereas 1-chloro-1,2-difluoropent-1-en-3-yne (III) exhibited the double bond stretching absorption at 5.90 μ. Similar shifts were noted for the other enynes. Only one peak in the double-bond region of the spectra was observed in $CH_3C{\equiv}CCF{=}CFCH{=}CH_2$, at 6.01 μ, which presumably is due to the difluoroethylene unit.

Perhalogenated ethylenes reacted readily with the lithium salt to give a mixture of *cis–trans*-substituted ethylenes wherever possible. Tetrafluoroethylene gave only the disubstituted difluoroethylene even with a 50% molar excess of the olefin. Presumably the presence of the triple bond in III causes a drift of electrons away from the difluoromethylene group, thus making it more susceptible to further attack than the difluoromethylene groups in tetrafluoroethylene. Thus no monoelimination product (III) was isolated. In this respect, propynyllithium is different from butyllithium, for Dixon[2] has reported the formation of 80% of 1,1,2-trifluoro-1-hexene in the reaction with tetrafluoroethylene.

$$\mathrm{II} + CF_2{=}CF_2 \longrightarrow \underset{\mathrm{III}}{CH_3C{\equiv}C{-}CF{=}CF_2} + LiF \xrightarrow{\mathrm{II}} \underset{\mathrm{IV}}{CH_3C{\equiv}C{-}CF{=}CF{-}C{\equiv}C{-}CH_3} + LiF$$

Trifluorovinyl bromide normally reacts with nucleophilic reagents to give products formed by attack on the difluoromethylene carbon atom. However, methyl- and butyllithium form trifluorovinyllithium and the alkyl halide.[3] It therefore was of some interest to note that propynyllithium attacked in the normal manner to give the bromenyne.

$$CH_3Li + CF_2{=}CFBr \longrightarrow CH_3Br + CF_2{=}CFLi$$

$$C_4H_9Li + CF_2{=}CFBr \longrightarrow C_4H_9Br + CF_2{=}CFLi$$

$$CH_3C{\equiv}CLi + CF_2{=}CFBr \longrightarrow CH_3C{\equiv}CCF{=}CFBr + LiF$$

Neither vinylidene fluoride nor trifluoroethylene gave any of the desired products. Most of the former olefin was recovered. These olefins are lower boiling than most of the others employed, but this is not a contributing factor since tetrafluoroethylene also is volatile. It thus appears that the hydrogen present in these molecules is responsible for their behavior. The compounds may be acid enough to cause the conversion of the propynyllithium to methylacetylene.

Park[4] has recently reported that hexafluorocyclobutene reacts with Grignard reagents to give 75–80% yields of mono- and disubstituted derivatives, and Dixon[2] earlier had found that lithium reagents gave similar results. However, under conditions which gave products with other fluoroolefins, hexafluorocyclobutene gave a black solid product which was not evaluated.

Perfluoropropylene did not give so good a yield of simple products as did the perhalogenated ethylenes. It will be noted that 1,1,2-trifluoro-1,3-butadiene reacted well with propynyllithium to give a conjugated dienyne. A conjugated diynene was obtained from tetrafluoroethylene so that the reaction is a synthetic route to highly conjugated compounds.

The products of the reaction were colorless liquids which generally were thermally unstable. 3,4-Difluorohepta-1,3-dien-5-yne, for example, decomposed at 86° and rapidly turned black at room temperature.

The products from the reaction of propynyllithium and the fluoroolefins are shown in Table I.

It will be noted that increasing the size of the group in $CF_2{=}CFX$ leads to increasing amounts of the less sterically hindered *trans* isomer, thus bromotrifluoroethylene gives a ratio of *trans–cis* isomer of 1:3, whereas the larger substituents, such as $-CF_3$ and vinyl, give exclusively the *trans*-substituted ethylene.

The chemical properties of 1-chloro-1,2-difluoropent-1-en-3-yne (III) were studied. Normally acetylenic compounds react with anhydrous hydrogen fluoride to give a vinyl fluoride or difluoroalkane. Compound III reacted at 85° with hydrogen fluoride to give a mixture of fourteen products. At 25°, no reac-

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(1) See D. C. England, L. R. Melby, M. A. Dietrick, and R. V. Lindsey Jr., *J. Am. Chem. Soc.*, **82**, 5112 (1960), for some reactions and references to earlier work.

(2) S. Dixon, *J. Org. Chem.*, **21**, 400 (1956).

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