solution. The combined residues were recrystallized from benzene, using Norit-A to give 0.32 g. (4.0%) of the amide melting at 185–186°.

Acknowledgment.—The authors wish to express their gratitude to Dr. Velmar A. Fassel and Mr. Marvin Margoshes of the Institute for Atomic Research for carrying out the infrared analyses.

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Derivatives of ζ-Truxinic Acid

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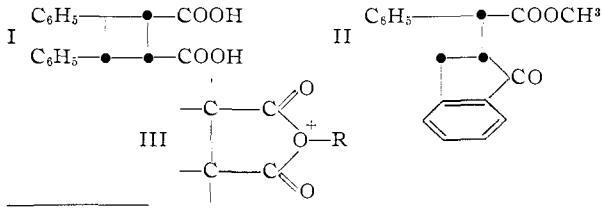
RECEIVED AUGUST 1, 1955

ζ-Truxinic acid (I by the Linstead convention), the resolvable *cis*-truxinic acid,[1] contains two nonequivalent carboxyl groups. Six positionally isomeric pairs of unsymmetrical derivatives of the acid functions have been characterized and the attachments of the substituents to the carboxyl groups, arbitrarily designated a and b, correlated throughout the series.[2] From the observation[2] that ζ-truxinic a-chloride b-methyl ester, but not its isomer, gave methyl ζ-truxinonate (II), in small yield,[3] on treatment with aluminum chloride, the a-carboxyl group was inferred to be the one *cis* to the adjacent phenyl group. The formulation of the keto ester as the hydrindone II rather than the possible tetralone rests on analogy to the facile cyclizations of truxillic acids and on pyrolysis of the truxinonic acid to cinnamic acid,[4] and seems probable but not proved. Further, serious difficulty with the argument arises from the recent demonstration by Cason and Smith[5] that Friedel–Crafts reactions of ester halides of 1,2-dicarboxylic acids may proceed through the symmetrical cation III. In ester chlorides of cyclobutane *trans*-diacids, formation of an intermediate such as III and consequent migration of an alkoxyl group are sterically prevented, and the structural assignments of unsymmetrical derivatives of *neo*-truxinic[4] and *epi*-truxillic[6] acids from Friedel–Crafts cyclizations agree with considerations of steric hindrance and inversion. However, substituents may easily shift between the carboxyl groups of ζ-truxinic acid: for example, the a-anilic acid with methanolic hydrogen chloride gave the ester of the b-anilic acid, presumably by way of the anil.[2] The two ζ-truxinic ester chlorides should give identical products on attempted cyclization, and the isolation of II from only one appears fortuitous.



(1) R. Stoermer and F. Scholtz, *Ber.*, **54**, 85 (1921).

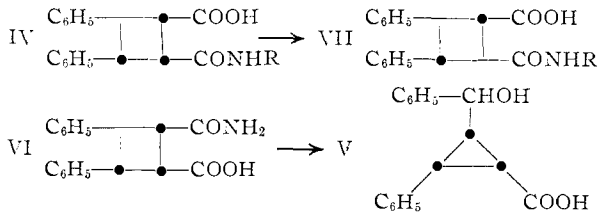
(2) R. Stoermer and P. Klockmann, *ibid.*, **58**, 1164 (1925).

(3) The product from 2 g. of ester chloride was insufficient for complete purification.

(4) R. Stoermer and E. Asbrand, *Ber.*, **64**, 2796 (1931).

(5) J. Cason and R. D. Smith, *J. Org. Chem.*, **18**, 1201 (1953); *cf.* B. H. Chase and D. H. Hey, *J. Chem. Soc.*, 553 (1952).

(6) R. Stoermer and F. Moeller, *Ber.*, **68**, 2124 (1935).



When ζ-a-truxinamic acid, previously formulated as IV (R = H), was subjected to the Hofmann reaction and the resultant amino acid nitrosated,[7,8] the product was the lactone of an all *cis*-substituted[7,9] cyclopropane V. Since the phenyl and carboxyl groups that are *cis* in V would be *trans* in IV, such a ring contraction would imply configurational inversion of the migrating group, in contradiction to established knowledge of carbonium ion rearrangements, including similar degradations of other truxinic and truxillic acids. However, as previous authors[7,8] noted, V would be the expected product from the ζ-amido acid VI. The proper deduction is that ζ-a-truxinamic acid is VI and the old allocation of structures must be reversed.

The conclusion that the a-carboxyl group of I is *trans* to the adjacent phenyl group is confirmed by independent evidence. The a-position is the less hindered[10]; in particular, the anhydride, imide and anil undergo cleavage of the heterocyclic rings by addition exclusively[11] to the a-carbonyl group. Furthermore, the ζ-b-amido and anilic acids are isomerized by base, under conditions that do not affect the a-compounds, to the half amides (VII, R = H or C_6H_5) of δ-truxinic acid.[2] The configuration of δ-truxinic acid is established by its formation from all other truxinic acids on fusion

(7) F. Schenck, *J. prakt. Chem.*, [2] **134**, 215 (1932). The deamination was cited from Rasenack (Dissertation, Rostock, 1928).

(8) I. S. Goldstein and H. I. Bernstein, THIS JOURNAL, **66**, 760 (1944).

(9) The complete stereochemistry of the deamination product (Schenck's[7] lactone Ia, obtained also from γ-truxillic acid) can be plausibly defined by the postulate that the phenyl group on the lactone ring is *cis* to the hydrogen atoms at the ring junctions. The deamination product is formed in acid from both epimeric alcohols V and apparently is more stable than the epimeric lactone of V, in which the phenyl groups may be in contact. Furthermore, the directly correlated configurations of the carboxyl epimers of V (Schenck's series III, of which IIIa is obtained from α-truxillic and δ-truxinic acids) would agree with the course of Meerwein–Ponndorf reduction of 1-benzoyl-2-*cis*-phenylcyclopropane-3-*trans*-carboxylic ester according to Cram's rule of asymmetric induction (D. J. Cram and F. A. Abd Elhafez, *ibid.*, **74**, 5828 (1952)). Application of the Cram–Abd Elhafez rule to the reduction of 1-benzoyl-2-*trans*-phenylcyclopropane-3-*cis*-carboxylic ester indicates that the lactonized product (Schenck's IIb, obtained from β-truxinic and ε-truxillic acids) has the same configuration about the lactone ring as that assumed for Schenck's Ia. The stereochemical result at the newly exocyclic carbon atom of the cited, principal ring contractions would be retention of configuration for truxillic and inversion for truxinic acids, formally as if the oxygen atom approached from the direction of the carboxyl group. Lactonization, if possible, and ring contraction may be simultaneous, but the attachment of the oxygen atom to the benzyl group need not be concerted with the rearrangement, notably in deaminations with nitrosyl bromide, where bromo acids may intervene, and may proceed simply to give the more stable product.

(10) Partial esterification gave the a-ester, and the a-amido acid was more rapidly hydrolyzed by acid than its isomer.[2] Esterification of the b-amido acid was anomalously difficult, presumably because of interaction of carboxyl and amide groups.

(11) The *cis*-phenyl group must retard attack from the opposite side at the adjacent b-position, which would drive the carbonyl oxygen atom toward the phenyl group.

with alkali,[12] with adoption of the most stable arrangement, like that of ϵ-truxillic acid, having no *cis* adjacent groups, by the failure to cyclize δ-truxinic acid to a hydrindone,[2] and by Hofmann degradation and deamination.[13] Since in base an amide group should form an enolate more readily than does a carboxylate ion, selective inversion of the amide portion of an amido acid would be anticipated, and has been demonstrated for the transformations of β-truxinamic to *neo*-a-truxinamic[4] and of *peri*-truxillamic to *epi*-b-truxillamic[6] acid. Inversion of the amide group of VII gives formula IV for the ζ-b-derivatives.[14]

(12) The reported isomerization[1] of β- to δ-truxinic acid by concentrated hydrochloric acid during six hours at 160° would represent a unique inversion of a phenyl substituent in *acid*. The change seems questionable, however, for a subsequent publication (R. Stoermer and F. Bachér, *Ber.*, **55**, 1860 (1922)) described the conversion of *neo*-truxinic acid by concentrated hydrochloric acid during four hours at 170–180° to a mixture that melted higher than the δ-acid and contained the β-acid.

(13) R. Stoermer and E. Asbrand, *ibid.*, **64**, 2793 (1931).

(14) Base-catalyzed isomerization of an a-half ester of I would lead to a new truxinic acid. The so-called μ- and ω-truxinic acids of M. M. Shemiakin (*Compt. rend. acad. sci. U.R.S.S.*, **24**, 768 (1939); **29**, 199, 202 (1940); [*Brit. Chem. Physiol. Abstr.*, **AII**, 169 (1941)]; *Zhur. Obshchei Khim.*, **11**, 219 (1941); [*C. A.*, **35**, 7944 (1941)]) appear to be lactonic acids.

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Steric Effects in Grignard Couplings with Alkoxysilanes[1]

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RECEIVED SEPTEMBER 19, 1955

Some years ago we described[3] a general method for the preparation of difficultly accessible trialkylsilyl compounds which involved the reaction of alkyl Grignard reagents with ethyl orthosilicate. The utility of this type of synthesis is evidenced by

$$RMgX + (EtO)_4Si \longrightarrow R_3SiOEt$$

the frequent use which has been made of it.[4] The success of the method depends on the fact that in general only three of the ethoxy groups of ethyl orthosilicate are replaced by alkyl Grignard reagents even under forcing conditions. For this reason an excess of Grignard reagent may be used to drive the reaction to the formation of a good yield of the trisubstituted derivative[5] without fear of over-stepping to the formation of by-product tetra-alkylsilane.[6,7] We now wish to report a more detailed investigation completed shortly after our earlier work,[3] which suggests that steric factors[8] play an important role in stopping the substitution at the desired stage.

In delineating the scope of the reaction we have found that ethyl and *n*-propyl Grignard reagents do not replace the fourth ethoxy group of ethyl orthosilicate even when a large excess of the organometallic compound is used and the reaction mixture is heated at 100°.[9] On the other hand methyl and phenyl Grignard reagents readily replace the fourth ethoxy group, giving tetramethylsilane and tetraphenylsilane respectively.[10] That this behavior is dependent more upon steric factors than upon Grignard reactivity or polar factors is suggested by the aforementioned results coupled with the following observations. Phenylmagnesium bromide does not replace the ethoxy group of triethylethoxysilane even under forcing conditions. Yet *n*-propylmagnesium bromide replaces the ethoxy group of trimethylethoxysilane with formation of *n*-propyltrimethylsilane.[11]

Experimental

Grignard Reagents with Ethyl Orthosilicate. A. Methylmagnesium bromide.—The Grignard reagent was prepared in the usual manner from 525 g., 21 moles, of magnesium turnings, 1.5 liters of liquid methyl bromide and seven liters of anhydrous ether. To the solution of organometallic reagent was added in thirty-five minutes with stirring and tap water cooling 1460 g., 7.0 moles, of ethyl orthosilicate.[12] Upon standing the reaction mixture separated into two layers, the lower of which solidified during the night. Fractional distillation of the seven-liter upper layer gave an ether fraction b. 25–35°, containing about two moles, 30% yield,

(1) Paper 49 in a series on organosilicon chemistry. For the preceding paper see THIS JOURNAL, **77**, 2485 (1955).

(2) Deceased, 1947.

(3) P. D. George, W. A. Strong, L. H. Sommer and F. C. Whitmore, THIS JOURNAL, **68**, 1380 (1946).

(4) No complete record has been kept but the following references are representative: (a) L. H. Sommer, D. L. Bailey, R. E. Van Strien and F. C. Whitmore, paper presented before the 109th American Chemical Society Meeting in April, 1946; (b) L. H. Sommer, E. W. Pietrusza and F. C. Whitmore, THIS JOURNAL, **68**, 2282 (1946); (c) H. Gilman and F. J. Marshal, *ibid.*, **71**, 2066 (1949); (d) N. S. Marans, L. H. Sommer and F. C. Whitmore, *ibid.*, **73**, 5127 (1951); (e) E. Larsson and R. Marin, *Acta Chem. Scand.*, **5**, 1173 (1951); (f) A. D. Petrov and L. L. Shchukoskaya, *Izvest. Akad. Nauk S.S.S.R., Otdel Khim. Nauk*, 564–565, 1952; (g) E. Larsson, *K. Fysiogr. Sällskap. Lund, Förh.* (*Lund*), **22**, No. 15, 1–4 (1952).

(5) Poor yields of trialkylsilyl derivatives are obtained upon coupling Grignard reagents with silicon tetrachloride: see for example C. R. Noller and H. W. Post. THIS JOURNAL, **74**, 1361 (1952).

(6) The preparation of tetra-*n*-butylsilane from the reaction of *n*-butylmagnesium bromide and ethyl orthosilicate under forcing conditions was erroneously reported by H. W. Post and C. H. Hofrichter, *J. Org. Chem.*, **5**, 572 (1940). Their product was probably Bu_3SiOEt—see P. D. George, Doctoral Dissertation, Pennsylvania State University, 1946; R. O. Sauer, THIS JOURNAL, **68**, 954 (1946); H. Gilman and R. N. Clark, *ibid.*, **69**, 967 (1947).

(7) Organolithium reagents are apparently much more reactive toward ethyl orthosilicate for they readily give symmetrical and unsymmetrical tetra-alkylsilanes: see H. Gilman and R. N. Clark, *ibid.*, **68**, 1675 (1946); H. Gilman and F. J. Marshall, *ibid.*, **71**, 2066 (1949); M. G. Voronkov, B. N. Dolgov and N. P. Zapevalova, *Uchenye Zapiski, Leningrad. Gosundarst. Univ.* No. **163**, Ser. Khim. Nauk No. 12, 161–176 (1953); *C. A.*, **49**, 5272*g* (1955).

(8) The role of steric factors in other reactions involving substitution at a silicon atom have been demonstrated repeatedly. For leading references see H. Gilman and C. G. Brannen, THIS JOURNAL, **73**, 4640 (1951). More recent references include: C. Eaborn, *J. Chem. Soc.*, 2840 (1952); H. Gilman and G. N. R. Smart, *J. Org. Chem.*, **19**, 441 (1954); L. H. Sommer and L. J. Tyler, THIS JOURNAL, **76**, 1030 (1954); L. H. Sommer, R. M. Murch and F. A. Mitch, *ibid.*, **76**, 1619 (1954).

(9) Findings have been reported recently which confirm these results and extend them to higher alkyl Grignard reagents: E. Larsson, *Kgl. Fysiograph. Sällskap. Lund, Handl.*, **63**, No. 12, 1–8 (1952).

(10) Another Grignard reagent recently reported to form a tetraorganosilane from ethyl orthosilicate is 3,3,4,4,5,5,5-heptafluoropentylmagnesium bromide: E. T. McBee, C. W. Roberts, G. F. Judd and T. S. Chao, THIS JOURNAL, **77**, 1292 (1955).

(11) Related studies involving competitive reactions of Grignard reagents with trialkylmonochlorosilanes have been described: L. H. Sommer, G. T. Kerr and F. C. Whitmore, THIS JOURNAL, **70**, 434 (1948).

(12) The ethyl orthosilicate used in this work was a technical grade purchased from Carbide and Carbon Chemical Corp. Careful fractional distillation of a random sample showed that it contained substantially no ethanol or siloxane polymers. Well over 90% of the material was ethyl silicate which had b.p. 164–164.8° at 725 mm., $n^{20}D$ 1.3838, d^{20} 0.9336, and η^{22} 0.762 centistokes.