action of catalyst in breaking a particular bond was shown by the action of aluminum chloride and ferric chloride on triphenylmethyl acetate: the former produced triphenylchloromethane and the latter triphenylcarbinol.

3. Aluminum chloride reacts with triphenylmethyl ethyl ether in the cold, the products being $(C_6H_5)_3CCl$ and $Al(OC_2H_5)_2Cl$.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

SOME HIGHLY PHENYLATED ALIPHATIC NITRO COMPOUNDS

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RECEIVED AUGUST 13, 1929 PUBLISHED FEBRUARY 6, 1930

Although aliphatic nitro compounds have been the subject of many excellent investigations they still present a number of problems of theoretical interest. Little is known about the factors that influence the stability of the *aci* forms and the manner in which these pass into true nitro compounds, the extent to which the nitro and iso-nitro groups are modified by conjugation with ethylenic linkages, the intimate structure of nitro and iso-nitro groups. Since the life of the *aci* forms of simple nitro compounds is short, we have studied a number of phenylated derivatives in the expectation that the saturated representatives would be more tractable than the simpler compounds which have been studied heretofore, and that a comparison between the unsaturated members and the correspondingly phenylated carbonyl compounds would be instructive.

Our starting materials were nitro styrene and nitro stilbene. Owing to the ease with which it polymerizes, the former proved comparatively useless for our purpose, but the latter enabled us to prepare and study still more highly phenylated saturated and unsaturated nitro compounds. It reacts with phenyl magnesium bromide as readily as does the corresponding unsaturated ketone—benzaldesoxybenzoin—and like the unsaturated ketone it forms, apparently exclusively, a 1,4-addition product

$$\underset{\text{I}}{C_6H_5CH{=}C(C_6H_5)NO_2} \longrightarrow \underset{\text{II}}{(C_6H_5)_2CHC(C_6H_5){=}N(OMgBr)O} \longrightarrow$$

$$\underset{\text{III}}{(C_6H_5)_2CHC(C_6H_5){=}N(OH)O}$$

From the product of the Grignard reaction it is easy to secure the corresponding *aci* nitro compound. In its chemical reactions this iso-nitro compound closely resembles its simpler analogs; it forms sodium, copper and silver salts; it gives the characteristic color reactions with ferric chloride and phenyl diazonium chloride; and it reacts with bromine in the usual manner. But this iso-nitro compound differs much from its simpler analogs both in the degree and in the quality of its instability. It can be isolated without too much difficulty in the form of a crystalline solid, which, when perfectly pure, may undergo relatively little change for several weeks. Its persistence varies greatly with its purity, hence it deteriorates more rapidly in a closed vessel than in the open or in a vacuum, more rapidly also in solution than by itself. In the end all specimens degenerate into red oils.

While this iso-nitro compound, like all others, is unstable, it exhibits little if any tendency to undergo spontaneous rearrangement into a true nitro compound. The oily degradation products, whether formed from the solid or in solution, contain barely a trace of the isomer. They are composed largely of triphenyl ethylene, triphenyl ethanone and triphenylethanone oxime, but contain a number of other substances—products which are due to intramolecular oxidation and reduction, and to hydrolysis.

$$\underset{\mathrm{IV}}{(C_6H_5)_2C{=}CHC_6H_5} \longleftarrow (C_6H_5)_2CHC(C_6H_5){=}N(OH)O \longrightarrow$$

$$\underset{\mathrm{V}}{(C_6H_5)_2CHC({=}NOH)C_6H_5} \longrightarrow \underset{\mathrm{VI}}{(C_6H_5)_2CHCOC_6H_5}$$

Another peculiarity of the nitro compound that seems at first surprising, is that its isomerization to the true nitro compounds is not promoted by acids; weak acids and very small concentrations of strong acids appear to retard deterioration and strong acids promote hydrolysis to triphenyl ethanone. In order to bring about isomerization it is necessary to employ bases. Strong bases like sodium hydroxide form salts that are sparingly soluble and apparently perfectly stable in strongly alkaline solutions. But when a dilute aqueous solution of such a salt is kept, it gradually becomes cloudy and more alkaline, and in time it deposits an equivalent quantity of the true nitro compound. The process is accelerated by boiling and it takes place rapidly when an organic base is added to a methyl alcoholic solution of the *aci* nitro compound.

The α-bromo substitution product of the true nitro compound is readily obtained by the action of bromine on the *aci* form, its sodium salt, or the magnesium halide derivative that is formed in the Grignard reaction. It is also easy to eliminate hydrogen bromide from it, and thus obtain a phenylated nitro stilbene—triphenyl nitro ethylene

$$(C_6H_5)_2CHC(C_6H_5){=}N(OH)O \longrightarrow \underset{\mathrm{VII}}{(C_6H_5)_2CHCBr(C_6H_5)NO_2} \longrightarrow$$

$$\underset{\mathrm{VIII}}{(C_6H_5)_2C{=}C(C_6H_5)NO_2}$$

We tried in vain to introduce a fourth phenyl group into triphenyl nitro ethylene, but had no difficulty in introducing methyl, ethyl and benzyl groups. In contrast with the corresponding unsaturated ketone, $(C_6H_5)_2C{=}C(C_6H_5)COC_6H_5$, the unsaturated nitro compound combines readily with aliphatic magnesium compounds, and despite the accumulation of phenyl groups about the conjugated system the reaction consists, apparently exclusively, of 1,4-addition. After acidification the product is in each case an iso-nitro compound

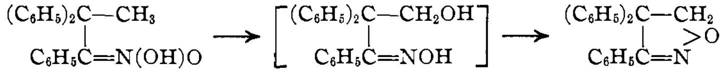
$$(C_6H_5)_2C(CH_3)C(C_6H_5){=}N(OH)O \qquad (C_6H_5)_2C(C_2H_5)C(C_6H_5){=}N(OH)O$$

IX X

$$(C_6H_5)_2C(CH_2C_6H_5)C(C_6H_5){=}N(OH)O$$

XI

These new *aci* nitro compounds, the most highly branched aliphatic nitro compounds that are known, behave in the main like *aci*-triphenyl nitro ethane. They give nearly all the characteristic reactions of the simplest *aci* nitro compounds but they do not react normally with bromine and for some unknown reason it was also impossible to make well-defined bromine compounds by the action of bromine on their metallic derivatives. Like all other *aci* nitro compounds they rapidly deteriorate both by themselves and in the presence of acid, but under these conditions they neither undergo rearrangement to true nitro compounds like the simple nitro paraffins, nor hydrolysis to the corresponding ketone like *aci*-triphenyl nitro ethane. The readjustment is involved, and it leads to more than one substance, but the principal product is a cyclic compound that is doubtless due to internal oxidation and reduction. Thus when hydrochloric acid is added to a methyl alcoholic solution of *aci*-triphenyl nitro propane, 70% of the product is triphenyl isoxazoline



$$\begin{array}{c}(C_6H_5)_2C{-}CH_3\\ |\\ C_6H_5C{=}N(OH)O\end{array} \longrightarrow \left[\begin{array}{c}(C_6H_5)_2C{-}CH_2OH\\ |\\ C_6H_5C{=}NOH\end{array}\right] \longrightarrow \begin{array}{c}(C_6H_5)_2C{-}CH_2\\ |\quad >O\\ C_6H_5C{=}N\end{array}$$

XII

All the true nitro compounds that we have studied are perfectly stable both in solid form and in solution. A solution of tetraphenyl nitro propane in pure dry ether has not undergone any change in the three years during which it has been kept under observation. Since, in ethereal solution, the iso-nitro compound completely disappears in a few weeks, it seems reasonable to conclude that this solution contains no *aci* form whatsoever and that the true nitro compounds do not spontaneously undergo rearrangement.

From a study of these substances we have, therefore, reached the conclusion that the scheme

$$(R)_2\ CHNO_2 \rightleftarrows (R)_2\ C{=}N(OH)O$$

does not represent reality. No quantitative results are available but, since the *iso* form is an acid, our qualitative results appear to be in complete accord with Lowry's mechanism for such rearrangements.

Experimental Part

I. Experiments with Nitro Stilbene

Nitro stilbene reacts readily both with methylmagnesium iodide and with phenyl magnesium bromide. Since the reaction with methyl magnesium iodide gave no well-defined product it will not be described. In the case of phenyl magnesium bromide at least 90% of the reaction consists in 1,4-addition to the conjugated system C=C—N=O. This follows not only from the fact that the resulting magnesium derivative is a salt of an acid which gives all the characteristic reactions of iso-nitro compounds, but also from a series of transformations which show that the phenyl group goes into the β-position.

$$\underset{\text{II}}{(C_6H_5)_2CHC(C_6H_5){=}NO(OMgBr)} \longrightarrow (C_6H_5)_2CHC(C_6H_5)BrNO_2 \longrightarrow$$

$$(C_6H_5)_2C{=}C(C_6H_5)NO_2 \longrightarrow (C_6H_5)_2CO$$

While it is possible to isolate pure iso-nitro compound by manipulating the reaction mixture which contains the magnesium derivative II in the usual manner, it is much better to secure it by way of the sodium salt. The procedure finally adopted was as follows.

A solution obtained by dissolving 12 g. of magnesium in 80 g. of bromobenzene and 500 cc. of ether was cooled in ice water. To this solution was added, gradually, with constant cooling and stirring, 60 g. of finely ground nitro stilbene. The resulting clear liquid was boiled for fifteen minutes, then cooled again and diluted with an equal volume of chilled low-boiling petroleum ether. The unused Grignard reagent, diphenyl, and other impurities remained in solution, while fairly pure magnesium derivative was precipitated as a pale yellow paste which generally solidified. After decanting the ether–petroleum ether layer and replacing it with 100 cc. of alcohol-free ether, the magnesium derivative was decomposed with iced acid and the ethereal layer separated and washed in the usual manner. When this ether solution was shaken with 10% aqueous sodium hydroxide it yielded an almost perfectly pure, colorless, crystalline sodium salt of the iso-nitro compound.

For the purpose of isolating the iso-nitro compound itself, the ethereal layer was decanted and replaced with fresh alcohol-free ether, the mixture cooled in a freezing mixture and gradually acidified with excess of iced hydrochloric acid. The resulting ethereal solution when dried for a few minutes with calcium chloride and then concentrated under diminished pressure deposited pure iso-nitro compound. The yield was 90%.

Anal. Calcd. for $C_{20}H_{17}O_2N$: C, 79.2; H, 5.6. Found: C, 79.1; H, 5.4.

Aci-triphenyl-nitro-ethane (III) crystallizes in colorless prisms and melts, with decomposition, at about 91°. It is readily soluble in all common organic solvents except petroleum ether. When it is prepared from the sodium salt as described and kept in an open vessel it may remain solid for as long as several weeks, but when it is made directly from the magnesium derivative it generally turns to a red oil within twenty-four hours. The change is promoted by organic solvents and other impurities. When the pure solid is suspended in dilute hydrochloric acid it disintegrates more slowly than when it is kept by itself. Solutions of the iso-nitro compound in organic solvents generally become distinctly colored in twenty-four hours, and after a week they fail to give the delicate color reaction with ferric chloride.

The Sodium Salt, $(C_6H_5)_2CHC(C_6H_5){=}NO{-}ONa$.—The *aci* form of triphenyl nitro ethane is readily soluble in sodium carbonate as well as sodium hydroxide, forming a sodium salt that precipitates at once from the hydroxide and more slowly from the carbonate. It is soluble in alcohols and in acetone but is best purified by recrystallization from water, in which it is only moderately soluble at low temperatures.

Anal. Calcd. for $C_{20}H_{16}O_2NNa$: Na, 7.1. Found: Na, 7.4, 7.0.

The sodium salt crystallizes in downy needles, melts at 100–103°, and is not altered by heating to 120°. As it is stable it constitutes a convenient means of stocking the *aci* nitro compound.

Other Salts.—When a drop of ferric chloride solution is added to an ethereal solution of the *aci* nitro compound, it immediately produces a red color which is destroyed by addition of hydrochloric acid and regenerated when the acid is partially neutralized by bases. This reaction which is characteristic of iso-nitro compounds supplies a delicate method for observing the disappearance of the *aci* form in solution.

The *aci* nitro compound also readily forms a copper salt, which is obtained as a colorless crystalline precipitate when an ethereal solution is shaken with copper acetate and when an ethereal solution of the *aci* compound is added to methyl magnesium iodide it liberates methane and precipitates colorless magnesium halide similar to that obtained in the Grignard reaction.

Attempts to Alkylate.—A suspension of the sodium salt in anhydrous ether was boiled for eight hours with excess of methyl iodide, then filtered. The filtrate on concentration deposited a crystalline solid which after recrystallization from methyl alcohol melted at 173°.

Anal. Calcd. for $C_{20}H_{17}ON$: C, 83.6; H, 5.9. Found: C, 83.0; H, 5.7.

The composition and melting point indicated triphenyl ethanone oxime (V) and the identification was completed by comparison with a specimen made from the ketone. A repetition of the experiment, using methyl alcohol as solvent, likewise gave mainly oxime but along with it a small quantity of the true nitro compound due to rearrangement in the slightly basic medium. Instead of being alkylated, therefore, the sodium salt was merely reduced to the corresponding oxime.

Oxidation and Reduction.—A freshly prepared solution of the iso-nitro compound in ethyl bromide is not attacked by ozone and an aqueous solution of the sodium salt is not oxidized by a 10% solution of sodium peroxide. Aqueous solutions of the sodium salt reduced permanganate but gave only oily products. Solutions of the iso-nitro compounds in moist ether were readily reduced by aluminum amalgam and gave triphenyl ethanone oxime as the primary product but the process was either accompanied or followed by condensation reactions which gave intractable substances.

Hydrolysis.—Cold concd. hydrochloric acid was added slowly and with constant cooling to a freshly made ethereal solution of 2 g. of the iso-nitro compound until there were two distinct layers. The mixture was shaken for ten minutes, and then cautiously diluted. The ethereal layer on evaporation left 1.75 g. of practically pure triphenyl ethanone, which was identified by comparison with a sample on hand. The same process occurred when a methyl alcoholic solution of the sodium salt was acidified with excess of concentrated hydrochloric acid and kept at 50° for several hours, but the product was less pure and the yield smaller. Since no true nitro compound could be detected in either case it is evident that mineral acids readily hydrolyze but do not promote the rearrangement of the *iso* form.

Rearrangement to the True Nitro Compound.—A solution of 5 g. of the pure sodium compound in one liter of water was boiled for an hour, during which a solid separated in pale yellow crystals. The suspension was filtered and the feebly alkaline filtrate tested for unchanged *aci* nitro compound by acidification, extraction with ether and addition of ferric chloride to the ethereal extract. The *aci* nitro compound had disappeared completely.

The solid was washed with water and recrystallized from methyl alcohol. It separated in rectangular elongated prisms which were faintly yellow in color and melted at 130°. The yield was 90%.

Anal. Calcd. for $C_{20}H_{17}O_2N$: C, 79.2; H, 5.6. Found: C, 79.2; H, 5.6.

α,β,β-Triphenyl nitro ethane is readily soluble in acetone, in alcohol and in ether, very slightly soluble in petroleum ether, and insoluble in water. It separates from petroleum ether in colorless prisms but it is most conveniently recrystallized from methyl alcohol. Its ethereal solution does not develop any color when treated with ferric chloride, and it neither dissolves in dilute sodium hydroxide nor is extracted from ethereal solution by concd. alkalies.

Change from Nitro to Iso-nitro Compound.—While the nitro compound is not extracted from its ethereal solution by aqueous sodium hydroxide, it is rapidly removed by methyl alcoholic sodium methylate. Thus after an ether–petroleum ether solution containing 2 g. of the substance had been shaken for five minutes with 10 cc. of a concentrated solution of sodium methylate, it was found to be entirely free from nitro compound. By allowing the pale yellow alcoholate solution to evaporate and treating the residue with ice water, it was easy to isolate a sodium salt that on acidification gave the *aci* nitro compound in a yield of about 90%.

α,β,β-Triphenyl-α-bromo-nitro Ethane (VII).—Triphenyl nitro ethane does not react with bromine but its α-bromo derivative is readily made from the *aci* form or its sodium salt. It is most economical, however, to prepare the bromo compound by adding bromine to the ethereal solution that is obtained when nitro stilbene is added to phenyl magnesium bromide. Thus, in a typical case, the solution obtained by adding 60 g. of nitro stilbene to the requisite amount of phenyl magnesium bromide was boiled for fifteen minutes, then cooled in a freezing mixture and treated with 82 g. of dry bromine. The bromine was added drop by drop while the solution was stirred vigorously. It first produced a greenish-brown paste which was gradually converted into a fine crystalline solid as the reaction neared completion. After all the bromine had been added, the stirring was continued for another half hour, during which the temperature was allowed to rise. The solid was collected on a suction filter, washed with ether and recrystallized from acetone; yield, 95%.

Anal. Calcd. for $C_{20}H_{16}O_2NBr$: C, 62.8; H, 4.2. Found: C, 62.7; H, 4.6.

The bromo compound is very sparingly soluble in all common organic solvents except hot acetone. It crystallizes in small colorless prisms and melts with decomposition at 185°. It readily reacts with ethyl magnesium bromide and forms the magnesium bromide salt of *aci* triphenyl nitro ethane—an interesting transformation. When it is heated above the melting point it loses nitrous acid and passes into bromo triphenyl ethylene, but when it is digested with alcoholates it loses hydrogen bromide and forms the corresponding unsaturated nitro compound—triphenyl nitro ethylene.

II. Experiments with Triphenyl Nitro Ethylene

Preparation.—A suspension of 75 g. of the bromo compound described in the preceding paragraph in a solution obtained by dissolving 25 g. of sodium in 500 cc. of methyl alcohol was boiled for an hour, during which the colorless compound was replaced by a granular yellow precipitate. The solid was washed with water, methyl alcohol and ether, and then recrystallized from acetone; yield, 56 g.

Anal. Calcd. for $C_{20}H_{15}O_2N$: C, 79.7; H, 5.0. Found: C, 79.8; H, 5.2.

The nitro compound crystallizes in yellow prisms which melt at 170° and decompose a few degrees above the melting point. It is very sparingly soluble in alcohol and ether, moderately soluble in acetone.

Oxidation and Reduction.—In order to verify the structure, the nitro compound was both oxidized and reduced. It was readily oxidized both by chromic acid in glacial acetic acid and by ozone in chloroform. In each case the principal product was benzophenone. For the purpose of reduction 6 g. of zinc dust was gradually added to a boiling solution of 5 g. of the substance in 50 cc. of glacial acetic acid and 15 cc. of water. When all the color had disappeared the solution was poured into water. It precipitated a colorless nitrogen-free solid that after recrystallization melted at 136° and formed an oxime melting at 172°. The physical properties of the substance agree with those of triphenyl ethanone, but the melting point of the oxime is 10° below that given for the oxime of this ketone.[1] The oxime was, therefore, analyzed and, finally, to remove all doubt, triphenyl ethanone was prepared in a different manner and turned into oxime as directed by Kohler. The oxime thus obtained likewise melted at 172°, and a mixed melting point of the two preparations proved their identity. Zinc and acetic acid, therefore, reduce the unsaturated to the saturated nitro compound, which is then hydrolyzed to the corresponding ketone

$$(C_6H_5)_2C{=}C(C_6H_5)NO_2 \longrightarrow (C_6H_5)_2CHC(C_6H_5){=}NO{-}OH \longrightarrow (C_6H_5)_2CHCOC_6H_5$$

Reaction with Grignard Reagent.—At the temperature of ice water the finely ground nitro compound readily reacts with alkyl magnesium halides without evolution of gas; the solutions remain colorless but deposit a colorless crystalline derivative, the reaction is confined to the conjugated system, and the yield is in excess of 90%; but if the temperature is allowed to rise, the nitro group also becomes involved, gas is given off, the solution becomes yellow, and the yield falls off. The solution also slowly turns yellow when it is allowed to stand overlong at low temperatures but this appears to be due to a slow decomposition of the iso-nitro compounds and has only a slight effect on the yields. A typical procedure is illustrated by the following experiment with methyl magnesium iodide.

Ten grams of the finely ground nitro compound was slowly stirred into an ice cold solution prepared from 3.2 g. of magnesium, 18 g. of methyl iodide and 150 cc. of ether. As soon as the mixture had become colorless it was decanted into iced hydrochloric acid. The ethereal layer, when shaken vigorously, began to deposit the iso-nitro compound as a pale pink crystalline solid. The deposition was rapidly made as complete as possible, by addition of cold petroleum ether. The solid was collected on a filter and the ether-petroleum ether extracted with 10% aqueous sodium hydroxide. The solid was washed with water and ether and recrystallized from ether–petroleum ether; yield, 8 g. The combined sodium hydroxide extracts, treated in the usual manner, gave nearly 1 g. more of less pure compound.

The properties of the products obtained with the three magnesium compounds are summarized in the following table.

Reagent	Formula	Composition, %			M. p., °C. (dec.)	Yield, %
		C	H	N		
CH_3MgI	$(C_6H_5)_2C(CH_3)C(C_6H_5)N(OH)O$	79.3	6.2	4.6	120	88
	$(C_6H_5)_2C(CH_3)CH(C_6H_5)NO_2$	79.0	5.8		136	95
C_2H_5MgI	$(C_6H_5)_2C(C_2H_5)C(C_6H_5)N(OH)O$	79.0	6.1		120	85
	$(C_6H_5)_2C(C_2H_5)CH(C_6H_5)NO_2$	79.5	6.3		138	95
$C_6H_5CH_2MgI$	$(C_6H_5)_2C(CH_2C_6H_5)C(C_6H_5)N(OH)O$	82.0	6.2		140	85
	$(C_6H_5)_2C(CH_2C_6H_5)CH(C_6H_5)NO_2$	82.1	6.0		136	95

The stability relationships of these iso-nitro compounds are practically the same as those of *aci*-triphenyl nitro propane, as is also their behavior toward acids and bases, oxidizing, reducing and alkylating agents; only their behavior toward hydrolytic agents is different.

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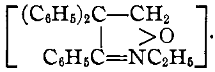
[1] Kohler, *Am. Chem. J.*, **36**, 193 (1906).

Action of Methyl Alcoholic Hydrochloric Acid, 3,4,4-Triphenyl Isoxazoline, XII.—A solution of 3 g. of the sodium salt in methyl alcohol was slowly added to a mixture of 150 cc. of absolute methyl alcohol and 120 cc. of concentrated hydrochloric acid which was stirred mechanically and kept at 50° for three hours. The light red reaction mixture was diluted with water and allowed to stand overnight. Since it yielded no solid product, it was extracted with ether. The ethereal solution was washed with sodium carbonate and water, dried with calcium chloride and concentrated. It deposited colorless needles which after one recrystallization from ether melted at 142°.

Anal. Calcd. for $C_{21}H_{17}ON$: mol. wt., 299; C, 84.2; H, 5.7. Found: mol. wt., 301; C, 83.9; H, 5.8.

The substance is remarkably stable and unreactive. It does not react with permanganate and it is not attacked by ozone. It was recovered after it had been boiled with sodium methylate and also after it had been dissolved in cold concentrated sulfuric acid or heated for fifteen minutes with 80% sulfuric acid on a steam-bath.

Ethylation of the Isoxazoline,  $\left[\begin{array}{l}(C_6H_5)_2C-CH_2\\ \qquad\quad | \quad >O\\ C_6H_5C{=}NC_2H_5\end{array}\right]\cdot FeCl_4$.—A solution of 0.5 g. of the isoxazoline in 3 g. of diethyl sulfate was heated for three hours at 120°, then diluted with hydrochloric acid and boiled for a few minutes to decompose the excess of sulfate. The clear solution was extracted with ether, then treated with 1 cc. of concd. ferric chloride. This precipitated an oil which soon solidified. The yellow solid was recrystallized from ethyl bromide and ether. The yield of pure product was 0.52 g.

Anal. Calcd. for $C_{23}H_{22}ON\cdot FeCl_4$: C, 52.5; H, 4.2. Found: C, 53.0; H, 4.2.

The substance is sparingly soluble in ether, readily soluble in ethyl bromide. It crystallizes from a mixture of these solvents in needles, and melts at 110–111°. Alkalies convert it into an ether-soluble pseudo base from which it is regenerated by hydrochloric acid and ferric chloride.

Summary

1. This paper contains directions for preparing pure highly phenylated aliphatic nitro and *iso*-nitro compounds.

2. It shows that neither form spontaneously passes into the other, that solutions do not contain an equilibrium mixture of the two forms, and that acids do not promote the rearrangement of the *iso* to the normal form.

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