165. *Researches on Acetylenic Compounds. Part XXX. Catalytic and Inhibitory Effects in the Reppe Carboxylation Reaction.*

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The extension of the Reppe carboxylation reaction to acetylenic halides has been investigated. 1-Iodoacetylenes are reduced by nickel carbonyl to the corresponding acetylenes, and simultaneously inhibit the normal reaction which the latter usually undergo with nickel carbonyl. Vinylacetylenes can be induced to react with nickel carbonyl by adding pyridine; dimeric products are obtained. Some complex salts obtained from nickel carbonyl are described.

During a systematic exploration of the Reppe carboxylation reaction, several types of acetylenic compounds have been treated with nickel carbonyl (Jones, Shen, and Whiting, *J.*, 1950, 230; 1951, 48). Some halogeno-acetylenic compounds have now been submitted to the reaction.

When 1-iodohex-1-yne was treated with nickel carbonyl under the usual conditions (*i.e.*, in aqueous-ethanolic acetic acid at about 70°) no exothermic reaction occurred, although a brown colour developed. No acidic product was obtained, but distillation of the neutral fraction gave, rather unexpectedly, an appreciable yield of the parent hex-1-yne, in addition to 20% of unchanged iodohexyne. In the same way, 1-iodo-2-phenylacetylene gave a 44% yield of phenylacetylene, 20% of the starting material being recovered. Presumably, the nickel carbonyl in these reactions is behaving as a reducing agent:

$$2R{\cdot}C{\equiv}C{\cdot}I + 2Ni(CO)_4 + 2AcOH \longrightarrow 2R{\cdot}C{\equiv}CH + Ni(OAc)_2 + NiI_2 + 8CO$$

This reduction proceeds slowly, whereas the carboxylation of hex-1-yne and phenylacetylene by nickel carbonyl normally occurs very rapidly, after a brief induction period, in these conditions. In order to account for the surprising fact that the acetylenic hydrocarbons produced in these reactions do not react subsequently with the nickel carbonyl present, it seemed reasonable to postulate the operation of some inhibiting influence.

It was at first thought possible that free iodine, which is very readily liberated from iodo-acetylenic compounds, might be acting as an inhibitor. However, in a control experiment in which phenylacetylene and a little iodine were treated with nickel carbonyl in aqueous-ethanolic acetic acid at 70°, the colour of the iodine was rapidly discharged as soon as the addition of the carbonyl began, and a normal reaction then ensued. The only difference from the usual results was the esterification of an abnormally large proportion of the atropic acid formed, presumably because of the catalytic effect of the nickel iodide present. It therefore appeared that the iodoacetylenes themselves might be capable of inhibiting the Reppe carboxylation; if so, and if their reduction proceeds to completion, the use of a large excess of nickel carbonyl should allow the normal vigorous carboxylation reaction to occur. This was found to be the case. When iodophenylacetylene was treated under the standard conditions at 70° with a large excess of nickel carbonyl, no detectable exothermic reaction occurred during 20 minutes; the usual, sudden, highly exothermic reaction then took place; working up gave a trace of atropic acid and a 32% yield of ethyl atropate (in this instance quite a large quantity of nickel iodide, evidently a good esterification catalyst, was present). No phenylacetylene or iodophenylacetylene could be isolated.

This evidence of inhibition by an acetylenic compound suggested the hypothesis that the "inert" acetylenic compounds referred to earlier (*locc. cit.*; see also following paper), which do not react vigorously with nickel carbonyl, may owe this inability to react to a self-inhibitory effect. If so, they should be able to hinder the carboxylation of typical "reactive" acetylenes. Therefore, mixtures, in various ratios, of a typical "inert" acetylene, 1-ethynyl*cyclo*hexyl acetate "(A)," and one which reacts normally, hex-1-yne "(B)," were treated with nickel carbonyl under the standard conditions. The results are tabulated below:

Molar ratio, B : A.	Exothermic reaction.	A recovered, %.	B recovered.	$Bu{\cdot}\underset{CO_2H}{C}{=}CH_2$, yield, %.
1	None	60	Yes	0
4	None	0	Yes	0
20	After long induction	0	None	27
A not present	Normal	—	None	35

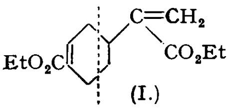
The evidence for the existence of such an inhibitory effect is convincing but it is impossible at this stage to estimate its importance and generality.

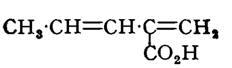
The behaviour of 1-bromohex-1-yne on treatment with nickel carbonyl was quite different from that of the iodo-compound. No exothermic reaction occurred, no hex-1-yne was formed and, despite the formation of much dark polymeric material, the bromo-compound was recovered in 46% yield. No acidic product was isolated.

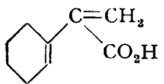
Attempts were made to apply the reaction to various other types of acetylenic halides. 1 : 4-Dichlorobut-2-yne underwent an exothermic reaction on treatment with nickel carbonyl, but distillation of the reaction product resulted in decomposition. 1-Bromopent-4-yne, however, reacted smoothly and gave the expected α-methylenic acid in 22% yield, together with about 18% of the corresponding ester.

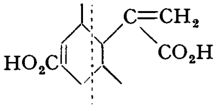
Because of the general similarity between the properties of alkyl halides and toluene-*p*-sulphonates, attempts were made to effect reactions between nickel carbonyl and the toluene-*p*-sulphonates of but-2-yne-1 : 4-diol, but-3-yn-1-ol, and pent-4-yn-1-ol. Unfortunately, rapid hydrolysis occurred instead in every case; no exothermic reactions were observed and a light-green precipitate of nickel toluene-*p*-sulphonate was formed in considerable quantity. In the case of pent-4-yn-1-yl toluene-*p*-sulphonate, however, isolation of the acidic fraction did give a small (1·5%) yield of a crystalline product which analysed as expected for the α-methylenic acid.

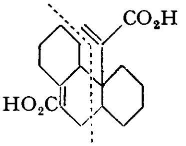
The failure of several substituted vinylacetylenes to undergo the Reppe carboxylation reaction under the normal conditions has already been described (*locc. cit.*). On the other hand, Reppe (" Acetylene Chemistry," translation, Meyer, 1949, p. 158) states that vinylacetylene reacts with nickel carbonyl in ethanol containing hydrochloric acid to give a dimer of the expected buta-1 : 3-diene-2-carboxylic acid, and suggests a possible structure (I) for it. An attempt to induce substituted vinylacetylenes to react essentially under our standard conditions has now been made by adding pyridine, which decomposes nickel carbonyl rapidly in acetic acid solution and might thus be expected to initiate the reaction. With the typical examples, pent-3-en-1-yne and 1-ethynyl*cyclo*hexene, no exothermic reactions ensued on slow addition of nickel carbonyl to their solutions in aqueous ethanolic acetic acid, containing one molecular proportion of pyridine, at 70°; but subsequent isolation gave appreciable quantities of acid. This in each case was separable into a crystalline fraction (m. p.s 230—232° and 251—252°, respectively) and a liquid portion which rapidly polymerised and was not investigated further. The crystalline acids gave analytical values expected for (II) and (III) respectively, but their physical properties suggested that they were dimeric, and in the case of the acid prepared from pent-3-en-1-yne this was proved by determination of the molecular weight of the dimethyl ester. Reppe's proposed structure (I) (the evidence upon which it was based has not yet been published) implies a Diels–Alder type of dimerisation, eminently plausible for primary products such as (II) and (III). If this interpretation is valid for the cases investigated, the products, (IV) and (V), should show the light absorption typical of αβ-unsaturated acids and esters; such is indeed the case. The product from 1-ethynyl*cyclo*hexene exhibits a maximum at a longer wave-length than that from pent-3-en-1-yne, as would be expected. There is therefore *prima facie* evidence for the correctness of the formulæ assigned, although various other possibilities cannot be excluded.


(I.)


$CH_3\cdot CH{=}CH\cdot\underset{CO_2H}{C}{=}CH_2$
(II.)


(III.)

(IV.)



(V.)

The results of adding pyridine to the reaction mixture in the cases of various other types of acetylenes were less remarkable. Vinylacetylene itself rather unexpectedly failed to give a crystalline product, although a certain amount of acidic material, which rapidly polymerised, was formed. The " inert " tertiary acetate, 1-ethynyl*cyclo*hexyl acetate, still gave the expected product in small yield (7%, as against 3% without pyridine). In the case of iodophenylacetylene, addition of pyridine did not alter the course of the reaction: slow reduction took place, followed (provided that sufficient nickel carbonyl was used) by rapid carboxylation of the phenylacetylene, and isolation of the products gave atropic acid and ester in 35% total yield. When phenylacetylene was treated with nickel carbonyl in the presence of pyridine the carboxylation reaction began without the normal induction period, and atropic acid was obtained in the usual yield, *i.e.*, 49%. It was also possible to effect the carboxylation of phenylacetylene (yield, 45%) when a mixture of pyridine, acetic acid, and water was used as solvent, in spite of the fact that this mixture rapidly decomposes the carbonyl.

It was noted, in the experiments with phenylacetylene just described, that when the reaction mixture cooled a deep-green solid separated. This appeared to be a complex salt of atropic acid, since the latter was precipitated on acidification of its aqueous solution. An apparently analogous salt was obtained by adding nickel carbonyl to an aqueous-ethanolic acetic acid solution of pyridine; it gave analytical figures for a dipyridine nickel diacetate dihydrate. The atropate, however, gave analytical values which could only be explained by assuming a solvate with one molecule of ethanol. Co-ordination complexes of nickel with two molecules of pyridine have not been described previously, but salts of copper containing only two amine molecules have recently been prepared (Broom, Ralston, and Thornton, *J. Amer. Chem. Soc.*, 1946, **68**, 67). It is of course possible that the organic acids are weakly co-ordinated to the nickel atom in these substances; in any case, their chemistry might repay investigation.

EXPERIMENTAL.

Reaction of 1-*Iodohex*-1-*yne with Nickel Carbonyl.*—To a solution of 1-iodohex-1-yne (10 g.; Grignard and Perrichon, *Ann. Chim.*, 1926, **5**, 5) in ethanol (20 c.c.), acetic acid (3 c.c.), and water (1 c.c.), nickel carbonyl (3 c.c.) in ethanol (7 c.c.) was added slowly at 70°. No exothermic reaction was observed, and the reaction mixture was kept at 75—80° for about 30 minutes. Removal of excess of nickel carbonyl by co-distillation with ether and isolation of the neutral fraction (care being taken to remove alcohol by washing and to avoid loss of volatile material), followed by distillation, gave (*a*) hex-1-yne (containing some alcohol) (2·5 g., ~60%), b. p. 65—72°, n_D^{19} 1·3853, and (*b*) recovered iodohexyne (2 g., 20%). Fraction (*a*) was recognised by its physical constants (pure hex-1-yne has b. p. 71°, n_D^{24} 1·3969), its odour, and its insoluble silver derivative. No appreciable acid fraction was present.

Reaction of Iodophenylacetylene with Nickel Carbonyl.—(*a*) To a solution of iodophenylacetylene (10·8 g.; prepared by the method of Grignard and Perrichon, *loc. cit.*) in ethanol (25 c.c.), water (1 c.c.), and acetic acid (3 c.c.), nickel carbonyl (5 c.c.) in ethanol (10 c.c.) was added slowly at 75—80°. The solution became dark brown, but no exothermic reaction was observed. After 20 minutes' heating isolation gave a negligible acidic fraction; the neutral fraction yielded phenylacetylene (2·1 g.; 44%), b. p. 81—83°/100 mm., n_D^{20} 1·5420 (Bourguel, *Ann. Chim.*, 1924, **3**, 229, gives b. p. 142—143°, n_D^{20} 1·548), and unchanged iodophenylacetylene (2·0 g., 18%), b. p. 123°/18 mm., n_D^{20} 1·6648. (Wieland and Fischer, *Annalen*, 1925, **446**, 67, give b. p. 114—116°/12 mm.)

(*b*) In a similar experiment in which 5·7 g. of iodophenylacetylene, 5 c.c. of nickel carbonyl, and 4 c.c. of acetic acid were employed, a period (10 minutes) when no conspicuous exothermic reaction occurred was followed by a sudden rise in temperature. Isolation then gave a trace of atropic acid, m. p. 102—104°, undepressed on admixture with an authentic specimen, and ethyl atropate (1·4 g., 32%), b. p. 67—71°/0·2 mm., n_D^{22} 1·526 (Auwers and Eisenlohr, *J. pr. Chem.*, 1911, **84**, 89, give b. p. 120·2—120·4°/14 mm., n_D^{16} 1·5260). The latter was characterised by alkaline hydrolysis (albeit in poor yield, as was usually the case) to atropic acid, m. p. 101—104°, undepressed on admixture with an authentic specimen (m. p. 106—107°).

(*c*) In a similar experiment in which phenylacetylene (7·7 g.), pyridine (2 c.c.), nickel carbonyl (5·5 c.c.), acetic acid (5 c.c.), water (1 c.c.), and ethanol (30 c.c.) were employed, no exothermic reaction occurred on addition of the carbonyl, although a deep green coloration was observed initially. After half the carbonyl had been added the solution became brown and 20 minutes after the commencement of the addition an exothermic reaction occurred suddenly. Atropic acid (0·18 g., 3%), m. p. 104—105°, and ethyl atropate (1·85 g., 32%), b. p. 85°/0·3 mm., n_D^{22} 1·5236, were obtained.

5-*Bromopent*-1-*ene*-2-*carboxylic Acid and its Ethyl Ester.*—5-Bromopent-1-yne (9·1 g.; Eglinton and Whiting, *J.*, 1950, 3650), acetic acid (3 c.c.), water (1 c.c.), and ethanol (25 c.c.) were treated with nickel carbonyl (3 c.c.) in ethanol (10 c.c.) at 70°. An exothermic reaction occurred; removal of excess of the carbonyl and isolation of the acidic and neutral fractions gave respectively the *acid* (2·6 g., 22%), b. p. 85°/0·05 mm., n_D^{20} 1·5047 (Found: C, 38·75, 38·5; H, 4·8, 4·8; Br, 40·5. $C_6H_9O_2Br$ requires C, 37·35; H, 4·7; Br, 41·4%), and the *ethyl* ester (2·5 g., 18%), b. p. 53°/0·02 mm., 113°/16 mm., n_D^{21} 1·4751 (Found: C, 43·9, 44·5; H, 6·05, 6·0; Br, 35·2. $C_8H_{13}O_2Br$ requires C, 43·45; H, 5·9; Br, 36·1%). Treatment of the acid with thionyl chloride and then with *p*-toluidine gave the corresponding p-*toluidide*, which formed plates, m. p. 78°, from benzene–light petroleum (Found: C, 55·85; H, 5·55; N, 4·85, 5·05; Br, 26·8. $C_{13}H_{16}ONBr$ requires C, 55·3; H, 5·7; N, 4·95; Br, 28·3%). No reasonable explanation for the consistently inaccurate analyses of these compounds, which appeared to be pure, can be suggested.

Toluene-p-*sulphonate of* 5-*Hydroxypent*-1-*ene*-2-*carboxylic Acid.*—A solution of pent-4-yn-1-yl toluene-*p*-sulphonate (12 g.; Eglinton and Whiting, *loc. cit.*) in acetone (2 c.c.), acetic acid (3 c.c.), and water (1 c.c.) was heated under reflux at 55—60° while a solution of nickel carbonyl (3 c.c.) in acetone (10 c.c.) was added during 15 minutes. A green precipitate slowly formed; no exothermic reaction occurred. Separation of the acidic fraction, after the removal of excess of carbonyl, gave an oil which partly solidified; crystallisation from benzene–light petroleum gave the *acid toluene*-p-*sulphonate* (0·2 g., 1·5%) as prisms, m. p. 85° (Found: C, 55·0; H, 5·8. $C_{13}H_{16}O_5S$ requires C, 54·95; H, 5·65%).

Reppe Carboxylation of Pent-2-en-4-yne.—A solution of pent-2-en-4-yne (4·6 g.; Eglinton and Whiting, *loc. cit.*), acetic acid (5 c.c.), water (3 c.c.), pyridine (5 c.c.), and ethanol (35 c.c.) was treated slowly with nickel carbonyl (4 c.c.) at 65—70°. The acidic fraction of the product partly solidified, and was separated into an oil (2·1 g.) which rapidly polymerised and was not investigated further, and a solid, m. p. 228—230° (1·2 g., 16%), which on recrystallisation from aqueous methanol gave the dimeric *acid* (IV?) as prisms, m. p. 230—232° [Found: C, 64·5; H, 7·25. $(C_6H_8O_2)_n$ requires C, 64·3; H, 7·2%]. Light absorption: End absorption, ε = 12,000 at 2160 A., assuming the doubled formula. The *methyl* ester, obtained with diazomethane had b. p. 115° (bath-temp.)/10^{-5} mm., n_D^{18} 1·4986 [Found: C, 66·3; H, 7·55; *M* (ebullioscopic), 241. $(C_7H_{10}O_2)_2$ requires C, 66·6; H, 8·0%; *M*, 252].

Reppe Carboxylation of 1-*Ethynyl*cyclo*hex*-1-*ene.*—Ethynyl*cyclo*hexene (5·4 g.; see Hamlet, Henbest, and Jones, forthcoming publication, for an improved method of preparation), water (2 c.c.), pyridine (5 c.c.), acetic acid (4 c.c.), and ethanol (20 c.c.) were treated slowly with nickel carbonyl (4 c.c.) in ethanol (10 c.c.) at 70°. No exothermic reaction occurred; the acidic fraction partly solidified, yielding, after crystallisation from ethyl acetate, the presumably dimeric *acid* (V?) (1·15 g., 15%), m. p. 251—252° [Found: C, 71·25; H, 7·75. $(C_9H_{12}O_2)_2$ requires C, 71·05; H, 7·95%]. Light absorption: Max., 2230—2260 A., ε = 9400.

Complex Salts from Nickel Carbonyl.—(*a*) On treatment of a solution of phenylacetylene and pyridine in aqueous ethanolic acetic acid with nickel carbonyl an exothermic reaction occurred immediately. When the solution was freed from excess of the carbonyl by co-distillation with ether and allowed to cool, deep green crystals separated. Recrystallisation from ethanol containing a few drops of pyridine gave a complex *salt* as bluish-green prisms, m. p. 150—154° [Found: C, 64·35; H, 5·0; N, 5·15. $C_{30}H_{30}O_5N_2Ni$, *i.e.*, $Ni(O{\cdot}CO{\cdot}CPh{:}CH_2)_2,2C_5H_5N,C_2H_5{\cdot}OH$ requires C, 64·65; H, 5·4; N, 5·0%]. Heating above 100° at 10^{-5} mm. converted it into grass-green prisms which decomposed, without melting, at 220°. Both this substance and the complex salt gave an immediate precipitate of atropic acid when their aqueous solutions were acidified.

(*b*) On addition of nickel carbonyl to a solution of pyridine in aqueous-ethanolic acetic acid the solution became warm and rapidly became green; on concentration it deposited blue crystals. Recrystallisation from aqueous ethanol containing a little pyridine gave greenish-blue prisms, m. p. 140—141° [Found: C, 45·6; H, 5·5; N, 7·3. $C_{10}H_{20}O_6N_2Ni$, *i.e.*, $Ni(O{\cdot}OC{\cdot}CH_3)_2,2C_5H_5N,2H_2O$ requires C, 45·3; H, 5·4; N, 7·55%].

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