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85. Catalytic Deoxygenation of Organic Compounds by Carbon Monoxide:

III[1]). The Reaction under Pressure of Aromatic Nitro Compounds in the Presence of *o*-Phthalaldehyde

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(14. I. 72)

Summary. The reaction of *o*-phthalaldehyde with several aromatic nitro compounds in the presence of carbon monoxide and catalytic quantities of hexarhodium-hexadecacarbonyl eventuated in the formation of the corresponding N-substituted isoindolinone as the major product. A reaction mechanism has been suggested incorporating deoxygenation of the nitro compound by carbon monoxide to a nitrene intermediate and the subsequent interception of the latter by *o*-phthalaldehyde.

Introduction. – Concurrent with the recent rapid growth of the chemistry of metal carbonyls, the application of carbon monoxide in the domain of organic syntheses has likewise gathered momentum. While such industrial processes as hydroformylation and hydrocarboxylation of olefins [2] conspicuously demonstrate the extensive exploitation of carbon monoxide as a carbonylating agent, its application as a reductant for organic compounds is confined to relatively few examples. For such studies, compounds containing the N–O linkage have constituted a fruitful substrate of frequent choice. The deoxygenating process here involved is accompanied by the oxidation of carbon monoxide to carbon dioxide.

The essentially stoichiometric reduction of nitrobenzene to aniline by alkaline solutions of iron carbonyl [3] is one of the earliest reports where deoxygenation by a carbon monoxide ligand is implied. Later [4] [5], iron pentacarbonyl was also found to effect the deoxygenation of amine oxides, azoxybenzenes, and nitrones, while nitro- and nitrosobenzenes were reduced, under the same conditions, to azo and/or amino compounds. The drastic conditions required for the reductive coupling of nitrobenzene to azobenzene by carbon monoxide alone [6] could be obviated by using catalytic quantities of iron pentacarbonyl [7]. Aryl isocyanates [8], or products derived therefrom [9] [10], were synthesized by the interaction between nitrobenzenes and carbon monoxide using selective catalyst systems. In the presence of a mixture

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[1]) For Part II, see reference [1].

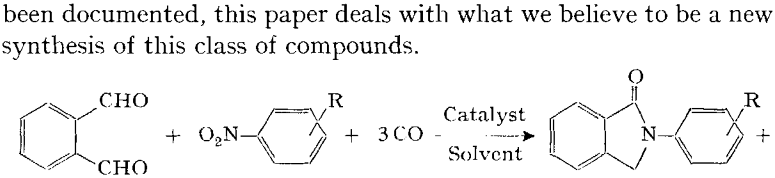
of hydrogen and carbon monoxide, the reduction process eventuated in the formation of the corresponding amines and/or urea derivatives [11] [12].

Thermolysis of established precursors of nitrene, such as aryl azides, to yield azobenzenes (cf. for example [13]) by dimerization, amines [14] by hydrogen abstraction from solvents, or isocyanates [15] in the presence of carbon monoxide, appears strongly evidential of the intervention likewise of nitrene or nitrenoid species in the formation of identical products by catalytic and non-catalytic reduction of nitro compounds by carbon monoxide. This view is further substantiated by the isolation of nitrenoid complexes from the reaction of iron carbonyls with aromatic azides and nitro compounds [16]. While consequently several authors have resorted to a nitrene mechanism in rationalizing the products of the aforementioned reactions [5] [7–10] [12], to our knowledge, no attempt has so far been undertaken to effect the conversion of such *in situ* deoxygenated intermediates with specific compounds. The only exceptions constitute instances where either carbon monoxide itself becomes attached to the nitrene to form isocyanate [8–10], or molecular hydrogen [11] [12] and organic solvents [5] [7] containing labile hydrogen atoms are employed in order to facilitate saturation of the reactive intermediate *via* hydrogen abstraction.

Interest was, therefore, stimulated for examining, as part of a programme for establishing a carbon-nitrogen bond, the catalytic deoxygenation of nitro compounds by carbon monoxide, conducted in the presence of various organic substrates considered capable of intercepting the deoxygenated intermediates.

Results and Discussion. – The rhodium carbonyl catalysed deoxygenation of nitro compounds to primary amines, in the presence of water, has been described in a previous communication [17]. The experimental facts were suggestive of a reaction mechanism involving the formation of a nitrenoid intermediate in a first step, followed by hydrogen transfer from water by way of a hydrido metal carbonyl. The crucial intervention of a nitrenoid species was subsequently postulated to explain the direct formation of *Schiff* bases [1] from monoaldehydes and nitro derivatives in the presence of carbon monoxide. We now report some results of investigations with *o*-phthalaldehyde in place of the monoaldehydes.

As we found, *o*-phthalaldehyde reacts with several aromatic nitro compounds and carbon monoxide under pressure to give the corresponding N-substituted isoindolinones, according to equation 1 below. Whereas the formation of isoindolinones *via* reaction of *o*-phthalaldehyde with amines [18], isocyanates and carbodiimides [19] has been documented, this paper deals with what we believe to be a new approach to the synthesis of this class of compounds.



(1)

[Ia–f]

Experimental conditions and results have been summarized in the Table. All products have been unequivocally identified by appropriate derivatives, mixed melting point, and by spectroscopic (IR. and NMR.) comparison with authentic specimens. No effort has been made to obtain optimal yields of the reaction, which will need to be studied in detail to allow any definite statement regarding the influence of ring substituents on the course and extent of isoindolinone formation.

The reaction of o-phthalaldehyde with aromatic nitro compounds and carbon monoxide to give N-substituted isoindolinone a)

Product	R =	Isoindolin-1-one yield [%] b)	Melting point c) [°C]	IR. (ν_{CO}) d) [μ]	¹H-NMR. Chemical Shifts δ [ppm] e)		
					–CH₂–	aromatic	–CH₃
Ia	H	58	161–162	5.92	4.81	7.1–8.0	–
Ia	H	0 f)					
Ib	*p*-OCH_3	42	144–145	5.99	4.66	6.75–7.95	3.74
Ic	*m*-Cl	55	190–191	5.92	4.78	7.1–8.0	–
Id	*m*-CH_3	40	143–144	5.91	4.73	6.8–8.0	2.36
Ie	*p*-CH_3	46	136–137	5.92	4.68	7.0–8.0	2.29
If	*p*-C_6H_5	0 f)					
If	*p*-C_6H_5	60	231–233	5.93	4.87	7.2–8.1	–

a) Constant reaction conditions: 0.01 mole *o*-phthalaldehyde, 0.011 mole nitro compound, 10^{-5} mole hexarhodium-hexadecacarbonyl, 5–6 ml pyridine, 150 atm initial carbon monoxide pressure, 165–170°C, 3 h, 30 ml rocking steel autoclave.

b) Raw yield based on *o*-phthalaldehyde (compare experimental section).

c) Melting points are uncorrected.

d) KBr disc.

e) Measured in $CDCl_3$.

f) Pyridine was replaced by benzene in these experiments.

As for previous, analogous reactions [1] [17], tertiary nitrogen bases also constitute essential solvents for the present synthesis. Thus, we failed to detect any isoindolinone on conducting the reaction in benzene, while up to 60% yields of the product could be isolated from reaction mixtures in pyridine. It is believed that the base promotes the formation of the catalytic rhodium carbonyl species, presumably by transiently absorbing the carbon dioxide formed and/or by incorporating itself into the coordination sphere of the metal carbonyl.

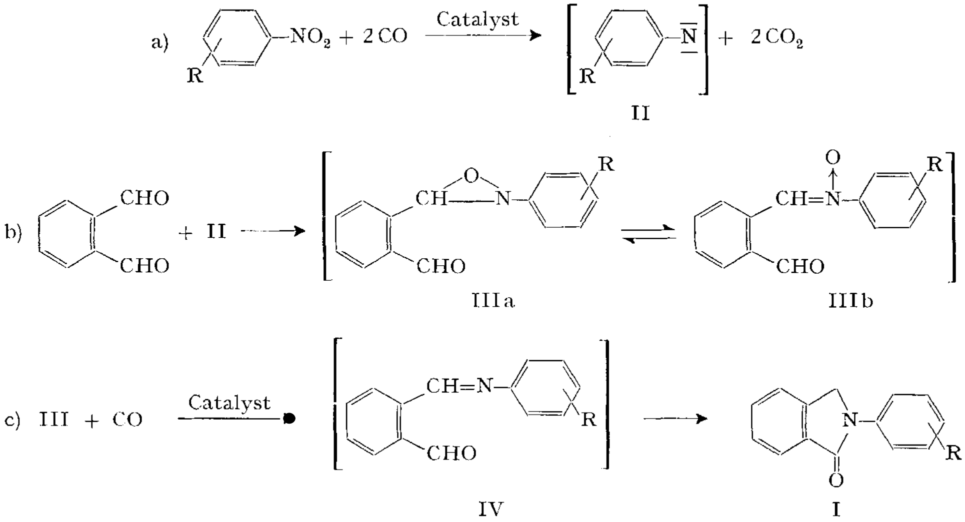
No isoindolinone is formed in the absence of a catalyst. A particularly suitable catalyst for the reaction is hexarhodium-hexadecacarbonyl, which may also be formed *in situ* from its precursors, such as rhodium salts or oxides. The yields of N-aryl-isoindolin-1-one vary in general between 50 and 60%, based on *o*-phthalaldehyde. In certain cases they are lowered by unavoidable manipulative losses. It proved expedient to carry out the reaction with a slight (*ca.* 10%) excess of the nitro component.

In search of an adequate mechanistic explanation of the above formation of isoindolinones, one might at first sight be tempted to formulate the nitro component as a possible precursor of isocyanate [8] or amine [5–7], both of which could subsequently react with *o*-phthalaldehyde [18] [19] to give the final product. However, control experiments with only nitrobenzene, carbon monoxide and hexarhodium-hexadecacarbonyl in pyridine failed to yield any isocyanate. Together with a negligible quantity of aniline, up to 30% of carbanilide was identified as the major product. The formation of the latter, though rendered possible by the presence of 1–2% hydrogen in commercial carbon monoxide, does not involve the carbonylation of intermediary aniline, as could be experimentally verified. In addition, replacement of the nitro by the corresponding amino compound in the reaction given by equation (1) led under identical conditions to intractable tars. Only a trace of isoindolinone could be isolated from the reaction mixture. In view of these results, the intermediacy of an amine or isocyanate is considered unlikely in this process.

The reductive carbonylation of nitrobenzene by commercially available carbon monoxide to carbanilide, on the other hand, prompted us to investigate the reaction of the latter with *o*-phthalaldehyde as a possible source of isoindolinone. While a survey of pertinent literature[2]) revealed very little about analogous reactions, we obtained fairly good ($> 50\%$) yields of isoindolinone by the interaction of *o*-phthalaldehyde and a number of diaryl ureas, both in melt and in solution.

None the less, these results, in our opinion, do not suffice as peremptory evidence for the intervention solely of urea derivatives during the direct synthesis of isoindolinones from nitro compounds and *o*-phthalaldehyde, essentially for two reasons. Firstly, from recent studies [21] it is very probable that in the above formation of urea a nitrenoid intermediate is involved, so that one must also take into account the possible interception of the nitrene by *o*-phthalaldehyde (*vide infra*) as a competitive step, leading ultimately to the isoindolinone. Moreover, stoichiometric control experiments have shown that the amount of urea, even if it be considered to intervene here, is inadequate to account for the observed yields of isoindolinone. Hence allowance must be made for additional or alternative reaction mechanism pathways.

The presumed mechanistic scheme below involves the intermediate III, formed along pathways envisaged for the analogous reaction of monoaldehydes [1].



The stepwise catalytic deoxygenation of the nitro derivative by carbon monoxide in the presence of a metal carbonyl is thougth to generate the aryl nitrene II – either

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[2]) For the reaction of *o*-phthalaldehyde with compounds containing the N—H bond, compare, for example [20].

discrete or complexed. The reaction of II with one carbonyl function of *o*-phthalaldehyde presumably leads to the oxazirane IIIa, in equilibrium with the tautomeric nitrone IIIb. Further catalytic reduction of III by carbon monoxide yields the imino aldehyde IV, which may be regarded as the immediate progenitor of isoindolinone I [19]. The rearrangement of IV to I entails an intramolecular shift of the hydrogen atom at the free carbonyl function. Beside being thermally initiated, such a transfer may conceivably take place *via* a hydrido metal carbonyl intermediate, analogous to those proposed for related reactions [22].

Experimental. – Carbon monoxide was purchased from *Organchemie*, Zürich, and used without further purification. The nitro compounds were freshly distilled or crystallized prior to reaction with *o*-phthalaldehyde (*Fluka/puriss*). Hexarhodium-hexadecacarbonyl was prepared by the reductive carbonylation of rhodium chloride in the presence of iron pentacarbonyl [23]. Pyridine (*Fluka/puriss*) and N-methylpyrrolidine were dried and distilled over potassium hydroxide.

M.p.'s are not corrected. ^{1}H-NMR. measurements were carried out in $CDCl_3$ with a *Varian* HA 60 IL instrument. For IR. spectra a *Grubb-Parsons* Spectromaster instrument was used.

Procedure for isoindolin-1-one formation from o*-phthalaldehyde and aromatic nitro compounds.* All reactions were carried out in stainless steel autoclave of 30 ml capacity, heated by an external rocking electric oven. Only one experiment, with *p*-nitrobiphenyl will be described here to exemplify the general experimental procedure adopted; the effect of varying conditions can be seen from the data presented in the Table.

A solution of *o*-phthalaldehyde (0.01 mole), *p*-nitrobiphenyl (0.011 mole) and hexarhodium-hexadecacarbonyl (10^{-5} mole) in 5 ml pyridine was allowed to react with carbon monoxide (150 atm). The content of the autoclave was heated during 40 min to 165–170° and kept at this temperature for 3 h. After cooling, the autoclave was discharged and pyridine evaporated from the mixture under vacuum. The residue was swirled with 10–15 ml of hot methanol and allowed to cool, upon which substantially pure micro-crystals of N-*p*-biphenyl-isoindolin-1-one separated out in 60% yield. The raw product may be recrystallized from methanol/chloroform 1:1. Yields and physical properties of the various isoindolin-1-ones are compiled in the Table.

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86. Equilibres conformationnels de glucides au niveau de liaisons σ sp²–sp³ C–C. IV[1]). Furannoses hybridés sp² en C(3)

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(17 I 72)

Summary. The conformation of 34 branched-chain unsaturated sugars, prepared by reacting different *Wittig* reagents with a series of 1,2-O-isopropylidene-furannosul-3-oses, has been studied by PMR spectroscopy. The position of each compound in the flexible conformational cycle has been established by using the known stereo-dependence of the allylic coupling constants and checked with the other parameters of the spectra. An 'isopropylidenic' ${}^4J_{2,4}$ coupling constant, present in all compounds whose H–C(4) is *endo* and absent in their C(4)-epimers has proved useful for configurational assignment at C(4).

L'analyse conformationnelle des sucres pyrannosiques et furannosiques dont tous les carbones sont hybridés sp^3 a fait l'objet de très nombreux travaux dont *Stoddart* a donné une revue récente [2]. La RMN. a beaucoup facilité ce développement dans la mesure surtout où la présence dans ces composés de nombreuses constantes de couplage vicinal dont la stéréodépendance est bien connue permettait une détermination sûre et précise de la conformation moyenne des furannoses alors que dans le cas des sucres pyrannosiques pour lesquels les barrières d'énergie entre conformations sont plus élevées la RMN. à différentes températures permettait même d'obtenir les paramètres cinétiques et thermodynamiques des équilibres conformationnels [3].

La présence, dans le cycle d'un sucre, de carbones hybridés sp^2 diminue le nombre des couplages vicinaux et par là même réduit considérablement la somme des informations pour l'analyse conformationnelle. Dans le cas des pyrannoses possédant une double liaison intracyclique, cet appauvrissement de l'information est compensé par une diminution considérable de la flexibilité de la molécule.

Une situation beaucoup plus difficile est rencontrée dans les dérivés furannosiques dont le carbone 3 est hybridé sp^2. Dans ces composés en effet un seul couplage vicinal (H–C(1)–H–C(2)) subsiste et la mobilité conformationnelle du cycle n'est pas réduite par la présence d'un carbone sp^2. Nous avons préparé un nombre assez important de dérivés de furannosul-3-oses (oximes, hydrazones, dérivés C-méthyléniques) et l'ana-

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[1]) La référence [1] constitue la troisième communication de cette série.