653. *Hydrogen Transfer. Part XVII.*[1] *Homogeneous Hydrogen Transfer Reactions from Dihydrides of Nitrogenous Heterocycles to Miscellaneous Acceptors.*

By (the late) E. A. Braude, J. Hannah, and Sir Reginald Linstead.

Diethyl 1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (the "Hantzsch ester") and 1,2-dihydroquinoline have been found to act as hydrogen donors in homogeneous solution in purely organic systems, and are capable of reducing a variety of hydrogen acceptors, such as suitably activated ethylenes, azomethines, and azo- and nitro-compounds. The process requires no catalyst.

The work presented in this paper is summarised in Tables 1 and 2. All the transfer reactions were of the same general form: stoicheiometric quantities of hydrogen donor and hydrogen acceptor were allowed to interact in homogeneous solution in sealed vessels, with variation in solvent and time and temperature of reaction. Most of the transfers were very slow and were rarely taken to completion. The ease of isolation of the four components varied widely, but in all cases the criterion of successful hydrogen transfer was isolation of the reduced acceptor or a derivative of it. Invariably there was more dehydrogenation of the donor than hydrogenation of the acceptor. This random oxidation of the hydro-heterocycle can generally be attributed to the presence of peroxides or dissolved oxygen in the solvent, but in certain experiments in which no transfer occurred, the considerable extent of donor oxidation can only easily be explained by the second component's exercising some catalytic dehydrogenation effect.

The corresponding reactions with quinone acceptors have been described in Part XVI.[1] The first homogeneous hydrogen transfer from the Hantzsch ester to maleic acid was effected at 66°. Higher temperature produced the expected increase in reaction velocity, with however, increasing evidence of decomposition of the donor. This effect of

[1] Part XVI, Braude, Hannah, and Linstead, preceding paper.

acidic decomposition [1] of the heterocycle was most marked when glacial acetic acid was tested as solvent (no. 8 and 9). The latter reaction mixture also contained 20 mg. of cupric acetate in solution: the only interesting effect observed was that a mirror of metallic copper was formed.

Reaction no. 4 was a test for the possible inhibition of the transfer to maleic acid. The solvent used was crude, discoloured, commercial tetrahydrofuran, which contained

TABLE 1. *Donor: diethyl* 1,4-*dihydro*-2,6-*dimethylpyridine*-3,5-*dicarboxylate.*

	Acceptor	Temp.	Time	Oxidn. of donor (%)	Redn. of acceptor (%)
1	Chloranil [1]	25°	15 min.	97	97
2	Maleic acid	66	20 hr.	?	49
3	,,	,,	70 hr.	?	62
4	,,	,,	90 hr.	?	72
5	,,	101	30 min.	70	29
6	,,	156	,,	>70	63
7	,,	172	,,	>70	61
8	,,	118	1 hr.	>60	49
9	,,	,,	,,	>60	33
10	Maleic anhydride	66	70 hr.	>95	93
11	,, ,,	,,	70 min.	>80	77
12	,, ,,	101	30 min.	95	91
13	Fumaric acid	,,	,,	9	8
14	Diethyl maleate	,,	,,	<5	<2
15	,, ,,	172	20 hr.	91	76
16	Diethyl fumarate	,,	,,	100	70
17	Dimethylmaleic anhydride	66	72 hr.	<2	not detected
18	,, ,,	172	90 hr.	>90	*meso*, 6; racemic, 47
19	Dimethylfumaric acid	66	72 hr.	0	0
20	3,4,5,6-Tetrahydrophthalic anhydride	101	30 min.	4	<4
21	,, ,, ,,	172	85 hr.	>80	*cis*, 70; *trans*, 0
22	3,4,5,6-Tetrahydrophthalimide	101	30 min.	>10	0
23	,, ,, ,,	172	50 hr.	>60	0
24	*trans-trans*-Muconic acid	101	101 hr.	>20	Probable
25	,, ,,	172	50 hr.	>95	,,
26	Cinnamic acid	66	24 hr.	<5	0
27	,, ,,	101	40 hr.	<5	,,
28	,, ,,	172	85 hr.	>60	Complex reaction.
29	Diphenylacetylene	66	24 hr.	5	Unlikely
30	,, ,,	101	40 hr.	10	,,
31	,, ,,	156	24 hr.	12	,,
32	1,4-Dihydronaphthalene	66	72 hr.	>20	,,
33	*trans*-Stilbene	156	24 hr.	30	0
34	*trans*-4-Nitrostilbene	,,	,,	60	$-NH_2$, 16; $-[CH_2]_2-$ possible
35	*trans*-4-Cyanostilbene	172	40 hr.	40	Possible
36	*trans-trans*-1,4-Diphenylbutadiene	156	24 hr.	>25	Unlikely
37	Nitrobenzene	66	,,	<3	Not detected
38	,,	172	,,	15	$-NH_2$, >8
39	Benzonitrile	,,	,,	10	0
40	,,	,,	100 hr.	50	,,
41	Benzophenone	66	24 hr.	6	Not detected
42	,,	172	85 hr.	>60	,,
43	Benzylideneacetophenone	156	24 hr.	42	$-[CH_2]_2-$, 25; $-CH(OH)$, unlikely
44	,, ,,	172	85 hr.	60	$-[CH_2]_2-$, 80; $-CH(OH)$, unlikely
45	Mesityl oxide	101	24 hr.	17	0
46	,,	200	20 hr.	>10	,,
47	*trans*-1,2-Diacetylethylene	101	24 hr.	Complex reaction	
48	Pyruvic acid	156	20 hr.	Decomposition	
49	,,	101	72 hr.	Complex reaction	
50	Ethyl pyruvate	,,	,,	14	0
51	Benzil	,,	50 hr.	7	Trace
52	,,	172	24 hr.	<40	$-CO\cdot CH(OH)-$23
53	Benzylideneaniline	156	,,	70	~25
54	Azobenzene	,,	,,	>90	~23
55	Anthracene	172	24 hr.	Trace	0

TABLE 2. *Donor:* 1,2-*dihydroquinoline.*

	Acceptor	Temp.	Time	Oxidn. of donor (%)	Redn. of acceptor (%)
56	Chloranil *	20°	30 min.	100	>93
57	3,4,5,6-Tetrahydrophthalic anhydride	20	256 hr.	?	0
58	,, ,,	101	50 hr.	80	15
59	Benzylideneacetophenone	,,	,,	?	$-[CH_2]_2-$, possible
60	Benzylideneaniline	,,	,,	?	77
61	Azobenzene	,,	,,	85	74
62	Maleic anhydride	20	8 min.	Quantitative condensation	

* Cf. reaction No. 62 for details.

water, peroxides, and other impurities: the acceptor, however, was smoothly reduced to succinic acid.

A series of reactions under identical conditions showed that maleic anhydride, maleic acid, fumaric acid, and diethyl maleate were reduced to the extent of 91%, 29%, 8%, and less than 2%, respectively.

When the reactions of the Hantzsch ester and maleic acid and anhydride were carried out in December 1953, we thought them to be the first examples of such hydrogen transfer. However, in 1939, Mumm and Diederichsen,[2] re-examining the structures in the 1,2- and 1,4-dihydropyridine series by the criterion of Diels–Alder reaction with maleic anhydride, treated the Hantzsch ester with maleic anhydride and, on the basis of the rapid interaction, classified this heterocycle as a 1,2-dihydropyridine; they pointed out, however, that no Diels–Alder adduct was formed, but that the dehydrogenated heterocycle and succinic anhydride were isolated. This observation was not followed up, and their main deduction was in fact incorrect, for it has now been shown by comprehensive ultraviolet spectral analyses that the Hantzsch ester belongs to the 1,4-dihydropyridine series.[3]

It at first appears surprising that under identical conditions there is very little difference in the extent of reduction of diethyl maleate and diethyl fumarate, whereas maleic acid is reduced almost three times faster than fumaric acid. However, the normally slow isomeric change of maleic to fumaric ester is markedly catalysed by secondary amines.[4] It seems probable, therefore, that with both the *cis*- and the *trans*-ester, the species being reduced is diethyl fumarate.

Hydrogen transfer from the Hantzsch ester to 3,4,5,6-tetrahydrophthalic anhydride was slow at 172°. The reduced acceptor was isolated as *cis*-cyclohexane-1,2-dicarboxylic acid in an extremely pure condition. No trace of the *trans*-isomer was detected. Because of the high temperature involved, the above result is not necessarily diagnostic of pure *cis*-addition of hydrogen to the double bond, and in fact a blank reaction, in which the pure *trans*-cyclohexane-1,2-dicarboxylic anhydride was heated in solution with the oxidised Hantzsch ester, showed considerable inversion to the *cis*-anhydride. The recovered acid was however not the pure *cis*-acid, and it is probable that in the transfer to the unsaturated anhydride, some trace of the *trans*-cyclohexane acid would have been detected if hydrogenation had involved an initial *trans*-addition.

Under similar conditions, dimethylmaleic anhydride was reduced in solution by the Hantzsch ester, and 6% of *meso*-αα′- and 47% of racemic αα′-dimethylsuccinic acid were isolated. The *meso*-material could hardly have been formed by inversion at the acid level and it is the *unstable* form at the anhydride level.[5] At first sight, therefore, it appears that the initial addition of hydrogen in the transfer reaction occurs (at least partially) *cis*. However, work described below on the reaction between maleic anhydride and 1,2-dihydroquinoline indicates that these reactions may follow a complex course.

3,4,5,6-Tetrahydrophthalimide did not act as an acceptor although considerable

[2] Mumm and Diederichsen, *Annalen*, 1939, **538**, 195.
[3] Berson and Brown, *J. Amer. Chem. Soc.*, 1955, 444.
[4] Davies and Evans, *Trans. Faraday Soc.*, 1955, 1506.
[5] Linstead and Whalley, *J.*, 1954, 3722.

oxidation of the Hantzsch ester was observed. This contrasts with the easy catalytic hydrogenation of imides such as maleimide, dimethylmaleimide, and 3,4,5,6-tetrahydrophthalimide, the anhydrides corresponding to which cannot be catalytically hydrogenated. No positive evidence can be produced for the homogeneous reduction of *trans-trans*-muconic acid [6] by the Hantzsch ester, although considerable oxidation of the donor occurred.

Cinnamic acid also showed no tendency to act as an acceptor at low temperatures, and the reaction at 172° caused some decomposition of donor material. In contrast, both cinnamic and *trans-trans*-muconic acid are smoothly reduced to the saturated compounds by metal-catalysed hydrogen transfer from cyclohexene at 66°.[7]

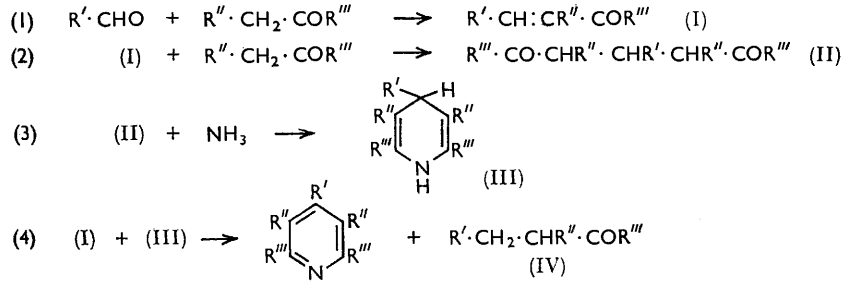
With hydrocarbon acceptors, previous work on hydrogen transfer has also shown that simple unactivated ethylenic and acetylenic bonds are easily reduced by cyclohexene in presence of palladised charcoal.[7] On the other hand the dihydropyridine donor in homogeneous solution failed to reduce diphenylacetylene, *trans*-stilbene, or *trans-trans*-1,4-diphenylbutadiene.

Attempts were then made to render the ethylene bond of *trans*-stilbene more susceptible to homogeneous reduction, by introducing strongly polarising groups in the 4-position of one ring. When 4-nitrostilbene was treated with the lutidine donor, little or no reduction of the ethylene bond could be observed, but the nitro-group was reduced to the primary amine.

Examination of nitrobenzene as an acceptor then showed that aniline is formed, but 4-nitrostilbene is much more readily reduced to 4-aminostilbene. Both 4-cyanostilbene and benzonitrile failed to act as hydrogen acceptors under similar conditions.

Reduction of the carbonyl function of aldehydes and ketones could not be effected by metal-catalysed hydrogen transfer from cyclohexene.[8] The ethylene bond of αβ-unsaturated aldehydes and ketones likewise was not reduced. The dihydropyridine donor in homogeneous solution gave parallel results in that simple keto-groups were not reduced to alcohols. One exception, however, was observed in both catalysed and non-catalysed transfer: the α-diketone benzil was reduced to the acyloin benzoin.

In contrast to the work on catalysed transfer, the αβ-unsaturated ketone, benzylideneacetophenone was reduced by the dihydropyridine donor to the saturated ketone. Two molecular equivalents of the donor were used, but no alcohol function could be detected in the product. Frank and Seven,[9] and Weiss,[10] in their studies on the Tschitschibabin pyridine synthesis have postulated that, for stoicheiometry, some transfer must occur (see formulæ). Here the 1,4-dihydropyridine intermediate has never been isolated, but



in one reaction, with benzylideneacetophenone, acetone, and ammonia, Frank and Seven [9] isolated benzylacetophenone. The present reduction of the same unsaturated ketone by

[6] Elvidge, Linstead, and Smith, *J.*, 1953, 708.
[7] Braude, Linstead, and Mitchell, *J.*, 1954, 3578.
[8] Braude, Linstead, Mitchell, and Wooldridge, *J.*, 1954, 3595.
[9] Frank and Seven, *J. Amer. Chem. Soc.*, 1949, 2629.
[10] Weiss, *J. Amer. Chem. Soc.*, 1952, 200.

diethyl 1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate supports the views of Frank and Seven and of Weiss.

The αβ-double bond of mesityl oxide was not reduced by the Hantzsch ester.

It was expected that *trans*-1,2-diacetylethylene would be reduced with ease comparable to that with fumaric acid. This was not realised in practice since some complex reaction and decomposition occurred.

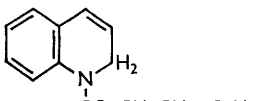
Mauzerall and Westheimer [11] examined the reaction between pyruvic acid and an excess of diethyl 1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate. The mixture was heated on a steam-bath for 18 hours with no solvent, and was then analysed by partition chromatography over silica gel.[12] 7% of lactic acid was found by titration and phenacyl lactate was isolated. We have found this to be an extremely complex reaction, involving extensive condensation between donor and acceptor. In contrast, ethyl pyruvate was not a hydrogen acceptor.

Abeles and Westheimer [13] recently reduced benzoylformic acid to mandelic acid in very low yield, again using the Hantzsch ester as a direct hydrogen donor.

Palladium-catalysed hydrogen transfer from cyclohexene causes hydrogenolysis of both benzylideneaniline and azobenzene to form aniline.[8] Homogeneous hydrogen transfer from the dihydropyridine donor to both of these compounds was achieved with the formation of benzylaniline and hydrazobenzene respectively.

A number of compounds in the series tested as hydrogen acceptors from the Hantzsch ester were also examined with 1,2-dihydroquinoline as donor. It was found that 1,2-dihydroquinoline effected the same type of reduction faster than the dihydropyridine donor. This might have been expected from kinetic data,[1] but the sequel to this paper provides good examples of kinetic predictions' being subordinate to the thermodynamic properties of any system.

The reaction between 1,2-dihydroquinoline and maleic anhydride in ether rapidly gave an unstable, crystalline product for which structure (V) is proposed. This compound dissolves with effervescence in cold aqueous sodium hydrogen carbonate and is reprecipitated by mild acidification. It is rapidly hydrolysed in cold concentrated hydrochloric acid to 1,2-dihydroquinoline and a maleic–fumaric acid mixture. It is thermally unstable, and controlled decomposition yields quinoline and succinic anhydride. Compound (V) therefore represents a half-way stage in the reduction of maleic anhydride by 1,2-dihydroquinoline, with thermal decomposition completing the hydrogen transfer.



(V)

The same process is thought to operate in the reduction of the substituted maleic anhydrides by both the dihydropyridine and the dihydroquinoline donor, with the slower reactions due to the steric and electronic contributions of the substituents.

Experimental

M. p.s were determined on the Kofler block. Unstable or volatile compounds were contained in sealed capillaries (about 0·2 mm. diameter), which lay flat on the glass slide of the Kofler block in the usual way.

Microanalyses and spectral measurements were carried out in the microanalytical (Miss J. Cuckney) and spectrographic (Mrs. A. I. Boston and Dr. R. L. Erskine) laboratories of this department.

Solvents used in the hydrogen-transfer reactions were tetrahydrofuran, dioxan, and phenetole, all of which were purified by prolonged refluxing over sodium, followed by fractional distillation through a 30 × 1 cm. column of Fenske helices. Refluxing in these solvents provided reaction temperatures of about 66°, 101°, and 172°, respectively.

[11] Mauzerall and Westheimer, *J. Amer. Chem. Soc.*, 1955, 2261.
[12] Bulen, Varner, and Burrell, *Analyt. Chem.*, 1952, **24**, 187.
[13] Abeles and Westheimer, *J. Amer. Chem. Soc.*, 1958, 5459.

Reaction apparatus consisted of long-necked, round-bottomed flasks of ~100 ml. capacity, all in one piece with a Liebig condenser topped with a B.19 socket.[14] Heating was by micro-burner, and the whole unit was shielded from draughts. In every case the mixtures were homogeneous at the boiling point, and were rapidly boiled until the vapour reached the condenser. The rate of heating was then reduced, and after a few seconds had been allowed for equilibration a " cold finger," fitted with a greased B.19 cone, was inserted to the level of the base of the condenser. Refluxing of the reaction solution then continued smoothly in an effectively sealed system.

As an additional precaution for the exclusion of oxygen, several reactions in phenetole solution were carried out in sealed Pyrex tubes. These mixtures were maintained at a constant temperature of 156° in a simple thermostat of boiling anisole vapour. The precaution was in general unnecessary.

In every case, exact equivalents of donor and acceptor were used, in terms of the hydrogen-transfer reaction being attempted.

The dihydropyridine donor and its oxidised form (diethyl 2,6-dimethylpyridine-3,5-dicarboxylate) were completely different in properties. The dihydropyridine donor, m. p. 189—190°, was yellow, non-basic, and insoluble in petroleum. The oxidised compound, m. p. 73·5—74·5°, was colourless, strongly basic, and easily soluble in petroleum. These differences were of great assistance in working up the products from the various reactions. The m. p. of the lutidine donor was markedly depressed by impurities, for example, 184—185° represents at least 97% purity.[1]

1,2-Dihydroquinoline and quinoline were more difficult to separate and, in general, the labile dihydroquinoline component in an incomplete transfer reaction was not worked up.

The solvent, time, and temperatures of reaction are given in Tables 1 and 2. Representative working up procedures are given below. The numbers refer to the examples in the Tables.

5. *Hantzsch Ester–Maleic Acid.*—Donor, 1·091 g.; acceptor, 0·500 g.; dioxan, 17 ml.; 101°; 30 min. Solvent was evaporated at reduced pressure, and the residue was extracted with an excess of warm aqueous sodium carbonate. The alkaline extract was acidified and continuous ether-extraction then yielded the acid component (0·53 g.), m. p. 125—179°. Titration of an aliquot part with 0·1N-potassium permanganate [15] showed that the maleic acid content had diminished by 29%. The remainder of the sample was oxidised with the permanganate reagent under the same conditions, and continuous ether-extraction of the mixture yielded crude succinic acid (0·121 g.), m. p. 167—175° (diphenacyl ester, m. p. and mixed m. p. 150—151°). The recovered donor component (0·980 g.) was separated by extraction with 4N-hydrochloric acid into crude unchanged donor (0·090 g.), m. p. 165—170°, and oxidised donor (0·715 g.), m. p. 71—72°.

15. *Hantzsch Ester–Diethyl Maleate.*—Donor, 1·091 g.; acceptor, 0·742 g.; phenetole, 15 ml.; 172°; 20 hr. Unchanged donor was precipitated from the cold solution by the addition of light petroleum (b. p. 40—60°) (50 ml.): filtration then gave yellow needles (0·101 g., 9%), m. p. 157—165°, raised to 181—183° by crystallisation from ethanol. Oxidised donor was extracted from the petroleum–phenetole filtrate with 4N-hydrochloric acid and was recovered as a colourless powder (0·410 g., 38%), m. p. 70—72°.

The petroleum–phenetole solution was evaporated on the steam-bath, and the residual phenetole solution of the ester was boiled under reflux with an excess of ethanolic potassium hydroxide. Water was added and the cold hydrolysis mixture was extracted with light petroleum to remove phenetole. The aqueous salt solution was then acidified and continuous ether-extraction gave the mixed acids as a pale brown solid (0·543 g., theor. 0·509 g.), m. p. 70—183°. Titration of an aliquot part with standard permanganate [15] showed that the original double bond value had diminished by 76%. The remainder of the recovered acids was fractionally crystallised from ethanol to give succinic acid (0·102 g.), m. p. and mixed m. p. 189—190°.

18. *Hantzsch Ester–Dimethylmaleic Anhydride.*—Donor, 0·880 g.; dimethylmaleic anhydride, 0·437 g.; phenetole, 14 ml.; 172°; 90 hr. Most of the solvent was distilled off at reduced pressure. The residue was dissolved in benzene and extracted with an excess of aqueous sodium carbonate. The alkaline extract was acidified to Congo Red and was continuously

[14] Braude, Jones, and Stern, *J.*, 1946, 401.
[15] Lange and Kline, *J. Amer. Chem. Soc.*, 1922, 2709.

extracted with ether, yielding a colourless solid (0·394 g.), m. p. 75—162°. Unchanged dimethylmaleic anhydride was dissolved from this mixture with boiling light petroleum (b. p. 40—60°) and was recovered as a colourless solid (0·122 g., 28%), m. p. and mixed m. p. 87—94° (pure m. p. 94—95°). The petroleum-insoluble residue (0·269 g.), m. p. 119—143°, was extracted with cold chloroform, leaving *meso*-dimethylsuccinic acid (0·030 g., 6%), which was crystallised from hot water as colourless prisms (0·027 g.), m. p. and mixed m. p. 204—206° (sealed capillary). Evaporation of the chloroform extract yielded racemic dimethylsuccinic acid (0·239 g., 47%), m. p. and mixed m. p. 123—127°. Oxidised donor (0·721 g., 83%) and crude unchanged donor (0·017 g., 2%) were recovered in the usual way from the original benzene solution.

21. *Hantzsch Ester–3,4,5,6-Tetrahydrophthalic Anhydride.*—Donor, 0·743 g.; acceptor, 0·447 g.; phenetole, 12 ml.; 172°; 85 hr. Light petroleum (b. p. 60—80°) (50 ml.) was added to the cold solution, and the precipitated unchanged donor (0·064 g.), m. p. 170—172°, was filtered off. Aqueous sodium carbonate extraction of the phenetole–petroleum filtrate, followed by acidification and constant ether-extraction of the aqueous extract, afforded a colourless solid (0·483 g.). This material was thoroughly extracted with boiling light petroleum (b. p. 60—80°). Insoluble material was *cis*-cyclohexane-1,2-dicarboxylic acid (0·353 g., 70%), m. p. and mixed m. p. 195·5—196°. [The *trans*-isomer has m. p. 221° (uncorr.).] Evaporation of the petroleum extract yielded a solid (0·109 g., 24%), m. p. 45—70°, which crystallised from light petroleum to give 3,4,5,6-tetrahydrophthalic anhydride, m. p. and mixed m. p. 68—73° (pure, m. p. 73—74·5°). In the usual way, oxidised donor (0·552 g., 75%) and crude unchanged donor (0·057 g., 16%) were recovered from the phenetole–petroleum solution.

Thermal Isomerism of trans- *to* cis-*Cyclohexane-1,2-dicarboxylic Anhydride.*—A solution of pure *trans*-cyclohexane-1,2-dicarboxylic anhydride (0·453 g.; m. p. 144—145°) and the oxidised donor (0·736 g.) in phenetole (12 ml.) was boiled under reflux in a sealed vessel for 90 hr. The mixture was worked up as in the above transfer and the recovered acid was found to be a mixture (0·470 g., 93%), m. p. 180—185°. M. p. tests in conjunction with the m. p. diagram for mixtures of *cis*- and *trans*-cyclohexane-1,2-dicarboxylic acid [16] suggested that the mixture contained about 30% of the *cis*- and 70% of the *trans*-isomer.

23. *Hantzsch Ester–3,4,5,6-Tetrahydrophthalimide.*—Donor, 0·837 g.; acceptor, 0·500 g.; phenetole, 13 ml.; 172°; 50 hr. Unchanged donor separated from the cold solution and was filtered off as yellow needles (0·236 g., 28%). The filtrate was evaporated at reduced pressure and the residue dissolved in benzene. Oxidised donor (0·475 g., 57%) was recovered from this solution by acid-extraction. The benzene solution was evaporated at reduced pressure, leaving a pale yellow powder (0·487 g.). Tetrahydrophthalimide and *cis*-hexahydrophthalimide are separated quantitatively by partition chromatography in wet benzene over silica gel containing 47% by weight of water: the unsaturated imide is eluted first. An aliquot part (0·190 g.) of the recovered imide was analysed by this procedure: unchanged tetrahydro-imide (0·179 g.), m. p. 169—173°, was isolated, but no trace of any other product could be found (pure 3,4,5,6-tetrahydrophthalimide, m. p. 173—174·5°; *cis*-hexahydrophthalimide, m. p. 135°).

24. *Hantzsch Ester–*trans-trans-*Muconic Acid.*—Donor, 1·782 g., 2·0 mol.; acceptor, 0·500 g., 1·0 mol.; dioxan, 70 ml.; 101°; 100 hr. Solvent was distilled off and the residue separated in the normal way for an acidic acceptor by extraction with aqueous sodium carbonate. Insoluble donor material was further separated by acid-extraction to give unchanged donor (1·26 g.; 71%) and oxidised donor (0·28 g., 16%). The sodium carbonate extract was acidified and the resultant precipitate of crude *trans-trans*-muconic acid (0·270 g., 54%) filtered off [m. p. 288—289° (decomp.; sealed capillary); pure, m. p. 297—300° (decomp.; sealed capillary)]. Continuous ether-extraction of the filtrate yielded a pale brown, sticky solid (0·230 g., 46%), m. p. 100—350°. Separation of this water-soluble product according to the literature [6] was unsuccessful. At each stage corresponding to one of the seven possible hydrogenation products, small quantities of solids with very wide melting ranges were isolated.

28. *Hantzsch Ester–Cinnamic Acid.*—Donor, 0·855 g., acceptor, 0·500 g.; phenetole, 13 ml.; 172°; 85 hr. Solvent was distilled off at reduced pressure, and the residue was dissolved in benzene and extracted with aqueous sodium carbonate. This extract on acidification yielded cinnamic acid (0·361 g., 72%), m. p. and mixed m. p. 128—134° (pure m. p. 133—134°). Oxidised donor (0·463 g., 54%) was extracted from the benzene solution with hydrochloric acid and precipitated with alkali. No unchanged donor was recovered. Evaporation of the benzene solution left a neutral yellow oil (0·245 g.), n_D^{20} 1·5677. Attempted fractional distillation of

[16] Price and Schwarcz, *J. Amer. Chem. Soc.*, 1940, 2894.

this product at 150°/0·002 mm. caused extensive decomposition, and gave only a trace of unidentified distillate (Found: C, 74·3; H, 6·8; N, 1·5%).

30. *Hantzsch Ester–Diphenylacetylene.*—Donor, 1·422 g., 2·0 mol.; acceptor, 0·500 g., 1·0 mol.; dioxan, 22 ml.; 101°; 40 hr. Solvent was evaporated at reduced pressure and the residue was extracted with 1 : 4 benzene–light petroleum. Insoluble unchanged donor (1·260 g., 87%) was filtered off. Oxidised donor (0·122 g., 9%) was recovered in the usual way by acid-extraction of the filtrate. Evaporation of the benzene–petroleum afforded the impure acceptor (0·500 g.), m. p. 47—68°, $\lambda_{max.}$ 279 and 296 mμ (ε 23,800 and 20,700) (diphenylacetylene, m. p. 62—63°; $\lambda_{max.}$ 281 and 298 mμ; ε 33,300 and 30,800) (Found: C, 92·8; H, 5·9. Calc. for $C_{14}H_{10}$: C, 94·3; H, 5·7%).

32. *Hantzsch Ester–1,4-Dihydronaphthalene.*—Donor, 0·970 g., acceptor, 0·500 g.; tetrahydrofuran, 20 ml.; 66°; 72 hr. The mixture was worked up as in reaction no. 30, to give 66% of unchanged donor and 18% of oxidised donor. The acceptor component was recovered as a yellow oil (0·43 g., 86%) from which 2,3-dibromotetralin (0·77 g., 79%), m. p. and mixed m. p. 70—72° (pure, m. p. 73—74°), was prepared by direct bromination in cold chloroform followed by fractional crystallisation.

34. *Hantzsch Ester–*trans-4-*Nitrostilbene.*[17]—Donor, 0·563 g., 1·0 mol.; acceptor, 0·500 g., 1·0 mol.; phenetole, 8 ml. The mixture was contained in a sealed Pyrex tube and kept at 156° for 24 hr. Unchanged donor (0·210 g., 37%) crystallised from the cold solution. Solvent was distilled off under reduced pressure and the residue was dissolved in benzene and treated with hydrochloric acid to remove oxidised donor. This produced a precipitate (85 mg.) of a primary aromatic amine hydrochloride. The compound was converted into the free base (65 mg.), m. p. 139—150°, which was in turn converted into the *N*-benzoyl derivative (93 mg.), m. p. 242—245°. Crystallisation from aqueous dimethylformamide gave straw-coloured leaflets (55 mg.), m. p. 247—248° (4-aminostilbene, m. p. 151—152°; *N*-benzoyl derivative, m. p. 245°). Only 29% of oxidised donor could be recovered from the hydrochloric acid solution, and evaporation of the benzene solution afforded a yellow, sticky solid (0·462 g.), m. p. up to 152°, $\lambda_{max.}$ 348 mμ (ε 18,000) [4-nitrostilbene, m. p. 157—158°, $\lambda_{max.}$ 348 mμ (ε 22,000)]. The formation of 4-aminostilbene (16%) required 48% of the donor, leaving a balance of only 15% donor oxidation, which is an average background value.

35. *Hantzsch Ester–*trans-4-*Cyanostilbene.*[18]—Donor, 0·618 g., 1·0 mol.; acceptor, 0·500 g., 1·0 mol.; phenetole, 10 ml.; 172°; 50 hr. The mixture was worked up as for 4-nitrostilbene (no. 34) to give 56% of unchanged donor (0·345 g.) and 16% of oxidised donor (0·095 g.). The crude acceptor was recovered as a yellow solid (0·592 g.), m. p. 112—118°, contaminated with the donor (~0·05 g.) which had remained in the cold phenetole solution. Purification by high-vacuum sublimation afforded a colourless powder (0·481 g., 96%), m. p. 100—117° (4-cyanostilbene, m. p. 119·5—120°). No convenient process was available to separate a possible trace of 4-cyanobibenzyl from 4-cyanostilbene, and the mixture was not further examined.

38. *Hantzsch Ester–Nitrobenzene.*—Donor, 3·09 g., 3·0 mol.; acceptor, 0·500 g., 1·0 mol.; phenetole, 40 ml.; 172°; 24 hr. Unchanged donor (2·47 g., 80%) crystallised from the cold solution which was then worked up for primary amine content. The *N*-benzoyl derivative was isolated as an oily solid (84 mg.), m. p. up to 155°. Recrystallisation from aqueous ethanol gave benzanilide (30 mg.), m. p. and mixed m. p. 163—164°. The working up process also yielded 12% of oxidised donor.

40. *Hantzsch Ester–Benzonitrile.*—Donor, 2·46 g., 2·0 mol.; acceptor, 0·500 g., 1·0 mol.; phenetole, 30 ml.; 172°; 100 hr. Unchanged donor (1·11 g., 45%) crystallised from the cold solution. The working-up process was based on the possibility that the cyano-group could have been reduced to the primary amine or to the aldimine stage. The phenetole solution was extracted with 4N-hydrochloric acid, and the aqueous acid solution was examined for traces of benzaldehyde and benzylamine: no trace of either was found. The aqueous acid extract yielded only crude, oxidised donor (0·71 g., 29%).

42. *Hantzsch Ester–Benzophenone.*—Donor, 0·695 g.; acceptor, 0·500 g.; phenetole, 11 ml.; 172°; 85 hr. Addition of light petroleum to the cold solution precipitated a small quantity of unchanged donor (0·027 g., 4%). Oxidised donor (0·404 g., 58%) was extracted from the solution with acid and precipitated with alkali. Evaporation of the phenetole–petroleum solution at reduced pressure gave the crude acceptor component as a sticky solid (0·64 g.,

[17] Pfeiffer and Sergiewskaja, *Ber.*, 1911, **44**, 1109.
[18] Meerwein, Büchner, and Van Emster, *J. prakt. Chem.*, 1939, **152**, 256.

theor. 0·50 g.). An aliquot part (0·23 g.) was treated with 3,5-dinitrobenzoyl chloride in pyridine but the only product was an oil (0·25 g.), found to be unchanged benzophenone (2,4-dinitrophenylhydrazone, m. p. 239—240°). The remaining acceptor (0·41 g.) was distilled at reduced pressure and gave only benzophenone (0·373 g., 91%), m. p. and mixed m. p. 45—47°.

43. *Hantzsch Ester–Benzylideneacetophenone.*—Donor, 1·215 g., 2·0 mol.; acceptor, 0·500 g., 1·0 mol.; phenetole, 20 ml. The mixture was kept in a sealed Pyrex tube at 156° for 24 hr. Unchanged donor (0·582 g., 48%) crystallised from the cold solution, which was then worked up as in reaction no. 42 to yield oxidised donor (0·509 g., 42%), and the acceptor component (0·551 g.), m. p. 35—68° (benzylideneacetophenone, m. p. 55—55·5°; benzylacetophenone, m. p. 71—72°). An aliquot part (0·100 g.), with 2,4-dinitrophenylhydrazine hydrochloride, gave an orange powder (0·130 g.), m. p. 160—210°, which was chromatographed in 1 : 3 benzene–petroleum over alumina. Only one homogeneous band was formed. A mixture of benzylidene- (m. p. 249—250°) and benzyl-acetophenone 2,4-dinitrophenylhydrazones (m. p. 185—185·5°) was likewise found to be non-separable by chromatography over alumina. A sample of benzylideneacetophenone was then brominated almost quantitatively in cold chloroform, yielding the two forms of the dibromide, m. p. 160—161° and 125—126°: both failed to react with 2,4-dinitrophenylhydrazine. The remainder of the acceptor component (0·45 g.) was therefore brominated and the products were treated with 2,4-dinitrophenylhydrazine sulphate in ethanol, forming an orange powder (0·180 g.), which was fractionally crystallised and chromatographed to give benzylacetophenone 2,4-dinitrophenylhydrazone (0·059 g.), m. p. and mixed m. p. 184—185·5°. Fractional crystallisation of the mother-liquors from the hydrazone gave the high-melting form of chalcone dibromide (47 mg.), m. p. and mixed m. p. 158—161°.

44. An identical mixture as in reaction no. 43 was boiled under reflux in a sealed vessel for 85 hr. The same working-up process afforded 40% of unchanged donor and 51% of oxidised donor. The recovered acceptor component (0·585 g.) was fractionally crystallised from light petroleum (b. p. 60—80°), to give benzylacetophenone (0·401 g., 80%), m. p. and mixed m. p. 70—72°. The combined petroleum mother-liquors yielded a sticky solid (0·124 g.) which still possessed strong ketonic properties. Treatment with α-naphthyl isocyanate at 100° for 30 min. yielded an oil.

46. *Hantzsch Ester–Mesityl Oxide.*—Donor, 1·290 g., 1·0 mol.; acceptor, 0·500 g., 1·0 mol.; tetrahydrofuran, 20 ml. The mixture was kept in a sealed Carius tube at 200° for 20 hr. After addition of pentane to the cold solution, unchanged donor (0·936 g., 62%) was filtered off, and oxidised donor (0·126 g., 10%) recovered in the usual way by acid-extraction and alkali-precipitation. The solvent was then distilled off through a Fenske column and an aliquot part of the residue was converted into the 2,4-dinitrophenylhydrazone (0·337 g., 95%). The 2,4-dinitrophenylhydrazones of mesityl oxide (red, m. p. 198—199°) and isobutyl methyl ketone (orange, m. p. 89—93°, constant after fractional crystallisation and chromatography over both alumina and bentonite–kieselguhr) were found to be separated quantitatively by chromatography in benzene over bentonite–kieselguhr (4 : 1 by wt.). The saturated derivative was rapidly eluted. Change of solvent to chloroform was required to elute the mesityl oxide derivative. Application of this process to the recovered acceptor derivative showed that no isobutyl methyl 2,4-dinitrophenylhydrazone was present, and only the mesityl oxide derivative (0·221 g., 62%) was recovered from the column.

50. *Hantzsch Ester–Ethyl Pyruvate.*—Donor, 4·37 g., acceptor, 2·00 g.; dioxane, 35 ml.; 101°; 72 hr. Unchanged donor (3·30 g., 76%) crystallised from the cold solution (~10% more would remain in solution). Reaction of an aliquot part of the filtrate with 2,4-dinitrophenylhydrazine hydrochloride showed that at least 95% of the ketone was present.

52. *Hantzsch Ester–Benzil.*—Donor, 1·205 g., 2·0 mol.; acceptor, 0·500 g., 1·0 mol.; phenetole, 17 ml.; 172°; 24 hr. Unchanged donor (0·722 g., 60%) crystallised from the cold solution. Solvent was distilled off at reduced pressure, leaving a sticky solid which was dissolved in benzene and extracted with dilute acid. Oxidised donor (0·176 g., 6%) was precipitated from the acid extract by alkali. Evaporation of the benzene solution yielded the acceptor component as a sticky yellow solid (0·670 g., theor. 0·505 g.). Testing this material with the sodium methoxide–methanol–benzil reagent [19,20] demonstrated that benzoin had been formed: a deep violet colour was at once produced. Comparison of the infrared spectra of

[19] McAllister, *J. Amer. Chem. Soc.*, 1929, 2824.
[20] Michaelis and Fetcher, *J Amer. Chem. Soc.*, 1937, **59**, 1246.

benzil and benzoin showed that the benzoin content of the mixture was ~17%: $\nu_{max.}$ 3449 cm.$^{-1}$: benzil, nil; benzoin, ε 40·2; mixture, ε 6·86. Since the recovered acceptor could only contain a maximum of 0·5 g. of benzoin, the effective hydrogen transfer value is 23%.

53. *Hantzsch Ester–Benzylideneaniline.*—Donor, 0·699 g.; acceptor, 0·500 g.; phenetole, 10 ml. The mixture was kept in a sealed Pyrex tube at 156° for 24 hr. Unchanged donor (0·144 g., 21%) crystallised from the cold solution. Solvent was distilled off at reduced pressure, and the last traces of unchanged donor (0·056 g., 8%) were precipitated from the residue by adding light petroleum (b. p. 60—80°). Evaporation of the petroleum filtrate left the mixture of oxidised donor and acceptor component as a colourless oil (1·000 g.). An aliquot part (0·638 g.) was benzoylated in pyridine solution: the neutral product was *N*-benzylbenzanilide (0·102 g., 25%), m. p. and mixed m. p. 106—107°.

54. *Hantzsch Ester–Azobenzene.*—Donor, 0·695 g.; acceptor, 0·500 g.; phenetole 7 ml. The mixture was kept in a sealed Pyrex tube at 156° for 24 hr. Phenetole was distilled off at reduced pressure and the residue was dissolved in 1 : 4 benzene–light petroleum (b. p. 60—80°). A trace of unchanged donor (0·035 g., 5%) was filtered off. Solvent was again evaporated, and the residue was added in ether (10 ml.) in small portions to ice-cold 5N-hydrochloric acid (10 ml.). The flask was shaken after each addition. Concentrated hydrochloric acid (5 ml.) was finally added to the mixture which was chilled to 0° for 30 min. then filtered. The product was a colourless powder (0·160 g., 23%) which was converted into the free base (0·098 g.), m. p. 115—149°, then dissolved in pyridine and benzoylated. The neutral product was *NN'*-dibenzoylbenzidine (0·195 g., 93%), m. p. and mixed m. p. 368—371°. 50% recovery of azobenzene was effected from the ethereal layer in the rearrangement; the hydrochloric acid layer yielded 72% of crude oxidised donor on being neutralised.

58. *1,2-Dihydroquinoline–3,4,5,6-Tetrahydrophthalic Anhydride.*—Donor, 0·432 g.; acceptor, 0·500 g.; dioxan, 10 ml.; 101°; 50 hr. An excess of aqueous sodium carbonate solution was added to the dioxan solution, then the donor component was removed by extraction with light petroleum (b. p. 40—60°). Petroleum was evaporated off and the dihydroquinoline content of the residue was estimated by reaction with chloranil:[1] 18% of tetrachloroquinol (0·145 g.), m. p. 226—232° (sealed capillary), was isolated (pure m. p. 234—236°). The basic component was recovered as a yellow oil (0·387 g., 91%) from which quinoline picrate (86%), m. p. and mixed m. p. 203—205° (sealed capillary) (pure m. p. 206—207°), was isolated. The sodium carbonate extract was acidified and continuous ether-extraction gave a yellow sticky solid (0·669 g.) (cf. reaction no. 21 with the Hantzsch ester). Extraction with boiling light petroleum (b. p. 60—80°) by decantation left a pale brown solid (0·136 g.), which crystallised from hot water as an off-white powder (0·082 g., 15%), m. p. 192—194°. The mixed m. p. with the pure *cis*-cyclohexane-1,2-dicarboxylic acid from reaction no. 21 was 192—195°. Evaporation of the petroleum extract afforded an orange gum from which 3,4,5,6-tetrahydrophthalic anhydride (0·094, 18%), m. p. and mixed m. p. 68—72°, was obtained.

59. *1,2-Dihydroquinoline–Benzylideneacetophenone.*—Donor, 0·315 g., 1·0 mol.; acceptor, 0·500 g., 1·0 mol.; dioxan, 10 ml.; 101°; 50 hr. The mixture was shaken with an excess of 4N-hydrochloric acid. Continuous extraction with light petroleum (b. p. 40—60°) then yielded the acceptor component as a viscous yellow oil (0·521 g., theory, 0·505 g.). This product was worked up as in reaction no. 43 by bromination (yield, 0·877 g.; theor. for 100% chalcone dibromide, 0·884 g.), treatment with 2,4-dinitrophenylhydrazine sulphate, and chromatography. The coloured product was a gum (77 mg.) which crystallised from the minimum volume of acetic acid as orange microcrystals (18 mg.), m. p. 155—225°.

60. *1,2-Dihydroquinoline–Benzylideneaniline.*—Donor, 0·362 g.; acceptor, 0·500 g.; dioxan, 10 ml.; 101°; 50 hr. Solvent was evaporated off and the residue was dissolved in quinoline and benzoylated. The neutral product was *N*-benzylbenzanilide (0·620 g., 77%), m. p. and mixed m. p. 105—106°.

61. *1,2-Dihydroquinoline–Azobenzene.*—Donor, 0·360 g.; acceptor, 0·500 g.; dioxan, 10 ml.; 101°; 50 hr. Solvent was evaporated off and the residue was subjected to the benzidine rearrangement as in reaction no. 54. The product was a colourless powder (0·522 g., 74%) which was converted almost quantitatively into free benzidine (0·364 g.), m. p. 123—124°. An aliquot part, benzoylated in pyridine, gave *NN'*-dibenzoylbenzidine (97%), m. p. and mixed m. p. 365—367°.

62. *1,2-Dihydroquinoline–Maleic Anhydride.*—A colourless solution of 1,2-dihydroquinoline (0·699 g.) in anhydrous ether (5 ml. + 2 ml.) was added at room temperature to a colourless

solution of maleic anhydride (0·500 g.) in anhydrous ether (10 ml.). A wine-red colour was immediately produced, fading quickly to pale yellow. The solution had been sealed at once under nitrogen, and after a few minutes, yellow needles began to separate. The mixture was chilled to 0° for 20 min., then the product (V) (0·986 g., 82%), m. p. 97·5—99°, was filtered off. Partial evaporation of the filtrate afforded similar needles (0·101 g., 8%), m. p. 96·5—100°. Attempted recrystallisation from benzene and from ether merely showed this product (1-β-*carboxyacryloyl*-1,2-*dihydroquinoline*) (V) to be unstable. A specimen was therefore analysed at once (Found: C, 67·8; H, 5·0; N, 6·1. $C_{13}H_{11}NO_3$ requires C, 68·1; H, 4·8; N, 6·1%), $\lambda_{max.}$ 231 and 309 mμ (ε 22,500 and 4500) in anhydrous ether, $\nu_{max.}$ 1715s, 1571s, and 1556s, and 2500m, 1774m, and 1622m cm.$^{-1}$.

Hydrolysis of Compound (V).—Compound (V) (0·200 g.) dissolved on trituration in cold concentrated hydrochloric acid to form an intensely yellow solution: in ~2 min. the colour faded completely. The solution was neutralised with sodium hydrogen carbonate and the resultant white precipitate was extracted with benzene. The benzene solution was treated at once with one of chloranil (0·215 g., 1·0 mol.) in benzene (20 ml.) at room temperature. A green colour appeared, fading almost instantly to yellow. After 30 min. at room temperature, solvent was distilled off, leaving a pale yellow-grey solid (0·326 g., 99%), m. p. in two stages, 109—113° with recrystallisation, and finally 163—175°. This product was probably a loose molecular complex of quinoline and the quinol.[1] Extraction with 4N-hydrochloric acid left an insoluble pale brown powder which was purified by sodium hydroxide extraction, filtration, and reprecipitation with acid to give tetrachloroquinol (0·201 g., 93%), m. p. and mixed m. p. 227—232° (sealed capillary) (pure m. p. 234—236°). The aqueous sodium hydrogen carbonate solution was then acidified and continuous ether-extraction yielded an off-white solid (0·102 g., theor. 0·101 g.), m. p. in two stages, 127—139° and 240—275° (decomp.). Titration of an aliquot part with 0·1N-potassium permanganate [15] showed that the acid was at least 97% unsaturated, confirming it as a maleic–fumaric acid mixture.

Thermal Decomposition of Compound (V).—This compound (0·200 g.) was contained in an ampoule with pure toluene (5 ml.). The mixture was frozen in liquid nitrogen, then the ampoule was evacuated to 0·08 mm. and sealed. At about 50° the mixture became a bright yellow homogeneous solution and was then suspended in a thermostat at 100° for 32 hr. The solution became very pale yellow, and on being cooled to 0° for 1 hr. deposited long colourless needles of succinic anhydride (0·034 g., 39%), m. p. and mixed m. p. 116—119° (pure m. p. 118—119·5°). Evaporation of the filtrate at reduced pressure left a sticky solid (0·163 g.) to which 2N-sodium hydroxide (5 ml.) was added. Extraction with ether yielded a colourless oil (0·098 g., 94%), which was characterised as quinoline by formation of the picrate (0·248 g., 93%), m. p. and mixed m. p. 202—205° (sealed capillary). The isolated succinic anhydride was dissolved in the sodium hydroxide solution which was acidified; continuous ether-extraction yielded the total acidic component as an off-white solid (0·092 g., 89%), m. p. 181—186°. Crystallisation from ethanol–benzene afforded succinic acid (0·058 g.), m. p. and mixed m. p. 186—188°.

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