Regioselectivity in the Intramolecular Carbon–Hydrogen Insertion in Metal-catalysed Decomposition of some *cis*-1-Methyl-3-arylcyclohexyl Diazomethyl Ketones. A Highly Efficient Homogeneous Nickel Catalyst for Carbenoid Insertion

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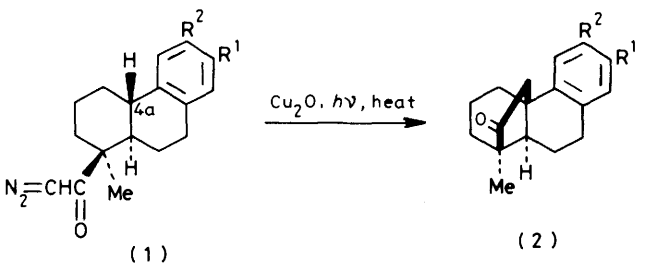
The comparative effectiveness of a variety of copper catalysts and a few transition-metal chelates [$Ni(acac)_2$, $Pd(acac)_2$, and $Co(acac)_3$] have been examined in the carbenoid decomposition of *cis,cis*-1,5-dimethyl-3-phenylcyclohexyl diazomethyl ketone (11), and *cis*-1-methyl-3-phenyl- and *p*-methoxyphenyl-cyclohexyl diazomethyl ketones (9) and (10) with reference to the formation of the respective regioisomeric bicyclo-octanones through intramolecular carbon–hydrogen bond insertion at C-3 and C-5. The most thoroughly studied case was that of (11), which clearly revealed that intramolecular competition in this case with most of the metal-catalysts only marginally favours insertion into Me–C–H bond leading to the bridged bicyclo[3.2.1]octanone (17) in comparison to that of Ph–C–H bond, resulting in the regioisomeric ketone (16). In the catalytic decomposition of (9) and (10) the intramolecular competition in each case strongly favours insertion into the tertiary benzylic bond leading mostly to (12) and (14) rather than the secondary ones, leading to the respective regioisomers (13) and (15). The homogeneous catalyst, $Ni(acac)_2$ has been found to be the most effective for these insertion reactions as well as the transformations of the octahydrophenanthrene diazo ketones (1a) and (1b) to the respective tetracyclic bridged-ketones (2a) and (2b). The key cyclohexanecarboxylic acids (3), (5), and (7) [for the diazo ketones (9), (10), and (11)], and the corresponding diastereoisomeric acids (4), (6), and (8) have been synthesised through a stereocontrolled route by lithium–ammonia and catalytic reduction of the corresponding benzylic γ-lactones (18), (19), and (20) respectively, and the conformational properties of their methyl esters (26)—(31) have been studied. A mechanism for the lithium–ammonia cleavage of the lactones with retention of configuration at the benzylic asymmetric centre has been advanced. Unambiguous synthesis of the bridged-ketones (12), (14), and (17) and the transformations of (12) and (14) to the respective *cis*-dicarboxylic acids (51) and (52) are reported.

The intramolecular carbon-hydrogen insertion through copper-catalysed thermolysis of appropriately substituted cyclohexyl or polycarbocyclic diazomethyl ketones constitutes an attractive method for the synthesis of bridged bicyclo[3.2.1]-octanones.[1,2] The course of this reaction in the alkyl substituted cyclohexyl diazo-ketones using $CuSO_4$, has been found [3] to be sensitive in terms of both conformational effects and the degree of alkyl substituents at the site of insertion. In connection with the synthetic studies towards complex diterpenoids we reported [4,5] copper-catalysed decomposition of the rigid tricyclic diazomethyl ketones (1a,b) and (1c) to the corresponding tetracyclic bridged ketones (2a—c) in good yield, as the only isolable carbon-hydrogen insertion products arising through reaction across the benzylic carbon-hydrogen bond (at C-4a) (Scheme 1). It was, however, not clear whether



(1) (2)

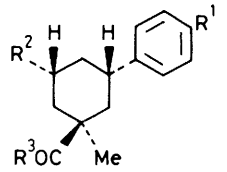
a, $R^1 = R^2 = H$; b, $R^1 = OMe$, $R^2 = H$; c, $R^1 = H$, $R^2 = OMe$

Scheme 1.

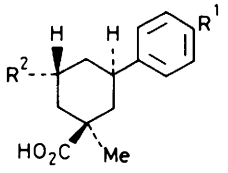
the presence of the aromatic moiety ensured the high regioselectivity in those substrates. In an effort to extend our understanding of the importance of the degree of substitution and the nature of the substituents (particularly that of aryl *vs.* alkyl substituents) at the site of the insertion as well as the influence of the nature of the metal catalyst on the yield and regioselectivity in the intramolecular carbenoid insertion reactions, the present studies were undertaken. We have developed a stereocontrolled synthetic route to the diastereoisomeric pairs of 1,5-dimethyl- and 1-methyl-3-aryl-cyclohexanecarboxylic acids (3)—(8) and studied their conformations by ^1H n.m.r. spectroscopy. We have also examined the carbenoid decompositions of the three conformationally favoured diazomethyl ketones (9)—(11) in the presence of a variety of copper and other transition-metal catalysts in which the corresponding regioisomeric bridged bicyclo[3.2.1]octanones (12) and (13); (14) and (15); and (16) and (17) are formed. We now describe in detail [6] the results of these studies revealing the comparative effectiveness of the various metal catalysts in terms of the yield and regioselectivity in the formation of the bridged-ring ketones which depend upon the degree and nature of the substituents at the site of insertion in the diazo ketones (9)—(11). We also give evidence, for the first time, that bis[pentane-2,4-dionatonickel(II)] or $Ni(acac)_2$ acts as a highly efficient homogeneous catalyst in intramolecular insertion reactions.

Results and Discussion

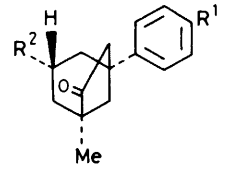
Synthesis of the Diastereoisomeric Acids (3)—(8) *and the Bridged Ketones* (12), (14), *and* (17).—The diastereoisomeric acid pairs (3) and (4); (5) and (6); and (7) and (8) have been synthesised by a stereocontrolled route *via* the γ-lactones (18), (19), and (20) respectively. Condensation of the known keto-



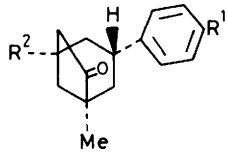
(3) $R^1 = R^2 = H$; $R^3 = OH$
(5) $R^1 = OMe$; $R^2 = H$; $R^3 = OH$
(7) $R^1 = H$; $R^2 = Me$, $R^3 = OH$
(9) $R^1 = R^2 = H$; $R^3 = CHN_2$
(10) $R^1 = OMe$; $R^2 = H$; $R^3 = CHN_2$
(11) $R^1 = H$; $R^2 = Me$, $R^3 = CHN_2$



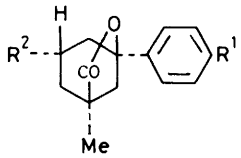
(4) $R^1 = R^2 = H$
(6) $R^1 = OMe$; $R^2 = H$
(8) $R^1 = H$, $R^2 = Me$



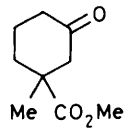
(12) $R^1 = R^2 = H$
(14) $R^1 = OMe$; $R^2 = H$
(16) $R^1 = H$; $R^2 = Me$



(13) $R^1 = R^2 = H$
(15) $R^1 = OMe$, $R^2 = H$
(17) $R^1 = H$, $R^2 = Me$



(18) $R^1 = R^2 = H$
(19) $R^1 = OMe$; $R^2 = H$
(20) $R^1 = H$; $R^2 = Me$



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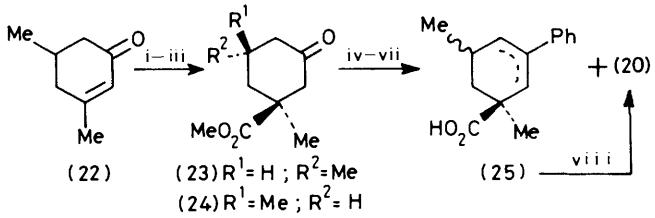
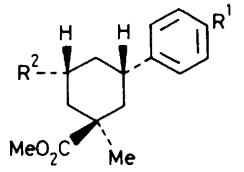
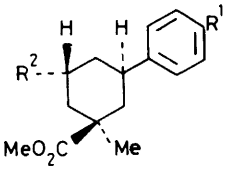


Scheme 2. *Reagents:* i, KCN–H_2O–EtOH; ii, KOH–H_2O; iii, MeOH–H_2SO_4–H_3BO_3; iv, PhMgBr–Et_2O; v, *p*-TsOH–C_6H_6 (heat); vi, KOH–H_2O–EtOH; vii, 6M-HCl (heat); viii, H_2SO_4 (99%) (−10 to −5 °C)



(26) $R^1 = R^2 = H$
(28) $R^1 = OMe$, $R^2 = H$
(30) $R^1 = H$; $R^2 = Me$



(27) $R^1 = R^2 = H$
(29) $R^1 = OMe$; $R^2 = H$
(31) $R^1 = H$; $R^2 = Me$

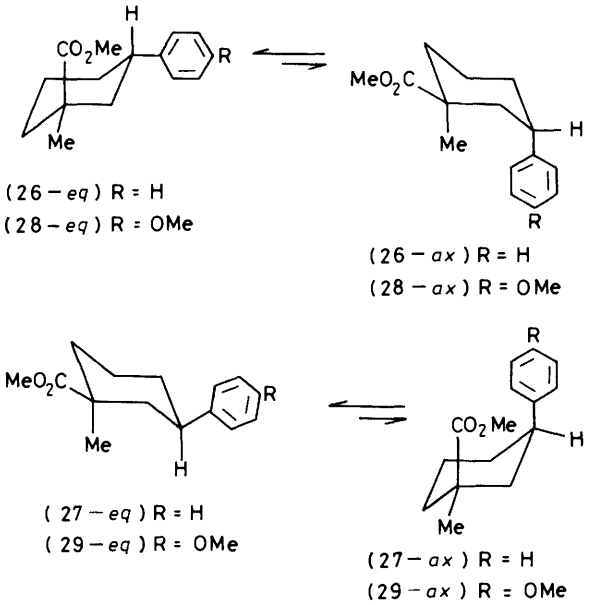
ester (21),[7,8] prepared in an improved yield (see Experimental section), with phenylmagnesium bromide in ether, followed by treatment of the crude product with toluene-*p*-sulphonic acid in refluxing benzene afforded the lactone (18) after saponification and acidic treatment. The remaining acidic product on lactonisation with sulphuric acid in benzene at low temperature gave more (18). Following a similar sequence (21) was treated with *p*-methoxyphenylmagnesium bromide to produce the lactone (19) in 84% yield. The spectral and analytical data are consistent with the assigned structure (see Experimental section).

The key intermediate keto ester (23)[8] required for the γ-lactone (20), has been prepared *via* a modified route[9] (Scheme 2). The conjugate addition of a hydrogen cyanide residue to the unsaturated ketone (22) with boiling aqueous ethanolic potassium cyanide followed by alkaline hydrolysis *in situ* afforded a semisolid acidic product. This was directly esterified to give a mixture of the diastereoisomeric methyl esters (23) and (24), in a ratio of *ca.* 80 : 20 (g.l.c.) in 49% overall yield. Since the conjugate addition of cyanide to (22) under the conditions used here is possibly reversible,[9,10] the major product derived from the reaction must be the stable epimer (23) with *cis*-dimethyl groups. This stereochemical inhomogeneity in the keto ester (23) however, created no problem in the subsequent steps (Scheme 2). The diastereoisomeric keto ester mixture was allowed to react with phenylmagnesium bromide and the resulting product on treatment with toluene-*p*-sulphonic acid in refluxing benzene followed by saponification and acidic treatment afforded the γ-lactone (20). The acidic product, presumably the isomeric unsaturated acids (25), gave an additional amount of the same lactone (20) (50% overall yield). The i.r. spectrum of (20) showed a strong γ-lactone band at 1 775 cm^{-1}. The ^1H n.m.r. spectrum exhibited a sharp methyl doublet at δ 1.01 (*J* 6 Hz) and a methyl singlet at δ 1.26. The assigned stereochemistry of (20) has been confirmed from its further transformations to the acids (7) and (8) as described below.

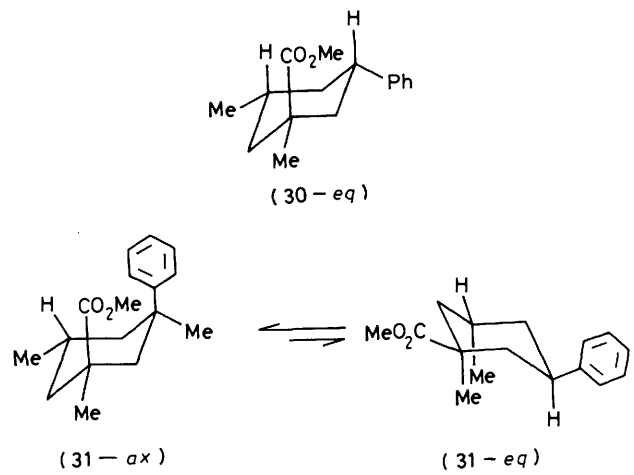
The reductive cleavage of the benzylic bond in the lactones (18), (19), and (20) with lithium in liquid ammonia following a method developed in this laboratory[11] produced mixtures (*ca.* 100%) of the respective diastereoisomeric acid pairs (3) and (4); (5) and (6); and (7) and (8) in *ca.* 77 : 23, 85 : 15, and 83 : 17 ratios respectively, involving *retention* and *inversion* respectively at the benzylic asymmetric centre. The pure epimeric acids (3), (5), and (7) could be easily separated from these mixtures by fractional crystallisation. On the other hand, catalytic hydrogenolysis of each of the lactones (18), (19), and (20) in the presence of palladium-charcoal in ethanol produced, in excellent yields, the epimeric acids, (4), (6), and (8) respectively as the sole products; this involved complete *inversion* at the benzylic chiral centre, in agreement with our earlier observations.[11] The configurational assignments of the diastereoisomeric acids have been based, in the first place, on their mode of formation in analogy with other systems.[11] However, independent assignments of these diastereoisomeric acid pairs have been made on the basis of the ^1H n.m.r. spectral data of the corresponding methyl esters (26) and (27); (28) and (29); and (30) and (31).

Thus, the diastereoisomeric pairs (26) and (27), and (28) and (29) should exist as (26-*eq*) and (27-*eq*), and (28-*eq*) and (29-*eq*) respectively, as the sole or highly predominant conformers in preference to the less favourable conformers (26-*ax*) and (27-*ax*), and (28-*ax*) and (29-*ax*) respectively (see Scheme 3). In these the methyl group is placed in equatorial and axial dispositions respectively.

It has been reported[12] that the axial methyl proton of *cis*, *trans*-1,3,5-trimethylcyclohexane is deshielded relative to the



Scheme 3.



Scheme 4.

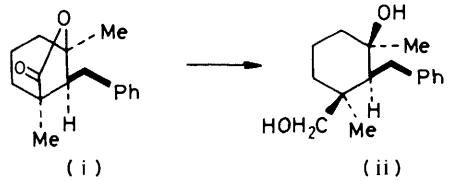
equatorial methyl protons by 0.14 p.p.m. Thus, while the ester (26) exhibits its 1-methyl singlet at δ 1.17 its epimer (27) shows it at δ 1.30. The difference in the observed chemical shift (Δδ 0.13 p.p.m.) of the methyl protons can be rationalised as a consequence of the conformational difference of the methyl group in (26-*eq*) and (27-*eq*) respectively, having equatorial and axial dispositions.* Also, the 1-methyl singlets in the diastereoisomeric methyl esters (28) and (29) appear at δ 1.16 and 1.28 respectively, indicating their respective predominating conformers as (28-*eq*) and (29-*eq*). The ^{1}H n.m.r. spectra of the diastereoisomeric methyl esters pair (30) and (31) show interesting features. The spectrum of (30) possessed a clean doublet at δ 0.95 for the C-5 methyl and two sharp singlets at δ 1.16 and δ 3.66 for the C-1 and ester methyl groups respectively; this is in accord with the assigned structure, which should exist in the conformer (30-*eq*). While the epimer (31) showed the 5- and 1-methyl groups as a doublet and singlet respectively at δ 1.01 and 1.16, positions close to those found with the epimer (30), the sharp ester methyl singlet shifted to an unusually high field at δ 3.06. This resulted from the perpendicular ring-current shielding effect [13] of the aromatic ring in conformation (31-*ax*). The magnitude of this shielding value (Δδ 0.61 p.p.m.) in (31) in comparison with the normal chemical shift of ester methyl protons [*e.g.* in (30)], clearly indicates that the energy involved in the 1,3-non-bonded interaction of phenyl-methoxycarbonyl groups as present in (31-*ax*) (Scheme 4) should be much less [14] than that of the 1,3-methyl interaction in the conformation (31-*eq*), thereby clearly ruling out the importance of the later conformer. In a number of 3,3,5,5-tetrasubstituted cyclohexanones or heavily substituted cyclohexanols having an aryl group as one of the substituents, the latter exhibits [13,15] a strong tendency to adopt an axial disposition in the ' biased ' mobile equilibrium between two chair-like conformers.

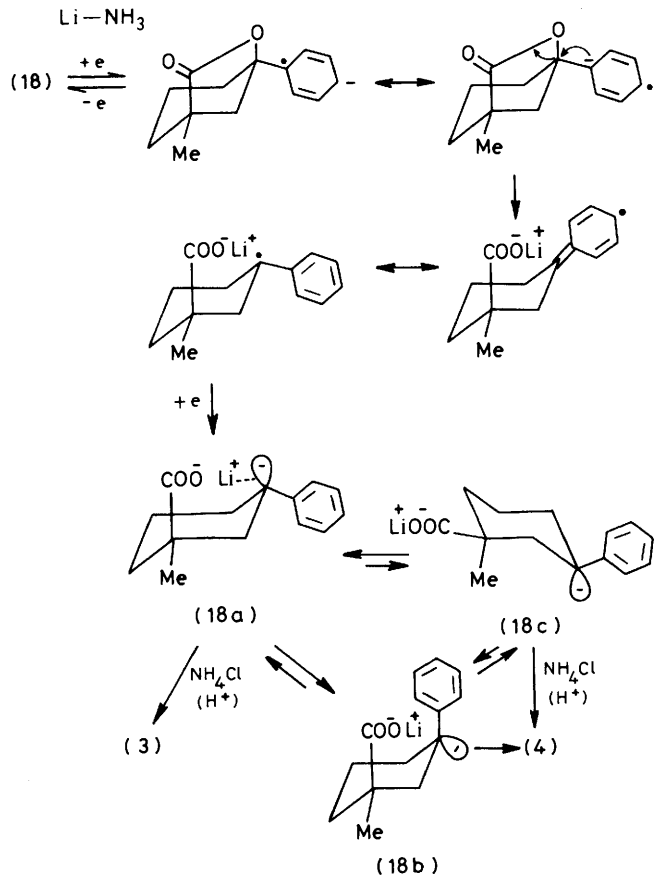
Stereocontrolled syntheses of the diastereoisomeric 3-arylcyclohexanecarboxylic acids (3)—(8), established in the present studies, illustrate the general applicability of the methods developed in our hands.[11] In particular, the stereochemical results of the lithium–ammonia induced cleavage reaction of the monocyclic lactones (18)—(20) provides substantial insight into the mechanistic course of this novel method for the reductive cleavage of a benzylic bond with retention of configuration.[11] These stereochemical observations are now rationally explicable by a mechanism in which the product structure is determined during the final protonation step of the carbanions [for example in (18a), (18b) and/or (18c) in the cleavage of (18)] *via* a generally accepted mechanism [16] for the metal–ammonia induced reductive cleavage of benzyl alcohols where the initial electron transfer is made to the aromatic ring * as depicted in Scheme 5.

The high stereoselectivity in the observed product (3) from (18), which possibly originates through protonation of a dianion, clearly suggests that the carboxylic acid function either directs the approach of a proton donor from its side or a dianionic intermediate such as (18a) is involved in lowering of the energy level where the *cis*-relationship between the carboxylate anion and the benzylic carbanion centre is maintained. This was suggested by Apsimon *et al.*[17] and others [18] in the metal–ammonia reduction of a double bond having a neighbouring carboxy group. The formation of the minor epimer (4) (in 23% yield) involving the carbanions (18b) and/or (18c) clearly indicates their involvement in the mobile equilibria (Scheme 5).

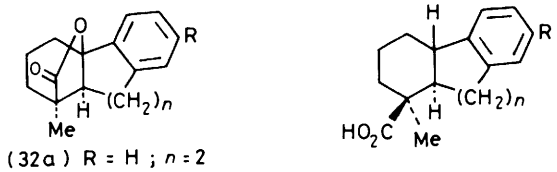
* It should be mentioned that *cis*, *trans*-1,3,5-trimethylcyclohexane is not a very good model for (26) and (27) owing to the presence of the aryl and methoxycarbonyl group in the latter. However, their subsequent chemical transformations do confirm the configurational assignments to these molecules.

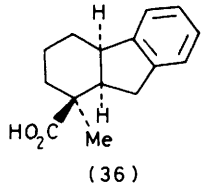
* An alternative path for electron transfer in (18)—(20) *via* the C=O group of the lactone, similar to that of the deoxygenation of hindered esters with lithium and ethylamine [A. G. M. Barrett, C. R. A. Godfrey, D. M. Hollinshead, P. A. Prokopiou, D. H. R, Barton, R. B. Boar, L. Joukhadar, J. F. McGhie, and S. C. Misra. *J. Chem. Soc., Perkin Trans. 1*, 1981, 1501], seems to be less probable since the non-benzylic lactone (i) [9] on reaction with lithium and liquid ammonia in the presence of ammonium chloride, under conditions of reductive cleavage, gave the diol (ii) in high yield (unpublished results by A. K. Chakraborti).





Scheme 5.

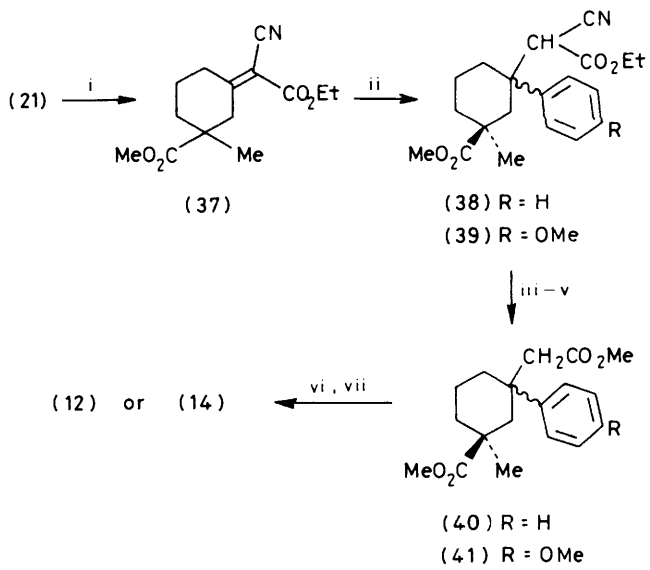




The earlier observations on the lithium–ammonia reductive cleavages of the hydrophenanthrene lactones [11a] (32a) and (32b) leading solely to the corresponding *trans*-acids (33a) and (33b), and the hydrofluorene lactone (34) [11b] to the *trans*- and *cis*-acids (35) and (36) in a ratio of 65 : 35 can now be rationalised by the mechanism postulated above.

To facilitate the structural identification of the possible insertion products from the diazo ketones (9)—(11), the three bridged-ketones (12), (14), and (17) have been synthesised *via* the following unambiguous route.[19]

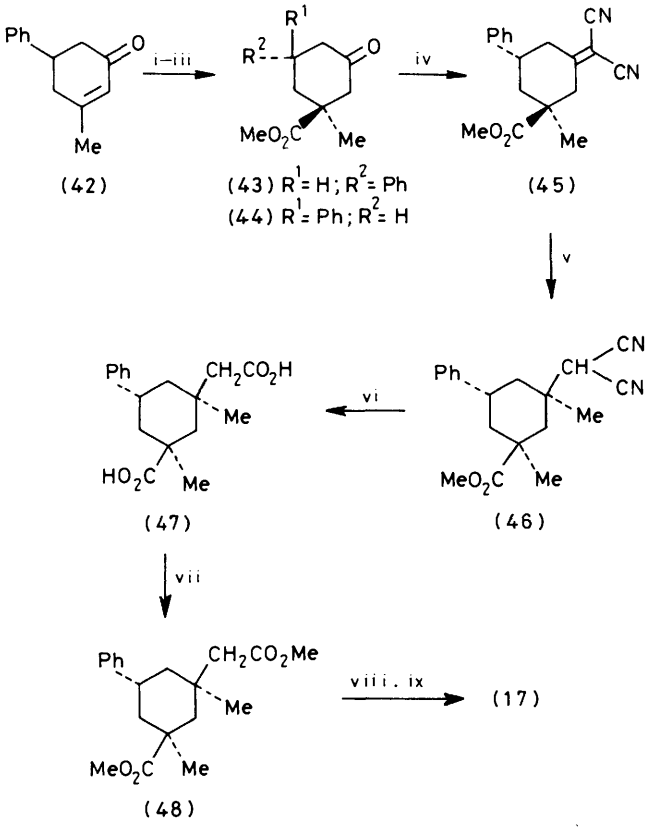
For the synthesis of (12) and (14) (Scheme 6) the keto ester



Scheme 6. *Reagents:* i, $CH_2(CN)CO_2Et$, HOAc, NH_4OAc, C_6H_6; ii, C_6H_5MgBr or *p*-$OMeC_6H_4MgBr$–CuI–Et_2O; iii, KOH–H_2O–$HOCH_2CH_2OH$; iv, 6M-HCl, heat; v, CH_2N_2–Et_2O; vi, Bu^tOK–C_6H_6; vii, 5% KOH–MeOH

(21) was condensed [19] with ethyl cyanoacetate to afford (37) (geometry undetermined) which underwent conjugate addition of phenylmagnesium bromide and *p*-methoxyphenylmagnesium bromide in the presence of cuprous iodide [20] to give diastereoisomeric mixtures of (38) (77%) and (39) (50%) respectively. The saponification of each of the cyano esters (38) and (39) followed by decarboxylation and esterification with ethereal diazomethane afforded a diastereoisomeric mixture of the respective diesters (40) and (41). Each of these diesters on Dieckmann cyclisation with potassium t-butoxide in benzene [21] followed by hydrolytic decarboxylation with methanolic potassium hydroxide gave the respective bridged-ketones (12) (43%) and (14) (25%). The i.r. spectra of (12) and (14) exhibited strong carbonyl bands at 1 735 and 1 730 cm^{-1} respectively, consistent with the presence of a cyclopentanone moiety. The ^1H n.m.r. spectra (at 60 MHz) of both the ketones showed a methyl singlet δ 1.05. The $COCH_2$ protons in (12) and (14) appeared at δ 2.38 (br d) and 2.37 (m) respectively.

The bridged ketone (17) was prepared (Scheme 7) *via* a 60 : 40 mixture of the diastereoisomeric keto esters (43) and (44), obtained from (42), adopting the same procedure as that described for the keto ester mixture (23) and (24). The stereochemistry of the major epimer (43) has been tentatively assigned from its mode of formation. The diastereoisomeric keto ester mixture on condensation with malononitrile in the presence of ammonium acetate and acetic acid in benzene selectively reacted with the major epimer (43), leading to a stereochemically homogeneous unsaturated dinitrile (45) in 40% yield. This underwent stereoselective addition [20b] of methylmagnesium iodide in the presence of cuprous iodide to give (45) (m.p. 116 °C in 88% yield) which on hydrolysis gave the crystalline diacid (47) in excellent yield. The corresponding dimethyl ester (48) (diazomethane) on Dieckmann cyclisation and hydrolytic decarboxylation with aqueous perchloric acid [21] gave the ketone (17) in 35% yield. It may be mentioned here that the isomeric unsaturated cyanoesters prepared from the aforementioned keto-ester (43) and (44) mixture with ethyl cyanoacetate failed to give the conjugate addition product with methylmagnesium iodide.



Scheme 7. *Reagents:* i, $KCN-H_2O-EtOH$; ii, $KOH-H_2O$; iii, $MeOH-H_2SO_4-H_3BO_3$; iv, $CH_2(CN)_2$–HOAc–$NH_4OAc-C_6H_6$; v, MeMgI–CuI–Et_2O; vi, H_2SO_4–HOAc–H_2O; vii, $CH_2N_2-Et_2O$; viii, $Bu^tOK-C_6H_6$; ix, 20% $HClO_4-H_2O$

The ^1H n.m.r. spectrum of (17) (at 60 MHz) showed two methyl singlets at δ 1.01 and 1.18, and the $COCH_2$ protons at δ 2.05 (br d); the corresponding values reported [3] for 1,5-dimethylbicyclo[3.2.1]octan-6-one are δ 0.95, 1.12, and 2.0. The absence of a diamagnetic shift for the $COCH_2$ protons in (17) confirm the assigned equatorial stereochemistry of the phenyl group in this and the intermediates (45)—(48), through which this bridged-ketone was obtained.

Preparation of the Diazo Ketones (9)—(11) *and the Intermolecular Insertion Reactions.*—The diazo ketones were prepared in excellent yields; following a standard method,[4] from the acids (3), (5), and (7), *via* the sequential treatment of the dry sodium salt of the corresponding acid with oxalyl chloride in benzene and an excess of diazomethane in ether in the presence of triethylamine.

We studied the carbenoid decomposition of the diazo ketone (11) with commonly used [1,2] heterogeneous copper catalysts (Cu_2O, $CuSO_4$, and CuO), $NiSO_4$, a homogeneous copper catalyst [copper(I) trifluoromethanesulphonate (CuTf)],[22] and other transition metal agents [$Ni(acac)_2$,[23] $Pd(acac)_2$,[24] and $Co(acac)_3$[25]]. This was the first time * these catalysts had been used to obtain the bridged-ketones (16) and (17), and we initiated the study in order or evaluate their efficiency in the regioselectivity of intramolecular carbon-hydrogen insertion reactions at the tertiary Me–C–H and Ph–C–H centres in (11). The quantitative evaluations of the products are outlined in Table 1. The distributions of the regioisomeric intramolecular insertion products (12) and (13), and (14) and (15) originating from the diazo ketones (9) and (10) with a limited number of the aforementioned catalysts are given in Tables 1 and 2.

Table 1. Distribution of the intramolecular insertion products (16) and (17) in the metal-catalysed decomposition of the diazo ketone (11)

Entry	Catalyst	Yield [a]	Product ratio [b–d] (16) : (17)
1	Cu_2O	60	48 : 52
2	CuO	65	43 : 57
3	$CuSO_4$	70	30 : 70
4	$NiSO_4$	65	35 : 65
5	$Ni(acac)_2$	92	45 : 55
6	$Pd(acac)_2$	70	45 : 55
7	$Co(acac)_3$	70	49 : 51
8	CuTf	65	48 : 52

[a] Purified product. [b] Determined by g.l.c. and ^1H n.m.r. [c] Average of at least three runs. [d] Purity of the product 95—98%.

Table 2. Distribution of the intramolecular insertion products (12) and (13) in the metal-catalysed decomposition of the diazo ketone (9)

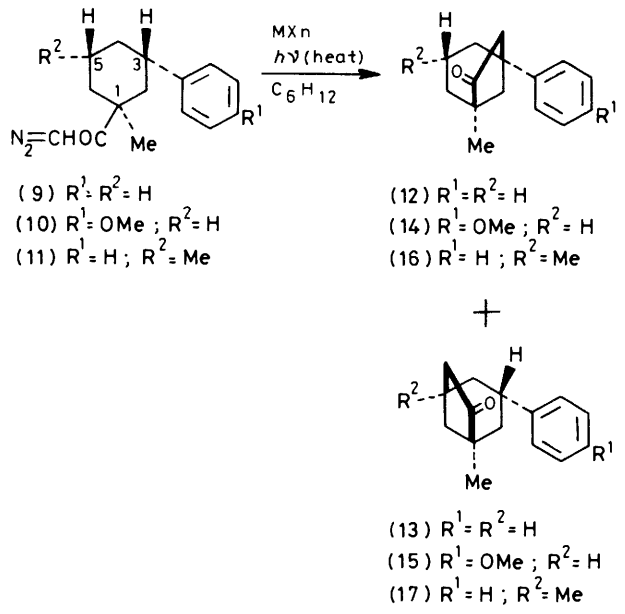
Entry	Catalyst	Yield [a]	Product ratio [b–d] (12) : (13)	Isolated yield (%) [e] of (12)
1	Cu_2O	60	85 : 15	42
2	CuO	65	85 : 15	43
3	$CuSO_4$	66	75 : 25	38
4	$Ni(acac)_2$	86	90 : 10	75
5	CuTf	60	85 : 15	40

[a] Purified product. [b] Determined by g.l.c. and ^1H n.m.r. [c] Average of at least three runs. [d] Purity of product 95—98%. [e] By fractional crystallisation.

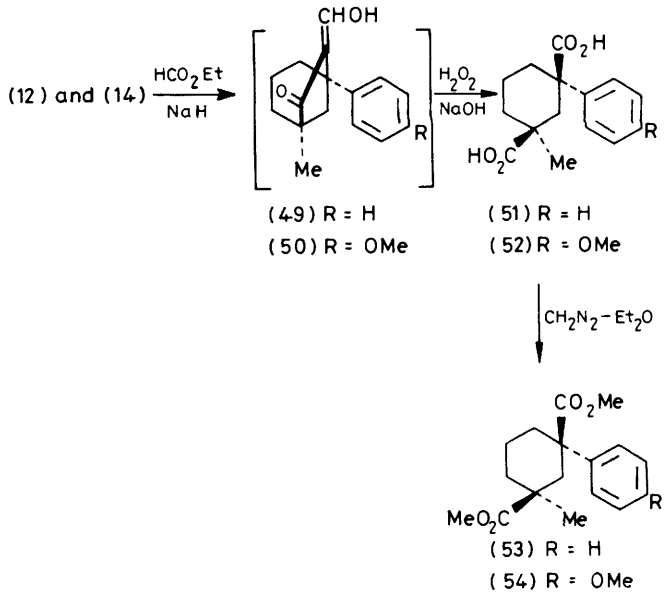
Although a variety of conditions were investigated for the insertion reactions the best results were obtained by slow addition (3—4 h) of dilute solutions (0.01—0.02M) of the diazo ketones in cyclohexane to irradiated (tungsten lamps; 250-W × 2) and refluxing suspensions or solutions of the catalyst in cyclohexane. The reactions were continued until disappearance of the diazo ketone band in the i.r. spectrum (total reaction time 6—10 h). The crude product isolated from each of the insertion reactions was purified by distillation or filtration through a column of neutral alumina and subjected to g.l.c. analysis. Intramolecular insertion products accounted for 95—98% of the total mixtures (Tables 1, 2, and 3). The unidentified materials are possibly the solvent insertion products.[2]

So far we have failed to separate the mixtures of (16) and (17) from the reactions of (11) (Scheme 8). Assignment of structure to the new ketone (16) is based upon the spectral and analytical data of the mixtures of (16) and (17), obtained from the decompositions of (11) in the presence of Cu_2O and

* Although some group 8 metal derivatives [Rh^{II} and Pd^{II} (ref. 26) and Co^{III} (ref. 27)] have been found to be highly effective catalysts for double-bond cyclopropanation reactions with diazo acetic esters and diazo ketones, only a single, unsuccessful, attempt at cyclopropanation using nickelocene has been recorded (ref. 28). All the reported carbon-hydrogen insertion reactions of diazo-compounds were carried out with heterogeneous copper or less frequently with silver catalysts. Since the completion of this work only one example (ref. 2) of an intramolecular C–H insertion of a diazo-methyl ketone and several examples of intermolecular C–H insertion reactions (ref. 29) of diazoacetic ester using Rh^{II} have been reported.



Scheme 8.



Scheme 9.

$Ni(acac)_2$ (entries 1 and 5 in Table 1). Both of these mixtures showed a single carbonyl band at 1 730 cm^{-1} in their i.r. spectra and gave elemental analyses corresponding to (16) and (17). The ^1H n.m.r. spectra of these materials exhibited a clean methyl doublet at δ 0.93 (*J* 6 Hz), revealing the presence of (16). The major regioisomeric ketones (12) and (14) from the reactions of the diazo ketones (9) and (10), however, could be easily separated by fractional crystallisation from the solid reaction products (Tables 2 and 3). The structures of the respective minor regioisomers (13) and (15) in the enriched mixtures (*ca.* 80% of isomeric purity) were assigned from the analytical and spectral data (see Experimental section).

The results obtained in the present studies clearly demonstrate that besides the degree [3] and nature of the substitution at the site into which C–H insertion may occur, the nature of the metal catalysts plays an important role in the regioselectivity of intramolecular carbenoid insertion reactions in the diazo ketones (9)—(11). In many respects these results show some degree of concordance. For example, insertion products from the diazo ketones (9) and (10), arising both from the heterogeneous and homogeneous metal promoters, excepting that of $CuSO_4$ (entry 3, Tables 2 and 3), show high regioselective preference for the tertiary benzylic C–H bond rather than the secondary C–H bond. In the case of (11), where selectivity between two tertiary C–H bonds is involved, the insertion reaction shows a slight preference in favour of the Me–C–H bond over that of the Ph–C–H bond (Table 1). Interestingly, $CuSO_4$ shows a relative reluctance towards directing insertion at the tertiary benzylic C–H bond, even for (9) and (10), and substantial amounts of the regioisomeric insertion products originating from the disfavoured secondary C–H bond [3] are formed. The same trend is maintained in the $CuSO_4$-catalysed reaction of (11) which exhibits substantial regioselectivity in insertion at the Me–C–H bond in preference to that at the Ph–C–H bond (entry 3, Table 1). The heterogeneous catalyst, $NiSO_4$, also shows similar behaviour in this reaction (entry 4, Table 1), thereby indicating that the nature of the anionic part of the metal salt catalysing the reaction, possibly has a role. The stabilisation of a partial charge (or a radical) by resonance involving the aromatic ring does not appear to be an important factor as revealed from the distributions of the regioisomeric insertion products from (11). The observed preference of insertion at the Me–C–H over that of Ph–C–H bond in (11) indicates the possible contribution of the inductive effect in this reaction.[30] However, the difference in the steric environment in these two reaction centres may also play a role.

Table 3. Distribution of the intramolecular insertion products (14) and (15) in the metal-catalysed decomposition of the diazoketone (10)

Entry	Catalyst	Yield [a] (%)	Product ratio [b–d] (14) : (15)	Isolated yield (%) [e] of (14)
1	Cu_2O	60	83 : 17	37
2	CuO	60	85 : 15	35
3	$CuSO_4$	75	70 : 30	25
4	$Ni(acac)_2$	85	85 : 15	71
5	CuTf	60	85 : 15	35

[a] Purified product. [b] Determined by g.l.c. and ^1H n.m.r. [c] Average of at least three runs. [d] Purity of product 95—98%. [e] By fractional crystallisation.

Perhaps the most significant outcome of the present work is the demonstration of the high efficiency of $Ni(acac)_2$ as a homogeneous catalyst for the intramolecular insertion reactions of the diazo ketones (9)—(11), which lead to the corresponding bridged ketones in excellent yields. Recently we have shown [31] the equal effectiveness of this catalyst in the intramolecular carbenoid addition reactions in some γ,δ-unsaturated α-diazomethyl ketones. To our knowledge these are the first reports of the successful use of a nickel catalyst [28] in carbenoid addition and insertion reactions of diazo-compounds. The efficacy of the homogeneous nickel catalyst, $Ni(acac)_2$, is exemplified for the regioselective intramolecular C–H insertion of the diazo ketones (1a) and (1b) to the corresponding tetracyclic ketones (2a) and (2b) in 80—82% isolable yields, the transformations of which were reported earlier from this laboratory [4] (Scheme 1) in the yields of *ca.* 40—55% by using $CuSO_4$ or Cu_2O.

As noted earlier (Tables 2 and 3) the $Ni(acac)_2$-catalysed reaction of the easily accessible diazo ketones (9) and (10) provide a simple preparative route to the angularly aryl-

methyl substituted bridged bicyclo[3.2.1]octanones (12) and (14) respectively in 71 and 75% isolable yields. Finally, to exemplify the synthetic usefulness, (12) and (14) have been transformed to the *cis*-1,3-disubstituted dicarboxylic acids (51) and (52) in excellent yields through their respective hydroxymethylene derivatives (49) and (50) followed by oxidation of the products with alkaline hydrogen peroxide.[4] These acids were further characterised by transformations to their corresponding di-esters (53) and (54) (Scheme 9).

Experimental

M.p.s were measured in open capillary tubes and are uncorrected. I.r. spectra of solids (KBr) and liquids (film) were recorded on a Perkin-Elmer model 298 and Beckman Acculab 4 spectrometers. U.v. spectra were recorded on a Beckman Du spectrophotometer for solutions in 95% ethanol. ^{1}H N.m.r. spectra were recorded at 60 or 100 MHz (if specified) on Varian Associates T-60A and HA-100 spectrometers, respectively, for solutions in CCl_4 or $CDCl_3$ (if specified), with $SiMe_4$ as internal standard. Analytical g.l.c. were performed on a Hewlett-Packard model 5730A Chromatograph equipped with a flame-ionization detector employing the following columns with N_2 as the carrier gas: 3% Poly-A-103 (6ft × ¼ in) on Gas Chrom-Q (100—120 mesh) (column A); 25% HVG-11 (6 ft × ⅛ in) (column B); 10% UCW-982 (20 ft × ⅛ in) (column C); 3% SE-52 on SIL-Rub (100—120 mesh) (6 ft × ¼ in) (column D); and 3% SE-30 (6 ft × ⅛ in) (column E). Elemental analyses were performed by C. Dutta and P. P. Bhattacharya of this laboratory. Column chromatography was performed on neutral (if specified) or basic alumina using aluminium oxide 'Standardised for chromatographic analysis acc. to Brockmann' (B.D.H., India). Petroleum and light petroleum refer to the fractions of b.p. 60—80 and 40—60 °C, respectively.

Methyl 1-*Methyl*-3-*oxocyclohexane*-1-*carboxylate* (21).—The keto-ester (21)[7,8] was prepared in an improved yield through a modified procedure. A solution of 3-methylcyclohex-2-enone (105 g, 0.95 mol) in 95% EtOH (400 ml) was heated under reflux with a solution of KCN (100 g, 1.53 mol) in water (500 ml) for 3 h. The cyano derivative was hydrolysed *in situ* by refluxing with KOH (86 g, 1.53 mol) in water (800 ml) for 36 h. EtOH was distilled out, and the reaction mixture acidified with 6M-HCl and extracted with Et_2O. The combined ethereal extracts were washed with 5% aqueous NaOH and the latter acidified with 6M-HCl and extracted with Et_2O to afford a thick semisolid acid (100 g). This was esterified with refluxing MeOH (500 ml), concentrated H_2SO_4 (30 ml), and a catalytic amount[32] of boric acid (2 g). The cold solution was poured into ice-cold brine and extracted with Et_2O; the extract was washed with 5% aqueous NaOH and brine and the solvent removed to afford the ester (21) (68 g), b.p. 125—130 °C at 10 mmHg (lit.,[8] b.p. 128.5—130.5 °C at 15 mmHg) as a colourless liquid. The recovered unchanged acid was re-esterified to increase the total yield to 79.8 g (49%); $\nu_{max.}$ 1 725 and 1 710 cm^{-1}. The 2,4-dinitrophenylhydrazone had m.p. 130 °C (lit.,[8] m.p. 130—131.5 °C). The *semicarbazone* (aq. EtOH) had m.p. 180 °C (Found: C, 52.8; H, 7.4. $C_{10}H_{17}N_3O_3$ requires C, 52.83; H, 7.54%).

Methyl cis- *and* trans-1,5-*Dimethyl*-3-*oxocyclohexane*-*carboxylates* (23) *and* (24).—A 80 : 20 mixture of (23) and (24) was prepared following the above described procedure from the unsaturated ketone (22)[33] (60 g, 0.48 mol) in 95% EtOH (200 ml) KCN (50 g, 0.77 mol) in water (250 ml). The cyano derivative was hydrolysed with KOH (44 g, 0.78 mol) in water (400 ml) and the acid (51.5 g) esterified with MeOH (250 ml), concentrated H_2SO_4 (20 ml), and boric acid (2 g) to give a mixture of (23) and (24) (44.1 g, 49.5%), b.p. 85—92 °C at 0.4 mmHg [lit.,[8] b.p. 95—96 °C at 1 mmHg for a stereochemically undefined mixture of (22) and (23)], $\nu_{max.}$ 1 725 and 1 710 cm^{-1}; $\lambda_{max.}$ 224 nm (log ε 1.26); g.l.c. on column A at 170 °C showed two components in a ratio of *ca.* 80 : 20; δ 1.16 and 1.30 (2 s, 2 × Me) and 3.66 and 3.60 (2 s, CO_2Me) [ratio *ca.* 80 : 20 due to (23) and (24)] (Found: C, 65.0; H, 8.6. $C_{10}H_{10}O_3$ requires C, 65.19; H, 8.75%). The 2,4-dinitrophenylhydrazone, m.p. 135—140 °C, was repeatedly crystallised from MeOH and formed shining yellow flakes, m.p. 160 °C (lit.,[8] m.p. 159.5—161 °C).

c-3-*Hydroxy*-1-*methyl*-t-3-*phenylcyclohexane*-r-1,3-*carbolactone* (18). To a well-stirred ice-cold solution of (21) (30 g, 0.17 mol) in dry Et_2O (100 ml) a solution (Et_2O) of PhMgBr [prepared from Mg turnings (5.5 g, 0.23 mol), PhBr (29.8 g, 0.19 mol) and dry Et_2O (50 ml)] was added dropwise for 2 h. The mixture was stirred at 0—5 °C for an additional 1 h and finally refluxed for 1 h. It was decomposed with ice-cold saturated aqueous NH_4Cl and extracted with Et_2O; the extracts were washed with water, aqueous $Na_2S_2O_3$ (5%), and water and then dried (Na_2SO_4). Evaporation of the solvent afforded a thick yellowish liquid; $\nu_{max.}$ 1 768 and 1 725 cm^{-1}. This was dissolved in benzene (200 ml) and refluxed for 12 h under a Dean-Stark water separator with *p*-TsOH,H_2O (0.5 g). The mixture was cooled and washed with water and the crude product isolated by evaporation of the solvent; the residue on distillation gave the following fractions: (i) 6.5 g, b.p. 110—130 °C at 4 mmHg, $\nu_{max.}$ 1 720 cm^{-1}; (ii) 5.3 g, b.p. 140—180 °C at 4 mmHg, $\nu_{max.}$ 1 775 and 1 725 cm^{-1}; (iii) 17.5 g, b.p. 150—180 °C at 0.2 mmHg, $\nu_{max.}$ 1 780 and 1 725 cm^{-1}. The combined fractions (ii) and (iii) (22.8 g) were refluxed for 2 h with a solution of KOH (8.4 g, 0.15 mol) in 95% EtOH (150 ml). Most of the ethanol was distilled under reduced pressure after dilution of the reaction mixture with water (50 ml); the unhydrolysed neutral material was extracted with Et_2O. The aqueous layer was acidified with an excess of 6M-HCl and heated on a steam-bath for 15 min after which the cooled mixture was extracted with Et_2O. The extracts were washed with aqueous Na_2CO_3 (5%) and water and then dried (Na_2SO_4). Removal of the solvent afforded (18) (14 g, 37%), m.p. 92—93 °C, after recrystallisation from Et_2O–petroleum; $\nu_{max.}$ 1 775 cm^{-1}; δ ($CDCl_3$, 100 MHz) 1.25 (s, 3 H, CH_3), 1.53—2.18 (m, 8 H, CH_2), and 7.34 (br s, 5 H, ArH) (Found: C, 77.7; H, 7.5. $C_{14}G_{16}O_2$ requires C, 77.75; H, 7.46%). The crude acidic material (6.7 g) isolated (Et_2O) from the aqueous alkali layer after acidification with 6M-HCl was lactonised by treatment with concentrated H_2SO_4 (100 ml) at −10 to −5 °C with stirring for 1 h. The red solution was poured onto crushed ice and work-up afforded the lactone (18) (5.1 g), m.p. 92—93 °C identical (mixed m.p. and i.r.) with the sample described above (total yield 50%).

c-3-*Hydroxy*-1-*methyl*-t-3-p-*methoxyphenylcyclohexane*-r-1,3-*carbolactone* (19).—The Grignard reaction of (21) (30 g, 0.17 mol) in dry Et_2O (100 ml), with *p*-$OMeC_6H_4MgBr$, prepared from *p*-$OMeC_6H_4Br$ (39.2 g, 0.21 mol), Mg (5.5 g, 0.23 g-atom) and Et_2O (60 ml) was carried out as described above. The crude product on distillation followed by treatment with *p*-TsOH,H_2O (0.5 g) in boiling benzene afforded on distillation the following fractions: (i) 3.5 g, b.p. 115—120 °C at 12 mmHg, $\nu_{max.}$ 1 720; (ii) 38.1 g, b.p. 105—135 °C at 0.4 mmHg, $\nu_{max.}$ 1 775 and 1 725. Fraction (ii) was hydrolysed with 10% ethanolic KOH (120 ml) and relactonised with 6M-HCl as described above to afford (19) (28.97 g, 66%), m.p. 89 °C after recrystallisation from Et_2O–petroleum; $\nu_{max.}$ 1 775; δ($CDCl_3$) 1.26 (s, 3 H, CH_3), 1.73—2.16 (m, 8 H, CH_2),

3.80 (s, 3 H, OCH_3), and 7.08 (AB_q, J_{AB} 8 Hz, 4 H, ArH) (Found: C, 73.0; H, 7.4. $C_{15}H_{18}O_3$ requires C, 73.14; H, 7.37%). The acidic products from the alkali washings on relactonisation with concentrated H_2SO_4 at −10 to −5 °C followed by work-up gave an additional quantity (7.8 g) of (19), m.p. and mixed m.p. 89 °C with the above sample, raising the total yield to 84%.

c-3-*Hydroxy*-1-t-5-*dimethyl*-t-3-*phenylcyclohexane*-r-1,3-*carbolactone* (20).—The Grignard reaction of the 80 : 20 mixture of (23) and (24) (10 g, 0.05 mol) in dry Et_2O (50 ml) with a solution of PhMgBr, prepared from PhBr (12.6 g, 0.08 mol), Mg (2 g, 0.08 g-atom), and Et_2O (50 ml) was carried out as described above. The crude product on distillation followed by treatment with *p*-$TsOH,H_2O$ (0.5 g) in boiling benzene afforded the following fractions: (i) 2.5 g, b.p. 130—150 °C at 25 mmHg, $\nu_{max.}$ 1 720; (ii) 8.0 g, b.p. 130—160 °C at 0.2 mmHg, $\nu_{max.}$ (neat) 1 775 and 1 725. Fraction (ii) was hydrolysed with a solution of KOH (5.6 g, 0.1 mol) in aqueous EtOH (100 ml; 50%) and relactonised as described above to afford (20) (4.86 g, 39%), m.p. 86 °C, $\nu_{max.}$ 1 775, $\lambda_{max.}$ 215nm (log ε 2.35), δ ($CDCl_3$) 1.01 (d, *J* 6 Hz, $CHCH_3$), 1.26 (s, 3 H, CH_3), 1.43—2.15 (m, 7 H, CH_2), and 7.33 (5 H, ArH) (Found: C, 78.05; H, 7.35. $C_{15}H_{18}O_2$ requires C, 78.25; H, 7.36%). The acids (25) [$\lambda_{max.}$ 259 nm (log ε 4.07)] (1.5 g) obtained on acidification of the alkali washings on relactonisation with concentrated H_2SO_4 as described above gave an additional amount (1.2 g) of (20), raising the total yield to 48%.

Hydrogenolysis of the Lactone (18) *with* Li–NH_3: 1-*Methyl*-t-3-*phenylcyclohexane*-r-1-*carboxylic Acid* (3). To a well stirred solution of (18) (1.5 g, 6.93 mmol) in dry Et_2O (20 ml), dry THF (20 ml), and anhydrous NH_3 liquid (200 ml) (directly distilled from the cylinder) was added freshly scraped Li wire (350 mg, 50.43 mg-atom) in small portions (5 min); the blue colour was discharged by the cautious addition of powdered NH_4Cl. Evaporation of NH_3 followed by extraction with ether afforded a solid acidic product (1.45 g, 96%), m.p. 95—105 °C. A small portion of this crude acid (100 mg) was esterified with CH_2N_2, which on g.l.c. analysis showed it to be a mixture of (26) and (27) (77 : 23). Repeated fractional crystallisation of the crude acid mixture from light petroleum afforded the pure epimeric acid (3) (760 mg, 50%) as colourless needles, m.p. 125—126 °C, $\nu_{max.}$ 1 700 and 1 600 cm^{-1} (Found: C, 76.9; H, 8.35. $C_{14}H_{18}O_2$ requires C, 77.0; H, 8.3%). The acid (3) (100 mg) was esterified with CH_2N_2 and on evaporative distillation at b.p. 130 °C at 0.1 mmHg afforded the ester (26), homogeneous by g.l.c. on column B at 170 °C (R_t 10.5 min); $\nu_{max.}$ 1 725 and 1 600 cm^{-1}; δ ($CDCl_3$) 1.17 (s, 3 H, CH_3), 1.40—2.46 (m, 9 H, CH_2), 3.70 (s, 3 H, $COOCH_3$), and 7.18 (s, 5 H, ArH) (Found: C, 77.5; H, 8.75. $C_{15}H_{20}O_2$ requires C, 77.55; H, 8.6%). The mother liquor afforded the epimeric acid (4) (110 mg, 7%), m.p. and mixed m.p. 109—110 °C with a sample described in the following experiment.

Hydrogenoylsis of (18) *with* Pd–C: 1-*Methyl*-c-3-*phenylcyclohexane*-r-1-*carboxylic Acid* (4).—The lactone (18) (200 mg, 0.93 mmol) in EtOH (10 ml) was hydrogenated over 10% Pd–C (100 mg) to afford a white solid (4) (200 mg, 99%), m.p. 109—110 °C, which crystallised from petroleum to give the acid (4) as rosettes, m.p. 109—110 °C; $\nu_{max.}$ 1 700s and 1 600m cm^{-1} (Found: C, 77.0; H, 8.4. $C_{14}H_{18}O_2$ requires C, 77.03; H, 8.31%). The acid (100 mg) was esterified with CH_2N_2 and the product purified by bulb-to-bulb distillation, b.p. 125—130 °C at 0.2 mmHg, to give the ester (27); homogeneous by g.l.c. on column B at 170 °C (R_t 13.5 min); $\nu_{max.}$ 1 725 and 1 600 cm^{-1}; δ($CDCl_3$, 100 MHz) 1.30 (s, 3 H, CH_3), 1.56—2.70 (m, 8 H, CH_2), 2.92 (m, 1 H, $CHAr$), 3.63 (s, 3 H, CO_2OCH_3), and 7.22 (s, 5 H, ArH) (Found: C, 77.5; H, 8.65. $C_{15}H_{20}O_2$ requires C, 77.55; H, 8.68%).

Hydrogenolysis of (19) *with* Li–NH_3: 1-*Methyl*-t-3-p-*methoxyphenylcyclohexane*-r-1-*carboxylic Acid* (5).—Hydrogenolysis of (19), (1.9 g, 7.71 mmol) in dry Et_2O (25 ml) and dry THF (25 ml) was carried out as described above with anhydrous liquid NH_3 (250 ml) and Li wire (400 mg, 57.6 mg atom) to afford a white solid (1.9 g, 99%), m.p. 115—125 °C. The crude acid (100 mg) was esterified with CH_2N_2. The ^1H n.m.r. spectrum of this ester showed two methyl singlets at δ 1.15 and 1.26 in a ratio of *ca.* 85 : 15 corresponding to the epimeric esters (28) and (29). Repeated fractional crystallisation of the crude acid mixture from Et_2O–petroleum afforded the pure epimeric acid (5) (1.1 g, 57.4%), m.p. 138 °C; $\nu_{max.}$ 1 700 and 1 600 cm^{-1} (Found: C, 72.7; H, 8.1. $C_{15}H_{20}O_3$ requires C, 72.55; H, 8.12%). The acid (5) (100 mg) was esterified with CH_2N_2 and on evaporative distillation at 140 °C and 0.2 mmHg gave the ester (28); $\nu_{max.}$ 1 725 and 1 600 cm^{-1}; δ 1.15 (s, 3 H, CH_3), 1.66—2.36 (m, 9 H, CH_2 and CH), 3.70 (s, 3 H, CO_2OCH_3), and 6.82 (AB_q, J_{AB} 8 Hz, 4 H, ArH) (Found: C, 73.0; H, 8.35. $C_{16}H_{22}O_3$ requires C, 73.25; H, 8.45%).

Hydrogenolysis of (19) *with* Pd–C: 1-*Methyl*-3-c-p-*methoxyphenylcyclohexane*-r-1-*carboxylic Acid* (6).—The lactone (19) (400 mg, 1.62 mmol) in EtOH (20 ml) was hydrogenated over 10% Pd–C (100 mg) to afford a colourless solid (400 mg, 99%), m.p. 118 °C. Crystallisation once from petroleum afforded the acid (6) as rosettes, m.p. 118 °C; $\nu_{max.}$ 1 700 and 1 600 cm^{-1} (Found: C, 72.6; H, 8.1. $C_{15}H_{20}O_3$ requires C, 72.55; H, 8.12%). The acid (6) (100 mg) was esterified with CH_2N_2 and the crude ester was purified by bulb-to-bulb distillation, b.p. 140 °C at 0.2 mmHg to afford the pure ester (29); $\nu_{max.}$ 1 725 and 1 600 cm^{-1}; δ 1.28 (s, 3 H, CH_3), 1.55—1.81 (m, 8 H, CH_2), 3.60 (s, 3 H, CO_2CH_3), and 6.88 (AB_q, J_{AB} 9 Hz, 4 H, ArH) (Found: C, 73.1; H, 8.25. $C_{16}H_{22}O_3$ requires C, 73.25; H, 8.45%).

Hydrogenolysis of the Lactone (20) *with* Li–NH_3: 1-t-5-*Dimethyl*-t-3-*phenylcyclohexane*-r-1-*carboxylic Acid* (7).—Hydrogenolysis of (20) (3.1 g, 13.46 mmol) in dry Et_2O (25 ml) and dry THF (25 ml) was carried out as described for (18) with anhydrous liquid NH_3 (500 ml) and Li wire (500 mg, 72 mg-atom) to afford a white solid (3 g, 96%), m.p. 123—126 °C, $\nu_{max.}$ 1 705 and 1 600 cm^{-1}. G.l.c. analysis of the methyl ester from a sample of the crude acid (CH_2N_2) showed the presence of (30) and (31) (84 : 16). Repeated fractional crystallisation of the crude acid mixture from petroleum afforded the pure epimeric acid (7) (1.9 g, 60%) as colourless cubes, m.p. 133 °C (Found: C, 77.85; H, 8.9. $C_{15}H_{20}O_2$ requires C, 77.55; H, 8.68%). The mother liquor from the crystallisation of (7) failed to afford pure epimeric acid (8). The acid (7) (100 mg) was esterified with CH_2N_2 to afford the ester (30); homogeneous by g.l.c. on column C at 185 °C (R_t 1.12 min), δ 0.95 (d, *J* 7 Hz, 3 H, $CHCH_3$), 1.16 (s, 3 H, 1-CH_3), 1.75—2.61 (m, 8 H, CH_2 and CH), 3.66 (s, 3 H, CO_2OCH_3), and 7.11 (s, 5 H, ArH).

Hydrogenolysis of (20) *with* Pd–C: 1-t-5-*Dimethyl*-c-3-*phenylcyclohexane*-r-1-*carboxylic Acid* (8).—Hydrogenation of (20) (250 mg, 1.08 mmol) in EtOH (20 ml) over 10% Pd–C (200 mg) in the usual manner gave the acid (8) as a viscous liquid (250 mg) which was purified by evaporative distillation, b.p. 150 °C at 0.2 mmHg; $\nu_{max.}$ 1 700 and 1 600 cm^{-1} (Found: C, 77.85; H, 8.9. $C_{15}H_{20}O_2$ requires C, 77.55; H, 8.68%). The acid (8) (135 mg) was esterified with CH_2N_2 and the ester (31) purified by bulb-to-bulb distillation, b.p.

120 °C at 0.2 mmHg; $\nu_{max.}$ 1 725 and 1 605 cm^{-1}; δ 1.01 (d, *J* 7 Hz, 3 H, $CHCH_3$), 1.16 (s, 3 H, CH_3), 1.31—2.55 (m, 8 H, CH_2 and CH), 3.05 (s, 3 H, CO_2CH_3), and 7.15 (br s, 5 H, ArH).

Preparation of the Diazo-Ketones (9)—(11).—r-1-*Diazoacetyl*-1-*methyl*-t-3-*phenylcyclohexane* (9). The acid (3) (4.04 g, 18.5 mmol) in MeOH (40 ml) was converted into its sodio-salt by neutralising the acid with a dilute solution (*ca.* 2%) of NaOMe in MeOH using phenolpthalein as indicator. After removing the solvent under reduced pressure, traces of moisture were removed by azeotropic distillation with dry benzene (2 × 30 ml) and the residue finally dried at 100 °C (at 10 mmHg) for 1 h. To the ice-cold suspension of the sodio-salt in dry benzene (30 ml) containing a catalytic amount of anhydrous pyridine (*ca.* 0.3 ml) oxalyl chloride (3 ml, 35 mmol) was added dropwise and the reaction flask occasionally shaken. After 30 min in the ice-bath, the reaction mixture was warmed at 60 °C for 1.5 h. The cold reaction mixture was filtered off and the filtrate concentrated under reduced pressure. The crude acid chloride in dry Et_2O (60 ml) was added dropwise to a magnetically stirred ice-cold dry ethereal diazomethane (generated from 15 g of *N*-methylnitrosourea) containing dry triethylamine (1 ml) during 1 h; the reaction mixture was then left overnight at room temperature. The reaction mixture was filtered and the filtrate concentrated and passed through a short column of basic alumina; it was eluted with petroleum–Et_2O (75 : 25) to afford pure (9) (4.04 g, 90%); $\nu_{max.}$ 2 115 and 1 630 cm^{-1}; δ 1.05 (s, 3 H, CH_3), 1.25—2.61 (m, 9 H, CH and CH_2), 5.38 (2 H, s, $COCH_2$), and 7.10 (br s, 5 H, ArH).

r-1-*Diazoacetyl*-1-*methyl*-t-3-p-*methoxyphenylcyclohexane* (10).—The crude acid chloride, prepared through the sodio-salt of the acid (5) (1.8 g, 7.2 mmol) in benzene (30 ml) with oxalyl chloride (1.3 ml, 15 mmol), was dissolved in dry Et_2O and treated with diazomethane (generated from 5 g of *N*-methylnitrosourea) in ether in the presence of triethylamine as above to afford (10) as a viscous yellow oil (1.8 g, 91%); 2 120 and 1 630 cm^{-1}; δ 1.05 (s, 3 H, CH_3), 3.70 (s, 3 H, OCH_3), 5.37 (s, 1 H, $COCHN_2$), and 6.90 (q, *J* 9 Hz, 4 H, ArH).

r-1-*Diazoacetyl*-1,t-3-*dimethyl*-t-3-*phenylcyclohexane* (11).—The crude acid chloride, prepared *via* the sodio-salt of the acid (7) (1.62 g, 6.97 mmol) in benzene with oxalyl chloride (1.3 ml, 15 mmol), was dissolved in dry Et_2O and treated with diazomethane in ether in the presence of triethylamine as above to afford (11) (1.65 g, 92%) as a thick yellow oil; $\nu_{max.}$ 2 120 and 1 640 cm^{-1} δ 0.93 (d, *J* 6 Hz, 3 H, CH_3), 1.08 (s, 3 H, CH_3), 5.36 (s, 1 H, $COCHN_2$), and 7.13 (br s, 5 H, ArH).

Unambiguous Synthesis of the Bicyclo[3.2.1]*octanones* (12), (14), *and* (17): *Ethyl* 3-*Methoxycarbonyl*-3-*methylcyclohexylidenecyanoacetate* (37).—The keto ester (21) (3 g, 17.62 mmol) was condensed with ethylcyanoacetate (4 g, 35.36 mmol) in benzene (20 ml) and acetic acid (1 ml) in the presence of ammonium acetate (500 mg, added in 4 lots) by refluxing for 20 h in a flask fitted with a Dean-Stark water separator. The reaction mixture was poured into water and extracted with Et_2O; the extracts were washed with water and dried (Na_2SO_4). On removal of the solvent and the low-boiling products, the unsaturated cyano ester (37) (3.2 g, 68%) was distilled, b.p. 145—147 °C at 0.6 mmHg (bath-temp.) (Found: C, 63.2; H, 7.4. $C_{14}H_{19}NO_4$ requires C, 63.38; H, 7.22%); $\nu_{max.}$ 2 223, 1 730, and 1 605 cm^{-1}; $\lambda_{max.}$ 235 nm (log ε 4.23); δ 4.2 and 4.17 (2 q, 3 H, *J* 7 Hz), 3.65 and 3.6 (2 s, 3 H), 3.37—1.2 (m, 14 H with t at 1.36, *J* 7 Hz and s at 1.27 and s at 1.2 due to stereoisomers).

Ethyl 3-*Methoxycarbonyl*-3-*methyl*-1-*phenylcyclohexylcyanoacetate* (38).—Cuprous iodide (300 mg) was added to a solution of the unsaturated cyano ester (37) (3.0 g, 11.3 mmol) in dry Et_2O (15 ml) and the mixture was stirred for 5 min. To this mixture was added at 0 °C with stirring, a solution of PhMgBr, prepared from Mg (600 mg, 24.68 mg-atom) and PhBr (3.6 g, 22.9 mmol) in dry Et_2O (20 ml). The mixture was left at room temperature for 16 h, refluxed for 30 min, and decomposed with 3M-HCl (30 ml). Work-up followed by distillation under reduced pressure furnished the saturated cyano ester (38) (3 g, 77%), b.p. 178—180 °C at 0.4 mmHg (bath-temp.) (Found: C, 70.2; H, 7.4. $C_{20}H_{25}NO_4$ requires C, 69.95; H, 7.34%); $\nu_{max.}$ 2 245 and 1 730 cm^{-1}; the ^1H n.m.r. spectrum showed the presence of diastereoisomers and indicated clearly the incorporation of the phenyl moiety.

Methyl 3-*Methoxycarbonyl*-3-*methyl*-2-*phenylcyclohexylacetate* (40).—The cyano ester (38) (3 g, 8.73 mmol) was hydrolysed by refluxing with KOH (6 g), ethylene glycol (16 ml) and water (4 ml) for 24 h. The reaction mixture was cooled, poured into water, and after removal of the unchanged neutral material by extraction with Et_2O the aqueous part was acidified with 6M-HCl and extracted with Et_2O; the extracts were washed with brine and dried (Na_2SO_4). The residue, after removal of the solvent was heated on an oil-bath at 180—200 °C for 30 min, cooled, dissolved in ether, and extracted with aqueous NaOH (2%). The alkali washings were acidified with 6M-HCl, worked up with Et_2O, and treated with a cold ethereal solution of CH_2N_2 (prepared from 8 g of *N*-methylnitrosourea). After removal of the solvent the residue on evaporative distillation [b.p. 150 °C at 0.6 mmHg (bath-temp.)] afforded the diester (40) (1.2 g, 45%) (Found: C, 70.9; H, 8.1. $C_{18}H_{24}O_4$ requires C, 71.02; H, 7.95%); $\nu_{max.}$ 1 730 cm^{-1}; δ 7.32—7.00 (m, 5 H), 3.67 (s, 3 H), 3.32, 3.25 (2 s, 3 H), and 2.87—1.00 (m, 13 H with s at 1.10 and s at 1.00 due to isomers). G.l.c. analyses indicated the presence of two isomers in the ratio of 1 : 3.

5-*Methyl*-1-*phenylbicyclo*[3.2.1]*octan*-6-*one* (12).—A solution of the diastereoisomeric mixture of the dimethyl esters (40) (1 g, 3.28 mmol) in benzene (10 ml) was added under a N_2 atmosphere to dry potassium t-butoxide [from K (400 mg, 10.25 mg-atom)] suspended in dry benzene (5 ml). The mixture was refluxed for 2.5 h, cooled, acidified with 6M-HCl and extracted with Et_2O; the extracts were washed with water, dried (Na_2SO_4), and evaporated. The neutral product was chromatographed on neutral alumina (15 g) and eluted with petroleum to afford the ketone (12) (300 mg, 48%), m.p. 80 °C (from light petroleum) (Found: C, 84.0; H, 8.45. $C_{15}H_{18}O$ requires C, 84.0; H, 8.5%); $\nu_{max.}$ 1 735 cm^{-1}; δ 1.05 (s, 3 H, CH_3), 1.68 (m, 6 H, CH_3), 2.01 (br s, 2 H, 8-CH_2); 2.38 (br s, 2 H, $COCH_2$), and 7.26 (br s, 5 H, ArH); R_t (column E) 5.4 min at 185 °C.

Ethyl 3-*Methoxycarbonyl*-3-*methyl*-1-(p-*methoxyphenyl*)-*cyclohexylcyanoacetate* (39).—The conjugate addition of *p*-$OMeC_6H_4MgBr$, prepared from *p*-bromoanisole (4.1 g, 21.9 mmol) and Mg (600 mg, 24.68 mg-atom) in dry Et_2O (30 ml) to the unsaturated cyano ester (37) (3.0 g, 11.3 mmol) afforded the saturated cyano ester (39) (2.1 g, 50%), b.p. 180 °C at 0.4 mmHg (bath-temp) (Found: C, 67.5; H, 7.3. $C_{21}H_{27}NO_5$ requires C, 67.54; H, 7.29%). The complex n.m.r. spectrum indicated the presence of the diastereoisomers of (39).

Methyl 3-*Methoxycarbonyl*-3-*methyl*-1-(p-*methoxyphenyl*)-*acetate* (41).—The cyano ester (39) (3.24 g, 8.67 mmol) was hydrolysed with KOH (6 g) in ethylene glycol (15 ml) and water (4 ml) under N_2 as described for (38). The crude product was decarboxylated and esterified with ethereal CH_2N_2 to afford the diester (41) (1.16 g, 40%), b.p 155 °C at 0.6 mmHg (bath-temp) (Found: C, 68.0; H, 7.6. $C_{19}H_{26}O_5$ requires C, 68.24; H, 7.84%); $\nu_{max.}$ 1 730 cm^{-1}. The ^1H n.m.r. spectrum indicated the presence of two isomers.

5-*Methyl*-1-(p-*methoxyphenyl*)*bicyclo*[3.2.1]*octan*-6-*one* (14).—Dieckmann condensation of (41) (1.0 g, 2.99 mmol) with Bu^{t}OK [from K-metal (313 mg, 8.02 mg-atom)] in benzene (12 ml) followed by hydrolysis of the crude product with 5% methanolic KOH (10 ml) as described for (40) gave (14) (182 mg, 25%), m.p. 70 °C (light petroleum) (Found: C, 78.6; H, 8.35. $C_{16}H_{20}O_2$ requires C, 78.65; H, 8.25%); $\nu_{max.}$ 1 730 and 1 610 cm^{-1}; δ 1.05 (s, 3 H, CH_3), 1.65 (m, 6 H), 1.93 (br s, 2 H, 8-CH_2), 2.37 (m, 2 H, $COCH_2$]), 3.70 (s, 3 H, OCH_3), and (6.90 q, J_{AB} 8 Hz, 4 H, ArH); R_t (column E) 1.8 min at 185 °C.

Methyl cis- *and* trans-1-*Methyl*-3-*oxo*-5-*phenylcyclohexane-carboxylates* (43) *and* (44).—A 60 : 40 mixture of (43) and (44) * was prepared following the procedure described for (21) from the unsaturated ketone (42) [8] (55.8 g, 0.28 mol) in 95% EtOH (200 ml), with KCN (47.5 g, 0.73 mol) in water (200 ml); the hydrolysis was effected *in situ* with KOH (45 g, 0.80 mol) in water (450 ml) and the esterification with MeOH (300 ml), concentrated H_2SO_4 (25 ml), and H_3BO_3 (2 g). The mixture of esters (43) and (44) (50 g, 70%) was distilled at 165—170 °C at 0.4 mmHg (bath temp); $\nu_{max.}$ 1 720 and 1 600 cm^{-1}. The ^1H n.m.r. spectrum exhibited two CO_2Me and methyl singlets at δ 3.70 and 3.60 and 1.31 and 1.20 respectively in a ratio of *ca.* 60 : 40. The proportion of the two isomeric esters varied from 60 : 40 to 70 : 30.

3-*Methoxycarbonyl*-cis-3-*methyl*-5-*phenylcyclohexylidene-malononitrile* (45).—The above diastereoisomeric mixture of the keto esters (43) and (44) (10 g, 40.65 mmol) was condensed with malononitrile (4.16 g, 62.9 mmol) in benzene (120 ml) and acetic acid (1 ml) in the presence of ammonium acetate (1 g; added in 4 lots) by refluxing for 36 h under a Dean-Stark water separator. Work-up and distillation gave a glassy solid (6.57 g, 55%), b.p. 185 °C at 0.4 mmHg, which solidified when kept. This on recrystallisation twice from Et_2O gave stereochemically homogeneous (45) (4.78 g, 40%), m.p. 118 °C (Found: C, 73.3; H, 6.3. $C_{18}H_{18}N_2O_2$ requires C, 73.45; H, 6.16%); $\nu_{max.}$ 2 225, 1 725, and 1 605 cm^{-1}; $\lambda_{max.}$ 240 nm (log ε 4.3); δ ($CDCl_3$) 1.38 (s, 3 H, CH_3), 3.75 (s, 3 H, $COOCH_3$), and 7.2 (br s, 5 H, ArH).

c-3-*Methoxycarbonyl*-1,t-3-*dimethyl*-t-5-*phenyl*-1-r-*cyclo-hexylmalononitrile* (46).—Conjugate addition of MeMgI [prepared from methyl iodide (4.54 g 32 mmol) and Mg (0.76 g, 31.59 mg-atom)] to the unsaturated nitrile (45) (4.50 g, 15.2 mmol) in anhydrous Et_2O in the presence of cuprous iodide (320 mg) following the method described for (37), finally afforded the saturated nitrile (46) (4.17 g, 88%), m.p. 116 °C (from Et_2O) (Found: C, 73.3; H, 7.3. $C_{19}H_{22}N_2O_2$ requires C, 73.52; H, 7.14%), $\nu_{max.}$ 2 240 and 1 725 cm^{-1}; $\lambda_{max.}$ 238 (log ε 3.92); δ (CCl_4) 1.25 (s, 3 H, CH_3), 1.3 (s, 3 H, CH_3), 3.75 (s, 3 H, $COOCH_3$), and 7.15 (br s, 5 H, ArH).

Methyl c-3-*Methoxycarbonyl*-1,t-3-*dimethyl*-t-5-*phenyl*-r-1-*cyclohexylacetate* (48).—The nitrile (46) (2.5 g, 8.05 mmol) was refluxed with a mixture of acetic acid (4 ml), concentrated sulphuric acid (4 ml), and water (4 ml) for 25 h. It was cooled diluted with ice-cold water (50 ml), extracted with ethyl acetate and the combined ethyl acetate extracts were washed with 2% ice-cold aqueous NaOH. The combined alkaline washings were acidified with 6M-HCl and extracted with ethyl acetate; the extracts were washed with water, dried, and evaporated to give the diacid (47) (1.98 g, 85%), m.p. 228 °C (from Et_2O) (Found: C, 70,3; H, 7.6. $C_{17}H_{22}O_4$ requires C, 70.32; H, 7.64%); $\nu_{max.}$ 1 700 cm^{-1}. The diacid (47) (70 mg, 0.24 mmol) was treated with an ethereal solution of CH_2N_2 to give the diester (48) (73 mg, 96%), b.p. 155 °C at 0.2 mmHg (Found: C, 71.5; H, 8.1. $C_{19}H_{22}O_4$ requires C, 71.67; H, 8.23%); $\nu_{max.}$ 1 720 cm^{-1}; δ 1.01 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 3.7 (s, 3 H, OCH_3), 3.8 (s, 3 H, OCH_3), and 7.1 (br s, 5 H, ArH).

1,5-*Dimethyl*-exo-3-*phenylbicyclo*[3.2.1]*octan*-6-*one* (17).—Dieckmann cyclisation of (48) (1 g, 3.14 mmol) in dry benzene (20 ml) with Bu^{t}OK, prepared from K-metal (1 g, 25.6 mg-atom) under N_2 as described for (40) and subsequent hydrolytic decarboxylation of the crude β-keto ester with aqueous perchloric acid (8 ml; 20%) under reflux for 8 h and chromatography of the crude product on neutral alumina (8 g) using petroleum as eluant afforded (17) (250 mg, 35%), m.p. 52 °C (light petroleum) (Found: C, 84.1; H, 8.9. $C_{16}H_{20}O$ requires C, 84.16; H, 8.83%); $\nu_{max.}$ 1 730 cm^{-1}; δ 1.01 (s, 3 H, CH_3), 1.18 (s, 3 H, CH_3), 1.38—1.71 (m, 6 H), 2.05 (br d, 2 H, $COCH_2$), 2.68 (m, 1 H, C*H*Ar), and 7.08 (s, 5 H, ArH); R_t (column D) 12.0 min at 170 °C.

α-*Ketocarbenoid Insertion Reactions of the Diazo Ketone* (11): exo-3,5-*Dimethyl*-1-*phenylbicyclo*[3.2.1]*octan*-6-*one* (16) *and* (17).—(*A*) *With heterogeneous catalysts.* (*a*) With Cu_2O. A solution of the diazo ketone (11) (0.5 g, 1.95 mmol) in anhydrous cyclohexane (100 ml) (freshly distilled over $LiAlH_4$) was added dropwise over a period of 3 h under a N_2 atmosphere to a magnetically stirred, refluxing suspension of freshly prepared anhydrous Cu_2O (2 g, 14 mmol) in dry cyclohexane (100 ml) which was irradiated with two 250-W tungsten lamps. Refluxing was continued for a further 5 h when the diazoketone i.r. band had disappeared. Filtration and evaporation afforded a yellow oil which, on evaporative distillation [125—130 °C at 0.1 mm Hg (bath-temp)] gave a colourless ketone mixture (267 mg, 60%), $\nu_{max.}$ 1 730 cm^{-1}. G.l.c. analyses of this mixture revealed the presence of (17) and (16) in a ratio of 52 : 48 (*ca.* 96% purity) with R_t values of 13 and 12 and 15 and 13 min respectively on column A and column D at 170 °C, by co-injection with the authentic sample of (17) (*vide supra*). The ^1H n.m.r. spectrum showed a 3-Me doublet at δ 0.93 (*J* 6 Hz) and a 5-Me singlet at δ 1.05 for (16); the 1- and 5-Me singlets for (17) appeared at δ 1.01 and 1.18 respectively, and the aromatic protons for (17) and (16) showed singlets at δ 7.10 and 7.15 respectively in a ratio of *ca.* 54 : 46. This mixture was chromatographed on neutral alumina (11 g) with light petroleum–Et_2O (1 : 1) as eluant to give a mixture of (17) and (16) (52 : 48) (100% purity by g.l.c.) (Found: C, 84.1; H, 8.8. $C_{16}H_{20}O$ requires C, 84.16; H, 8.83%).

Decomposition of (11) (0.5 g; 1.95 mmol) under the conditions described above using 12—15 mmol of 'activated CuO',[34] anhydrous $CuSO_4$, and anhydrous $NiSO_4$ gave in each case a mixture of (17) and (16) in 95—98% (g.l.c.) purity. The results are given in Table 1.

(*B*) *With homogeneous catalysts.* (*a*) With $Ni(acac)_2$. A solution of the diazo ketone (11) (0.5 g, 1.95 mmol) in dry cyclohexane (200 ml) was added dropwise over a period of

* Preparation of a keto ester of this structure, with undefined stereochemistry, in lower yield has been reported (ref. 8).

3 h, to a magnetically stirred, refluxing solution of anhydrous $Ni(acac)_2$ [23] (260 mg, 1 mmol) in dry cyclohexane under a N_2 atmosphere, which was irradiated with two 250-W tungsten lamps. Refluxing was continued for a further 7 h when the diazo ketone i.r. band had disappeared. The green solution was filtered through neutral alumina (30 g) and the column was further eluted with petroleum–benzene (9 : 1). Evaporation of the combined elutes under reduced pressure afforded a mixture of (17) and (16) as a colourless liquid (410 mg, 92%) of 98% purity (g.l.c.) which was subjected to g.l.c. and ^1H n.m.r. analyses (Table 1).

Decomposition of (11) (0.5 g, 1.95 mmol) with $Pd(acac)_2$ [24] (300 mg, 0.98 mmol), $Co(acac)_3$ [25] (300 mg, 0.84 mmol), $CuTf\cdot\frac{1}{2}C_6H_6$ (200 mg, 1.01 mmol) under the conditions described above gave in each case a mixture of (17) and (16) in 96—98% purity (g.l.c.). The results are given in Table 1.

α-Ketocarbenoid Insertion Reactions of the Diazo Ketone (9): *The Bridged Ketone* (12) *and* exo-1-*Methyl*-3-*phenylbicyclo*[3.2.1]*octan*-7-*one* (13). (*A*) *With heterogeneous catalysts.* (*a*) With Cu_2O. A solution of the diazo ketone (9) (760 mg, 3.13 mmol) in dry cyclohexane (200 ml) was subjected to an insertion reaction with anhydrous Cu_2O (2 g, 14 mmol) in dry cyclohexane (100 ml) under the conditions described above for the corresponding reaction of (11). Distillation of the crude product at 125—130 °C at 0.4 mmHg (bath-temp) afforded mainly a mixture of (12) and (13) (403 mg, 60%); $\nu_{max.}$ 1 735 cm^{-1}; the ^1H n.m.r. spectrum showed two methyl singlets at δ 1.05 and 1.0 (*ca.* 85 : 15). G.l.c. analyses of the sample in column E at 185 °C showed besides a minor (*ca.* 5%) component at R_t 3.5 min (possibly the solvent insertion product), the ketones (12) and (13) in a ratio of 85 : 15 with R_t values of 4.55 and 5.4 min respectively by co-injection with an authentic sample of (12) (*vide supra*). With time, the liquid distillate solidified and this, on recrystallisation from light petroleum, afforded (12) (282 mg, 42%), m.p. 80 °C, identical with an authentic sample (mixed m.p., i.r. and g.l.c.).

(*b*) With CuO. Decomposition of (9) (760 mg, 3.13 mmol) with 'activated CuO' [34] (1.2 g, 15.09 mmol) following the above conditions and purification of the crude product by distillation afforded a colourless liquid (436 mg, 65%) consisting of (12) and (13) (96% purity by g.l.c.) (Table 2), which solidified when kept. Recrystallisation from light petroleum gave (12) (289 mg, 43%) identical (mixed m.p., i.r. and g.l.c.) with the sample described above.

(*c*) With $CuSO_4$. Decomposition of (9) (760 mg, 3.13 mmol) with anhydrous $CuSO_4$ (3.5 g, 21.9 mmol) following the aforementioned conditions gave a mixture of (12) and (13) (443.0 mg, 66%) (95% purity, g.l.c.) after distillation of the crude product, which was subjected to g.l.c. analyses (Table 2). The solidified distillate on recrystallisation from light petroleum afforded the pure ketone (12) (255 mg, 38%), m.p. 80 °C, identical (mixed m.p., i.r., and g.l.c.) with the sample described above. The mother liquor after separation of (12) was carefully chromatographed on neutral alumina (30 g). Initial eluates with light petroleum afforded the crystalline ketone (12). Further elution with the same solvent afforded an oil (140 mg, 20%) consisting of (12) and (13) in a ratio of 20 : 80 (g.l.c.) which did not solidify. This was purified by evaporative distillation at 125—130 °C (bath-temp.) at 0.4 mmHg; *m/z* 214 (M^+); $\nu_{max.}$ 1 735 cm^{-1}; ^1H n.m.r. spectrum of this mixture showed two methyl singlets at δ 1.0 and 1.05 in a ratio of 80 : 20 corresponding to (13) and (12) and a multiplet at 82.70 for the benzylic proton of (13) (Found: C, 84.0; H, 8.3. $C_{15}H_{18}O$ requires C, 84.07; H, 8.47%).

(*B*) *With homogeneous catalyst.* (*a*) With $Ni(acac)_2$. Decomposition of (9) (760 mg, 3.13 mmol) with a solution of $Ni(acac)_2$ (308 mg, 1.2 mmol) under the conditions described for (11) and filtration of the reaction mixture through a column of neutral alumina (35 g) and elution with petroleum–benzene (9 : 1) afforded a mixture of (12) and (13) (578 mg, 86%) as a colourless solid, which was subjected to g.l.c. analysis (Table 2). This on recrystallisation from light petroleum afforded the ketone (12) (504 mg, 75%), m.p. 80 °C, identical (mixed m.p., i.r., g.l.c.) with the sample described above.

(b) With $CuTf\cdot\frac{1}{2}C_6H_6$. Decomposition of (9) (500 mg, 2.05 mmol) with $CuTf\cdot\frac{1}{2}C_6H_6$ (200 mg, 1 mmol) in cyclohexane under the conditions described for (11) gave a mixture of (12) and (13) as a colourless semisolid (265 mg, 60%), which was subjected to g.l.c. and ^1H n.m.r. analyses (Table 2). The pure ketone (12) (176 mg, 40%) was isolated from the mixture by recrystallisation from light petroleum.

α-Ketocarbenoid Insertion Reactions of the Diazo Ketone (10): *the Bridged Ketone* (14) *and* exo-1-*Methyl*-3-p-*methoxyphenylbicyclo*[3.2.1]*octan*-7-*one* (15). (*A*) *With heterogeneous catalysts.* (*a*) With Cu_2O. A solution of the diazo ketone (10) (844 mg, 3.1 mmol) in dry cyclohexane (200 ml) was subjected to an insertion reaction with anhydrous Cu_2O (2 g, 14 mmol) in dry cyclohexane (100 ml) under conditions identical with those described for the reaction of (11). The decomposition of the diazo ketone was completed in 6 h. Distillation of the crude product at 120—125 °C at 0.2 mmHg (bath-temp) afforded a mixture of (14) and (15) (454 mg, 60%), in a ratio of 83 : 17 with R_t values of 15.6 and 18 min respectively (96% purity), on column E at 185 °C; $\nu_{max.}$ 1 730 cm^{-1}; the ^1H n.m.r. spectrum showed two Me singlets at δ 1.05 and 1.0 (*ca.* 83 : 17). Recrystallisation of this mixture from light petroleum gave the pure ketone (14), (280 mg, 37%), m.p. 70 °C, identical with an authentic sample (*vide supra*) (mixed m.p., i.r. and g.l.c.).

(*b*) With 'activated CuO.' Repeating the decomposition of (10) (844 mg, 3.1 mmol) with 'activated CuO' (1.2 g, 15 mmol) under the above conditions gave, after distillation, a mixture of (14) and (15) (455 mg, 60%) in 95% purity (g.l.c.), which was subjected to ^1H n.m.r. and g.l.c. analyses (Table 3). On recrystallisation from light petroleum the mixture gave the pure ketone (14) (265 mg, 35%).

(*c*) With $CuSO_4$. Decomposition of (10) (844 mg, 3.1 mmol) with anhydrous $CuSO_4$ (3.5 g, 21.9 mmol) following the conditions described for (9) gave a mixture of (14) and (15) (567 mg 75%) (96% purity by g.l.c.) after distillation of the crude product, b.p. 120—125 °C at 0.2 mmHg; $\nu_{max.}$ 1 730 and 1 600 cm^{-1}, which was subjected to g.l.c. and ^1H n.m.r. analyses (Table 3). On careful chromatography of this mixture on neutral alumina (40 g) the initial elutions with light petroleum gave the ketone (14) (189 mg, 25%), m.p. 70 °C (from light petroleum), alone or in admixture with an authentic sample. Further elutions with the same solvent afforded an oil which did not solidify. G.l.c. analyses indicated this to be a mixture of (14) and (15) in a ratio of *ca.* 25 : 75 (99% purity). The ^1H n.m.r. spectrum of this mixture showed two Me singlets at δ 1.05 and 1.00 for (14) and (15), and a multiplet at δ 2.66 due to a benzylic proton of (15) as well as two methoxy singlets at δ 3.70 and δ 3.73 for (14) and (15), respectively (Found: C, 78.4; H, 8.05. $C_{16}H_{20}O_2$ requires C, 78.65; H, 8.25%).

(*B*) *With homogeneous catalyst.* (*a*) With $Ni(acac)_2$. Decomposition of (10) (844 mg, 3.1 mmol) with a solution of $Ni(acac)_2$ (308 mg, 1.2 mmol) under the conditions described for (11) and filtration through a column of neutral alumina (40 g) afforded a mixture of (14) and (15) (643 mg, 85%) as a colourless solid. This was subjected to g.l.c. and ^1H n.m.r. analyses (Table 3) and recrystallised from light petroleum to give the ketone (14) (536 mg, 71%), m.p. 70 °C, identical (mixed m.p., i.r. and g.l.c.) with the sample described above.

(*b*) With $CuTf\cdot\frac{1}{2}C_6H_6$. Decomposition of (10) (844 mg, 3.1 mmol) with $CuTf\cdot\frac{1}{2}C_6H_6$ (400 mg, 2 mmol) as described for (11) gave a mixture of (14) and (15) (454 mg, 69%) which was subjected to g.l.c. and ^1H n.m.r. analyses (Table 3). The pure ketone (14) (265 mg, 35%) was isolated from the mixture by recrystallisation from light petroleum.

Intramolecular Insertion Reaction of the Diazo Ketone (1a): (±)-19,20-*Cyclopodocarpa*-8,11,13-*trien*-19-*one* (2a).—A solution of the diazo ketone (1a) [4b] (536 mg, 1.99 mmol) in a mixture of anhydrous cyclohexane and tetrahydrofuran (9 : 1) was added during 3 h to a magnetically stirred refluxing solution of $Ni(acac)_2$ (260 mg, 1 mmol) in dry cyclohexane (200 ml) under irradiation of two 250-W tungsten lamps; the refluxing was continued for a further 9 h when the diazo ketone i.r. band had disappeared. The green solution was filtered through neutral alumina (35 g) and the column was eluted with light petroleum–benzene (9 : 1). Evaporation of the combined organic layers gave (2a) (393 mg, 82%), as a white solid, m.p. 116—117 °C. Recrystallisation once from light petroleum gave analytically pure (24), m.p. 118 °C (lit.,[4a,b] m.p. 118 °C) identical (mixed m.p., i.r., ^1H n.m.r.) with the sample prepared earlier.[4a,b]

Intramolecular Insertion Reaction of the Diazo Ketone (1b): (±)-13-*Methoxy*-19,20-*cyclopodocarpa*-8,11,13-*trien*-19-*one* (2b).—Decomposition of the diazo ketone (1b) [4b] (536 mg, 1.99 mmol) with $Ni(acac)_2$ (260 mg, 1 mmol) under the conditions described above for (1a) required 12 h for completion of the reaction. The chromatography of the reaction mixture on neutral alumina (35 g) and elution with petroleum–benzene (9 : 1) gave the bridged-ketone (2b) (462 mg, 80%), m.p. 128—129 °C. Recrystallisation once from light petroleum afforded the analytically pure sample of (2b), m.p. 130 °C (lit.,[4a,b] m.p. 130 °C), identical (mixed m.p., i.r. and ^1H n.m.r.) with the sample prepared earlier.[4a,b]

Transformation of (12) *to* 1-*Methyl*-t-3-*phenylcyclohexane*-r-1,3-*dicarboxylic Acid* (51).—To an ice-cold stirred suspension of NaH (1 g; 50% dispersion) in dry benzene (15 ml) under N_2 was added dropwise a solution of (12) (350 mg, 1.63 mmol) in benzene (25 ml) followed by the addition of one drop of MeOH. Ethyl formate (2 g, 27 mmol) was then added dropwise and the stirring was continued for an additional 2 h; the reaction mixture was then left overnight. The excess of NaH was decomposed with a small amount of MeOH, diluted with water, acidified with 6M-HCl, and extracted with Et_2O. The ethereal layer was extracted with 2% NaOH solution. The combined basic layers were acidified with 6M-HCl and extracted with Et_2O. The ether layer was washed with brine and dried (Na_2SO_4). Evaporation of the solvent afforded the crude hydroxymethylene derivative, $\nu_{max.}$ 1 710 and 1 670 cm^{-1}. To a magnetically stirred cooled (5—10 °C) solution of this crude hydroxymethylene derivative in NaOH (90 ml; 10%) was added dropwise H_2O_2 (60 ml; 30%). After the vigour of the reaction subsided, further NaOH (10 ml; 10%) was added followed by H_2O_2 (10 ml; 30%); the mixture was then allowed to stand overnight. The reaction mixture was diluted with water and extracted with Et_2O. The aqueous layer was acidified with 6M-HCl and extracted with ethyl acetate. The organic layer was washed with brine and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure afforded (51) (402 mg, 94%), m.p. 209—210 °C (ether–petroleum); $\nu_{max.}$ 1 700 cm^{-1} (Found: C, 68.6; H, 7.1. $C_{15}H_{18}O_4$ requires C, 68.68; H, 6.92%).

The diacid (51) (100 mg) was esterified with an excess of diazomethane in Et_2O to afford the dimethyl ester (53) (100 mg), m.p. 74 °C (light petroleum); $\nu_{max.}$ 1 730 cm^{-1}; δ 1.16 (s, 3 H), 1.4—2.0 (m, 8 H), 3.50 (s, 3 H), 3.63 (s, 3 H), and 7.2 (m, 5 H) (Found: C, 70.0; H, 7.5. $C_{17}H_{22}O_4$ requires C, 70.32; H, 7.64%).

Transformation of (14) *to* 1-*Methyl*-t-3-p-*methoxyphenylcyclohexane*-r-1,3-*dicarboxylic Acid* (52).—The crude hydroxymethylene derivative, prepared from the ketone (14) (500 mg, 2.04 mmol) with ethyl formate (0.5 ml, 6.2 mmol) in the presence of NaH (0.5 g, 20.8 mmol) in benzene as described for (12), was oxidised with H_2O_2 (15 ml; 30%; added in two lots) in NaOH solution (25 ml, 10%, added in two lots) as described above to afford the dicarboxylic acid (52) (568 mg, m.p. 196—197 °C (ether–petroleum) (Found: C, 65.45; H, 6.75. $C_{16}H_{20}O_5$ requires C, 65.74; H, 6.90%).

The acid (52) (100 mg) was esterified with diazomethane in Et_2O to afford the dimethyl ester (54) (100 mg), m.p. 103—104 °C (petroleum); $\nu_{max.}$ 1 730 cm^{-1}; δ 1.16 (s, 3 H), 1.30—2.66 (m, 8 H), 3.50 (s, 3 H), 3.6 (s, 3 H), 3.73 (s, 3 H), and 6.95 (AB_q, J_{AB} 8 Hz, 4 H) (Found: C, 67.3; H, 7.6. $C_{18}H_{24}O_5$ requires C, 67.48; H, 7.55%).

Acknowledgements

The financial support from S.E.R.C./D.S.T. Scheme (New Delhi) under Grant No. 23 (3p-8)/81-STP/II is gratefully acknowledged.

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Received 3rd *June* 1983; *Paper* 3/902