BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 47(8), 2081—2082 (1974)

The Reductive Amination of *d*-Camphor with the Methylamine and Carbon-13 NMR of the Reaction Products

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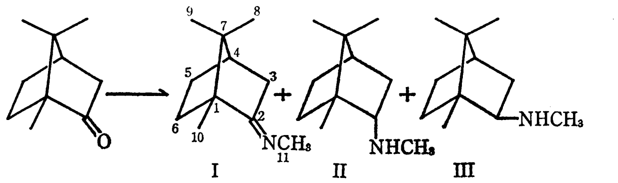
(Received January 7, 1974)

Synopsis. The effects of catalysts (Raney Ni, 5% Pd–C, and PtO_2) in the title reactions have been discussed. The PtO_2 catalyst is excellent in reductive power and in selectivity. The CMR spectra of the reaction products (I, II, and III) are assigned, and the *N*-protonation shifts are further measured.

The reductive amination reactions using *d*-camphor and methylamine have not been investigated. The present paper reveals the reductive power and selectivity of some catalysts in the reactions. Generally, the reductive amination reactions of ketone with a primary amine are carried out in the presence of the Raney Ni catalyst and hydrogen, while the yields of the reactions are decreased by the sterically-enhanced bulkiness about the carbonyl groups and amino groups.[1] Raney Ni, 5% Pd–C, and PtO_2 were employed as catalysts. The reaction mixtures of methylamine and *d*-camphor, together with one of the three catalysts in an autoclave, were stirred at 120 °C for 24 hr. The basic oil obtained after the reaction was quantitatively analyzed by gas-chromatography. Three peaks appeared on the chromatogram. The structures of the three components (I, II, and III) were comfirmed by a comparison with the retention times of authentic samples (*N*-methylcamphorimine, *N*-methylbornylamine, and *N*-methylisobornylamine) prepared by known methods.[2–4]



I II III

Table 1. The catalytic effects of the reductive amination

	Mixture yields (%)	Ratio of products (%) I	II	III
Raney Ni	65	82.8	1.3	15.9
5% Pd–C	61	30.4	3.9	65.7
PtO_2	70	3.7	4.6	91.7
No catalyst	70	100.0		

Table 1 shows the yields and ratios of the products resulting from the effects of each catalyst. The remarkable differences in the reductive power of the catalysts were clarified. The reaction using the W-1 Raney Ni catalyst gave scarcely any Compounds II, and III, while the reaction using the PtO_2 catalyst gave mostly Compound III. Consequently, the PtO_2 catalyst is superior to the other catalysts in reductive powder and in selectivity, as shown by the ratios of the products of Compounds II and III, in the reductive amination reaction using ketones with sterically bulky groups, such as *d*-camphor. Similar results regarding the reductive power of the catalyst have been previously obtained by Goldberg and Lam.[5] As the reaction using no catalysts gave only Schiff base I, it may be assumed that the Schiff base was reduced to give Compounds II, and III in the reactions using catalysts. Moreover, the fact that Compound III was afforded as the main product means that the Schiff base was reduced by the *cis* addition of hydrogen from the endo side. Next, the ^{13}C NMR spectra of the three products in $CDCl_3$ and TFA (trifluoroacetic acid) were measured. Table 2 shows the observed chemical shifts, the multi-

Table 2. ^{13}C chemical shifts ($\delta^{13}C$)[a] and *N*-protonation shifts ($\Delta\delta^{13}C$)[b]

Compd		C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11
I	$\delta^{13}C$ in $CDCl_3$	53.6	183.5	35.2	43.9	27.5	32.1	47.1	*19.6	*19.1	11.3	39.3
	Off-resonance	s	s	t	d	t	t	s	q	q	q	q
	$\delta^{13}C$ in TFA	60.0	209.4	38.6	44.9	26.8	32.6	52.0	19.6	18.6	9.8	35.5
	$\Delta\delta^{13}C$	−6.4	−25.9	−3.4	−1.0	+0.7	−0.5	−4.9	0.0	+0.5	+1.5	+3.8
II	$\delta^{13}C$ in $CDCl_3$	48.3	69.2	38.3	45.2	27.4	37.0	46.6	*20.6	*20.5	12.0	35.3
	Off-resonance	s	d	t	d	t	t	s	q	q	q	q
	$\delta^{13}C$ in TFA	50.6	72.0	35.5	46.6	27.5	37.6	48.8	20.6	20.4	11.8	34.7
	$\Delta\delta^{13}C$	−2.3	−2.8	+2.8	−1.4	−0.1	−0.6	−2.2	0.0	+0.1	+0.2	+0.6
III	$\delta^{13}C$ in $CDCl_3$	48.6	65.6	37.6	45.0	27.5	28.4	48.4	*19.8	*18.7	14.3	36.0
	Off-resonance	s	d	t	d	t	t	s	q	q	q	q
	$\delta^{13}C$ in TFA	51.2	70.3	34.5	46.1	28.9	28.9	50.5	19.8	18.7	13.8	35.4
	$\Delta\delta^{13}C$	−2.6	−4.7	+3.1	−1.1	−1.4	−0.5	−2.1	0.0	0.0	+0.5	+0.6

a) ^{13}C chemical shifts are given in ppm from TMS and considered accurate to ±0.1 ppm. b) The plus and minus signs mean the upfield and downfield protonation shifts. * The asterisks designate pairs of shifts which have been assigned for consistency with other shift data, although there is a possibility that the assignments should be interchanged.

plicities observed in the off-resonance proton decoupled spectra, and the *N*-protonation shifts. The assignments of the ^{13}C signals of Compounds I, II, and III were decided with the aid of the CMR studies of norbornyl derivatives by Grutzner *et al*,[6] of camphor by Wenkert *et al*,[7] and of general substituent effects, the so-called α and β effects.[8]

Assignment of the ^{13}C NMR Spectra of N*-methylbornylamine II.* The 69.2 ppm resonance peak in the lowest field are immediately identified as C-2 attached to the methylamino group. The 45.2 ppm absorption appearing as a doublet in the off-resonance decoupled spectrum must be C-1 and C-7. Further, it is assumed, on the basis of the β effect of the substituent, that the line of C-1 is in a lower field than C-7. The lowest field peak at 38.3 ppm in the three triplet peaks when partially decoupled must belong to C-3, caused by a substantial downfield shift at positions β to the amino group. There are two absorptions, at 27.4 and 37.0 ppm, which appear as triplets', they must be C-5 and C-6. The C-6 is situated at positions β to the C-10 methyl group. The 35.3 ppm absorption appears as a quartet in the off-resonance decoupled spectrum and thus must be methyl carbon. The resonance line of methyl carbon agrees with the assignment given to the *N*-methyl groups.[9] The peak at 12.0 ppm was identified as C-10 according to Wenkert's work.[7] The remaining absorptions, at 20.5 and 20.6 ppm, must belong to C-8 and C-9. The assignment of C-8 and C-9 can not be decided on the basis of our present information. According to the general procedure described above, the ^{13}C chemical shifts of I and III have been assigned. The protonation-induced shifts are also shown in Table 2. It has been observed by Morishima *et al.*[10] that almost all the ^{13}C signals move to a higher field upon the *N*-protonation of some saturated amines. They concluded that, by the protonation of saturated amines, the C–H bond is polarized to produce the C^{-}–H^{+} structure and that the electron on the hydrogen atom is transmitted through the carbon skeleton onto the positively-charged nitrogen atom. However, the observed protonation shifts of I, II, and III were downfield shifts at C-1, C-2, C-4, C-6, and C-7. It is especially notable that the protonation shift at C-2 of (I) was −25.9 ppm.

Experimental

General Procedure of Reductive Amination. To a 200-ml autoclave containing 20 g of *d*-camphor in 80 ml of a 30% methylamine-methanol solution, a catalyst (W-1 Raney Ni (5 g), 5% Pd–C (20 g), or PtO_2 (1.5 g)) was added. The autoclave was then filled with hydrogen at 60 kg/cm^2 (room temperature) and stirred magnetically at 120 °C for 24 hr. After cooling, 60 ml of 10% hydrochloric acid was added to the reaction mixture. The catalyst and the unreacted camphor were then filtered off. The filtrate was made strongly basic with 30% sodium hydroxide and extracted with ether, and the ethereal solution was dried over sodium hydroxide pellets. The evaporation of ether afforded a basic oil. The mixture oil was subsequently analyzed by gas chromatography. Four grams of the oil were chromatographed on 120 g of alumina. Elution with benzene afforded (I) (bp$_{757}$ 203 °C), which was identified as *N*-methylcamphorimine (by means of infrared and PMR spectra). Further elution with a 10% ethanol-benzene solution yielded a mixture (bp 83—97 °C 10 mmHg), the identity of which were confirmed by comparing the retention times of the oily mixture on the gas chromatogram with those of *N*-methylbornylamine (II) (bp 89—96 °C/10 mmHg) and *N*-methylisobornylamine (III) (bp 82—83 °C 10 mmHg), both prepared by known methods.[3,4]

Gas-chromatographic Analysis. The gas chromatography was carried out with a Shimadzu GC-3AF Model apparatus. A $3\phi\times2000$-mm stainless steel column was packed with THEED (15%) on Shimalite F (20—80 mesh). Nitrogen was used as the carrier gas. The column temperature was 100 °C. The percentages of the constituents of the oil were calculated from the areas of the peaks of the gas chromatogram.

CMR Spectral Measurement. All the ^{13}C spectra were obtained at natural abundance in 8-mmϕ tubes by means of a JNM-PS-100/PFT-100 spectrometer operating at 25.15 MHz (28 °C). The chemical shifts were determined with reference to the internal TMS from spectra taken with noise decoupling, which removed all the ^{13}C–H coupling. The repetition time of the pulse was 1—4 s. The numbers of scans were 1000—2000. Further, the off-resonance proton decoupling technique was applied to all samples. $CDCl_3$ and TFA were employed as the solvents. The concentrations of the samples were approximately 100 mg/ml.

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