ELSEVIER

Journal of Organometallic Chemistry 553 (1998) 405–415

Journal of Organometallic Chemistry

C(3) aurated 1,4-benzodiazepin-2-ones. Synthesis and characterization. Crystal structure of (L)Au[P($C_6H_4CH_3$-4)$_3$] (HL = 7-chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one, DIAZEPAM)

Giovanni Minghetti [a,*], Antonio Zucca [a], Maria Agostina Cinellu [a], Sergio Stoccoro [a], Mario Manassero[b,*], Mirella Sansoni [b]

[a] *Dipartimento di Chimica, Università di Sassari, via Vienna 2, 07100 Sassari, Italy*

[b] *Dipartimento di Chimica Strutturale e Stereochimica Inorganica, Università di Milano, Centro CNR, via Venezian 21, 20133 Milano, Italy*

Received 26 July 1997

Abstract

The synthesis of a series of gold(I) metallated derivatives of some 1,4-benzodiazepin-2-ones is described. They include mononuclear (L)Au(PR_3) (R = C_6H_5, $C_6H_4CH_3$-4 or C_2H_5) aswell as dinuclear species (L)Au($Ph_2P(CH_2)_nPPh_2$)Au(L), $n = 2$, 3 (HL = 7-chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one, DIAZEPAM or 7-chloro-1-(cyclopropylmethyl)-1,3-dihydro-5-phenyl-2H-1,4-benzodiazepin-2-one, PRAZEPAM). The deprotonated ligand is bonded to the $AuPR_3$ moiety through the C(3) atom. Activation of the C(sp^3)–H bond is achieved by means of a strong base in the presence of the phosphinegold chloride intermediate. The structure of (L)Au[P($C_6H_5CH_3$-4)$_3$] has been determined by X-ray diffraction. Some aspects of the reactivity of the metallated species is also reported. © 1998 Elsevier Science S.A.

Keywords: Gold; 1,4-benzodiazepin-2-ones; DIAZEPAM; PRAZEPAM

1. Introduction

1,4-Benzodiazepines are psychotropic drugs widely employed in therapy for their anti-anxiety, sedative, hypnotic, myorelaxing and anti-convulsive properties [1–3].

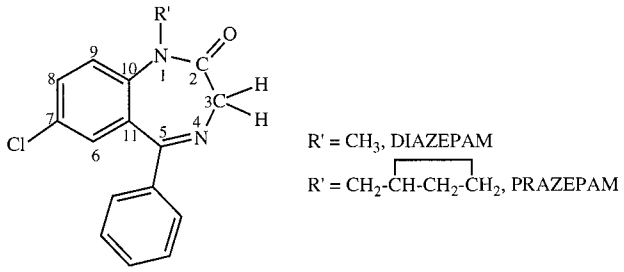
Complexes of neutral 1,4-benzodiazepin-2-ones with transition metal ions [4–14] have been reported; in most cases the ligand is bonded through the N(4) atom. Metal derivatives of deprotonated 1,4-benzodiazepin-2-ones are likewise known: besides N(1) bonded molecules arising from N(1)-unsubstituted ligands [8], examples include C-bonded molecules where C is an *ortho* carbon atom of the 5-phenyl substituent [13,15]. The C(sp^2)–metal bond is usually assisted by coordination of the N(4) atom, to give a five-membered C,N ring. In contrast, at least to the best of our knowledge, no metal derivative has been synthesized with the ligand bonded through the C(3) atom of the seven-membered 1,4-diazepine ring.

Here we report the synthesis of some C(3) aurated 1,4-benzodiazepin-2-ones, HL: they include mononuclear (L)Au(PR_3) (R = C_6H_5, $C_6H_4CH_3$-4 or C_2H_5) as well as dinuclear species (L)Au($Ph_2P(CH_2)$nPPh_2)Au(L), $n = 2$, 3 (HL = 7-chloro-1, 3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one, DIAZEPAM or 7-chloro-1-(cyclopropylmethyl)-1,3-dihydro-5-phenyl-2H-1,4 - benzodiazepin-2-one, PRAZEPAM).

The new gold(I) derivatives have been fully characterized in solution by ^{1}H, ^{13}C{^{1}H} and ^{31}P{^{1}H} NMR spectra. The structure of (L)Au[P($C_6H_4CH_3$-4)$_3$] (HL = DIAZEPAM) has been solved by an X-ray structure determination.

* Corresponding authors.

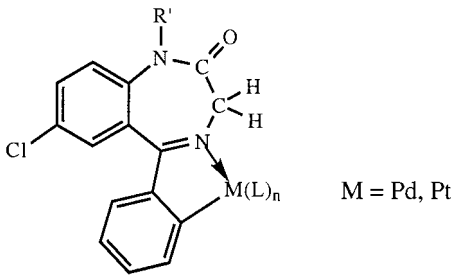
Some of the aurated 1,4 benzodiazepin-2-ones are able to coordinate a $[Au(PR_3)]^+$ fragment through the N(4) atom, giving cationic derivatives $[(L)\{Au(PR_3)\}_2]^+$.



Ligands with numbering scheme

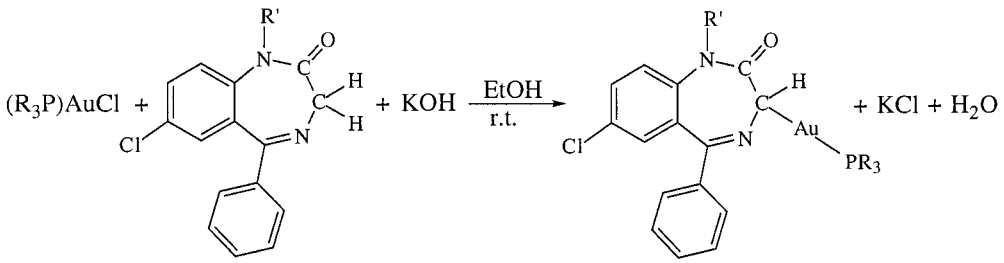
2. Results and discussion

Although the reactivity of 1,4-benzodiazepin-2-ones with transition metal ions has been the subject of several studies, very few metallated 1,4-benzodiazepin-2-ones have been reported. Actually they are restricted to palladium(II) [9,15] and platinum(II) [13] derivatives where the metal–carbon(sp^2) bond is supported by coordination of the N(4) atom to give a five-membered cyclometallated C,N ring.



In the field of gold chemistry, adducts of both Au(III) [7] and Au(I) [8] have been described previously but no activation of C–H bonds has been achieved in spite of several attempts carried out under different experimental conditions.

We describe here that under controlled conditions, C(3) aurated 1,4-benzodiazepin-2-ones **1**–**5** can be obtained in fairly good yields according to reaction 1.



(1)

1-5

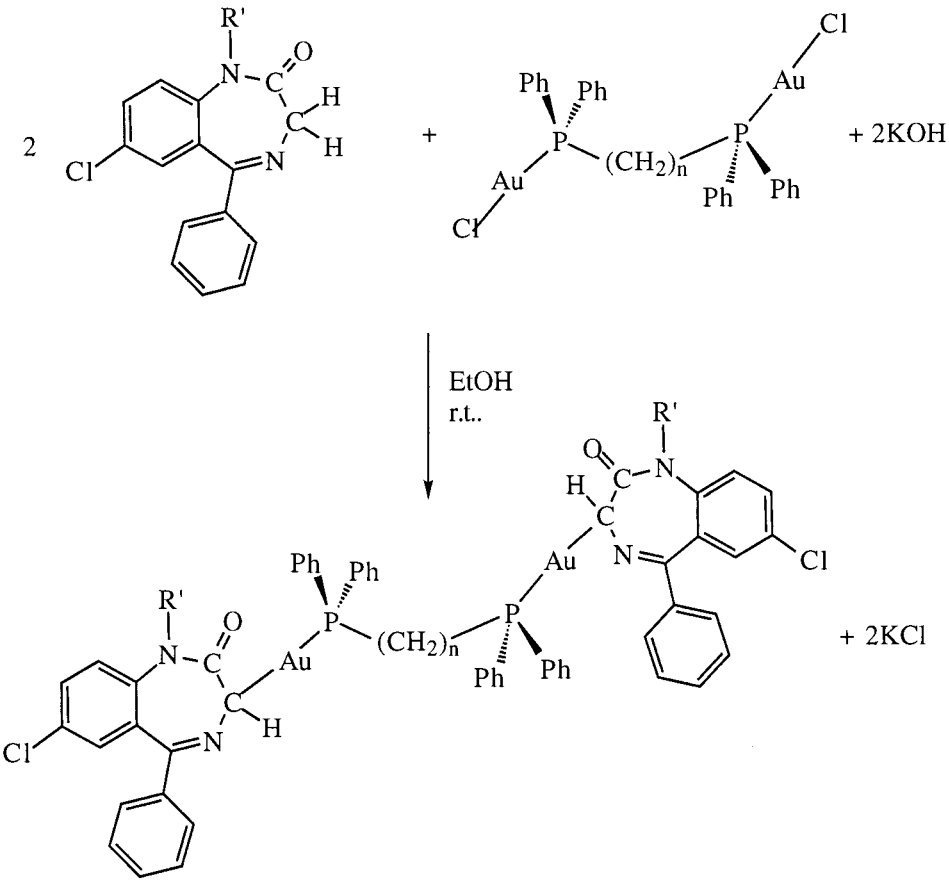
R'=CH_3;R=C_6H_5(**1**), C_2H_5(**2**), $C_5H_4CH_3$-4 (**3**)

R'=CH_2-$\overline{CH-CH_2-CH_2}$: R=C_6H_5(**4**), C_2H_5 (**5**)

The reaction requires that the ethanolic solution of the base is added at room temperature drop by drop to a suspension of (R_3P)AuCl and the ligand in the same solvent; in many cases a certain amount of the starting gold complex is recovered.

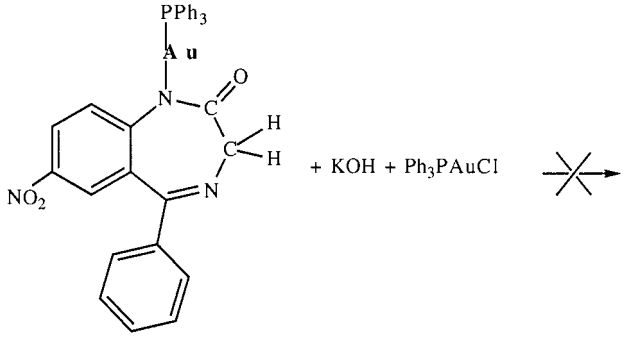
It is worth noting that the auration is achieved by means of the gold chloride complex $(R_3P)AuCl$ and does not require the tris(triphenylphosphinegold)oxonium cation, $[\{(R_3P)Au\}_3O]^+$, which is known to display a remarkable 'aurating' ability [16,17].

Reaction 1 can be extended to the synthesis of dinuclear species,



6, 7

Under the same experimental conditions, complex **8**, an N(1)-aurated species previously described [8], does not react to give the corresponding C(3) aurated derivative:



8

The new species **1**–**5** are white solids stable to air, soluble in most of the common organic solvents. The IR spectra show strong absorptions in the range 1700–1500 cm^{-1} typical of the ligands, suggesting that the diazepine ring is untouched. Evidence for the C(3) auration is given mainly by NMR spectra. In the ^1H spectra the AB spin system due to the diastereotopic C(3) protons is missing and a new signal, corresponding to one proton, appears at lower field (see Table 1): a small coupling to the ^{31}P nucleus is observed ($^3J(HP)$ = ca. 10 Hz).

Table 1
^{1}H and $^{31}P\{^{1}H\}$ NMR data[a]

Compound	CH_3	$CH_2-\overline{CH-CH_2-CH_2}$	$CH_2-\overline{CH-CH_2-CH_2}$	H(3)	Aromatics	Other signals	^{31}P
1	3.33 s			5.55 d [9.5]	7.04–7.66 (m, 23H)		39.9
2	3.32 s			5.27 d [9.6]	7.12–7.65 (m, 8H)	0.94 (dt, 9H)[17.8](7.7) CH_3-CH_2 1.49 (dq, 6H)[9.3](7.7) CH_3-CH_2	39.3
3	3.33 s			5.53 d [9.5]	7.03–7.65 (m, 20H)	2.37 (s, 9H)($C_6H_4CH_3$)	38.1
4		0.91 (m, 1H) CH 0.04–0.43 (m, 4H) CH_2	3.53 dd (6.4) (14.4) 4.13 dd (7.8) (14.4)	5.52 d [9.6]	6.94–7.65 (m, 23H)		40.2
5		ca 0.9 (CH)[b] 0.06–0.40 (m, 4H)	3.51 dd (6.1) (14.4) 4.10 dd (7.8) (14.4)	5.23 d [9.5]	7.11–7.63 (m, 8H)	0.94 (dt, 9H) [17.9](7.6) CH_3-CH_2 1.48 (dq, 6H) [9.3](7.6) CH_3-CH_2	39.5
6	3.29 s			5.49 m	6.83–7.62 (m, 36H)	2.10 (m, 4H) CH_2	38.5, 38.6
7	3.29 s			5.46 d [9.5]	6.98–7.62(m, 36H)	1.35–2.70 (m, 6H) CH_2	33.8, 33.9
9	3.48 s			5.34 d [8.7]	6.88–7.73 (m, 38H)		29.3, 40.1
10		1.01 (m, 1H) CH 0.18–0.60 (m, 4H) CH_2	3.74 dd (6.1) (14.4) 4.16 dd (7.9) (14.4)	5.32 d [8.8]	6.94–7.71 (m, 38H)		29.4, 40.2

[a] $CDCl_3$, room temperature, 300 MHz (1H), chemical shifts in ppm from internal TMS (1H) and external H_3PO_4 (^{31}P), coupling constants in Hz, J(H,H) in parentheses, J(P,H) in square brackets.
[b] Partially overlapping with CH_3-CH_2.

The $^{31}P\{^{1}H\}$ spectra of complexes **1**–**5** display one signal around δ 40 significantly at low field with respect to the shift of the gold complexes having a benzodiazepine bonded through a nitrogen atom [8].

In the $^{13}C\{^{1}H\}$ spectra, a resonance in the range δ 77–80, coupled to ^{31}P ($^{3}J(CP)$ = ca. 73 Hz) has been assigned to a methinic carbon through an APT (Attached Proton Test) experiment. The resonances at very close values, ascribed in the free ligand to the 2- and 5- quaternary carbons of the diazepine ring (e.g., DIAZEPAM: δ 170.1 and 169.1) split remarkably in the C(3) aurated derivatives (complex **1**: δ 179.6, $J(CP)$ = 4.6 Hz and 160.4, $J(CP)$ = 5.2 Hz) and cannot be unambiguously assigned.

In the NMR spectra of the dinuclear complexes **6** and **7** (r.t.), some of the signals are broad (^{1}H) or split into two resonances ($^{31}P\{^{1}H\}$) (e.g., **6**: δ 38.5 and 38.6) which very likely have to be assigned to the diastereomers due to the presence in the molecule of two asymmetric carbons.

All the C(3) aurated species **1**–**7** show in the mass spectra (FAB +) the molecular ion [M^+]: in addition peaks at higher mass, corresponding to dinuclear unities [$(L-H)\{Au_2(PPh_3)_2\}^+$] are sometimes observed, likely arising from reaction in vapour phase. Peaks at m/z 721 and 459 due to [$Au(PPh_3)_2^+$] and [$Au(PPh_3)^+$], respectively are present in the spectra of compounds **1** and **4**, as usually observed in the case of gold complexes of PPh_3.

The structure of complex **3** in the solid state has been solved by an X-ray determination.

The structure consists of the packing of (L)Au[$P(C_6H_4CH_3\text{-}4)_3$] and acetone molecules in the molar ratio 1:1 with no unusual van der Waals contacts. Principal bond lengths and angles are reported in Table 2. An ORTEP view of the complex molecule is shown in Fig. 1.

In the free DIAZEPAM molecule [18], the N1–C2–C3–N4–C5–C11–C10 seven membered ring is in a boat conformation and the sp^3 C3 atom is the bow of the boat; of the two hydrogen atoms bonded to C3, one points towards the inside of the boat and the other towards the outside. In the present metal complex the seven-membered ring retains the boat conformation and the gold atom replaces the C3 hydrogen atom that points toward the inside of the boat. The P–Au–C3 interaction is essentially linear [angle 172.2(3)°] with Au–P and Au–C3 distances of 2.289(3) and 2.109(11) Å, respectively. These values are very similar to those found in fluorenyl (triphenylphosphine) gold [19], where the sp^3 carbon atom bonded to gold belongs to a fused cyclopentadiene ring: Au–P 2.275 and Au–C

Table 2
Selected bond distances (Å) and angles (°) with e.s.d.'s in parentheses for (L)Au[$P(C_6H_4CH_3\text{-}4)_3$], compound **3**

Au–P	2.289(3)	Au–C3	2.109(11)
N1–C2	1.435(16)	C2–O	1.204(13)
C2–C3	1.496(15)	C3–N4	1.448(13)
N4–C5	1.290(15)	C5–C11	1.501(15)
C11–C10	1.392(13)	C10–N1	1.414(14)
C11–C6	1.391(16)	C6–C7	1.401(17)
C7–C8	1.357(15)	C7–Cl	1.760(13)
C8–C9	1.362(18)	C9–C10	1.435(16)
C10–N1	1.414(14)	N1–C18	1.485(16)
C5–C12	1.469(14)	C12–C13	1.389(15)
C12–C17	1.408(18)	C13–C14	1.395(18)
C14–C15	1.338(20)	C15–C16	1.387(19)
C16–C17	1.371(17)	P–C19	1.821(11)
P–C26	1.824(12)	P–C33	1.820(11)
P–Au–C3	172.2(3)	AU–C3–C2	111.3(7)
Au–C3–N4	112.9(7)	N1–C2–O	119.4(1.0)
N1–C2–C3	115.4(9)	C3–C2–O	125.3(1.1)
C2–C3–N4	114.1(9)	C3–N4–C5	121.7(9)
N4–C5–C11	123.5(9)	C5–C11–C10	122.0(1.0)
C11–C10–N1	121.4(1.0)	C10–N1–C2	122.4(9)
C10–N1–C18	119.7(1.0)	C2–N1–C18	116.0(9)
C5–C11–C6	118.1(9)	C10–C11–C6	119.9(1.0)
C11–C6–C7	119.5(9)	C6–C7–C8	120.7(1.1)
C6–C7–Cl	118.2(8)	C8–C7–Cl	121.0(1.0)
C7–C8–C9	121.6(1.1)	C8–C9–C10	119.1(1.0)
C9–C10–C11	119.3(1.0)	C9–C10–N1	119.3(9)
N4–C5–C12	118.8(9)	C11–C5–C12	117.6(9)
C5–C12–C17	121.1(1.0)	C5–C12–C13	123.4(1.1)
C13–C12–C17	115.5(1.0)	C12–C13–C14	121.8(1.2)
C13–C14–C15	121.6(1.2)	C14–C15–C16	118.1(1.1)
C15–C16–C17	121.3(1.3)	C16–C17–C12	121.6(1.1)

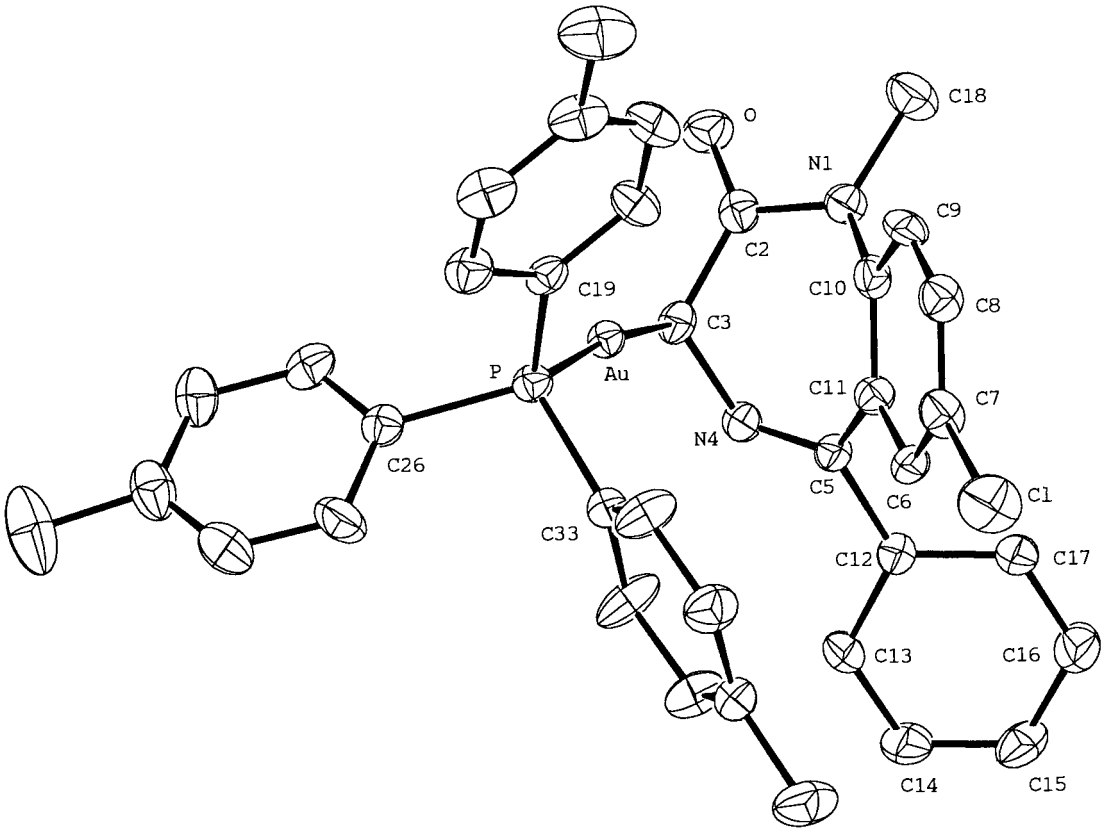
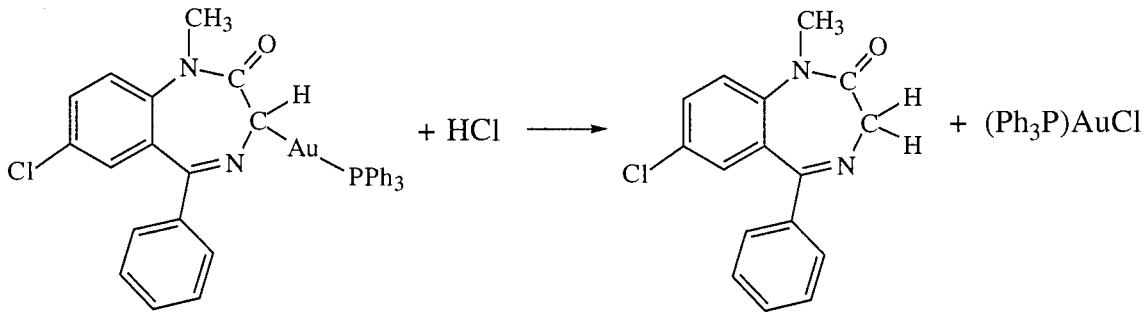


Fig. 1. An ORTEP view of (L)Au[P($C_6H_4CH_3$-4)$_3$], compound **3**. Thermal ellipsoids are drawn at the 30% probability level.

2.102 Å (each value is the average of three bond lengths found in three crystallographically independent molecules). Bond lengths and angles within the C3-coordinated DIAZEPAM molecule are very similar to those found in the free ligand [18] and in the N4-bonded DIAZEPAM molecule found in Pt(L)(HL)Cl (**11**) [13]. The most significant differences are the lengthening of the N1–C2 bond length [1.435(16) Å here, 1.365(2) and 1.378(6) Å in DIAZEPAM and **11**, respectively] and the increase of the N4–C3–C2 and C3–N4–C5 angles [114.1(9) and 121.7(9)° here, 110.5(2) and 118.1(2) in DIAZEPAM, 109.4(3) and 118.2(3)° in **11**, respectively]. In the present seven-membered ring the N1–C2–N4–C5 atoms are strictly coplanar and form dihedral angles of 50.9(7) and 40.6(8)° with the bow and stern planes of the boat, formed by atoms C2–C3–N4 and N1–C10–C11–C5, respectively. The C6–C11 and C12–C17 aromatic rings are also strictly planar.

Reaction 1 is reversible: the gold–carbon bond can be cleaved by HCl to give the free ligand (reaction 2):

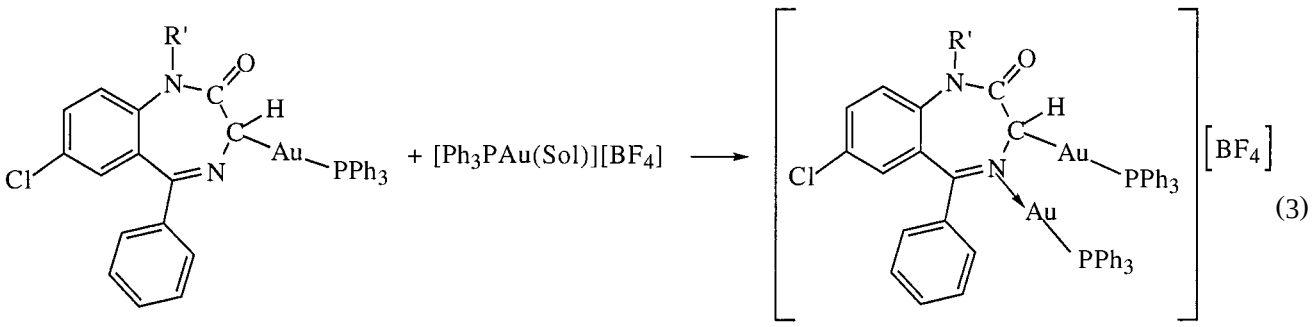


(2)

1

Reaction with bromine is more complex, as reported in the case of the simple gold(I) alkyl derivatives [16,17]. Although isolation of (Ph_3P)AuBr (molar ratio Au:Br = 1:1) or (Ph_3P)$AuBr_3$ (Au:Br = 1:2) gives evidence for the cleavage of the Au–C bond, we were unable to separate the expected 3-bromo-1,4-benzodiazepin-2-one.

The C3 aurated complexes react with $[(PPh_3)Au(Sol)]^+$ as obtained by removal of chloride from $(Ph_3P)AuCl$ with silver fluoborate in acetone solution, to give cationic species, according to reaction 3:



1, **4** **9**, **10** (3)

Clear evidence for the C3 and N4 bonding of the bridging ligand is given by the $^{31}P\{^1H\}$ NMR spectrum: the chemical shift of the two signals, δ 29.3 and 40.1, **9**, and 29.4 and 40.2, **10**, are comparable with that of compounds 1 and 2, and with that of the N(4) bonded adducts [8], respectively.

3. Experimental

Syntheses of compounds **2** and **5** were performed under dry nitrogen by using standard Schlenk techniques. Ligands DIAZEPAM and PRAZEPAM were provided by Roche and Parke-Davis, respectively.

^1H, $^{31}P\{^1H\}$ and $^{13}C\{^1H\}$ NMR spectra were recorded with a Varian VXR 300 spectrometer operating at 299.9 (^1H), 121.4 (^{31}P) and 75.4 MHz (^{13}C). Chemical shifts are given in parts per million relative to internal TMS (^1H and ^{13}C) and external 85% H_3PO_4 (^{31}P).

IR spectra were recorded with Perkin Elmer spectrophotometers 983 and 1310 using Nujol mulls. Mass spectra were obtained with a VG 7070 instrument operating under FAB conditions, with 3-nitrobenzyl alcohol as supporting matrix. Conductivity measurements were obtained using a Philips PW 9505 conductimeter at 25°C. Elemental Analyses were performed with a Perkin-Elmer elemental analyzer 240 B by Mr A. Canu (Dipartimento di Chimica, Università di Sassari).

*3.1. Synthesis of compounds: general procedure for the synthesis of (L)Au(PR_3) [HL = DIAZEPAM: (**1**), (**2**) and (**3**); PRAZEPAM: (**4**) and (**5**)]*

An ethanol solution (10 cm^3) of KOH (1.1 mmol) was added dropwise to an ethanol suspension (30 cm^3) of HL (1.0 mmol) and $(PR_3)AuCl$ (1.0 mmol). The mixture was stirred at room temperature, then filtered to separate some unreacted $(PR_3)AuCl$ and evaporated to dryness.The residue was taken up with dichloromethane, filtered and concentrated to small volume: addition of diethyl ether gave a white solid. Recrystallization from dichloromethane–diethyl ether gave the analytical sample.

*3.2. (L)Au(PPh_3) (**1**)*

Yield 63%, m.p. 162°C (dec.). Anal. Found: C, 53.64; H, 3.58; N, 3.86%. $C_{34}H_{27}AuClN_2OP.0.25CH_2Cl_2$ Calc.: C, 53.82; H, 3.63; N, 3.66%. IR (Nujol, cm^{-1}) ν: 1639 s, 1582 m, 1100 s, 690 s, 535 s, 504 s. ^{13}C NMR (CD_2Cl_2) δ: 35.1 (s, CH_3), 77.6 (d, $^2J(CP) = 73.8$ Hz, CH), 122.3, 128.3, 128.7, 129.0, 129.2, 130.0, 129.4 (d, $J(CP) = 10.9$ Hz), 131.6 (d, $J(CP) = 2.4$ Hz), 134.3 (d, $J(CP) = 13.7$ Hz), 160.4 (d, $J(CP) = 5.2$ Hz, CO or C=N), 179.7, (d, $J(CP) = 4.6$ Hz, CO or C=N); FAB mass spectrum (m/z): 742 [M^+], 721 [$Au(PPh_3)_2^+$], 459 [$Au(PPh_3)^+$], 1200 [$(L-H)(AuPPh_3)_2^+$].

*3.3. (L)Au(PEt_3) (**2**)*

Yield 66%, m.p. 105°C (dec.). Anal. Found: C, 44.32; H, 4.48; N, 4.67%. $C_{22}H_{27}AuClN_2OP$ Calc.: C, 44.12; H, 4.54; N, 4.68%. IR (Nujol, cm^{-1}) ν: 1627 s, 1411 s, 1305 m, 1253 m, 1104 s, 703 s, 539 s, 526 m. ^{13}C NMR

($CDCl_3$) δ: 8.6 (s, CH_3CH_2P), 17.6 (d, $J(CP) = 29.7$ Hz, CH_2P), 34.8 (s, CH_3N), 78.8 (d, $^2J(CP) = 72$ Hz, CH), 121.8, 127.3, 128.0, 128.5, 128.6, 128.9, 129.6, 145.7 and 180.5 (CO or C=N). FAB mass spectrum (m/z): 598 [M^+], 912 [$(L-H)(AuPEt_3)_2^+$].

3.4. (L)Au[P($C_6H_4CH_3-4$)$_3$] (3)

Yield 60%, m.p. 125–130°C (dec). Anal. Found: C, 54.06; H, 4.23; N, 3.21%. $C_{37}H_{33}AuClN_2OP \cdot 0.5CH_2Cl_2$ Calc.: C, 54.43; H, 4.14; N, 3.38%. IR (Nujol, cm^{-1}) ν: 1676 s, 1594 m, 1104 s, 700 s, 537 m, 524 s, 507 s, 498 s.

3.5. (L)Au(PPh_3) (4)

Yield 52%., m.p. 135°C (dec.). Anal. Found: C, 55.49; H, 4.12; N, 3.49%. $C_{37}H_{31}AuClN_2OP \cdot 0.25CH_2Cl_2$ Calc.: C, 56.62; H, 3.95; N, 3.48%. IR (Nujol, cm^{-1}) ν: 1636 s, 1435 s, 1100 s, 694 s, 533 m, 504 m. ^{13}C NMR (CD_2Cl_2) δ: 3.4, 4.8 and 10.9 (3xs, $\overline{CHCH_2CH_2}$), 51.2 (s, CH_2N), 77.8 (d, $^2J(CP) = 74.4$ Hz, CH), 124.8, 128.4, 128.5, 129.1, 129.4 (d, $J(CP) = 10.8$ Hz), 129.8, 131.6 (d, $J(CP) = 2.5$ Hz), 134.3 (d, $J(CP) = 13.6$ Hz), 160.3 (d, $J(CP) = 4.9$ Hz, CO or C=N), 178.6 (d, $J(CP) = 4.5$ Hz, CO or C=N). FAB mass spectrum (m/z): 783 [MH^+], 721 [$Au(PPh_3)_2^+$], 459 [$Au(PPh_3)^+$], 1240 [$(L-H)(AuPPh_3)_2^+$].

3.6. (L)Au(PEt_3) (5)

Yield 46%, m.p. 110–115°C (dec.). Anal. Found: C, 45.35; H, 4.53; N, 4.29%. $C_{25}H_{31}AuClN_2OP \cdot 0.25CH_2Cl_2$ Calc.: C, 45.94; H, 4.81; N, 4.24%. IR (Nujol, cm^{-1}) ν: 1627 s, 1288 m, 707 w, 591 m, 547 m, 496 w, 480 w. ^{13}C NMR ($CDCl_3$) δ: 3.2, 4.8 and 10.5 (3xs, $\overline{CHCH_2CH_2}$), 8.6 (s, CH_3CH_2P), 17.7 (d, $J(CP) = 29.7$ Hz, CH_2P) 50.6 (s, CH_2N); 79.1 (d, $^2J(CP) = 72.8$ Hz, CH), 124.3, 128.1, 128.4, 128.6, 128.8, 129.3 144.1 and 179.7 (CO or C=N). FAB mass spectrum (m/z): 638 [M^+], 952 [$(L-H)(AuPEt_3)_2$].

3.7. General procedure for the synthesis of [(L)Au]$_2$(P–P) [HL = DIAZEPAM: P–P = dppe (6); dppp (7)]

An ethanol solution (10 cm^3) of KOH (1.1 mmol) was added dropwise to an ethanol suspension (30 cm^3) of HL (1.0 mmol) and $(P-P)Au_2Cl_2$ (0.5 mmol). The mixture was stirred at room temperature for 36 h,32 + 13 then filtered and evaporated to dryness. The residue was taken up with dichloromethane, filtered and concentrated to small volume: addition of diethyl ether gave a white solid. Recrystallization from dichloromethane–diethyl ether gave the analytical sample.

3.8. [(L)Au]$_2$(dppe) (6)

Yield 25%, m.p. 160–165°C (dec.). Anal. Found: C, 50.15; H, 3.64; N, 3.92%. $C_{58}H_{48}Au_2Cl_2N_4O_2P_2 \cdot 0.5CH_2Cl_2$ Calc.: C, 50.10; H, 3.52; N, 3.99%. IR (Nujol, cm^{-1}) ν: 1637 s, 1481 s, 1104 s, 695s, 591 m, 583 m, 541 s m, 482 m. FAB mass spectrum (m/z): 1358 [M^+], 1075 [$M-L^+$].

3.9. [(L)Au]$_2$(dppp) (7)

Yield 25%, m.p. 135–140°C (dec.). Anal. Found: C, 50.21; H, 3.79; N, 3.86%. $C_{59}H_{50}Au_2Cl_2N_4O_2P_2 \cdot 0.5CH_2Cl_2$ Calc.: C, 50.45; H, 3.49; N, 3.96%. IR (Nujol, cm^{-1}) ν: 1637 s, 1435 s, 1103 s, 697 m, 542 m, 521 s, 483 w.

3.10. General procedure for the synthesis of [(L){Au(PPh_3)}$_2$][BF_4] [HL = DIAZEPAM: (9); PRAZEPAM: (10)]

A methanol solution of $AgBF_4$ (0.0708 g, 0.32 mmol) was added to a methanol suspension (15 cm^3) of PPh_3AuCl (0.1587 g, 0.32 mmol). After removal of AgCl, a methanol solution of $(L)AuPPh_3$ (0.32 mmol) was added. The resulting suspension was stirred for about 5 h at room temperature and then evaporated to dryness; the residue was dissolved in chloroform, filtered and concentrated to small volume. Addition of diethyl ether gave a yellow precipitate. Recrystallization from acetone–diethyl ether gave the analytical sample.

3.11. Compound **9**

Yield 85.3%, m.p. 158°C (dec). Anal. Found: C, 47.82; H, 3.15; N, 2.29%. $C_{52}H_{42}Au_2BClF_4N_2OP_2$ Calc.: C, 48.45; H, 3.28; N, 2.17%. Λ_M (5×10^{-4} M, acetone) 132 Ω^{-1} cm^2 mol^{-1}. IR (Nujol, cm^{-1}) ν: 1651 s, 1434 s, 1101 s, 1054 s (broad), 693 s, 544 s, 507 s. FAB mass spectrum (m/z): 1201 [M^+], 721 [$(PPh_3)_2Au^+$], 459 [$(PPh_3)Au^+$].

3.12. Compound **10**

Yield 88%, m.p. 148°C (dec.). Anal. Found: C, 49.28; H, 3.45; N, 2.23%. $C_{55}H_{46}Au_2BClF_4N_2OP_2$ Calc.: C, 49.70; H, 3.49; N, 2.11%. Λ_M (5×10^{-4} M, acetone): 116 Ω^{-1} cm^2 mol^{-1}. IR (Nujol, cm^{-1}) ν: 1643 s, 1101s, 1053 s (broad), 693 s, 544 s, 507 s. FAB mass spectrum (m/z) 1241 [M^+], 841 [$Au_2(PPh_3)_2$-Ph^+], 721 [$Au(PPh_3)_2^+$], 459 [$Au(PPh_3)^+$].

3.13. Reaction of (L)Au(PPh_3)(**1**) with Br_2 (molar ratio 1:1)

To a solution of (L)Au(PPh_3) (**1**) (0.1194 g, 0.16 mmol) in benzene was added Br_2 (0.16 mmol). The mixture was stirred for 45′ in a cold water bath, then concentrated to small volume; addition of *n*-hexane gave a white precipitate which was filtered off and recrystallized from benzene–*n*-hexane. The product was identified as (Ph_3P)AuBr; yield 87.5%

Table 3
Crystallographic data

Compound	$3\cdot(CH_3)_2CO$
Formula	$C_{40}H_{39}Au_1Cl_1N_2O_2P_1$
M	843.2
Colour	colourless
Crystal system	triclinic
Space group	$P\bar{1}$
a (Å)	9.956(2)
b (Å)	13.595(2)
c (Å)	14.215(2)
α (°)	87.29(1)
β (°)	89.44(1)
γ (°)	77.29(1)
U (Å^3)	1874.8(5)
Z	2
F(000)	840
D_c (g cm^{-3})	1.494
Crystal dimensions (mm)	$0.23\times0.28\times0.42$
μ (MoK α) (cm^{-1})	40.6
Min. and max. transmission factors	0.65–1.00
Scan mode	ω
Frame width/°	0.3
Time per frame (s)	20
No. of frames	2500
Detector-sample distance (cm)	5.50
θ-range (°)	2–25
Reciprocal space explored	$\pm h, \pm k, \pm l$
No. of reflections (total; independent)	21030; 8294
Unique observed reflections with $I > 3g s(I)$	5220
Final R and R' indices[a]	0.054, 0.076
No. of variables	424
Goodness of fit[b]	1.47
Max. and min. residual electron density (e Å^{-3})	+3.6(3), −2.1(3)

[a] $R=[\Sigma(|F_O-k|F_c||)/\Sigma F_O]$, $R'=[\Sigma w(F_O-k|F_C|)^2/\Sigma wF_O^2]^{1/2}$.
[b] $[\Sigma w(F_O-k|F_C|)^2/(N_O-N_V)]^{1/2}$, where $w=1/[\sigma(F_O)]^2$, $\sigma(F_O)=[\sigma^2(F_O^2)+(0.06F_O^2)^2]^{1/2}/2F_O$, N_O is the number of observations and N_V the number of variables.

3.14. Reaction of (L)Au(PPh_3) (**4**) with Br_2 (molar ratio 1:2)

Addition of Br_2 (1.0 mmol) to a suspension of (L)Au(PPh_3) (**4**) (0.3914 g, 0.5 mmol) in benzene resulted in an immediate colour change to red. The suspension was stirred for about 3 h and then filtered off. The solid product was identified as (Ph_3P)$AuBr_3$; yield 82%.

3.15. Reaction of (L)Au(PPh_3) (**1**) with HCl

Addition of 2M HCl (0.06 cm^3, 0.12 mmol) to a solution of **1** (0.0822 g, 0.11 mmol) in EtOH gave a white precipitate which was filtered off and identified as (Ph_3P)AuCl. The filtered solution was evaporated to dryness and extracted with diethyl ether: after removal of the solvent DIAZEPAM was recovered (80%).

Table 4
Fractional atomic coordinates with e.s.d.'s in parentheses for the non-hydrogen atoms of (L)Au[$P(C_6H_4CH_3\text{-}4)_3$](CH_3)$_2$CO (compound **3** (CH^3)2CO)

Atom	*x*	*y*	*z*
Au	−0.36473(4)	0.22459(3)	0.10803(3)
Cl	0.0421(4)	0.3698(3)	0.3198(3)
P	−0.4097(3)	0.1905(2)	0.2629(2)
O	−0.4368(8)	0.3722(6)	−0.1306(6)
O2	−0.102(2)	−0.325(2)	0.370(1)
N1	−0.2823(9)	0.4197(7)	−0.0347(6)
N4	−0.1525(9)	0.2010(7)	−0.0441(6)
C2	−0.349(1)	0.3461(8)	−0.0715(8)
C3	−0.299(1)	0.2404(8)	−0.0322(8)
C5	−0.062(1)	0.2392(8)	−0.0029(8)
C6	−0.022(1)	0.3115(8)	0.1485(8)
C7	−0.059(1)	0.3831(9)	0.2172(8)
C8	−0.166(1)	0.4633(9)	0.2026(9)
C9	−0.244(1)	0.4754(8)	0.1228(9)
C10	−0.209(1)	0.4030(8)	0.0514(8)
C11	−0.098(1)	0.3213(8)	0.0659(8)
C12	0.084(1)	0.1964(8)	−0.0192(8)
C13	0.138(1)	0.0939(9)	−0.027(1)
C14	0.277(1)	0.0566(9)	−0.049(1)
C15	0.366(1)	0.117(1)	−0.057(1)
C16	0.316(1)	0.220(1)	−0.049(1)
C17	0.179(1)	0.2589(9)	−0.031(1)
C18	−0.325(1)	0.524(1)	−0.077(1)
C19	−0.513(1)	0.2934(9)	0.3270(7)
C20	−0.593(1)	0.274(1)	0.4047(9)
C21	−0.663(1)	0.353(1)	0.4566(9)
C22	−0.658(1)	0.452(1)	0.4310(9)
C23	−0.580(2)	0.4700(9)	0.356(1)
C24	−0.508(1)	0.3895(9)	0.3030(8)
C25	−0.735(2)	0.538(1)	0.487(1)
C26	−0.487(1)	0.0814(8)	0.2798(8)
C27	−0.444(2)	0.007(1)	0.351(1)
C28	−0.507(2)	−0.075(1)	0.359(1)
C29	−0.605(1)	−0.090(1)	0.295(1)
C30	−0.646(1)	−0.015(1)	0.2239(9)
C31	−0.586(1)	0.068(1)	0.2156(8)
C32	−0.662(2)	−0.185(1)	0.301(1)
C33	−0.247(1)	0.1572(8)	0.3265(8)
C34	−0.136(1)	0.091(1)	0.2851(8)
C35	−0.005(1)	0.071(1)	0.329(1)
C36	0.014(1)	0.1118(9)	0.4148(9)
C37	−0.098(1)	0.174(1)	0.455(1)
C38	−0.229(1)	0.196(1)	0.4125(9)
C39	0.156(1)	0.086(1)	0.460(1)
C40	−0.051(2)	−0.293(1)	0.303(1)
C41	0.067(2)	−0.354(1)	0.253(1)
C42	−0.095(3)	−0.185(2)	0.274(2)

4. X-ray data collection and structure determination

Crystal data and other experimental details are summarized in Table 3. The diffraction experiment was carried out on a Siemens SMART CCD area-detector diffractometer at room temperature using MoK α radiation ($\lambda = 0.71073$ Å) with a graphite crystal monochromator in the incident beam and the generator working at 50 kV and 35 mA. Cell parameters and orientation matrix were obtained from the least-squares refinements of 90 reflections measured in three different sets of 15 frames each, in the range $2 < \theta < 23°$. At the end of data collection the first 50 frames, containing 379 reflections, were recollected to have a monitoring of crystal decay, which was not observed, so that no time-decay correction was needed. The 2500 collected frames were processed with the software SAINT, and an absorption correction was applied (SADABS, written by G. Sheldrick) to the 21 030 collected reflections, 8294 of which are unique with $R_{int} = 0.0287$ ($R_{int} = \Sigma|F_O^2 - F\text{mean}^2|/\Sigma F_O^2$).

The calculations were performed on an AST Power Premium 486/33 computer using the Personal Structure Determination Package [20,21] and the physical constants tabulated therein. Scattering factors and anomalous dispersion corrections were taken from Ref. [22]. The structure was solved by Patterson and Fourier methods and refined by full-matrix least-squares, minimizing the function $\Sigma w\ (F_O - k|F_c|)^2$. Anisotropic thermal factors were refined for all the non-hydrogen atoms. The hydrogen atoms of the solvent molecule were ignored. Those of the CH_3 groups of the complex molecule were detected in the final Fourier maps and included in the calculations but not refined. All the other hydrogen atoms were placed in their ideal positions (C–H = 0.97 Å, $B = 1.15$ times that of the carbon atom to which they are attached) and also not refined. The atomic coordinates of the structure model are listed in Table 4.

Acknowledgements

Financial support by C.N.R. (Rome) is gratefully acknowledged. We thank Roche (Milano) and Parke-Davis (Lainate) for a gift of DIAZEPAM and PRAZEPAM, respectively.

References

[1] L.H. Sternbach, J. Med. Chem. 22 (1979) 1.
[2] H. Schütz, Benzodiazepines, Springer-Verlag, Heidelberg, 1982.
[3] Schütz, Benzodiazepines II, Springer-Verlag, Heidelberg, 1989.
[4] A. Mosset, J.P. Tuchagues, J.J. Bonnet, R. Haran, P. Sharrock, Cu(II), Inorg. Chem. 19 (1980) 290.
[5] H. Miyamae, A. Obata, H. Kawazura, Cu(II), Acta Crystallogr., Sect. B 38 (1982) 272.
[6] J.A. Real, J. Borras, M.C. Munoz, A. Mosset, J. Galy, Cu(II), J. Inorg. Biochem. 31 (1987) 221.
[7] G. Minghetti, M.L. Ganadu, C. Foddai, M.A. Cinellu, F. Cariati, F. Demartin, M. Manassero, Au(III), Inorg. Chim. Acta 86 (1984) 93.
[8] M.A. Cinellu, S. Stoccoro, G. Minghetti, A.L. Bandini, F. Demartin, Au(I), Inorg. Chim. Acta 168 (1990) 33.
[9] M.A. Cinellu, M.L. Ganadu, G. Minghetti, F. Cariati, F. Demartin, M. Manassero, Pd(II), Inorg. Chim. Acta 143 (1988) 197.
[10] M. Cusumano, A. Giannetto, P. Ficarra, R. Ficarra, S. Tommasini, Pd(II), J. Chem. Soc., Dalton Trans., (1991) 1581.
[11] L. Antolini, G. Bruno, M. Cusumano, A. Giannetto, P. Ficarra, R. Ficarra, Pd(II), Polyhedron 21 (1992) 2795.
[12] A. Benedetti, A.C. Fabretti, C. Preti, G. Tosi, P. Zannini, Pt(II), J. Cryst. Spectrosc. Res. 17 (1987) 771.
[13] S. Stoccoro, M.A. Cinellu, A. Zucca, G. Minghetti, F. Demartin, Pt(II), Inorg. Chim. Acta 215 (1994) 17.
[14] M.C. Aversa, P. Bonaccorsi, M. Cusumano, P. Giannetto, D. Minnitti, Pt(II), J. Chem. Soc., Dalton Trans., (1991) 3431.
[15] M.A. Cinellu, S. Gladiali, G. Minghetti, S. Stoccoro, F. Demartin, J. Organomet. Chem. 401 (1991) 371.
[16] R.J. Puddephatt, in: R.J.H. Clark (Ed.), The Chemistry of Gold, Elsevier, Amsterdam, 1978.
[17] K.J. Grandberg, V.P. Dyadchenko, J. Organomet. Chem. 474 (1994) 1.
[18] A. Camerman, N. Camerman, J. Am. Chem. Soc. 94 (1972) 268.
[19] Yu.T. Struchkov, Yu.L. Slovokhotov, D.N. Kravtsov, T.V. Baukova, E.G. Perevalova, K.I. Grandberg, J. Organomet. Chem. 338 (1988) 269.
[20] B.A. Frenz, Comput. Phys. 2 (1988) 42.
[21] Crystallographic Computing 5, Chap. 11, Oxford Univ. Press, Oxford, UK, 1991, p. 126.
[22] International Tables for X-ray Crystallography, Vol. 4, Kynoch Press, Birmingham, UK, 1974.